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CONTENTS

Volume:2 Issue:1
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LETTER TO EDITOR

Turkey's First Traditional and Complementary Medicine Student Community

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Abstract

As known; In Turkey, Traditional and Complementary Medicine (TCM) Practices are continuing to build the infrastructure based on evidence under the control of the Ministry of Health.

Following these processes, it was realized that there was a need for a formal student organization that would accurately convey the important steps and developments taken to health students. Due to this need, the necessary step was taken in Duzce University Faculty of Medicine.

The purpose of this article is to introduce students to the process of integration and providing medical training TCM first year student community in the area of Turkey, which aims to create awareness starting from the TCM and purpose.

Dear Editor

Traditional and Complementary Medicine Practices have been used for therapeutic purposes in different cultures and in various ways, starting from the beginning of human history. It continues to be used more and more popularly since the 1990s.

These methods, which were used to include superstitions from time to time, mixed with cultural customs and were abused, continued to be applied with the same problems until our modern time. However, with the increasing demand in this field in recent years, important developments have taken place that will say 'stop' to this complexity. Traditional and Complementary Medicine practices that can be officially applied were determined in our country in 2014 with the regulation of traditional and complementary medicine practices[1]. These practices were collected under a heading called Traditional and Complementary Medicine (TCM).

According to the World Health Organization (WHO), "Traditional Medicine" is used in the prevention of physical and mental diseases, diagnosis, healing or treatment as well as good health, based on theories, beliefs and experiences specific to different cultures -which can or cannot be humorous- It is the sum of knowledge, skills and practices. "Complementary medicine", on the other hand, is the meaning gained as a result of the use of health practices believed to provide additional benefits together with conventional medicine. Integrative Medicine; It includes methods and practices that evaluate traditional and complementary medicine and evidence-based medicine practices as a holistic and defined as integrative / holistic medicine.

In 2014, the Department of Traditional and Complementary Medicine Practices was established within the General Directorate of Health Services pursuant to the Decree No. 663, and its regulation was also prepared. 15 application names that can be done in the unit and application centers are as follows. Acupuncture, Apitherapy, Phytotherapy, Hypnotherapy, Hirudotherapy, Homeopathy, Chiropractic, Cup application, Larva application, Mesotherapy, Prolotherapy, Osteopathy, Ozone application, Reflexology, Music Therapy [2].

While rapid advances in TCM in Turkey, to be implemented under more stairs of TCM practice and in exchange it -a amount justified-as completely TCM areas of the academic medical community and a group who realized their approach biased Duzce Medical School student,

doctor of the future in this area and decided to do something for the medical students who will have academics. It was first established a Community Health TCM Students in Turkey on 16.04.2018 in accordance with this decision. Reaching a management team of 30 people and more than 200 members in a very short time on the road set out with 6 volunteer physicians, our community continues to raise awareness of traditional medicine among healthcare students by conducting more than 15 social and scientific activities every year.

As the TCM student community started to bring together doctors and students specialized in traditional medicine, another great development took place on behalf of our university.

WHO, TCM area, considering a lot of factors, chose the leader of the country and supported Turkey. Turkey Duzce University specialization in the scope of the project Ministry of Health Faculty of Medicine specialization in project design TCM area where the teacher was accepted and Duzce University, was selected as the pilot area universities TCM.

Duzce University Traditional and Complementary Medicine Application and Research Center (DUGETAM) was established as a unit affiliated to Duzce University Rectorate in accordance with the decision of the Science Commission on 04.06.2018 with the permission of the TCM Department in line with the policies of the Ministry of Health. Our Center, which has made it a mission to apply the necessary treatments within the scope of Traditional and Complementary Medicine, to carry out education, research and application activities in the field of TCM and to help protect individuals from physical / mental diseases, cooperates with other actors in this field in line with its objectives and conducts evidence-based studies [3].

Turkey's only inpatient services, where the serious clinical research continues to assume the bridge between the largest and most comprehensive TCM establishment right next to the center of Duzce University research hospital has been a major source of motivation for Duzce TCM community of students and medical students with TCM center publishes international indexed journals

The main 5 visions and goals of the TCM student community are [4]

1. To get to know and then introduce Traditional and Complementary Medicine Practices as health students, to create awareness and curiosity in medical students
2. To be able to create a preliminary preparation starting from student years in order that these methods, which have been applied under the stairs for many years in our country, are under the supervision of healthcare professionals and doctors.
3. However, while investigating the evidence of methods based on scientific basis, participating in clinical studies of applications with insufficient evidence value, instilling both the process and research principles in students, and separating effective and scientific evidence-based practices from superstitions.
4. To break down certain walls of prejudice and get one step closer to the concept of Integrative Medicine, where Modern and Traditional Medicine can serve together arm in arm.
5. Participating in national and international congresses, workshops, courses and programs in the field of TCM by bringing health students to DUGETAM's work, education, scientific research and activities, as well as bringing students with our national and international experts.

To mention a few of the activities of our community: Duzce University Experimental Animals Center and DUGETAM, which are also scientific research centers of our university, publicity trips, hypnotherapy conferences and group trainings, Maggot therapy conference and literature review, publication in compilation, participation in the National Music Therapy Congress Active participation in the 1st and 2nd International TCM Congresses together with many important and stimulating conferences such as, active participation in the National Bee Venom workshop and the Medical Fungi workshop,

trainings on the Scientific aspects of Acupuncture, and poster presentation

As a result, he believes that our TCM student community will raise awareness in all current and future healthcare community students and future physicians, break their prejudices and create a more holistic perspective, and as a result, they will take important steps in bringing TCM practices to today's modern medicine and health system by strengthening the scientific foundations, I hope.

REFERENCES

1. Traditional and Complementary Medicine Practices Regulation, Official Newspaper http://www.resmigazete.gov.tr/eskiler/2014/10/20141027-3.htm
2. T.R. Ministry of Health Health Sciences University Etlik Zübeyde Hanım Gynecology Training and Research Hospital https://ezheah.saglik.gov.tr/TR,396642/TCM-geleneksel-ve-tamamlayici-tip-uygulamalari.html
3. Düzce University Traditional and Complementary Medicine Application and Research Center https://dugetam.duzce.edu.tr/
4. Düzce University Traditional and Complementary Medicine Student Community, Social Media Accounts https://duzce.edu.tr/16010-duyurus-TCM-ogrenci-toplulugu%E2%80%99ndan-universitemiz-geleneksel-ve-tamamlayici-tip-uygulama-ve-arastirma-merkezi%E2%80%99ne-ziyaret

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ORIGINAL RESEARCH

Effects of Therapeutic Massage on Fear, Anxiety, and Pain Levels of Critical Care Patients

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Abstract

Objective: Holistic health approach addresses the individual as a whole being consisting of different dimensions in clinical practice. In this study, it was aimed to investigate the effects of therapeutic massage (TM) on fear, anxiety, and pain levels of critically ill patients.

Material-Method: The sample of the study consisted of 50 patients in the intensive care unit (ICU). The patients were divided into two groups: control and experimental groups, each consisted of 25 patients. the data were collected using a questionnaire form containing sociodemographic and some medical parameters, Visual Analogue Scale for Anxiety (VAS-A), Visual Analogue Scale for Anxiety (VAS-A), and Visual Analogue Scale for Pain (VAS-P).

Results: Of the patients, 31 (62%) were male, 22 (44%) were 44 to 64 years old, 45 (90%) were married and 27 (54%) were primary school graduates. The reason for staying in the ICU was the diagnosis of respiratory distress in 21 (42%) of the patients and 37 (74%) were staying in the ICU for two days. There was a decrease in systolic blood pressure, diastolic blood pressure, and pulse in the experimental group compared to the control group; however, this was not statistically significant ($p>0.05$). It was further observed that high respiratory values decreased, and oxygen saturation values increased ($p<0.05$). A statistically significant decrease was observed in anxiety, fear, and pain levels of the patients in the experimental group ($p<0.05$).

Conclusion: TM may be used as a complementary method for anxiety, fear and pain treatment of critically ill patients. It is essential that healthcare professionals working with critically ill patients should be aware of the benefits of TM with a holistic approach.

Keywords: Anxiety, Fear, Holistic, Critical Care, Pain, Therapeutic Massage

INTRODUCTION

The integration of healthcare teams with a holistic model, which addresses the individual as a whole being consisting of all dimensions is crucial in the critical care units [1]. The goal is to improve quality of life in a multidimensional manner [2]. It has been demonstrated that display of genuine empathy, compassion, and physical touch are relevant for improving the healing capacity of patients [3,4].

'Therapeutic Massage' (TM), which is also known as the 'therapeutic tactile touch' or 'effleurage' is such a type of physical contact. TM is all light massages that are applied to large areas of the body with the palms in the direction of the return of the venous circulation to the heart, involving soft, patting movements, by sliding the hands on the skin, and do not cause pressure in the deep muscle masses. Today, it is used as a complementary therapy in palliative care, geriatric care and intensive care settings [5,6].

TM is a kind of tactile touch which may cause certain physiological effects on the body [7,8]. Researchers have evaluated the cortical dynamics of tactile contact [9–11], and how the brain encodes TM [12,13].

TM is transmitted primarily through stimulation of the nerve's unmyelinated C- fibers, that may contribute the treatment. The pathway runs in part through the spino- mesencephalic tract, engaging

the amygdala, insula and anterior cingulate cortex[8].

The physiological response to TM includes the release of certain neuro-transmitters that lead to neuro-endocrine impact; vagal stimulation; reduction of stress, pain and depression; and enhancement of immunity [7,14]. An interoceptive effect of TM may aid alterations to the insular cortex and limbic system [15]. These reactions may have a positive impact on the patient and may contribute to the treatment [8,16].

Intensive care units (ICU) differ from other units in terms of the characteristics of patients and diseases, treatment methods, physical characteristics and emotional environment [17]. Individuals are hospitalized in the ICU due to a life-threatening disease or sudden and serious changes in their health status [18].

TM has positive effects on anxiety, pain, nausea, fatigue and patients' quality of life [19]. It has been used to alleviate the pain and suffering of the patient, and to support the health and well-being of the patient, and to improve the quality of care provided [20]. It has been shown that Swedish massage reduced anxiety and improved vital signs in critically ill patients immediately after the massage and 30 minutes after the massage [21]. Clinical effectiveness of therapeutic touch has positive effects on pain, nausea, anxiety, fatigue, quality of life and biochemical parameters in cancer patients [22]. TM may lead to many positive results in preterm newborns babies in the neonatal intensive care unit who are exposed to a highly stressful environment (such as noise, bright light) and lack the tactile stimulation of the care of their mothers [23].

In a unit with critical importance such as intensive care, TM application is an easy and practical application that can be applied by nurses. It is very important as it can contribute to the increase in the comfort and well-being of the patients and to decrease their fear, anxiety and pain. However, there are limited ICU-studies published, concerning tactile touch or massage. The current study was conducted to determine the effect of TM application on fear, anxiety, and pain levels of intensive care patients.

MATERIALS AND METHODS

Type of the study

The research was planned and conducted as a quasi-experimental study in which the pre-test and post-test measurements were carried out and the experimental and control groups were used to determine the effect of TM applications on the level of fear, anxiety and pain in patients in intensive care. It was registered at the archive of the Databases of National Thesis Center of the Council of Higher Education (No:409467/2015).

The place and time of the study

The study was performed in Istanbul Şişli Hamidiye Etfal Training and Research Hospital between 1 November 2014 and 31 January 2015.

Universe and sample of the research

The universe of the research was composed of patients hospitalized in the intensive care at Istanbul Şişli Hamidiye Etfal Training and Research Hospital. The study sample consisted of 25 experimental group and 25 control group patients who were in the intensive care unit, who were in the general intensive care unit.

Inclusion criteria:

- Being in the ICU for at least 24 hours
- Being between the ages of 18 to 80
- Being conscious
- Not having a perception disorder
- Not having a cardiological disorder
- Agree to participate in the study

Application of the research

The 'TM protocol' was applied to the patients in the experimental group for 30 minutes every day for 3 days. In order to evaluate the anxiety, fear and pain experienced by the patient before and after the application, VAS-A, VAS-F and VAS-P were used. Physical parameters of the patient such as blood pressure, pulse, respiration, body temperature, O_2 saturation and glucose level were also evaluated before and after the application. No intervention was made to the patients in the control group, except for routine care in the unit.

It was recorded by applying the relevant measurement tools at specified times.

Application protocol

To the patients in the experimental group; TM applications (using the effleurage-quaking-massage maneuver) were performed for 3 days; 30 minutes between 18.00-20.00 every day on the following areas:

• Head (5min)
• Face area (cheek and forehead) (5min)
• Right hand and forearm, left hand and forearm (5min)
• Right shoulder, left shoulder (5min)
• Applied to the right foot and left foot areas (5 min),
• During the transition from one region to another, the patient was encouraged to breathe deeply 5 times with the command.

Research variables

The independent variables of the research are the age, gender, educational status, marital status, diagnosis, length of hospital stay, intubation status.

The dependent variables of the research are; the patient's systolic blood pressure, diastolic blood pressure, pulse, respiration, saturation, glucose, anxiety, fear and pain levels.

Data collection tools

In the study, the data were collected using a questionnaire form containing sociodemographic and some medical parameters, Visual Analogue Scale for Anxiety (VAS-A), Visual Analogue Scale for Anxiety (VAS-A), and Visual Analogue Scale for Pain (VAS-P). VAS-A, VAS-F, and VAS-P were used with scoring between 1 (none) and 5 (most), 1 (none) and 5 (most), 1 (none) and 10 (most), respectively.

Evaluation of the data

The data were evaluated in computer environment using SSPS 20.0 package program. Shapiro-Wilk test was used to determine whether numerical variables show normal distribution. In the analysis of the data; In descriptive statistics, percentages, arithmetic mean, and standard deviation values were used. Independent samples t test was used in binary group comparisons. One Way Anova test was used in multiple group comparisons. Pearson correlation analysis was used to evaluate the relationship between variables. In comparisons, $p < 0.05$ value was considered statistically significant.

Ethical aspect of research

In order to conduct the research, written permission from the institution where the research was conducted, and ethical committee approval was obtained from the Istanbul Medipol University Non-Interventional Clinical Research Evaluation Commission (No:197/2014). Verbal and written consent was obtained from the patients

Limitations of research

This research covered a limited number of patients who were hospitalized in the intensive care unit at a state hospital.

RESULTS

Table 1 shows the introductory disease-related characteristics of patients. It was seen that 31 of the patients (62.0%) were male, 22 (44.0%) were between 44-64 years old, 45 (90.0%) were married and 27 (54.0%) were primary school graduates. It was determined that 21 (42.0%) of the patients had been in intensive care with the diagnosis of respiratory distress, 37 (74.0%) had been in intensive care for 2 days and 45 (90.0%) were extubated.

Table 2 shows the vital signs of the patients. It was determined that there was no significant change in the body temperature, pulse and blood pressure values in the experimental group after TM application. There was a significant change in the distribution of respiratory values of the patients in the experimental group after TM application. After application, there was a significant difference in the 3 measurements in the experimental and control groups ($p < 0.05$). In TM application, respiratory values decreased on average in the experimental group, whereas in the control group not subject to TM application, the respiratory values increased on average. After application, there was a significant difference in

Table 1. Introductory disease-related characteristics of patients

Characteristics of Patients		Number (n)	Percent (%)
Gender	Female	19	38.0
	Male	31	62.0
Age	23-43 years old	8	16.0
	44-64 years old	22	44.0
	65 years and above	20	40.0
Marital status	Married	45	90.0
	Single	5	10.0
Educational Status	Literate	8	16.0
	Primary education graduate	27	54.0
	High school graduate and above	15	30.0
Diagnosis	Colon-abdominal diseases	10	20.0
	Pneumonia	4	8.0
	Cancer	9	18.0
	Respiratory distress	21	42.0
	Hypertension	6	12.0
Pre-Application Hospitalization Period	2 days	37	74.0
	3 days	7	14.0
	4 days	6	12.0
Intubation Status	Intubated	5	10.0
	Extubated	45	90.0

Table 2. Vital signs of patients

Vital Signs	Group	1st measure		2nd measure		3rd measure	
		Pre	Post	Pre	Post	Pre	Post
		Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Systolic Blood pressure	Experiment	141.00±24.28	132.08±21.01	138.04±21.97	134.16±17.04	135.20±16.91	128.76±15.58
	Control	126.96±22.04	129.28±23.39	129.48±24.05	132.04±24.77	126.32±22.25	129.76±22.16
	Test	***t=2.140***	***t=0.444***	***t=1.313***	***t=-0.352***	***t=1.588***	***t=-0.184***
		p=0.037	***p=0.659***	***p=0.195***	***p=0.726***	***p=0.119***	***p=0.854***
Diastolic Blood pressure	Experiment	70.36±16.11	68.36±16.09	72.08±14.52	69.76±14.35	70.40±13.02	67.88±13.45
	Control	63.40±13.33	65.20±12.72	65.60±15.36	66.88±15.54	63.44±12.65	63.76±11.78
	Test	***t=1.66***	***t=0.77***	***t=1.53***	***t=0.68***	***t=1.91***	***t=1.15***
		p=0.10	***p=0.44***	***p=0.13***	***p=0.49***	***p=0.06***	***p=0.25***
Pulse	Experiment	91.96±16.16	88.64±16.14	88.52±15.37	85.76±15.08	87.64±13.26	85.76±13.22
	Control	87.00±17.71	87.96±18.49	84.92±17.26	85.56±18.18	84.76±18.13	85.32±18.51
	Test	***t=1.03***	***t=0.13***	***t=0.79***	***t=0.04***	***t=0.64***	***t=0.09***
		p=0.30	***p=0.89***	***p=0.44***	***p=0.96***	***p=0.52***	***p=0.92***
Body temperature	Experiment	36.72±0.412	36.68±0.416	36.68±0.49	36.66±0.48	36.43±0.36	36.42±0.33
	Control	36.74±0.65	36.76±0.65	36.53±0.54	36.50.±0.51	36.46±0.46	36.47±0.47
	Test	***t=-0.07***	***t=-0.567***	***t=1.00***	***t=1.10***	***t=-0.30***	***t=-0.44***
		p=0.93	***p=0.57***	***p=0.32***	***p=0.27***	***p=0.76***	***p=0.65***
Respiratory	Experiment	20.00±5.17	17.64±4.37	18.64±5.07	16.84±5.04	17.44±4.97	15.88±5.03
	Control	20.20±4.25	21.08±4.48	18.72±3.12	19.44±3.79	18.68±3.57	19.48±3.66
	Test	***t=-1.49***	***t=-2.74***	***t=-0.06***	***t=-2.05***	***t=-1.01***	***t=-2.89***
		p=0.88	***p=0.009***	***p=0.94***	***p=0.04***	***p=0.31***	***p=0.006***
Glucose	Experiment	150.40±68.56	147.84±68.39	145.80±67.77	143.40±65.38	143.04±55.94	138.48±54.16
	Control	146.12±51.21	144.64±50.18	135.92±45.07	135.20±46.47	125.12±35.23	131.88±37.88
	Test	***t=0.25***	***t=0.18***	***t=0.60***	***t=0.51***	***t=1.35***	***t=0.49***
		p=0.80	***p=0.85***	***p=0.54***	***p=0.61***	***p=0.18***	***p=0.62***

the oxygen saturation values in all 3 measurements in the experimental and control groups (p<0.05). Saturation values in the TM application showed an average increase in the experimental group, while the saturation values in the control group that were not subject to TM application decreased on average.

Table 3 shows the VAS-A, VAS-F, VAS-P mean values of the patients. After the application, VAS-F values were found to be significantly different in the 3 measurements in the experimental and control groups (p <0.05). In the TM application, the VAS-F values decreased on average in the experimental group, while in the control group not subject to TM application, the VAS-F values increased on average. After the application, VAS-A values were significantly different in the 3 measurements in the experimental and control groups (p <0.05). In TM application, VAS-A values decreased on average in the experimental group, whereas in the control group not subject to TM application, VAS-A values increased on average. After the application, there were significant differences in the VAS-P values in the 3 measurements in the experimental and control groups (p <0.05). While the VAS-P values decreased significantly in the experimental group in TM application, there was no significant change in the control group not subject to TM application.

Table 4 shows the correlation of the post-application VAS-A, VAS-F, VAS-P mean values of the patients. After the application, it was determined that there was a positive correlation in pain, fear, anxiety mean scores, and pain, anxiety and fear feelings decreased in parallel (p≤0.001).

Table 3. VAS-A, VAS-F, VAS-P mean values of the patients.

Scales	Group	1st measure		2nd measure		3rd measure	
		Before	After	Before	After	Before	After
		Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
VAS-P	Experiment	4.96±1.69	2.04±1.81	4.96±1.56	1.92±1.57	4.72±1.40	1.52±1.08
	Control	6.36±2.17	6.32±2.21	5.56±2.20	5.72±2.37	5.76±2.16	5.88±2.14
	Test	***t=-2.53***	***t=-7.48***	***t=-1.11***	***t=-6.66***	***t=-2.01***	***t=-9.06***
		p=0.01	***p=0.00***	***p=0.27***	***p=0.00***	***p=0.04***	***p=0.00***
VAS-A	Experiment	3.40±1.11	1.44±0.86	3.28±0.89	1.20±0.81	3.24±0.77	1.08±0.70
	Control	3.08±0.86	3.28±0.89	3.16±0.80	3.36±0.81	3.12±0.83	3.32±0.85
	Test	***t=1.13***	***t=-7.39***	***t=0.50***	***t=-9.38***	***t=0.52***	***t=-10.14***
		p=0.26	***p=0.00***	***p=0.61***	***p=0.00***	***p=0.61***	***p=0.00***
VAS-F	Experiment	3.24±1.12	1.32±0.85	3.00±0.95	1.16±0.85	3.12±0.92	0.92±0.49
	Control	2.92±1.15	3.08±1.15	3.16±1.10	3.20±1.11	3.04±0.97	3.16±1.02
	Test	***t=0.99***	***t=-6.14***	***t=-0.54***	***t=-7.26***	***t=0.29***	***t=-9.82***
		p=0.326	***p=0.00***	***p=0.58***	***p=0.00***	***p=0.76***	***p=0.00***

Table 4. The Correlation of the post-application VAS-A, VAS-F, VAS-P mean values of the patients.

Scales	VAS-P	VAS-A	VAS-F
VAS-P	-	r=0.751** p=0.000	r=0.718** p=0.000
VAS-A	r=0.751** p=0.000	-	r=0. 924** p=0.000
VAS-F	r=0. 718 p=0.000	r=0. 924** p=0.000	-

** Pearson correlation (r) was used as a parametric correlation test, which measures a linear dependence between two variables.

DISCUSSION

Critically ill patients are admitted to ICU due to a life-threatening disease or sudden and serious changes in their health status.[18] Rapid change of the patient's condition, uncertainty, and the presence of mortality risk, as well as sounds of monitor systems, ventilators, liquid, or drug infusion pumps in the ICU, causes anxiety and fear in the patient.

Therefore, staying in ICU is a very traumatic and frightening experience for the patient. These feelings experienced by the patient can adversely affect many physical parameters and the

perception of pain [24].

In this study, 62% of the patients were male and 38% were female. In similar studies involving critically ill patients, the rate of male and female patients was reported to be 54.4% and 46.6% by Özer et al. (2006) and 51.9% and 48.1% by Gündöndü (2014), respectively, whereas Uysal et al. (2010) have reported that the distribution of male and female patients was equal in their study [25–27]. Considering the diagnoses of patients included in the study, health problems, such as respiratory distress (due to COPD, lung cancer, etc.) and colon-abdominal diseases (colon cancer, etc.) are more common in men in Turkey and the results obtained from this study support this finding [28]. Of the patients, 44% were aged between 44 and 64 years. In a study on critically ill patients conducted by Uçar and Tunçay (2010), the majority of patients were reported to be in the age group between 42 and 67 years; however, in the study conducted by Gündöndü (2014), it was reported that 42.2% of the patients were over 50 years of age [26,29]. In a study by Uysal et al. (2010), the mean age of the patients was 55 and the rate of geriatric patients (>65 years) was 38.0% [27]. Özer et al. (2006) reported the mean age of the patients as 57.8±17.5 years in their study [25]. The results of this study are compatible with the literature. According to the Turkey Demographic and Health Survey (TDHS), chronic diseases start in middle age and above in Turkish population, and therefore, the complications due to such diseases and requiring ICU indication develop during this period, and in consequence higher need for intensive care and hospitalization to these services in middle-aged and advanced-aged patients are expected [30].

In the present study, 90% of the patients were married. Gündöndü (2014) reported that 71.8% of patients were married [26]. The majority of patients included in our study consist of middle-aged and elderly patients. Compatible with TDHS 2013 data, the fact that most of the individuals in this age group are married is a common situation in Turkey[30].

The rate of patients who were primary school graduates was found to be 54%. In their studies, Uçar and Tunçay (2010) and Gündöndü (2014) reported that 50% and 53.1% of critically ill patients were secondary school graduates, respectively [26,29]. According to the TDHS 2013 data, the majority of the women (51.3%) and men (50.6%) in the age range of 45–49 years in Turkey are primary school graduates and this result is the same for men and women over 50 years of age [30]. Since the majority of the individuals included in the present study are in the age group of 44–64 years, the fact that the majority of them are in primary school graduates is compatible with the statistics related to the educational level in Turkey.

Considering the disease-related characteristics of the patients, 42% were hospitalized in ICU due to respiratory distress. Uysal et al. (2010) and Ceylan et al. (2001) reported that 30% and 29.8% of patients were admitted to the ICU with the diagnosis of respiratory failure and pulmonary disease, respectively, whereas Gürsel et al. (2002) stated that 66% of patients hospitalized in ICU had a diagnosis of chronic obstructive pulmonary disease (COPD) [27,31,32]. Although respiratory distress/failure may result from many reasons, the most important reason is the presence of a disease or condition that impairs lung function. Individuals with respiratory distress/failure are often monitored in the ICU since respiration is a vital function. Lung cancer and COPD are common chronic diseases in Turkey [32].

In this study, the length of stay in the ICU was two days in 74% of the patients. In a study by Uçar and Tunçay (2010), the length of stay in ICU was reported to be three days in 73.6% of the patients and the mean length of stay in ICU was 4.6 days in the study by Keleş et al. (2006) and 4.3 days in the study by Uysal et al. (2010). Treatment is planned according to the diagnosis of the patients and the length of their stay in ICU is affected by this [27,29,33]. In the current study, 90% of the patients were extubated. In their study, Ceylan et al. (2001) showed that 76.8% of the

patients were intubated [31]. Unconscious patients, patients with head trauma, head injury, neurological disease, and delirium that may affect the level of consciousness, and those with impaired perception were excluded from the study.

When repeated measurements of systolic blood pressure, diastolic blood pressure, and pulse parameters were examined, no statistical difference was observed in the experimental group after massage application. However, mean systolic blood pressure, diastolic blood pressure, and pulse values decreased in the experimental group as anxiety, fear, and pain levels of the patients decreased after TM application, whereas these values were observed to increase in the control group which did not receive TM application. Jarianin et al. (2011) reported that there was a decrease in systolic and diastolic blood pressure of the patients following the progressive muscle relaxation exercises [34]. Similarly, Post-White et al. (2003) reported in their study, in which they examined the TM and touch applications in improving cancer symptoms, that high values in all vital parameters (systolic and diastolic blood pressure, respiratory rate, pulse) have decreased to almost normal levels [35].

TM applications, which are applied as a non-pharmacological intervention, have been observed to not affect body temperature. No significant difference was found in the blood glucose levels of the patients in the experimental group following the TM application, whereas the mean values in the experimental group have decreased towards the normal levels.

When the respiratory values were examined, a significant difference was noted in the experimental group after TM application. There was a significant difference between the experimental and control groups in terms of respiratory values in all three measurements made following the application ($p<0.05$). Respiratory values of patients in the experimental group, who have received massage application, have decreased towards normal values whereas these values have increased in the control group not receiving TM application. Upon examination of saturation values, parameters related to respiration, a significant difference was found in the experimental group after TM application. There was a significant difference between experimental and control groups in all measurements in terms of saturation values after application ($p<0.05$). While saturation values increased in the experimental group receiving TM application, the values in the control group not receiving TM application decreased.

Several physiological symptoms occur in the body with the effect of stress hormones when an individual experiences stress or anxiety; blood pressure rises, respiratory rate increases, and blood glucose level rises. Stress hormones decrease as the level of stress and anxiety decreases and in parallel, these findings return to normal levels [36]. In this study, these physical symptoms accompanying anxiety and fear have improved since TM application reduced the anxiety and fear levels of patients. Furthermore, during TM application, breathing exercise was repeated five times following the completion of the application related to each body part and then, TM was applied to another body part. We believe that this is associated with the improvement in the respiration rate and saturation levels of the patients in the experimental group.

There was a significant change in the anxiety level of the patients after TM application. There was a decrease in the mean anxiety levels in the experimental group receiving TM whereas there was an increase in the mean anxiety levels of the patients in the control group. Considering the fear levels of the patients, there was a decrease in the mean fear levels in the experimental group following TM intervention whereas there was an increase in the control group. Fear and anxiety are feelings that accompany each other most of the time. They increase and decrease in direct proportion. In this study, both feelings have decreased in the experimental group. In a study by Henricson (2008) on TM intervention in ICU, a

decrease was reported in the anxiety levels of the patients receiving TM intervention [5]. In a study conducted by Homayouni et al. (2012), they showed that TM interventions caused a significant reduction in stress levels [6]. Abolhasani et al. (2007) reported that the anxiety levels of the patients decreased by massage [37]. Similarly, Terzioğlu and Gönenç (2012) found that massage and acupressure reduced the state anxiety scores of patients [38]. Cooke (2013) reported that relaxation exercises and biofeedback therapy caused a decrease in anxiety levels among patients with cancer.[39] Jarianin et al. (2011) reported that there was a decrease in anxiety levels of the patients following the progressive muscle relaxation exercises [34]. In a study conducted on cancer patients by Post-White et al. (2003), anxiety levels of the patients following the TM and therapeutic touch interventions were reduced [35]. While the pain levels significantly decreased in the experimental group, no significant difference was noted in the control group that did not receive TM intervention. Soykan and Kumbasar (1999) emphasized the importance of psychiatric approaches in the treatment of chronic pain and reported that therapeutic touch treatments and other psychiatric treatment modalities significantly reduced the pain levels of the patients [40]. Similarly, Post-White et al. (2003) found that therapeutic massage and touch reduced pain [35]. In this study, no significant correlation was found between the demographic characteristics (gender, age, marital status, and educational level) and diagnoses with fear, anxiety, and pain levels of patients. Similarly, Şeker (2014) did not find a correlation between the educational level of the participants and their tendency to stress ($p>0.05$) [41]. In a study by Rattray et al. (2005), no correlation was detected between the age, gender, and length of stay in the ICU, and anxiety and depression levels of the patients[42]. Hintisyan (2009) reported that emotional states did not have a statistically significant correlation with the age, gender, educational level, marital status, occupation, diagnosis, and length of stay in the ICU [43]. Our results are compatible with the literature. Regardless of gender, age, marital status, and educational level, all patients are affected negatively by the rapid change in their condition, uncertainty, and the presence of mortality risk, as well as sounds of monitor systems, ventilators, liquid, or drug infusion pumps in the ICU. Staying in the ICU is a very traumatic and frightening experience for the patient. We found a statistically significant relationship between the length of stay in the ICU and fear and anxiety levels of the patients in the control group; anxiety and fear levels increased as the length of stay in ICU prolonged ($p<0.05$). A significant relationship was observed between fear, anxiety, and pain levels of the patients in the experimental group following the intervention. Fear, anxiety, and pain levels of the patients were found to decrease in parallel with each other ($p\leq0.001$). In a study by Henricson (2008) on TM in ICU, TM intervention was reported to reduce anxiety levels of patients staying in ICU [5]. Similarly, Homayouni et al. (2012) found that TM interventions significantly reduced the stress levels of the patients [6]. Similarly, Post-White et al. (2003) found that TM and touch treatments reduced pain [35]. Since therapeutic touch interventions give messages such as closeness, care, trust, courage, sincerity, warmth, empathy, respect, support, understanding, acceptance, and willingness to help, it is an expected result that these practices reduce negative feelings such as fear and anxiety and decrease the perception of pain that increases in parallel with these feelings.

CONCLUSION

Complementary methods such as TM may be used for anxiety, fear and pain treatment of the critically ill patients. Therefore, it should be integrated into routine care of the critically ill patients. Healthcare professionals should be aware of the close relationship between the vital signs of the patients and their fear, anxiety and pain levels. It is suggested to perform TM

regularly in the critical care. It is recommended to provide sufficient number of nurses who can integrate complementary therapies into the time they allocate for routine care. Primary care professionals can play a crucial role to integrate services with a holistic model. Further studies on the effects of therapeutic massage or touch on the critical care patients are needed.

REFERENCES

1. Sixty-seventh World Health Assembly. *Strengthening of Palliative Care as a Component of Comprehensive Care throughout the Life Course*.; 2014.
2. Mercadante S, Gregoretti C, Cortegiani A. Palliative care in intensive care units: Why, where, what, who, when, how. *BMC Anesthesiology*. 2018;18(1):106.
3. Dinç L, Gastmans C. Trust in nurse-patient relationships: A literature review. *Nursing Ethics*. 2013;20(5):501-516.
4. Foster T, Hawkins J. The therapeutic relationship: dead or merely impeded by technology? *British journal of nursing (Mark Allen Publishing)*. 2005;14(13):698-702.
5. Henricson M. Tactile touch in intensive care : Nurses' preparation, patients' experiences and the effect on stress parameters. Published online 2008.
6. Homayouni K, Zaher H, Borhani F, Abbaszadeh A, Jahromi M, Jahromi MM. Effect of tactile touch on stress in patients with myocardial infarction. *Iranian Journal Of Critical Care Nursing*. 2013;5(4):183-187.
7. Papathanassoglou EDE, Mpouzika MDA. Interpersonal Touch: Physiological Effects in Critical Care. *Biological Research for Nursing*. 2012;14(4):431-443.
8. Linden DJ. *Touch: The Science of the Hand, Heart, and Mind*. Penguin; 2016.
9. Guest S, Dessirier JM, Mehrabyan A, McGlone F, Essick G, Gescheider G, Fontana A, Xiong R, Ackerley R, Blot K. The development and validation of sensory and emotional scales of touch perception. *Attention, Perception, and Psychophysics*. 2011;73(2):531-550.
10. Hertenstein M, Weiss S, eds. *The Handbook of Touch: Neuroscience, Behavioral, and Applied Perspectives*. Springer Publishing Company; 2011.
11. McGlone F, Wessberg J, Olausson H. Discriminative and Affective Touch: Sensing and Feeling. *Neuron*. 2014;82(4):737-755.
12. Ackerley R, Backlund Wasling H, Liljencrantz J, Olausson H, Johnson RD, Wessberg J. Human C-tactile afferents are tuned to the temperature of a skin-stroking caress. *Journal of Neuroscience*. 2014;34(8):2879-2883.
13. Morrison I, Björnsdotter M, Olausson H. Vicarious responses to social touch in posterior insular cortex are tuned to pleasant caressing speeds. *Journal of Neuroscience*. 2011;31(26):9554-9562.
14. Rapaport MH, Schettler P, Bresee C. A preliminary study of the effects of a single session of Swedish Massage on hypothalamic-pituitary-adrenal and immune function in normal individuals. *Journal of Alternative and Complementary Medicine*. 2010;16(10):1079-1088.
15. Zimmerman A, Bai L, Ginty DD. The gentle touch receptors of mammalian skin. *Science*. 2014;346(6212):950-954.
16. Sandkühler J, Gruber-Schoffnegger D. Hyperalgesia by synaptic long-term potentiation (LTP): An update. *Current Opinion in Pharmacology*. 2012;12(1):18-27.
17. Gürkan A. Holistic Approach: Family Members with Patients at the Intensive Care Unit. *Intensive Care Nurses Magazine*. 2009;13(1):1-5.
18. Kulaksizoglu IB. Yoğun Bakım Şartlarında Deliryum ve Psikiyatrik Sorunlar. *Turk J Intense Care*. 2006;4(1):77-82.
19. Maksum, Sujianto U, Johan A. Effects of Therapeutic Touch to Reduce Anxiety As a Complementary Therapy: A Systematic Review. *KnE Life Sciences*. Published online October 9, 2019:162–175-162–175.
20. Airosa F, Falkenberg T, Öhlén G, Arman M. Tactile Massage as Part of the Caring Act: A Qualitative Study in Short-Term Emergency Wards. *Journal of Holistic Nursing*. 2016;34(1):13-23.
21. Alves da Silva T, Stripari Schujmann D, Yamada da Silveira LT, Caromano FA, Fu C. Effect of therapeutic Swedish massage on anxiety level and vital signs of Intensive Care Unit patients. *Journal of Bodywork and Movement Therapies*. 2017;21(3):565-568.
22. Tabatabaee A, Tafreshi MZ, Rassouli M, Aledavood SA, AlaviMajd H, Farahmand SK. Effect of Therapeutic Touch in Patients with Cancer: a Literature Review. *Medical archives (Sarajevo, Bosnia and Herzegovina)*. 2016;70(2):142-147.
23. Chhugani M, Sarkar S. Therapeutic Touch Modalities and Premature Neonate's Health Outcome: A Literature Review. *Journal of Neonatal Biology*. 2014;3(4):0-0.
24. Meehan TC. Therapeutic touch as a nursing intervention. *Journal of Advanced Nursing*. 1998;28(1):117-125.
25. Özer Balın Ş, Aktaş Şenol A. Evaluation of Hospital Infections in Intensive Care Unit. *Klimik Dergisi*. 2017;30(3):108-113.

26.Gündöndü D. Ameliyat sonrası yoğun bakıma alınan hastalarda ağrı yönetimiyle anksiyete düzeyi arasındaki ilişki [Postoperative pain management in intensive care patients received relationship between the anxiety levels] (in Turkish). Published online 2014.
27.Uysal N, Gündoğdu N, Börekçi Ş, Dikensoy Ö, Bayram N, Uyar M, Bayram H, Filiz A, Ekinci E, Mutlu GM. Prognosis of Patients in a Medical Intensive Care Unit of a Tertiary Care Centre. *Yoğun Bakım Dergisi*. 2010;1:1-5.
28.*Türkiye Kanser İstatistikleri*.; 2016. [Turkey Cancer Statistics; 2016] (in Turkish). Accessed January 2, 2021.
29.Tunçay GY, Uçar H. Opinions of Patients on Physical Environmental Features of Intensive Care Units. *Hacettepe University Faculty of Health Sciences Nursing Journal*. 2010;1:33-46.
30.*Türkiye Nüfus ve Sağlık Araştırması*;2013. [Turkey Demograhic and Health Survey; 2013] (in Turkish). Accessed January 2, 2021.
31.Ceylan E, İtil O, Arı G, Ellidokuz H, Uçan ES, Akkoçlu A. Factors Affecting Mortality and Morbidity in Patients Followed in Medical Intensive Care Unit. *Toraks Dergisi*. 2001;2(1):6-12.
32.Gürsel G, Erel Kırışoğlu C, Bilgin Mullaoğlu S, Çetin N. Intensive Care Unit Characteristics of Patients with Chronic Respiratory Failure During Acute Exacerbations. *Yoğun Bakım Dergisi*. 2002;2(4):261-267.
33.Tezcan Keleş G, Topçu İ, Kefi A, Ekici Z, Sakarya M. Obstetric Patients in Intensive Care Unit. *Fırat Tıp Dergisi*. 2006;11(1):62-65.
34.Jariani M, Saki M, Momeni N, Ebrahimzade F, Seydian A. The Effect of Progressive Muscle Relaxation Techniques on Anxiety in Patients with Myocardial Infarction. *Yafteh*. 2011;13(3):22-30.
35.Post-White J, Kinney ME, Savik K, Gau JB, Wilcox C, Lerner I. Therapeutic Massage and Healing Touch Improve Symptoms in Cancer. *Integrative Cancer Therapies*. 2003;2(4):332-344.
36.Baltaş Z, Atakuman Y, Duman Y. Standardization of the Perceived Stress Scale: Perceived stress in middle managers. In: *Stress and Anxiety Research Society 19 the International Conference*. Vol 3. Boğaziçi University; 1998.
37.Abolhassani S. Sensory Stimulation effect on Patient Anxiety in Coronary Care Unit. *J Med Sci Kurdistan*. 2007;12:46-52.
38.Gönenç İM, Terzioğlu F. The Effect Of Massage And Acupressure On Pregnant Women Anxiety Level. *Ankara Sağlık Bilimleri Dergisi*. 2012;1(3):129-143.
39.Cooke H. Progressive Muscle Relaxation. *CAM-Cancer Journal*. 2013;1(1):1-6.
40.Soykan A, Kumbasar H. Psychiatric Interventions in Chronic Pain Treatment. *J Clin Psy*. 1999;2(2):109-116.
41.Şeker M. Güreş eğitim merkezlerindeki güreşçilerin depresyon, kaygı ve stres düzeylerinin incelenmesi [Wrestling wrestlers education centers study of depression, anxiety and stress levels] (in Turkish). Published online 2014.
42.Rattray JE, Johnston M, Wildsmith JAW. Predictors of emotional outcomes of intensive care. *Anaesthesia*. 2005;60(11):1085-1092.
43.Hintistan S, Nural N, Öztürk H. Experiences of the Patients in Intensive Care Unit. *Yoğun Bakım Hemşireliği Dergisi*. 2009;13(1):40-46.

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ORIGINAL RESEARCH

An Investigation of the Knowledge and Attitudes of Medical Faculty Students on Traditional and Complementary Medicine

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Abstract

Objective: Traditional and complementary medicine, which is being used more and more all over the world, has also become widespread in our country. However, the medical school could not find enough place in the curriculum. In this study, it was aimed to show the level of knowledge and awareness of medical faculty students about traditional and complementary medicine.

Material-Method: In the study, an e-questionnaire was delivered to the 1st and 6th grade students of the medical faculty with the help of "Google Forms". A 24-question survey consisting of TCM application methods and some descriptive questions was applied to the participants. Analyzes were analyzed by SPSS.

Results: A total of 166 medical faculty students participated in the study. Most of the students were female students (% 62). Students from all classes participated in the study. The students stated that they knew the most about acupuncture and the least about prolotherapy. Nearly half of the students (46.4%) thought that TCM applications should be included in the medical school curriculum. It was observed that towards upper grades, students stated their TCM knowledge level more.

Conclusion: It was observed that medical faculty students were frequently interested in TCM applications, but they did not find their knowledge sufficient on this subject. In this sense, new education models and curriculum arrangements are needed.

Keywords: Traditional Medicine, Complementary Medicine, Medical Education

INTRODUCTION

Traditional and complementary medicine, which is being used more and more all over the world, has also become widespread in our country [1]. Complementary medicine covers applications that are used with modern medical practices in the treatment of diseases but are not known at the desired level [2]. On the other hand, traditional medicine was all of the knowledge, skills and practices used to prevent and diagnose mental and physical diseases, based on beliefs and experiences fed by different cultures for centuries [3-5]. In this sense, the Traditional and Complementary Medicine (TCM) Practices Regulation was published by the Ministry of Health in 2014 in our country. Fifteen different TCM methods are defined in this regulation. Those application area acupuncture, apitherapy, phytotherapy, hypnosis, leech therapy, homeopathy, chiropractic, cupping therapy, prolotherapy, maggot therapy, mesotherapy, osteopathy, ozone therapy, reflexology, music therapy. Many universities, hospitals and Educational Research is designated as the central unit. In addition, in this regulation, which aims to prevent inappropriate TCM methods and increase inspections, the indications/contraindications, personnel and materials that must be present in the application center are explained in detail [6].

Although TCM methods are applied in many centers and units, they have not found enough

place in the medical school curricula [7,8]. Although researches with TCM methods have increased in recent years, it is still limited. In this study, it was aimed to show the level of knowledge and awareness of future physicians on this issue.

MATERIALS AND METHODS

Our study is a descriptive cross-sectional study. The study was applied to 1st-6th grade students studying at Duzce University Faculty of Medicine in the form of an e-questionnaire, via "Google Forms" in December and November 2020. Written permission was obtained from the students who wanted to participate in the study. A 24-question survey consisting of TCM application methods and some descriptive questions was applied to the participants.

Statistical analysis

While performing the statistics of the study, numerical data were given as mean and standard deviation in descriptive statistics, and category data as numbers and percentages. The distribution of numerical data was viewed with histogram graphics. While numerical data in two different groups were analyzed by student's t test, comparisons of categorical data were analyzed by chi-square test. In addition, one-way ANOVA test was used. P significance value was accepted as <0.05. SPSS 23.0 (SPSS, version 23X, IBM, Armonk, New York 10504, NY, USA) package program was used for analysis.

RESULTS

A total of 166 medical faculty students participated in the study. 62% (n = 103) of the participants were female and 38% (n = 63) were male. All students from the 1st to the 6th grade participated in the study, with a maximum of 24.7% (n = 41) 3rd grade students (Figure 1).

The students participating in the study were asked to score their own knowledge on TCM between 0-10. The answers given and the number of students are shown in Figure 2. Average knowledge level was calculated as 4.75 ± 2.52.

The answers given by the participating students to some questions about TCM applications were evaluated. Most of the students (66.3%) stated that they knew that they could obtain a certificate as a doctor and apply TCM applications in the future. 36.1% (n = 60) of the students stated that they have prejudices against TCM applications. Again, 21.1% (n = 35) of the students stated that they believed the benefits of TCM applications consisted of placebo. Most of the students stated that TCM applications should be included in the medical school curriculum with 46.4% (n = 77). Answers to other questions are shown in Table 1.

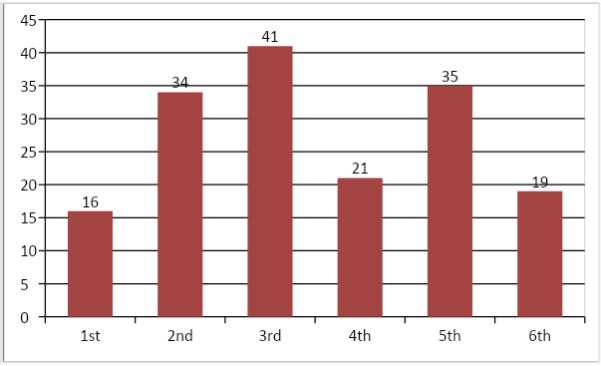

Figure 1. Classes and numbers of students participating in the study

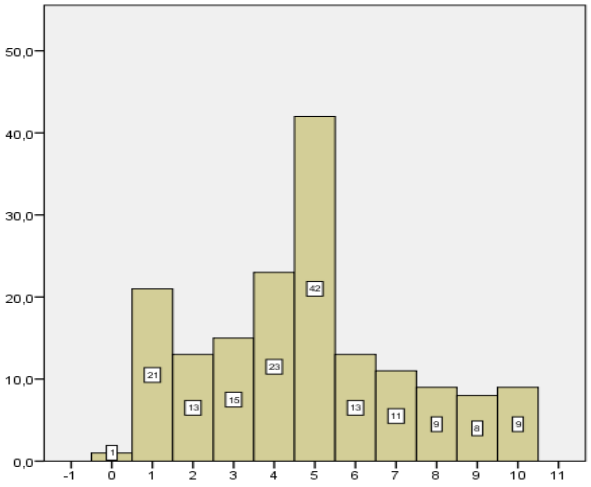

Figure 2. The level of knowledge score that students give to them about TCM

13.9% of students (N=23) said they would make an effort to eliminate information pollution about TCM. 67.5% (n = 112) of the students stated that they could be used in treatments as supportive of TCM applications. The students were asked who can apply TCM applications and the answers given can be seen in Figure 3.

Students were asked if they knew about which TCM app. 83.7% (139) expressed knowledge about acupuncture, while at least 6.0% (n=10) expressed knowledge about prolotherapy. 83.7% (139) expressed knowledge about acupuncture, while at least 6.0% (n=10) expressed knowledge about prolotherapy. The answers regarding other TCM applications are shown in Table 2.

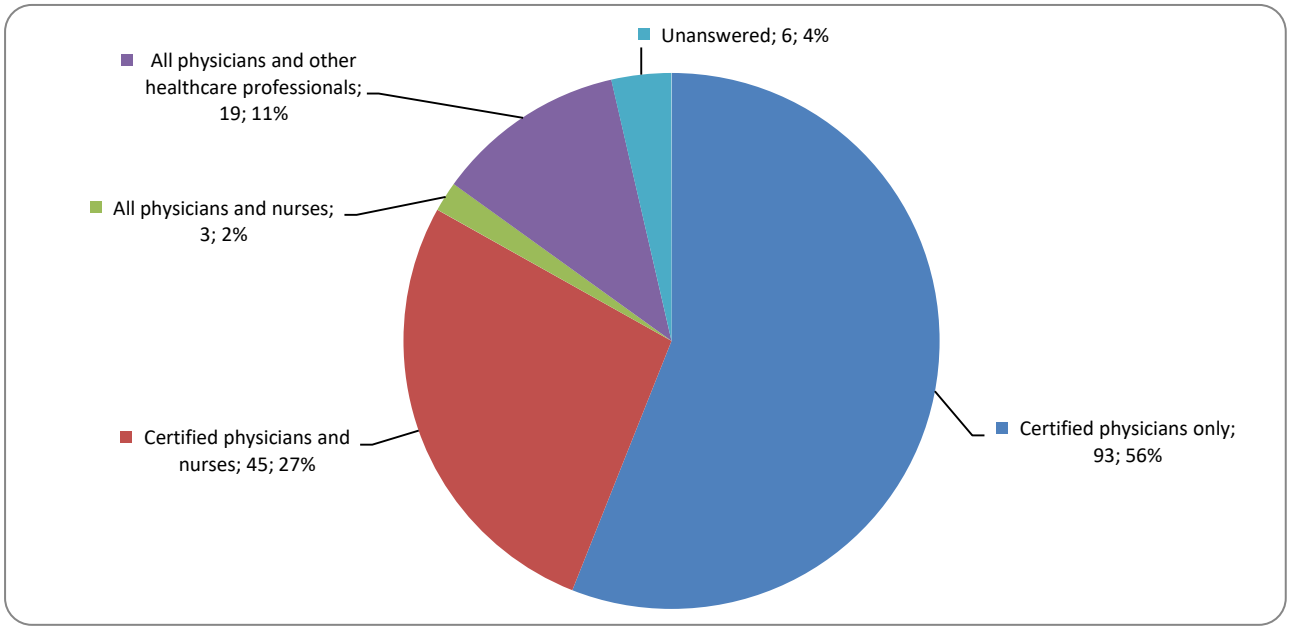

Figure 3. Answers of students about who can apply TCM applications

Table 1. The answers given by the students participating in the study to some questions about TCM applications

	Yes n /%	No n /%	I am indecisive n /%
Want to know more about TCM?	61/36.7	32/19.3	73/440
Do you know that you can get a certificate and apply TCM applications as a doctor in the future?	110/66.3	52/31.3	4/2.4
Would you like to get a certificate for TCM applications?	66/39.8	46/27.7	54/32.5
Does having information about TCM provide a more holistic approach to patients?	100/60.2	38/22.9	28/16.9
Do you have prejudices against TCM practices?	60/36.1	65/39.2	41/24.7
If you were sure that only certified physicians applied TCM applications, would you have prejudice?	32/19.3	96/57.8	38/22.9
Is it necessary for every physician to know the effects and side effects of traditional methods used by their patients?	145/87.3	8/4.8	13/7.8
Is TCM just a placebo?	35/21.1	81/48.8	49/29.5
Do you think that TCM applications will be as useful as modern medicine in the right indications?	42/25.3	81/48.8	43/25.9
Was it helpful for the Ministry of Health to allow 15 TCMs?	75/45.2	25/15.1	66/39.8
Have you ever used TCM methods?	39/23.5	122/73.5	5/3.0
Are there people around you who benefit from TCM methods?	68/41.0	71/42.8	27/16.3
Would you mind drinking linden or mint-lemon when you have flu?	8/4.8	156/94.0	2/1.2
Do you think TCM applications should be included in the medical school curriculum?	77/46.4	55/33.1	34/20.5
Would you direct your patients to specialist physicians in TCM centers in the future?	77/46.4	45/27.1	43/25.9

Table 2. The knowledge of the students participating in the study about TCM applications

TCM Applications	Yes (n /%)	No(n/%)
Larval treatment	77/46.4	89/53.6
Prolotherapy	10/6.0	156/94.0
Music therapy	105/63.3	61/36.7
Mesotherapy	47/28.3	119/71.7
Osteopathy	24/14.5	142/85.5
Chiropractic	35/14.5	131/85.5
Homeopathy	33/21.1	133/78.9
Ozone therapy	89/19.9	77/80.1
Reflexology	30/18.1	136/81.9
Cup treatment	126/77.9	40/24.1
Leech therapy	137/82.5	29/17.5
Phytotherapy	77/46.4	89/53.6
Apitherapy	61/36.7	105/63.3
Hypnotherapy	110/66.3	56/33.7
Acupuncture	139/83.7	27/16.3

Some other parameters were compared with the states of students applying TCM methods. It was observed that students who wanted TCM applications to be added to the medical school curriculum used TCM applications significantly more (p = 0.001). Students who thought that TCM applications were placebo applied significantly less than TCM applications (p <0.001). It was observed that students who had bias towards TCM applications applied significantly less than TCM applications (p = 0.007). No significant relationship was found between the number of applications to TCM applications with gender and grade (p> 0.05) (Table 3).

Table 3. Comparison of students' application to TCM methods and some other parameters

		Have you ever used TCM methods?			
		Yes	No	I am indecisive	p
Do you think TCM applications should be included in the medical school curriculum?	Yes	29	45	3	0.001
	No	6	47	2	
	I am indecisive	4	30	0	
Is TCM just a placebo?	Yes	1	34	0	<0.001
	No	32	48	1	
	I am indecisive	6	39	4	
Want to know more about TCM??	Yes	26	35	0	<0.001
	No	3	27	2	
	I am indecisive	10	60	3	
Do you have prejudices against TCM practices?	Yes	9	51	0	0.007
	No	21	43	1	
	I am indecisive	9	28	4	
Gender	Woman	19	81	3	0.140
	Man	20	41	2	
Class	1	2	14	0	0.107
	2	8	23	3	
	3	8	33	0	
	4	4	15	2	
	5	9	26	0	
	6	8	11	0	

The level of knowledge score given by the students about TCM was evaluated according to gender and classes. There was no significant difference in scores according to gender (p = 0.534). It was observed that there were significantly higher scores in the upper classes compared to the lower classes (p = 0.002) (Table 4).

Table 4. Assessment of students by gender and class with the knowledge level score they give them

	n	Average	standard deviation	p
Woman	103	4.65	2.30	**0.534**
Man	62	4.90	2.85	
1st Class	16	4.44	2.80	**0.002**
2nd Class	33	4.64	2.65	
3rd Class	41	4.27	2.47	
4th Class	21	3.38	1.53	
5th Class	35	5.63	2.61	
6th Class	19	6.11	1.85	

DISCUSSION

TCM practices are more important to physicians in our country, especially after the Ministry of Health issued regulations are practiced by many physicians. In this sense, it is extremely important to work with medical faculty students, who will be the doctors of the future.

Participants from each class appear to have participated in the study. This situation is also seen in other studies [7,8]. In our study, it was observed that the students did not find themselves adequate in terms of TCM knowledge. This situation overlaps with similar results in other studies [9-11]. It is obvious that there is a need for curriculum changes in medical faculties, especially when we consider the curiosity of students in these subjects. It has been stated in studies that the rate of using an alternative medicine method in individuals aged 18 and over in Turkey is 70 % [12]. Therefore, the training to be given about TCM means that medical faculty students will be able to perform these practices more as physicians in the future. Thus, more patients will not be victims by those who perform these applications, except for health institutions.

Although most of the students said that they knew that they could obtain a certificate and apply TCM applications in the future, it was observed that many students also had prejudices about TCM. This situation has been expressed similarly in other studies [8.] In the study, the students mostly knew who could apply TCM applications. This situation can be explained by the fact that the Ministry of Health TCM regulation is frequently the subject of meetings and symposiums [6]. In addition, the increase of faculty members who are interested in TCM applications in medical faculties is an important factor in this regard. In our study, it was observed that the students stated that they had the most knowledge about acupuncture and at least about prolotherapy. In similar studies, both physicians and students stated the most commonly used method as acupuncture [3,13]. This can be explained by the fact that acupuncture is the most widely used TCM method worldwide and krotherapy is relatively uncommon compared to other applications. It was observed that students who thought that TCM applications consisted of placebo and had prejudices about these applications applied less to TCM applications. This situation confirms the need for additions to the curriculum in order to introduce TCM applications to medical students. In our study, it was observed that students had higher scores in upper grades while expressing their own knowledge of TCM. This suggests that as their time on the faculty increases, they learn more about it and consider themselves more adequate.

CONCLUSION

As a result, we believe that TCM practices are methods that are often used by people, but are often used by people who are not qualified, and doctors should receive more training in this regard. For this purpose, only post-graduate certified training programs and TCM applications, which are only accessible to a limited number of physicians, should be delivered to medical school students before graduation with a curriculum. Thus, the awareness and application status of TCM applications among physicians will increase.

REFERENCES

1. Ünal M, Dağdeviren HN. Geleneksel ve tamamlayıcı tıp yöntemleri. *Eurasian Journal of Family Medicine*. 2019;8(1):1-9.
2. Taştan K. Ülkemizde Geleneksel ve Tamamlayıcı Tıbbın Kilometre Taşları. *Ankara Medical Journal*. 2018;18(3):458-9.
3. Samanci R, Samanci VM, Günel MG, Yildiz SN, Ataoğlu S. Investigation of the Knowledge and Attitude of Physicians About Traditional and Complementary Medicine. *International Journal of Traditional and Complementary Medicine Research*. 2020;1(3):118-24.
4. Organization WH. WHO global report on traditional and complementary medicine 2019: *World Health Organization;* 2019.
5. Siti Z, Tahir A, Farah AI, Fazlin SA, Sondi S, Azman A, Maimunahb A, Hanizab M, Siti Haslindab M, Zulkarnainb

A, Zakiaha I, WanZalehab W. Use of traditional and complementary medicine in Malaysia: a baseline study. *Complementary therapies in medicine*. 2009;17(5-6):292-9.
6. Resmi Gazete. Geleneksel ve tamamlayıcı tıp uygulamaları yönetmeliği. http://www.resmigazete.gov.tr/eskiler/2014/10/20141027-3.htm/adresinden 15.02.2021 tarihinde erişilmiştir.
7. Sönmez CI, Başer DA, Küçükdağ HN, Kayar O, İdris A, Güner PD. Tıp fakültesi öğrencilerinin geleneksel ve tamamlayıcı tıp ile ilgili bilgi durumlarının ve davranışlarının değerlendirilmesi. *Konuralp Tıp Dergisi*. 2018;10(3):276-81.
8. Ayraler A, Yavuz E, Oruç MA, Öztürk O. Tıp Fakültesi Öğrencilerinin Geleneksel ve Tamamlayıcı Tıp Hakkındaki Bilgi Düzeyleri ve Görüşleri. *Türkiye Aile Hekimliği Dergisi*. 2020;24(4):196-202.
9. Ergin A, Hatipoğlu C, Bozkurt Aİ, Mirza E, Kunak D, Karan C, Özçelik G, Teğin C, Pazir Y, Pirti İ. Uzmanlık ve tıp öğrencilerinin tamamlayıcı-alternatif tıp hakkındaki bilgi düzeyleri ve tutumları. *Pamukkale Tıp Dergisi*. 2011(3):136-43.
10. Yeo AS, Yeo JC, Yeo C, Lee CH, Lim LF, Lee TL. Perceptions of complementary and alternative medicine amongst medical students in Singapore–a survey. *Acupuncture in Medicine*. 2005;23(1):19-26.
11. Doğanay S, Guzel D, Öztürk D, Tanyeli A. Complementary and alternative medicine: understanding, attitude and usage among Turkish health sciences and medical students. *J Contemp Med*. 2018;8(1):48-54.
12. Tan M, Uzun O, Akçay F. Trends in complementary and alternative medicine in Eastern Turkey. *Journal of Alternative & Complementary Medicine.* 2004;10(5):861-5.
13. Ozcakir A, Sadikoglu G, Bayram N, Mazicioglu MM, Bilgel N, Beyhan I. Turkish general practitioners and complementary/alternative medicine. *The Journal of Alternative and Complementary Medicine*. 2007;13(9):1007-10.

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ORIGINAL RESEARCH

Knowledge Level and Opinions of Secondary School Students about Traditional and Complementary Medicine

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Abstract

Objective: The place of traditional and complementary medicine (T&CM) practices in modern health services has been under intensive debate over recent years. Currently, integrative medicine is not included in the curricula across educational levels below the bachelor's degree. In this study, the level of awareness and opinions about T&CM were investigated among secondary school students.

Material-Method: In this cross-sectional study, the level of awareness and opinions about T&CM were examined among secondary school students. A survey was administered to students attending the 9th-12th grades at randomly selected schools in the Asarcık and Canik districts of Samsun.

Results: This study included 459 students. Most of the participating students were males (59.7%). It was determined that; of the approaches in T&CM, the highest level of awareness was about 'hypnosis' (67.7%). It was found out that information about T&CM approaches was mostly acquired from the media (32.0%). Of the student opinions about T&CM, 40.7% were positive. The percentage of students thinking that conventional medicine and T&CM can be integrated and complement each other was 32.5% (n=149). Most of the students with a family member utilizing T&CM were wishing to work in the health sector in the future (32.1%) (p=0.02) and aiming to have an integrated medicine related occupation more than other participants (32.7%) (p=0.001).

Conclusion: The level of awareness about T&CM was found to be low among secondary school students. If health literacy education in schools is organized better, awareness of evidence-based integrative medicine may grow.

Keywords: Evidence-Based, Traditional Medicine, Complementary Medicine, Integrative Medicine

INTRODUCTION

In Turkey, 15 forms of T&CM therapies were authorized by the Regulation on Practices of T&CM; which was put into force in 2014 by the Ministry of Health of Turkey [1]. The regulation legitimized T&CM treatments and started forestalling inappropriate practices.

The secondary school system in Turkey is an intermediate process to follow the preceding eight-year compulsory primary school period and serve as the path to university. The secondary school system in Turkey covers all generalist, vocational, and technical education in institutions that provide at least a four-year program that can be compulsory, formal, or non-formal [2]. Although the secondary school curriculum includes topics about general health, nutrition, healthy lifestyle, and addictions; it does not contain any topics about integrative medicine. However, there is information pollution about this topic, which is often regarded positively or negatively in the social and national media in routine daily life. It is important that secondary school students, too,

should acquire information about integrative medicine and have an evidence-based opinion on T&CM.

MATERIALS AND METHODS

This is a cross-sectional survey study. An 8-item sociodemographic data form and a 13-item questionnaire that inquired about the awareness and opinions on T&CM were administered in the period between May 2019 and June 2019 to students attending the 9th, 10th, 11th, and 12th grades as the grades of the secondary school education. The secondary schools were selected out of the schools in the Asarcık and Canik districts of Samsun. Of the questions regarding T&CM; one was designed as a 2-point Likert-type scale, 8 were designed as a 3-point Likert-type scale, and 3 were designed as a 4-point Likert-type scale. One question had 15 options and one participant could select more than one option to respond. Body mass indexes (BMI) of the students were calculated using the height and weight information reported by the students. A student having a BMI value below 18.5 kg/m2 was accepted as underweight, students with BMI values of 18.5-25 kg/m2 were accepted as normal weight, and students with BMI values more than 25 kg/m2 were accepted as overweight [3].

Questionnaires were administered after obtaining permission from the respective institutions and teachers. Percentage (%) and mean ± standard deviation values were used in descriptive statistics. The chi-square test was used in comparative analyses. The statistical analysis was performed using the SPSS 20.0 package software. A p-value of less than 0.05 was accepted as significant. To carry out the study, ethics committee approval was obtained from 19 Mayıs University's Clinical Research Ethics Committee (OMU KAEK 2019/154).

RESULTS

The study included 459 students. Of the participants, the mean age was 15.75 ±1.26 years, the mean height was 165.75 ± 9.06 cm, and the mean weight was 56.47 ±11.30 kg. Of the participants, 68.6% (n=315) were in the normal BMI range. Of the male and female students, 26.6% and 9.7% were smokers, respectively (Table 1).

Table 1. Demographic data

	Parameter	Frequency (n)	Percentage (%)
Grade	9	178	38.8
	10	74	16.1
	11	133	29.0
	12	74	16.1
Gender	Girls	185	40.3
	Boys	274	59.7
BMI	<18,5 kg/m^2	116	25.3
	18,5-25 kg/m^2	315	68.6
	>25 kg/m^2	28	6.1
Desired occupation sector	Health	56	12.2
	Non-health	403	87.8
Chronic Disease	Yes	29	6.3
	No	430	93.7
Smoking	Girls	18	9.7
	Boys	73	26.6

Of the T&CM practices, the highest level of awareness was about hypnosis followed by music therapy and the least known practice was chiropractic with the following numbers (rates) of students as 311 (67.7%), 218 (47.4%), and 16 (3.4%), respectively (Table 2).

Table 2. T&CM awareness

T&CM Practices	Frequency (n)	Percentage (%)
Hypnosis	311	67.7
Music therapy	218	47.4
Wet cup	212	46.1
Homeopathy	95	20.6
Acupuncture	84	18.3
Reflexology	83	18.0
Mesotherapy	69	15.0
Apitherapy	52	11.3
Ozone	50	10.8
Osteopathy	42	9.1
Larva Application	40	8.7
Prolotherapy	35	7.6
Phytotherapy	31	6.7
Hirudotherapy	20	4.3
Chiropractic	16	3.4

It was found that information about T&CM practices was mostly acquired from the media (32.0%). Of the participants wishing to choose an occupation in the health sector, 35.7% were

aiming to do so in integrative medicine. While 40.7% (n=187) of the students had a positive opinion about T&CM, 21.6% (n=99) of them had a negative opinion. The rate of those, who thought that conventional medicine and T&CM could be integrated and complement each other, was 32.5% (n=149). The rate of those who had a family member that benefited from T&CM was 20.7% (n=95). The rate of those, who thought that the number of T&CM centres in Turkey needed to be increased, was 46.4% (n=213). According to 38.6% of the students, everyone completing the respective training could perform T&CM practices. The rate of those; who heard positive news about T&CM approaches in the media was 40.7% (n=187); while the remaining participants heard about T&CM in negatively commenting news in the media or they did not hear about T&CM in the news at all. Those, who heard T&CM practices in positive news, had a more positive opinion regarding such practices (p=0.003). The rate of those, who thought that T&CM could boost student success, was 35.5% (n=163). About spiritual practices such as amulet, prayer, and magic; 12.6% (n=58) of the participants thought that these were among T&CM practices but 24.0% (n=110) of the participants were hesitant.

There was not a difference by gender in terms of wishing to have an occupation related to T&CM; however, the wish of having an occupation in the field of conventional medicine was higher in females and female students had more positive opinions on T&CM (p=0.39 , p<0.001, p=0.02; respectively) (Figure 1).

By the BMI categories, no differences were observed in terms of wishing to have an occupation related to T&CM or conventional medicine, or in terms of having a different opinion on T&CM (p=0.45, p=0.79, p=0.34; respectively).

In terms of being a smoker or not, no differences were observed in terms of wishing to have an occupation related to T&CM or in the field of conventional medicine (p=0.38 and p=0.80. However, the opinions of non-smokers on T&CM were more positive (p=0.03).

Wishing to have an occupation related to T&CM or conventional medicine was not different in the student group having the misconception that spiritual approaches such as amulet, prayer, and magic were authorized T&CM practices (p=0.52, p=0.26). However, the students thinking the opposite had more positive opinions regarding T&CM (p<0.001) (Figure 2).

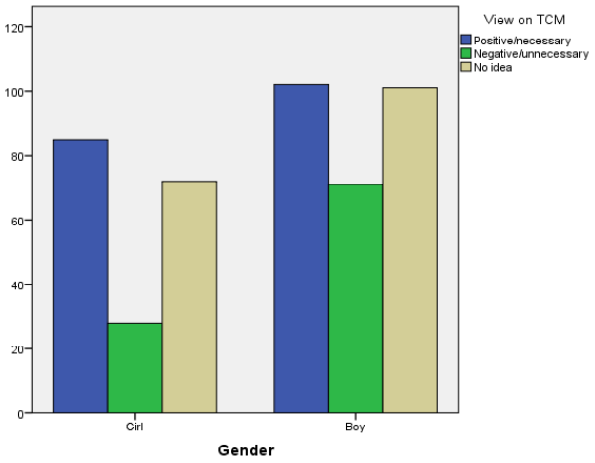

Figure 1. View on T&CM by gender

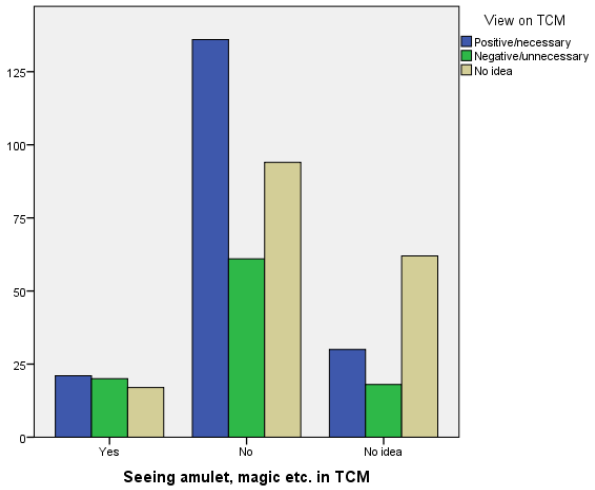

Figure 2. View on T&CM by seeing amulet, magic etc. in T&CM

The opinions about T&CM among the participating students with a chronic disease were not different from those not having a chronic disease (p=0.66). When the participating students were compared by the wish of having an occupation in the health sector or not, no differences were observed between the two groups in terms of participants' opinions on T&CM

(p=0.55). The percentage of students wishing to have an occupation in the health sector was significantly higher (32.1%) in the group of students having family members utilizing T&CM compared to the group of students with family members, who did not utilize T&CM (19.1%) (p=0.02). In the group of students having a family member utilizing T&CM, the rate of students wishing to have a T&CM-related occupation was higher (32.7%) compared to the students, who did not wish to have such an occupation (14.4%) (p=0.001).

DISCUSSION

Concerning the study participants, this study is the first in the literature to the best of our knowledge. Therefore, the study may potentially shed light on future studies. Information pollution in the field of T&CM places a major hurdle in front of individuals wishing to utilize integrative medicine practices [4]. Patients usually suffer from a lack of information and unrealistic expectations.

A significant issue is to create awareness on the potential health protection benefits of knowing and utilizing integrative medicine starting from the early years of life. Establishing a general culture of health would provide many benefits in more than one aspect.

When the literature is reviewed, it is seen that studies about the awareness and practices of T&CM were conducted on medical students, medical doctors, students/professionals from other fields of medicine, and patients. Our findings will be compared with those of other studies that included different groups of participants since no other study included secondary school students. The number of studies from Turkey, conducted on physicians and medical students to investigate awareness levels and attitudes about T&CM practices, is increasing [5-9]. It has also been shown that the interest of students varies according to age, gender, and the type of school and the grade that the student was currently attending [10-13]. If an appropriate curriculum is developed about evidence-based integrative medicine, it will not be wrong to expect the occurrence of a certain interest among secondary school students. However, studies are available showing low levels of knowledge of evidence-based T&CM among medical students despite their high levels of interest [6,14]. This finding should be considered as a natural consequence since no universally accepted curricula are available regarding integrative medicine.

In the study conducted by Altan et al., it was determined that "media" was the most frequently used tool among medical students to gather information about T&CM. That study found out that "massage" and "herbal therapy" were the most commonly known T&CM practices8. In many studies, it has been seen that the media, especially the internet, is the most frequently used tool [14,15]. Consistent with the information in the literature, we found in our study that the media was the most commonly used source of information. As is known, the reliability of information to be acquired from the media is not absolute in any discipline, not even to mention controversial ones such as T&CM. Therefore, it is necessary to educate people.

Because most studies on T&CM were conducted before the respective regulation that was put into effect in 2014, studies conducted in our country are not adequate to provide information about the rates of the use of the currently authorized T&CM methods. In the study conducted by Sonmez et al. in 2018, it was found that medical students most frequently used phytotherapy and cup therapy practices among T&CM methods [9]. In our study, we found out that hypnosis and music therapy were the most commonly known methods. However, this is not a commonly reported finding in the literature and might have occurred in our study depending on the emergence of popular social media topics followed by secondary school students.

Chiropractic has been found as one of the least known T&CM methods in many studies [6,8,14,15]. Sönmez et al., too, obtained a similar result in their study in 2018, reporting that the participants had never heard of mesotherapy, osteopathy, larva treatment, and chiropractic [9]. In our study, chiropractic was found to be the least known

practice consistent with the information in the literature.

In the study by Doğanay et al., the rate of those reporting that T&CM methods could not be applied without the supervision of a certified health professional was only 47%. In that study, the rate of those thinking that T&CM methods could be as successful as conventional medical practices was 29% [14]. In our study, the percentage of participants was lower reporting that T&CM methods could be applied in the presence of a supervising certified health professional. This result can be explained by the lack of awareness and experience among secondary school students. Furthermore, it was observed in our study that participants mostly did not have an idea about the adequacy of T&CM or conventional medicine therapies alone or in combination.

When the studies conducted on different participant groups were examined, it was seen that 37% of medical students, 50% of nurses, and 27% of physicians used T&CM methods [14,17]. In another study, the rate of using an alternative medicine method in people aged 18 and older in Turkey was determined as 70% [16]. The usability of T&CM was not questioned in our study. Furthermore, it was not expected that secondary school students would have a clear opinion about treatment methods. Therefore, a future study that will include not only students but also their family members may reflect the actual percentages better.

In the study conducted by Cook et al., the negative attitude towards T&CM was found to increase with increasing age in adult patients admitted to an inpatient internal medicine unit [18]. According to Erci, attitudes were found to be significantly negative in males and singles [19]. Featherstone et al. found that positive attitudes in females were significantly higher compared to males [20]. In some studies conducted on patients, the rate of positive attitudes was found out to be high in higher education levels [21,22]. In our study, it was observed that female students had more positive opinions about T&CM compared to male students but they wished to have an occupation in conventional medicine more than males. This shows that female students are more interested in and informed about the health sector. The awareness of T&CM among our participants was low and the most commonly known practices were associated with the topics in the popular culture. These findings might have occurred because students were not educated about evidence-based integrative medicine and it appears that they searched for information about T&CM in association with their areas of interest. Considering the high rate of positive opinions regarding T&CM among students, who did not think of some spiritual approaches such as amulet, prayer, and magic as methods of T&CM; it can be suggested that perceptions of these students were based on science rather than belief. As scientific aspects of T&CM come to the forefront, evidence-based integrative medicine may be taken more seriously.

Secondary school students are under significant pressure because of the upcoming local and national exams. The majority of students in the study believed that T&CM could contribute to their academic achievements. Apitherapy has been shown to improve children's athletic abilities. Aromatherapy and music therapy have calming effects. These are examples of how T&CM can help [23,24]. Basic education can promote the use of T&CM in younger age groups by increasing awareness.

Topics about bodyweight are popular today. In our study, we calculated the BMI values of participating students and found out that the distribution of BMI values in our study was similar to that of the Turkish population. Individuals wishing to lose or gain weight often search for different methods. Therefore, individuals with high or low BMI values may acquire more information about T&CM practices. However, our findings did not support this assumption. Young people may be concerned about body image, but they may not have adequate information about T&CM to consider such practices to obtain benefits for their concerns.

The multifaceted fight against smoking continues. Smokers often feel desperate and seek different

methods. Therefore, smokers can be expected to become more interested in T&CM. However, according to the results of our study, non-smokers think more positively about T&CM. This relationship is promising and may become stronger as health awareness increases.

It is not surprising that people with a chronic disease have expectations about T&CM. However, in our study, the opinions of students with chronic diseases were not different and these students were not more likely to wish to have a T&CM-related occupation. This finding can be associated with the small sample size and inadequate acquisition of information about T&CM.

Today, the health science courses in the curriculum are mandatory in Turkey; comprising 20 hours to be completed in the 9th grade. The main titles of the health science courses in the curriculum are as follows: i) Personal and social health, ii) Adolescence, iii) Nutrition and physical activity, iv) Mental-emotional and social health, v) Harmful habits for health and substance use, vi) Basic first aid knowledge [25]. In the curriculum change put into force by the Ministry of National Education on July 18, 2017; acquisitions named as the 21st-century skills were specified among the basic competencies and skills aimed to be acquired by students. In addition to the curriculum components that are implemented in line with the course contents and requirements; personal, interpersonal, and cognitive skills such as sociocultural awareness and literacy (health literacy, scientific literacy, environmental literacy, financial literacy, technology literacy, information literacy, media literacy, etc.) were included under the title of the 21st-century skills [26]. According to the results of our study, it may be an appropriate revision to include the provision of information about T&CM under the health literacy skill category. Thus, evidence-based information can be provided to students about what T&CM is, what it deals with, and how it deals with. In the study of Gardiner et al., it was shown that a high health literacy level was associated with more T&CM experience in all participant groups [27]. Evidence-based integrative medicine literacy will not only contribute to health and forestall inappropriate use but will also open up new prospects for career planning and planning higher education accordingly. Having acquired the integrative medicine literacy previously, medical students will have the option to ask for education on the evidence-based T&CM, which is not provided by all medical schools currently.

CONCLUSION

It was observed that awareness and attitude levels about T&CM were low in secondary school students. The media is obviously the most powerful tool to gather and acquire information. Students, who have family members having experienced T&CM practices, are more interested in such methods. It is important that health literacy education at schools should include the evidence-based integrative medicine content and that information pollution should be fought against.

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CONFLICT OF INTEREST

There is no conflict of interest.

REFERENCES

1. Ministry of Health. Traditional and Complementary Medicine Practices Regulation. Official Newspaper.
2. Türk E, ed. Türk Eğitim Sistemi ve Ortaöğretim. Ortaöğretim Genel Müdürlüğü; 2015.
3. Ergün A, Erten SF. Öğrencilerde Vücut Kitle İndeksi ve Bel Çevresi Değerlerinin İncelenmesi. Ankara Üniversitesi Tıp Fakültesi Mecmuası. 2004;57(2):1.
4. Şahin S. Geleneksel, tamamlayıcı, alternatif tıp uygulamalarına genel bir bakış. Turkish Journal of Family Practice. 2017;21(4):159-162.

5. Yildirim Y, Parlar S, Eyigor S, Sertoz O, Eyigor C, Fadiloglu C, Uyar M. An analysis of nursing and medical students' attitudes towards and knowledge of complementary and alternative medicine (CAM). Journal of Clinical Nursing. 2010;19(7-8):1157-1166.
6. Ergin A, Hatipoğlu C, İhsan Bozkurt A, Mirza E, Kunak D, Karan C, Özçelik G, Teğin C, Pazır Y, Pırtı İ. Uzmanlık ve tıp öğrencilerinin tamamlayıcı-alternatif tıp hakkındaki bilgi düzeyleri ve tutumları [Knowledge and attitudes of residents and medical students on complementary-alternative medicine]. Pamukkale Tıp Dergisi. 2011;(3):136-143.
7. Akan H, Izbirak G, Kaspar ET, Kaya, ÇA, Aydın S, Demircan N, Bucaktepe PG, Özer C, Şahin HA, Hayran O. Knowledge and attitudes towards complementary and alternative medicine among medical students in Turkey. BMC Complementary and Alternative Medicine. 2012;12.
8. Altan S, Rahman S, Çam S. Tıp Fakültesi Öğrencilerinin Tamamlayıcı ve Alternatif Tıp Yöntemleri ile İlgili Bilgi ve Tutumları. Türkiye Klinikleri Tıp Etiği-Hukuku-Tarihi Dergisi. 2014;22(3):81-88.
9. Sönmez CI, Ayhan Başer D, Küçükdağ HN, Kayar O, Acar İ, Döner Güner P. "Evaluation of Knowledge and Behaviors of Traditional and Complementary Medicine of Medical School Students." *Konuralp Tıp Dergisi*. 2018;10(3):278-281.
10. Sahar T, Sallon S. [Attitudes and exposuer of Israeli medical students to complementary medicine-a survey]. *Harefuah*. 2001;140(10):907-910.
11. Lie DA, Boker J. Comparative survey of Complementary and Alternative Medicine (CAM) attitudes, use, and information-seeking behaviour among medical students, residents & faculty. *BMC Medical Education*. 2006;6.
12. Furnham A, McGill C. Medical students' attitudes about complementary and alternative medicine. *Journal of Alternative and Complementary Medicine*. 2003;9(2):275-284.
13. Yeo ASH, Yeo JCH, Yeo C, Lee CH, Lim LF, Lee TL. Perceptions of complementary and alternative medicine amongst medical students in Singapore - A survey. *Acupuncture in Medicine*. 2005;23(1):19-26.
14. Doğanay S. Tamamlayıcı ve Alternatif Tıp: Türk Sağlık Bilimleri ve Tıp Öğrencileri Arasında Bilgi, Tutum ve Kullanma Durumları. *Journal of Contemporary Medicine*. 2018;8(1):48-54.
15. Ayraler A, Öztürk O, Oruç MA. Knowledge Levels and Attitudes of Medical Faculty Personnel on Traditional and Complementary Medicine. *Education in Medicine Journal*. 2019;11(4):37-45.
16. Bal B. Hemsire ve hekimlerin tamamlayici ve alternatif tedavilere iliskin görüsleri [The thoughts of the physicians and nurses related to the complementary and alternative therapies]. Published online 2009.
17. Uzun Ö, Tan M. Nursing students' opinions and knowledge about complementary and alternative medicine therapies. *Complementary Therapies in Nursing and Midwifery*. 2004;10(4):239-244.
18. Cook TF, Frighetto L, Marra CA, Jewesson PJ. Patterns of use and patients' attitudes toward complementary medications: a survey of adult general medicine patients at a major Canadian teaching hospital. *Can J Clin Pharmacol*. 2002;9(4):183-189.
19. Erci B. Attitudes towards holistic complementary and alternative medicine: A sample of healthy people in Turkey. *Journal of Clinical Nursing*. 2007;16(4):761-768.
20. Featherstone C, Godden D, Gault C, Emslie M, Took-Zozaya M. Prevalence Study of Concurrent Use of Complementary and Alternative Medicine in Patients Attending Primary Care Services in Scotland. *American Journal of Public Health*. 2003;93(7):1080-1082.
21. Buda Laslo, Lampek K, Tahin T. [Correlations of alternative medicine, health status and health care in Hungary]. *Orvosi Hetilap*. 2002;143(17):891-896.
22. Liu EH, Turner LM, Lin SX, Klaus L, Choi LY, Whirtworth J, Ting W, Oz MC. Use of alternative medicine by patients undergoing cardiac surgery. *Journal of Thoracic and Cardiovascular Surgery*. 2000;120(2):335-341.
23. Kumar Gupta R, Stangaciu S. Apitherapy: Holistic healing through the honeybee and bee products in countries with poor healthcare system. In: *Beekeeping for Poverty Alleviation and Livelihood Security: Vol. 1: Technological Aspects of Beekeeping*. Springer Netherlands; 2014:413-446.
24. Akın B, Karaca Saydam B. Algılanan Doğum Ağrısının Azaltılmasına Yönelik Yeni Bir Yaklaşım: Doğum Dansı. *Gümüşhane Üniversitesi Sağlık Bilimleri Dergisi*. 2017;6(3):218-224.
25. *Ortaöğretim Sağlık Bilgisi ve Trafik Kültürü Dersi Öğretim Programı*. T.C. Millî Eğitim Bakanlığı; 2018.
26. *Müfredatta Yenileme ve Değişiklik Çalışmalarımız Üzerine...*; 2017.
27. Gardiner P, Mitchell S, Filippelli AC, Sadikova E, White LF, Paasche-Orlow MK, Jack BW. Health literacy and complementary and alternative medicine use among underserved inpatients in a safety net hospital. *Journal of Health Communication*. 2013;18(SUPPL. 1):290-297.

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ORIGINAL RESEARCH

The Use of Natural Preservative Propolis and *Hypericum perforatum* Oil in Herbal Cream Production

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Abstract

Objective: Consumers' preference for products produced with natural additives has accelerated the search for natural substances that are alternative to synthetic materials in cosmetics and food production. The aim of the study is to obtain a herbal cream by using the natural preservative effect of propolis and the moisturizing effect of St. John's wort fixed oil of *Hypericum perforatum* plant which grows naturally in our country.

Material-Method: The chemical content of the obtained propolis ethanolic extract was determined by Liquid Chromatography Mass Spectrometry (LC-MS/MS) analysis. *Hypericum perforatum* fixed oil was obtained by maceration and the chemical content of the oil was determined by gas chromatography mass spectrometry (GC-MS) analysis. Herbal cream was prepared using PEG400 to facilitate dispersion of *Hypericum perforatum* oil and propolis extract obtained in water-based cream formulations and to provide a creamy consistency. Microbiological stability tests were carried out with reference to ISO21149, ISO16212, ISO18416, ISO22717 and ISO21150 standards and ISO11930: 2012 standard for challenge test (preservative efficacy tests).

Results: The total phenolic content of propolis ethanol extract was determined as 66.096 ± 1.546 mg gallic acid equivalent (GAE) / mL sample, dry weight and flavonoid content as 13.375 ± 0.185 quercetin equivalent (QE) / mL sample. An extract rich in phenolic components such as quercetin, p-coumaric acid, ferulic acid, trans-cinnamic acid, benzoic acid was obtained. Component analysis showed that propolis ethanolic extract could show preservative efficiency. The presence in the GC-MS analysis of *Hypericum perforatum* oil that it contains fatty acids widely used in the cosmetic and pharmaceutical industry clearly demonstrated that the oil can be used safely in cream formulations.

Conclusion: The test results of the creams were prepared using *Hypericum perforatum* and propolis clearly revealed that the obtained propolis extract provided protective efficacy. The thickener property of PEG400, which is used to ensure homogeneous distribution, reduced the need for an extra thickener additive.

Keywords: Natural Preservative, Herbal Cream, Propolis, *Hypericum perforatum* L., St. John's Wort

INTRODUCTION

Natural products are widely used in the treatment of diseases and in the food and cosmetic industries from past to present. With the discovery of the side effects of synthetic products and reporting the health hazards, the demand for natural products is increasing day by day. This has led to a rapid increase in search for natural products that can replace synthetic cosmetic additives. These natural products include widely used bee products and herbal products. In the present study, the natural preservative effect of propolis and the moisturizing and the wound healing effect of *Hypericum perforatum* oil were combined.

It is known that the therapeutic properties of

propolis have been used since ancient times. Like other bee products, propolis is widely used for the prevention and treatment of various diseases and is known to have rich biological activity. Propolis is also used as an alternative to synthetic preservatives in the cosmetics and food industry with its antibacterial, antifungal and antioxidant qualities [1]. The biological activities of the components in the propolis chemical composition have made propolis an important bee product. There are many studies showing that propolis has antimicrobial, antibacterial, antiviral, antifungal, antioxidant, anti-inflammatory, wound healing, tissue regenerating and anesthetic effects [2-5]. Studies on propolis have shown that this substance also contains vitamins, minerals and elements that are very important and essential for human health. Propolis also has anti-cancer, liver preservative, local anesthetic and antimutagenic activities [6,7]. Its antibacterial, antifungal and antioxidant qualities show that propolis can be an alternative additive to chemical preservatives [8].

Propolis contains 50% resin and herbal balm, 30% beeswax, 10% essential and aromatic oils, 5% pollen and 5% various organic components. Wax and organic components are usually removed by extraction. More than 300 ingredients have been identified in unprocessed propolis, including polyphenols, terpenoids, steroids, sugar and amino acids [9,10]. Propolis is beneficial for health since it contains high amounts of chemicals such as epicatechin, naringenin, catechin, genistein, kaempferol, chlorogenic acid, quercetin, apigenine, o-coumaric acid, protocatechuic acid, syringic acid, p-coumaric acid, gallic acid, ferulic acid, caffeic acid [5,10,11]. Hexane and ethanol extracts of propolis have been reported to show high antimicrobial activity against the tested microorganisms, as they contain the main phenolic components of pinbanxin and naringenin [12]. All these studies clearly reveal the suitability of propolis as a natural preservative.

Since propolis shows little solubility in water and hydrocarbon solvents and quite high in alcohols, its commercially available form is mostly 96% ethanol extract [7]. Usually it contains waxes, resins, water, inorganic ingredients, phenols and essential acids. The main biologically active ingredients of propolis are not very well soluble in water, oil and other solvents commonly used in the pharmaceutical industry. The active ingredients of propolis are easily soluble in ethanol, but ethanolic extracts cannot be used in the treatment of some diseases encountered in ophthalmology and pediatrics. Therefore, there are many studies investigating the chemical composition, radical scavenger and antimicrobial activities of propolis extracts, in which different solvents are used as extraction solvents. It is possible to obtain propolis extract with chemical content similar to ethanolic extract in extractions performed by adding additives that increase polarity such as vegetable glucose, sorbitol, glycerol and polyethylene glycol to water [13]. Comparing the total phenolic compound amount of polyethylene glycol 400 (PEG400) and water mixture or PEG400 extracts with olive oil-water mixture extract and ethanol extract, it was observed that the antimicrobial activity was equal or better than ethanolic extract. It was observed that the products of extractions performed in pure water or oil at room temperature did not show enough antimicrobial activity since they contain 5-10 times less amount of phenolic compounds [14]. In the study, PEG400 was used to increase the solubility of propolis in water-based cream formulations and to provide a homogeneous distribution. PEG400 is known to be a non-irritating hydrophilic substance that does not easily penetrate the skin. Since they are water soluble, they can be easily removed from the skin by washing with water. Aqueous PEG solutions can be used as suspending agents in topical ointments or to adjust the viscosity and consistency of other suspending agents [15]. For this reason, the use of PEG400 is suitable in the food and cosmetic industry to increase the solubility of propolis in water-based products.

Turkey is an agricultural country with a rich flora of medicinal and aromatic plants. *Hypericum perforatum* plant, which has been used in the treatment of many diseases since ancient times, is

a widely used plant to heal burns and wounds [16,17]. *Hypericum* species contain a large number of secondary metabolites, including naphrodiantrons, flurogonol derivatives, flavonoids, organic acids, essential oils, amino acids, xanthones, tannins, proxyanidines and other water-soluble components [18,19]. Although *Hypericum perforatum* has many bioactive compounds in its structure, the most active in terms of pharmacological properties are hyperforin, a phloroglucinol derivative, and hypericin, a naphthodianthron derivative [20]. Hypericin, a colored pigment that gives oil its red color, is the most important component [21]. It has been stated that oil prepared by maceration from *Hypericum perforatum* flowers reduces inflammation in wound healing, increases collagen synthesis in fibroblasts, positively affects epithelial regeneration, and has antibacterial and antiviral effects [16,22-25]. In studies where the extract obtained from *Hypericum perforatum* was applied topically and its effectiveness in wound healing was examined, it was found that the plant was quite effective in wound healing [26,27].

The use of *Hypericum perforatum* oil in wounds, burns, crushes and ulcers, pain relief and diuretic effects are supported by pharmacological research [28-32]. It has been reported that the ointment containing *Hypericum perforatum* oil shortens the burn healing time and shows antiseptic effect.

First-degree burns treated with the ointment healed within 48 hours, while second- and third-degree burns healed rapidly without scarring on the skin [26].

Propolis extract, which can replace synthetic substances used as preservatives in cream production, was used in the study. Propolis were obtained from beekeepers in three different regions in Duzce region of Turkey. The use of ethanolic extract was preferred because it is known that the active ingredients of propolis are easily soluble in ethanol. Since ethanolic extract was not dispersed homogeneously in water-based cream formulations, homogeneous distribution was achieved by using PEG400. PEG400 is known to be non-toxic. In addition to providing the distribution of oil-based additives in the water-based cream formulation, PEG400 also acted as a thickener in the formulation due to its thickener effect.

MATERIALS AND METHODS

Obtaining *Hypericum perforatum* oil (Maceration)

Three hundred grams of commercial olive oil was added over 100 grams of *Hypericum perforatum*. It was kept in a jar for 5 days with its lid open to see the sunlight and 45 days with its lid closed. In this process, the mixture was stirred in the jar every other day. After 50 days of maceration, the mixture was manually pressed through a cotton swab and dried over anhydrous sodium sulfate[33].

Hypericum perforatum oil content analysis

The maceration product was analyzed by GC/MS. The study was carried out on an Agilent 7890A GC System coupled to an Agilent 5975C inert MSD with Triple Axis Detector. Agilent HP5-MS (30 m × 0.25 mm × 0.25 µm) column was used as GC column. The oven temperature was held at 80 ^{o}C for 0 min., then ramped at 10 ^{o}C/min. to 130 ^{o}C for 1 min., then ramped at 10 ^{o}C/min. to 170 ^{o}C and held at this temperature for 0 min., then ramped 5 ^{o}C/min. to 215 ^{o}C for 12 min., then ramped 40 ^{o}C/min at 230 ^{o}C and held at this temperature for 3 min. The total run time was 31.87 min. The injector temperature was fixed at 280 ^{o}C and splitless mode was used with helium carrier gas. The ion source was electron ionization and the MS source temperature was set at 230 ^{o}C. The injection volume was 1.0 µL.

Propolis extract content analysis

The mass-spectrometer measurements were performed on a hybrid triple quadrupole/linear ion trap mass spectrometer API 4000 QTRAP (Applied Biosystems, Darmstadt, Germany) with electrospray ionization (ESI). LC separations were performed in a C18 analytical column (Gemini® 5 µm particle size, 110 Å pore size, 50 mm x 2 mm, fully porous organo-silica LC Column) using a mobile phase consisting of 0.1% aqueous formic acid solution (phase A), and Methanol (phase B) at a flow rate of 0.3 mL min−1.The gradient profile started at 15% of B until 1.5 min; then it

went to 55% B in 0.1 min and kept until 3 min; then it went to 90% B in 0.1 min and kept until 4 min. Finally it was back to 15% B in 0.1 min.The run time for each injection was *5.5* min, the temperature of the column was 40 ◦C and the injection volume was10 µL. The mass-spectrometer was working with an electro spray ion source (ESI) in positive mode under the selected ion monitoring (SIM) or Selected Reaction Monitoring (SRM) condition including 0,70 amu width (the nebulizer pressure was 55psi, the drying gas (He) temperature was 40 ◦C, the drying gas flow was 1 mL/min and the skimmer voltage were among *20-80* V. Data acquisition was carried out with Workstation Method Builder) shown in Table 1. The ionization source parameters were: source temperature *50 ◦C;* curtain gas (nitrogen) 55 psi, ion spray voltage 5000V on needle, 600V on shield, 70V on capillary and 1800V on detector ; and GAS 1 and GAS 2 (both of them nitrogen) were set to 55 psi.

Herbal cream preparation

PEG400 was added to 115 mL of water, stirring slowly and thoroughly on a magnetic stirrer until thickening was achieved. After the desired consistency was achieved, a herbal cream was obtained by adding all additives in the amounts specified in the table 1.

Table 1. Additives in cream formulation

Additive, INCI name	**Amount***
Aqua	115 mL
Sodium Polyacrylate (and) Dicaprylyl Carbonate (and) Polyglyceryl-3 Caprate	2.5 g
PEG400	15 g
Propolis Extract, in solution form	1.5 g
Coco-Caprylate	10.5 g
Hypericum perforatum Oil	15 g
Perfume	3 g
Sodium Stearoyl Glutamate	0.45 g

* Amounts for ~150 g cream.

Microbiological analysis test

ISO21149[34], ISO16212[35], ISO18416[36], ISO22717[37] and ISO21150[38] standards were taken as reference for microbiological analysis aimed at determining the presence of microorganism in the cream. In the analysis, *Staphylococcus aureus* (ATCC 6538), *Pseudomonas aeruginosa* (ATCC 9027), *Escherichia coli* (ATCC 8739), *Candida albicans* (ATCC 10231), aerobic mesophilic microorganism and mold-yeast microorganisms were investigated. Briefly; In the determination of aerobic mesophilic microorganism and mold-yeast; 1 mL/gr sample was placed in 9 mL neutralizer and homogenized. 0.1 mL was taken from this mixture and transferred to Tryptic Soy Agar (TSA) medium containing Polysorbate 80 and Lecithin for aerophilic mesophilic determination and Saboraud 4% Dextrose Agar (SDA) for mold and yeast determination. Bacteria were incubated at 32.5 ± 2.5 °C for 48-72 hours and mold-yeast for 3-5 days at 22.5 ± 2.5 °C and colony counts were made at the end of the period. In the analysis of pathogen strains, in addition to those mentioned above, the neutralized sample mixture was enriched by incubating at 32.5 °C for 24 hours. At the end of the period, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Escherichia coli* were incubated at TSA, *Candida albicans* SDA for 48 hours at 32.5 °C. Since the pathogen microorganisms should not be present in 1g or 1 mL of the product, it was checked for its existence.

Antimicrobial efficacy test

The antimicrobial efficacy test, also known as the challenge test, determines the effectiveness of the preservative by calculating the logarithm of the number of viable microorganisms remaining on the product on days 7, 14 and 28 after artificial contamination on the product. This analysis of propolis extracts used as a preservative in the cream was made with reference to the ISO11930:2012[39] standard. Microorganisms used to create contamination were *Pseudomonas aeruginosa* (ATCC 9027)*, Staphylococcus aureus* (ATCC 6538), *Escherichia coli* (ATCC 8739), *Candida albicans* (ATCC 10231) and *Aspergillus brasiliensis* (ATCC 15404). Briefly; Working cultures were created by making subcultures from stock cultures. Microorganisms were suspended in diluent and calibrated to 10^6-10^7cfu/mL. Ten fold dilutions were made and bacteria were incubated

at TSA, yeast SDA and mold PDA for 32.5±2.5 C for 24-48 hours. 20 grams of propolis cream sample was placed in sterile containers, and 0.2 mL of different microorganisms were added to each container to ensure homogeneity. The inoculated containers were incubated at 22.5 ± 2.5 °C in the dark for 28 days. For the 7th day, 1 g of cream sample was taken from the containers and homogenized in 9 mL of neutralizer. The mixture, which was kept at room temperature for 30±15 minutes, was diluted to correspond to 1/10 and 1/100. This dilution was transferred to the SDA medium for TSA yeasts and the PDA for molds. The colonies in the petri dishes incubated under appropriate conditions were counted and logarithmic evaluation was done and according to the ISO11930: 2012 standard Criterion A was interpreted. The same procedures were carried out on the 14th and 28th days.

RESULTS

Hypericum perforatum oil analysis

It was determined that the oil of *Hypericum perforatum*, which was obtained from Duzce region of Turkey, contained fatty acids widely used in the cosmetics and pharmaceutical industry in the GC-MS analysis (Table2). Palmitic acid derivatives found in *Hypericum perforatum* masere oil can prevent the formation of wrinkles and delay skin aging. They also play a role in increasing water retention of the skin and moisturizing the skin. Linoleic acid, oleic acid, elaidic acid molecules are used in the cosmetic industry as solubilizer and plasticizer. Stearic acids are widely used in cosmetic formulations such as creams, lotions, eye makeup products, shampoos, and hair care auxiliary products [40,41]. Oleic acid derivatives are used as emulsifying and dissolving agents in addition to being used as excipients in pharmaceuticals and cosmetics [42]. The use of *Hypericum perforatum* oil in cream formulations can provide a supportive role in reducing scars and acne blemishes as well as moisturizing the skin. **Propolis extract analysis**

Many studies have been conducted to evaluate the chemical composition and potential pharmacological activities of propolis produced by different bee species. Various solvents were used in these studies. Both the chemical composition and biological properties of propolis extracts depend greatly on the type of solvents used for extraction.

Table 2. GC-MS library scan results

Compound Name	RT (min)	% of Total
Hexadecanoicacid, methyl ester (Methylpalmitate)	13.47	4.7
Linoleicacidmethyl ester	16.27	40.8
(E)-9-Octadecenoic acidmethyl ester (Elaidicacidmethyl ester)	16.37	50.7
Octadecanoicacidmethyl ester (Stearicacid, methyl ester)	16.79	3.0
cis-11-Eicosenoic acidmethyl ester	20.57	1.0

The most commonly used solvent for the extraction of propolis is ethanol[43]. Therefore, the chemical content of the ethanolic extract in Duzce region of Turkey propolis used in the study was determined by LC-MS/MS analysis. The total phenolic content of the extract was determined as 66.096 ± 1.546 mg gallic acid equivalent (GAE) / mL sample, dry weight and flavonoid content as 13.375 ± 0.185 quercetin equivalent (QE) / mL sample. In addition to the total flavonoid content, it was determined that the caffeic acid compound with high free radical activity was found in high amounts in the propolis ethanol extract. An extract rich in phenolic components such as quercetin, p-coumaric acid, ferulic acid, trans-cinnamic acid, benzoic acid responsible for biological activity was obtained. When the analysis results were evaluated, it was clearly observed that the chemical content of the ethanolic extract would be suitable for use as a natural preservative (Table3).

Microbiological analysis test

As a result of the analysis, the total number of aerobic mesophilic microorganisms and mold-yeast in all samples was found as <10 cfu/g. Based on this analysis, it was found that the cream sample containing propolis and *Hypericum perforatum* oil were found to comply with the"Guidelines on Microbiological Control of Cosmetic Products" (Table 4).

Antimicrobial efficacy test

Analysis of the efficacy of the preservative by creating artificial contamination corresponds to Criterion A in the ISO11930: 2012 standard and according to the results of the analysis, it has been determined that the preservative is protected against microbial reproduction. The reduction values equation (Rx = logN0 -logNx) was used for logarithmic calculations (Table 5).

Table 3. Chemicalcomposition of propolisextract

Chemicalcompounds	Mean ± SD (mg/g)
Pinostrobin	4620.00± 5.46
Kaempherol	0.00
o-coumaric	58.632 ± 4.92
m-coumaric	48.30 ± 3.86
FerulicAcid	0.00
Clorogenic	3.70 ± 1.65
SinapicAcid	20.80 ± 2.78
CaféicAcid	56.90 ± 4.68
ProtocatheuicAcid	0.00
Daidzein	106.10 ± 1.43
RosemarinicAcid	417.23 ± 9.30
SyringicAcid	269.33 ± 5.60
QuercetinHyrate	7.13 ± 8.74
Trans-Chalcone	6.21± 2.69
CAPE (caffeicacidphenethyl ester)	90.30 ± 3.45
Hesperidin	111.33 ± 0.00
(±)-Catechin	57.57 ± 7.22
Trans-3-Hydroxy-Cinamic Acid	28.63 ± 2.87
GallicAcid	235.00 ± 0.00
(±) Naringenin	51.03 ± 8.16
p-CoumaricAcid	13.60 ± 7.09
3-4 DimethoxycinnamicAcid	22.57 ± 8.10
Apigenin	91.67 ± 5.02
BenzoicAcid	28.52 ± 3.18
Trans-CinnamicAcid	6.88 ± 4.92
EllagicAcid	77.77 ± 6.00
Emodin	147.17 ± 7.51
Quercetin	777.67 ± 1.77

DISCUSSION

Preservatives are substances that prevent deterioration of cosmetics and care products and microorganism contamination [44], and preservative efficacy tests that measure antimicrobial activity in the finished state of the product are performed[39]. The use of preservatives is inevitable in order to prevent corruption in cream formulations and to keep the shelf life long. Since the side effects of synthetic additives are reported, it is important to search for substances isolated from natural products as preservatives. It is known that bee product propolis has a natural preservative effect that can replace the preservative additives used in the cosmetic industry. Therefore, in the study, it was investigated whether the contents of propolis samples are suitable for use as a preservative. The chemical content of the ethanol extract of propolis samples collected as a result of beekeeping activities in Duzce region of Turkey were determined. The rich content of phenolic compounds known to be responsible for the preservative effect of propolis strengthened the idea that it could be suitable for use as a preservative in cream formulations. In addition, the moisturizing oil used in cream formulations was obtained from the *Hypericum perforatum* plant, which grows naturally in Duzce region of Turkey. In the content analysis of the oil used, it was determined that fatty acids, which are frequently used as moisturizing, plasticizing and dissolving agents in the cosmetic industry, were present. Since the use of *Hypericum perforatum* oil in the treatment of wounds and burns in traditional treatments has been known from past to present, it was thought that it could contribute to the healing of wounds and acne scars as well as its moisturizing effect. Preservative effectiveness tests of the prepared herbal cream were carried out. The most used preservative in cosmetics is paraben derivatives. In the preservative activity study with paraben derivatives; when two different paraben derivatives are used in the same combination, the log cfu/mL of most bacteria is <1 on the fourteenth day, <1 was found on the twenty-first day whensoever used alone. Log cfu/mL of yeast and mold; as using a single derivative, it was <1 on the twenty-first day, while in the use of two paraben derivatives, <1 was found mostly on the fourteenth day. In the same study, the preservative activity of isothiazolinones

derivatives was investigated, it had an effect on *Staphylococcus aureus* and *Escherichia coli* on the fourteenth day (log cfu/mL <1), and *Pseudomonas aeruginosa* had an effect on the twenty-first day (log cfu/mL <1). On the other hand, it was not effective on yeast and mold species in the twenty-eight day test[45].

Table 4. Microbiological analysis test results of cream sample

Microorganisms	Unit	Result	Standart No	Limit values
Total aerobic mesophilic microorganism	cfu/g	<10	ISO21149	<100
*Staphylococcus aureus*ATCC 6538	cfu/g	Negative	ISO21149	Negative
Pseudomonas aeruginosa ATCC 9027	cfu/g	Negative	ISO22717	Negative
Escherichia coli ATCC 8739	cfu/g	Negative	ISO21150	Negative
*Candida albicans*ATCC 10231	cfu/g	Negative	ISO18416	Negative
Mold and yeast	cfu/g	<10	ISO16212	<100

Sample of propolis used in our study reduced log cfu/mL values of all microorganisms below <1 on the fourteenth day. Our data show that propolis can be as effective as paraben derivatives and can be better than isothiazolinones derivatives. The results of our analysis have shown that propolis can be used as a preservative thanks to its antimicrobial activity and naturalness.

Table 5. Antimicrobial efficacy data of the cream sample containing propolis ethanol extract

Microorganisms	0 hours		7th day			14th day	28th day
	cfu/g	log cfu/g	cfu/g	log cfu/g	Log reduction	cfu/g	cfu/g
Staphylococcus aureus (ATCC 6538)	2,60E+07	7,41	3,00E+03	3,5	3,94	<10	<10
Pseudomonas aeruginosa (ATCC 9027)	2,50E+07	7,40	2,00E+03	3,3	4,10	<10	<10
Escherichia coli (ATCC 8739)	2,40E+07	7,38	4,00E+03	3,6	3,78	<10	<10
Candida albicans (ATCC 10231)	1,60E+06	6,20	2,00E+03	3,3	2,90	<10	<10
Aspergillus brasiliensis (ATCC 15404)	2,00E+05	5,30	2,00E+02	2,3	3,00	<10	<10

CONCLUSION

In this study, the total phenolic content of Propolis ethanol extract was determined as 66.096 ± 1.546 mg gallic acid equivalent (GAE)/mL sample, dry weight and flavonoid content as 13.375 ± 0.185 quercetin equivalent (QE)/mL sample. An extract rich in phenolic components such as quercetin, p-coumaric acid, ferulic acid, trans-cinnamic acid, benzoic acid was obtained. Component analysis clearly demonstrated that propolis ethanolic extract could show protective activity. The presence in the GC-MS analysis of *Hypericum perforatum* oil, which contains fatty acids widely used in the cosmetics and pharmaceutical industries, showed that the oil can be used safely in cream formulations. The results of microbiological analysis and antimicrobial efficacy tests of creams prepared using *Hypericum perforatum* and propolis clearly revealed that the obtained propolis extract provided protective efficacy. Thickener property of PEG400, used to provide homogeneous distribution, reduced the need for extra thickener additives.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare that are relevant to the content of this article.

REFERENCES

1. Silici S, Kutluca S. Chemical composition and antibacterial activity of propolis collected by three different races of honeybees in the same region. *Journal of ethnopharmacology.* 2005;99(1):69-73.
2. Pascual C, Gonzalez R, Torricella R. Scavenging action of propolis extract against oxygen radicals. *Journal of Ethnopharmacology.* 1994;41(1-2):9-13.
3. Scheller S, Wilczok T, Imielski S, Krol W, Gabrys J, Shani J. Free radical scavenging by ethanol extract of propolis. *International Journal of Radiation Biology.* 1990;57(3):461-465.
4. Kusano Bucalen Ferrari C, Percário S, Carlos Costa Baptista Silva J, Aparecida Ferraz da Silva Torres E. An apple plus a Brazil nut a day keeps the doctors away: antioxidant capacity of foods and their health benefits. *Current pharmaceutical design.* 2016;22(2):189-195.
5. Ozdal T, Ceylan FD, Eroglu N, Kaplan M, Olgun EO, Capanoglu E. Investigation of antioxidant capacity, bioaccessibility and LC-MS/MS phenolic profile of Turkish propolis. *Food Research International.* 2019;122:528-536.
6. Scheller S, Krol W, Owczarek S, Swiacik J, Gabrys J, Shani J. Antitumoral property of ethanolic extract of propolis in mice-bearing Ehrlich carcinoma, as compared to bleomycin. *Zeitschrift für Naturforschung C.* 1989;44(11-12):1063-1065.
7. Nagai T, Inoue R, Inoue H, Suzuki N. Preparation and antioxidant properties of water extract of propolis. *Food chemistry.* 2003;80(1):29-33.
8. Atik A, Gümüş T. Propolisin gıda endüstrisinde kullanım olanakları. *Akademik Gıda.* 2017;15(1):60-65.
9. Nakajima Y, Shimazawa M, Mishima S, Hara H. Water extract of propolis and its main constituents, caffeoylquinic acid derivatives, exert neuroprotective effects via antioxidant actions. *Life sciences.* 2007;80(4):370-377.
10. Marcucci M. Chemical composition, plant origin and biological activity of Brazilian propolis. *Current Topics Phytochem.* 1999;2:115-123.
11. Burdock G. Review of the biological properties and toxicity of bee propolis (propolis). *Food and Chemical toxicology.* 1998;36(4):347-363.
12. Arslan S, Silici S, Percin D, Koç AN, Er Ö. Antimicrobial activity of poplar propolis on mutans streptococci and caries development in rats. *Turkish Journal of Biology.* 2012;36(1):65-73.
13. Bakkaloğlu Z, Arıcı MJAFJAG. Farklı Çözücülerle Propolis Ekstraksiyonunun Toplam Fenolik İçeriği, Antioksidan Kapasite ve Antimikrobiyal Aktivite Üzerine Etkileri. 2019;17(4).
14. Kubiliene L, Laugaliene V, Pavilonis A, Maruska A, Majiene D, Barcauskaite K, Kubilius R, Kasparaviciene G, Savickas AJBc, medicine a. Alternative preparation of propolis extracts: comparison of their composition and biological activities. 2015;15(1):156.
15. Raymond C. Rowe PJS, Siân C. Owen. Handbook of pharmaceutical excipients *Pharmaceutical Press London.* 2006;1.
16. Sönmez M, Seval M. Fitoterapik Yara Bakımında Sarı Kantaron Yağının Etkisi. *Journal Academic Studies on Natural.* 2019:201.
17. Altan A, Damlar İ, Aras M, Alpaslan CJAKTD. Sarı Kantaronun (*Hypericum Perforatum*) Yara İyileşmesi Üzerine Etkisi. 2015;24(4):578-591.
18. Greeson JM, Sanford B, Monti DAJP. St. John's wort (*Hypericum perforatum)*: a review of the current pharmacological, toxicological, and clinical literature. 2001;153(4):402-414.
19. Tanaka N, Takaishi YJP. Xanthones from Hypericum chinense. 2006;67(19):2146-2151.
20. Patocka JJJoAB. The chemistry, pharmacology, and toxicology of the biologically active constituents of the herb *Hypericum perforatum* L. 2003;1(2):61-70.
21. Topal A, Çelebi F. Hiperisin'in İzole Edilmiş Şıçan Midesinde Mide Asit Sekresyonu Üzerine Etkisi. *Atatürk Üniversitesi Veteriner Bilimleri Dergisi.* 2011;6(3):201-208.
22. Lavagna SM, Secci D, Chimenti P, Bonsignore L, Ottaviani A, Bizzarri BJIF. Efficacy of Hypericum and Calendula oils in the epithelial reconstruction of surgical wounds in childbirth with caesarean section. 2001;56(5-7):451-453.
23. Öztürk N, Korkmaz S, Öztürk YJJoe. Wound-healing activity of St. John's Wort (*Hypericum perforatum* L.) on chicken embryonic fibroblasts. 2007;111(1):33-39.
24. Süntar IP, Akkol EK, Yılmazer D, Baykal T, Kırmızıbekmez H, Alper M, Yeşilada EJJoE. Investigations on the in vivo wound healing potential of Hypericum perforatum L. 2010;127(2):468-477.
25. Medina MA, Martínez-Poveda B, Amores-Sánchez MI, Quesada ARJLs. Hyperforin: more than an antidepressant

bioactive compound? 2006;79(2):105-111.
26. Saddiqe Z, Naeem I, Maimoona AJJoe. A review of the antibacterial activity of Hypericum perforatum L. 2010;131(3):511-521.
27. Süntar I, Akkol EK, Keleş H, Oktem A, Başer KHC, Yeşilada EJJoe. A novel wound healing ointment: a formulation of Hypericum perforatum oil and sage and oregano essential oils based on traditional Turkish knowledge. 2011;134(1):89-96.
28. Boon H, Smith M. *The botanical pharmacy: the pharmacology of 47 common herbs.* Quarry press; 1999.
29. Fernie WT. *Herbal simples approved for modern uses of cure.* Vol 19352: Lulu. com; 2006.
30. Kıyan S, Uyanikgil Y, Altunci YA, Cavusoglu T, Cetin Uyanikgil EO, Karabey FJTJoT, Surgery E. Investigation of acute effects of *Hypericum perforatum* (St. John's Wort-Kantaron) treatment in experimental thermal burns and comparison with silver sulfadiazine treatment. 2015;21(5):323-336.
31. Pekşen M, Kurt A, Soylu S, Tuzcu M, Bostancı M, Mollaoğlu M, Akabay U, Şen MJB, Sciences C. Comparison of the healing effects of silver sulfadiazine cream 1% and the essential oil of *Hypericum perforatum* on scald burn wound in a rat model. 2014;3(1):1-8.
32. Yücel A, Kan Y, Yesilada E, Akın OJJoe. Effect of St. John's wort (*Hypericum perforatum*) oily extract for the care and treatment of pressure sores; a case report. 2017;196:236-241.
33. Achat S, Tomao V, Madani K, Chibane M, Elmaataoui M, Dangles O, Chemat F. Direct enrichment of olive oil in oleuropein by ultrasound-assisted maceration at laboratory and pilot plant scale. *Ultrasonics Sonochemistry.* 2012;19(4):777-786.
34. ISO21149. Cosmetics—Microbiology—Enumeration and Detection of Aerobic Mesophilic Bacteria.
35. ISO16212. Cosmetics—Microbiology—Enumeration of Yeast and Mould.
36. ISO18416. Cosmetics—Microbiology—Detection of Candida albicans.
37. ISO22717. Cosmetics—Microbiology—Detection of Pseudomonas aeruginosa.
38. ISO21150. Cosmetics—Microbiology— Detection of Escherichia coli.
39. ISO11930:2012. Cosmetics—Microbiology—Evaluation of the Antimicrobial Protection of a Cosmetic Product.
40. Zhang C, Guo S, Huang CJAJoAC. Determination of compositions in cosmetics by multiple-instrument. 2011;2(8):857.
41. Kalustian PJJotAOCS. Pharmaceutical and cosmetic uses of palm and lauric products. 1985;62(2):431-433.
42. Chen X, Lee K-M, Yoon J-YJBotKCS. A polydiacetylenes-based sensor for discriminating oleic acid from stearic acid and elaidic acid. 2011;32(10):3775-3778.
43. Sun C, Wu Z, Wang Z, Zhang HJE-BC, Medicine A. Effect of ethanol/water solvents on phenolic profiles and antioxidant properties of Beijing propolis extracts. 2015;2015.
44. Majeed M, Paliwal P, Mohamed A. New Era in Preservatives–SabiLize®-New. *Cosmetic Science Technology.* 2012.
45. Smaoui S, Hlima HBJBs. Effects of parabens and isothiazolinone on the microbiological quality of baby shampoo: The challenge test. 2012;17(3):135-142.

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REVIEW

Overview of Apitherapy Products: Anti-Cancer Effects of Bee Venom Used In Apitherapy

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Abstract
While Brazil and the United States of America are in the first place in world Apitherapy research, our country is in the fifth place after Japan and China. While the studies on apitherapy are continuing rapidly in the world, it has started to become widespread in our country especially in 2014 with the regulation of traditional and complementary medicine practices, and Apitherapy units and application centers have started to be established. Apitherapy is the use of bee products to protect and improve health, to strengthen the immune system and to complement the treatment process of some diseases. While bee products such as honey, propolis, bee pollen have been known and used for a long time, studies on apilarnil, royal jelly and bee venom have started to increase in recent years. These products have been used both as foodstuffs and as a source of healing from wound healing to anticancer effect for many years due to their rich content. With scientific studies, the interest in apitherapy products has increased even more.
Cancer is known as the leading cause of death in our country and all over the world. Side effects, costs, etc. Such adverse conditions have led researchers to research natural treatment methods. These natural treatments are used to increase the effectiveness of existing traditional treatments. In this review, literature information about Apitherapy, which is one of the traditional and complementary medicine applications, chemical content and physiological effects of bee products, is given and the therapeutic effect of bee venom on cancer is mentioned. Studies on the anticancer activity of bee venom in almost all types of cancer have been conducted and promising results have been obtained. This situation indicates that this apitherapeutic product will take place as a supplement in cancer treatment in the near future.
Keywords: Apitherapy, Bee Venom, Honey, Propolis, Neoplasms, Traditional Medicine

INTRODUCTION

What is apitherapy?

Apitherapy is one of the 15 therapies defined according to the Traditional and Complementary Medicine Practices Regulation that entered into force in the Official Gazette No. 29158 dated October 27, 2014. Other therapies that are legally permitted to be used; Acupuncture, Phytotherapy, Hypnosis, Leech Application, Homeopathy, Chiropractic, Cup Application (Cupping Application=Cupping), Larva Application, Mesotherapy, Prolotherapy, Osteopathy, Ozone Application, Reflexology, and Music Therapy.

It is the way of using bee and bee products (honey, propolis, bee pollen, bee bread, royal jelly, apilarnil, bee venom) as support and complementary application method in the treatment of some diseases in order to protect and improve health and strengthen the immune system[1].

Apitherapy applications are carried out by a certified Apitherapy Specialist in an Apitherapy Unit or Apitherapy Application Center approved by the Ministry of Health. It should be determined whether there is an allergy before the application. It should not be applied to those with allergies and hypersensitivity. For the application of bee venom to the skin, live bee stings or injections containing bee venom containing extracts or ointments

containing bee venom are used. Chemical analyzes should be made for oral bee products (honey, propolis, royal jelly, pollen, apilarnil, etc.) and these products should be in accordance with the Turkish Food Codex Regulation and the Turkish Standards Institute instructions, and their quality control should be done.

What are bee products?

Bee products; Honey, propolis, bee pollen, bee bread, royal jelly, apilarnil, and bee venom are examined under seven headings.

While honey, propolis, bee pollen, and bee bread are products created by adding their own secretions to plant products (such as pollen, resinous substances, nectar) collected by bees from plants, royal jelly, apilarnil, and bee venom are products secreted directly by the bee or produced from its own body [2].

Honey

Honey, which contains about 200 types of components in its structure, is defined according to the Turkish Standards Institute 3036 Honey Standard and the Codex as a sweet product that results from the collection of nectar secreted from the flowers or other living parts of plants by honey bees (Apis mellifera), changing their composition in their bodies and maturing after being stored in the honeycomb cells [3-5]. Honey, which has rich content, varies according to the vegetation and honey source, but it has an average of 80% carbohydrates (monosaccharides (55-85%), disaccharides (2-15%), and trisaccharides (1-7%), 0.5% proteic substances, 0.1-0.2% polyphenolic compounds, 0.01% lipids, very small amounts of vitamins and minerals [6-10]. In addition, about 500 different volatile compounds in honey [11]. Detailed information about the content is given in Table 1.

It is known not only as food with delicious taste and nutritious qualities but also as a medicine that has been used in traditional medicine for centuries to protect health and treat some diseases [12]. As the most interesting product among apitherapy products, it has been known for many years that honey has a protective effect on the stomach against acute or chronic stomach injuries, has significant effects on the digestive system with its prebiotic properties, has a high healing potential in a wound and burn treatment, and its strong antimicrobial property is also supported by clinical studies [13-15]. The beneficial effects of honey are mainly due to its polyphenolic compound content [16] and have a high antioxidant capacity due to these compounds [17,18]. So much so that honey is considered to have higher antioxidant activity than antioxidant vitamins such as Vitamins C and E [19]. Thanks to this feature, it can reduce oxidative stress by eliminating the harmful effects of oxidizing molecules such as free radicals in the body [20]. It accelerates wound healing by providing tissue regeneration [21]. It has started to attract attention in recent years with its antiviral, antifungal, anti-inflammatory, antiallergic, anticancer, hepatoprotective, antiatherogenic, antinociceptive, and immunostimulant effects [22-24] and has been included in many studies. Compared to sweeteners such as sucrose and fructose in clinical studies, it has been found that honey consumption reduces postprandial glycemic response and provides a beneficial effect on diabetes by lowering serum glucose levels in patients with diabetes [25]. Honey, which has protective effects in addition to its therapeutic properties, has protective roles for many systems from the digestive system to the respiratory system, from the cardiovascular system to the nervous system [16].

Propolis

Although its content generally varies according to the vegetation, it is a product prepared by bees by collecting resinous substances and plant secretions from the leaves, buds, and branches of plants and adding some beeswax by subjecting them to enzymatic changes for the purposes of ensuring hygiene of the hive, preventing insects and other animals from entering the hive, and repairing cracks in the combs [26-28]. Recently, with the realization of its rich content, interest in propolis has increased and it has become popular with its positive effects on human health. It is known that propolis contains nearly 300 compounds as chemical content. The carbohydrate content of propolis, which has a high lipid content is

relatively low and it is only found in small amounts in resinous substances. The content of propolis; consists of 45-55% resinous substances, 25-35% wax and fatty acids, 10% essential oil, 10% polyphenolic compounds, 5% pollen, and 5% other organic compounds, vitamins, and minerals. In addition, it has been determined that there are 24 amino acids in its structure [22,29,30].

Due to the phenolic compounds, it contains, propolis is antimicrobial, antibacterial, antifungal, antiviral, antiallergic, antioxidant, anticancer, cytotoxic effect against tumor cells, hepatoprotective, cardioprotective, neuroprotective, renal protective, anti-aging, anti-ulcer, wound healing effect, anti-inflammatory effects against infections. Prominent with its immunomodulatory effect, propolis has been reported to reduce blood pressure and cholesterol levels [26,29,31-33].

Bee pollen

In flowering plants, the pollens that enable the fertilization of female cells are the structures that make up the plant's male reproductive cells. Bee pollen is defined as the product formed by the blending of pollen collected by bees from plants with their own body fluids (enzymes such as amylase and catalase secreted from salivary glands) [34,35]. This product is delivered to the hive by bees in pollen sacs on their hind legs and at all stages of development [36,37]. As with other bee products, the composition of bee pollen depends on a significant amount of plant source, climatic characteristics, and geographical conditions [38-40].

It has been known since ancient times that bee pollen, known as the "life-giving dust" in ancient Egyptian civilization, is both a healing and nutritious food and has been used as traditional medicine for a long time. [40-42]. With the content analysis of bee products, its importance has increased even more in recent years and has been rapidly included in the human diet. Bee pollen has also been recognized as a valuable dietary supplement for humans [38]. It is also anti-inflammatory, antiosteoporosis, anti-neurodegenerative, antioxidant, antibacterial, antiviral, antifungal, hepatoprotective, radioprotective, cholesterol-lowering, immunostimulant, probiotic, antiallergic, due to its phytosterol content. It has been reported to have positive effects on anticancer, antinociceptive, antiulcer, and wound healing [35,37,41-45]. Its use as a support in the treatment of asthma is also beneficial [35]. Bee pollen, which is valuable for humans and has many benefits, has been standardized in our country as in some countries, and the features that should be included in it are specified in TS 10255 Pollen standard.

Although its content varies according to the plant source, it is known that there are about 200 substances in bee pollen. Bee pollen, rich in proteic substances and carbohydrates, is also a rich source of lipids, vitamins, minerals, and polyphenolic compounds. It contains 22 amino acids that people need. Due to its polyphenolic compounds, it has a high antioxidant capacity with its scavenging effect, without causing oxidative damage to free radicals that cause many diseases [34,43,46-48]. Detailed information about the content is given in Table 1.

Bee bread (Perga)

The product formed within two weeks after the honey bees deliver the pollen they collect to the hive and these pollens are mixed with honey and other bee secretions and exposed to lactic acid fermentation which is called bee bread [49]. Bee bread, which is an important source of protein, oil, and vitamins in the feeding of bees, also constitutes the raw material of royal jelly production [50]. It has also been used by humans for nutrition and treatment since ancient times [51]. Recently, it has become a preferred product to treat many diseases with its rich bioactive substance content.

Although its content varies according to plant origin, it consists mainly of carbohydrates, proteins, and lipids, as well as phenolic compounds such as anthocyanins and flavonoids, lactic acid, volatile compounds, various vitamins, and minerals [52-54]. Although it is mainly composed of pollen, it is different in the content; while it contains richer carbohydrates and lactic acid than pollen, it contains less protein and fat [55].

Although the studies on bee bread are limited, more literature information will be obtained as its importance is understood. According to current information, it has been reported to have in vitro antibacterial, antiviral, antimicrobial, anti-inflammatory, antioxidant, hepatoprotective, radioprotective, immunomodulatory, anti-tumor, and adaptogenic properties [8,56-59]. It has positive effects on the liver, endocrine, and nervous system functions. Crisin and kaempferol isolated from bee bread have neuroprotective, anxiolytic, and anticonvulsant effects. It increases the regeneration of tissues and is important for physical and mental health [51,55].

Royal jelly

Royal jelly secreted from the upper pharynx and jaw glands of young worker bees is a product used for feeding the larvae [60]. Its nutritional value is quite high and it has a special nutritious environment that enables the queen bee to differentiate. While worker bees can only benefit from this food store in the first three days of their larval stages, it is the only nutritional product for the queen bee [61]. The chemical content analysis of royal jelly started in the mid-19th century and continues today [62]. Royal jelly, which has a highly mixed content, contains carbohydrates, proteins, amino acids, lipids, organic acids, steroids, esters, phenolic compounds, minerals, and trace elements. Fresh royal jelly contains 50-70% water, 7-18% carbohydrates, 9-18% proteins, 3-8% lipids, 0.8-3% minerals, and low amounts of vitamins and polyphenolic compounds. Lyophilized royal jelly contains <5% water, 22-31% carbohydrates, 27-41% proteins, and 15-30% lipids. Royal jelly, which contains all the amino acids required for humans, has 29 defined amino acids and derivatives, mainly glutamic acid and aspartic acid. This product, which is different from other products in terms of lipid content, has short-chain and long-chain fatty acids, which are also responsible for their biological activities [63-67]. Detailed information about the content is given in Table 1. With its rich content, this product, which provides food for worker bees for a short time and the queen bee for a lifetime, has also attracted the attention of humans. Studies increasing day by day include anti-aging, anti-inflammatory, antioxidant, antibacterial, antifungal, antiviral, antihypertensive, immunomodulatory, preventing osteoporosis risk, hepatoprotective, cardioprotective, antiulcer, neuroprotective, anticancer, growth promoting, wound healing, stated that it has antirheumatic, antidepressant, antiallergic, and balancing effects of high cholesterol levels [68-75]. Since it has estrogen-like activity, current studies are investigating that it can be a traditional solution for postmenopausal symptoms and reduce complaints [76].

Royal jelly, a natural product that is frequently used and preferred in the fields of traditional medicine and cosmetics, is being used as a supportive treatment for Alzheimer's, cancer, diabetes, and cardiovascular diseases, It is inevitable that the anti-aging effect will cause royal jelly to increase its popularity and even to remain in the for a long time [77].

Apilarnil

Apilarnil in Turkey is unknown yet, however, while the male bee larvae pupae collected during the period of 3-7 days the larvae before they found the result is a lyophilized product consisting of bees. It has high biological activity due to the sum of nutrient compounds found in both the egg and larval body [78,79].

Its chemical composition changes with the effect of many factors such as the production period, the age of the larva, and the flora in which the colony is located. Although it is similar to royal jelly in content, it has less protein and carbohydrate and more water content. In the studies, moisture content was determined between 65-80%, total protein ratio 9-12%, total lipids 5-8%, phenolic substance 0.8%, and total sugar between 6-10%. From sugar profiles; fructose 0.11-0.60%, glucose 3.40-6.74%, sucrose 0.00- 0.14% [78-82]. It can be considered as a good source of amino acids due to the essential and non-essential amino acids in its composition. In apilarnil, calcium, magnesium, phosphorus, iron, manganese, copper, zinc, sodium, potassium minerals have been determined [83] vitamin A, vitamin B1, vitamin B2, niacin,

Table 1. Chemical contents of apitherapy products.

	Honey	Propolis	Bee pollen	Bee bread	Royal jelly (fresh)	Apilarnil	Bee venom (dry venom)
Carbohydrates	80% Monosaccharides (55-85%): fructose, glucose Disaccharides (2-15%): sucrose, maltose, turanose. Trisaccharides (1-7%):erlose, maltotriose …	It contains 45-55% resin.	15-60% Reduced sugars (glucose, fructose), sucrose	24-35% Monosaccharides (93-94%): Fructose, glucose. Disaccharides: turanose, maltose, trehalose and erlose	7-18% (More than 90% of total sugar content glucose and fructose). Other sugars; sucrose, maltose, trehalose, melibiose, ribose, and erlose	6-10% (0.11-0.60% Fructose, 3.40-6.74% glucose, 0.00-0.14% sucrose, maltose, trehalose)	2-4% (Glucose, fructose)
Proteic substances	0.5% 26 amino acids, enzymes (glucose oxidase, invertase, amylase ...) Choline, acetylcholine Approximately 50% of the amino acid content is proline	24 amino acids	7.5-35% Proteins Amino acids (including essential) Enzymes	14-24% Peptides and amino acids Enzymes (Saccharose, amylase, phosphatases)	9-18% Proteins Amino acids (proline, lysine, glutamic acid, phenylalanine, aspartate serine)	9-12% Proteins Amino acids (glycine, proline, lysine, glutamic acid, aspartic acid, valine, isoleucine) Enzymes Hormones (testosterone, estradiol, progesterone, prolactin)	48-58% Small proteins and peptides (Melittin, apamin, MCD et al.) 15-17% Enzymes (Phospholipase A2 and B, hyaluronidase et al.) 0.13-1% Amino acids
Lipids	0,01%	Contains 10% essential oil. It contains 25-35% Beeswax and fatty acids.	4-7% Essential fatty acids, phospholipids, phytosterols, cholesterol	5-11% Medium and long chain saturated fatty acids, polyunsaturated fatty acids (oleic, palmitic and stearic acid)	3-8% 80--85% fatty acids, 3-4% steroid and 0.4--0.8% phospholipids	5-8% Saturated fatty acids (palmitic acid, stearic acid, myristic acid etc.) Mono and polyunsaturated fatty acids (oleic acid et al.)	4-5% Phospholipids (6-phospholipids)
Polyphenolic compounds	0.1-0.2% Flavonoids (crisis, luteolin, quercetin, kaempferol, apigenin, galangin…) Phenolic acids (caffeic acid, gallic acid, chlorogenic acid ... Procyanidins Coumarins	10% Polyphenols Flavonoids KAFE-caffeic acid phenylethylester; pinosembrine, gakangin, pinobanksin, seizure, quercetin, kaempferol	1.6% Flavonoids (rutin, quercetin, kaempferol, naringin…) Phenolic acids (gallic acid, vanillic acid…)	12-25% Flavonoids (quercetin, rhamnoside, rutin, luteolin, apigenin, kaempferol, isorhamnetin…) Phenolic acids (gallic acid, vanillic acid…)	Flavonoids (quercetin, luteolin, apigenin, kaempferol, galangin, fisetin, naringin, hesperidin, crisisin)	0,8 %	

Vitamins	C, K, B1, B2, B3, B5, B6	B1, B2, B3, B5, B6, C, E	C, β-carotene, E, B1, B2, B3, B5, B6, B9	C, B1, B2, B3, B5, B6, folic acid, biotin, inositol, choline	B1, B2, B3, B5, B6, folic acid, biotin, inositol, vitamin C (in trace amounts)	A, C, B1, B2, B3, B5, B6 (trace amounts), folic acid, choline, inositol	
Minerals	P, S, Ca, Mg, K, Na, Zn, Fe, Cu, Mn, Se	Na, K, Mg, Ca, Ba, Bo (eser), Sr, Zn, Cd, Al, Si, Se (trace), Fe, Ni, Cr, Mn, Ti), Ag, Co, V	Fe, Ca, Mg, Zn, Cu, K, Na,	Na, K, Mg, Ca,Mn, Zn, P, Cu, Fe, Se	0,8-3% K, Ca, Na, Mg, Zn, Fe, Cu, Mn	K, Ca, Na, Mg, Zn, Fe, Cu, Mn, P	3-4% P, Ca, Mg
Water	15-20%	2-4%	6-18%	5-6%	50-70%	65-80%	-

Table 2. Comparison of biological activities of apitherapy products

Effect / Apitherapy products	Honey	Propolis	Bee pollen	Bee bread	Royal jelly	Apilarnil	Bee venom
Antibacterial	✓	✓	✓	✓	✓		✓
Antiviral	✓	✓	✓	✓	✓		✓
Antifungal	✓	✓	✓		✓		✓
Antioxidant	✓	✓	✓	✓	✓	✓	✓
Hepatoprotective	✓	✓	✓	✓	✓	✓	✓
Anti-inflammatory	✓	✓	✓	✓	✓		✓
Radioprotective		✓	✓	✓			✓
Anti-cancer	✓	✓	✓	✓	✓	✓	✓
Imunstimulant	✓	✓	✓	✓	✓	✓	✓
Antiallergic	✓	✓	✓		✓		✓
Wound healing effect	✓	✓	✓	✓	✓		✓
Antiatherogenic	✓	✓	✓		✓		✓
Antinociceptive	✓	✓	✓				✓
Anti-Neurodegenerative	✓	✓	✓	✓	✓		✓
Anti-osteoporosis			✓		✓		
Antirheumatic		✓			✓		✓
Anti-ulcer	✓	✓	✓		✓		
Anti-aging		✓			✓	✓	✓

pantothenic acid, vitamin B6, vitamin C, folic acid, inositol, and choline was found [84].

It shows androgenic and anabolic activity because it contains testosterone, estradiol, progesterone hormones. For this reason, it has been a preferred product to treat infertility. It has been reported that it has immunomodulatory, hepatoprotective, antioxidant, anti-aging, anticancer, hypolipidemic effects and contributes to body development [85]. Although information about Apilarnil is limited, more data will be obtained with the increase of studies on this product whose value has been understood.

Bee venom

Bee venom, also called apitoxin, is a substance that can be obtained from all honey bee species (such as Apis mellifera, Apis cerena, Apis florea, and Apis dorsata) and produced in venom sacs in the abdominal cavity of bees. Approximately 0.3mg of bee venom can be produced in this venom sac [86,87]. It is mainly composed of peptides such as melittin, apamin, mast cell degranulating peptide (MCD), enzymes such as hyaluronidase and phospholipase A_2, and biologically active amines such as histamine and dopamine. It has a very complex chemical content. The protein content consists of 48-58% small proteins and peptides, 15-17% enzymes, 0.13-1% amino acids, and a small amount of biologically active amines, while the carbohydrate content is 2-4%, the lipid content is 4-5%, the volatile component (pheromone) content is 4-8% and the mineral content is 3-4% [88,89].

Bee venom rich in peptides is an apitherapeutic agent used in degenerative diseases such as autoimmune and osteoarthritis such as rheumatoid arthritis, some neurodegenerative diseases such as Alzheimer's and Parkinson's, and skin diseases. Since it has an antinociceptive effect, it has traditional use to reduce pain and treat chronic pain. Positive effects on the nervous system have been found due to biologically active amines (apamin et al.) [90,91]. It also has a radioprotective feature [92]. Bee venom, which has increased its popularity as a natural treatment method, has been examined in detail in terms of content, and it has been revealed as a result of research from which material the biological effects originate. For example, the highest amount of melittin is responsible for anti-inflammatory, antiarthritic, antibacterial, antiviral, antifungal, antinociceptive, and cytotoxic effects against cancer cells [93,94]. Apamine is anti-inflammatory, antinociceptive, and cytotoxic effects [95]. MCD peptide is anti-inflammatory, antinociceptive and causes low-dose histamine release while inhibiting high-dose histamine release [96]. Adolapine peptide also has anti-inflammatory and analgesic effect [97]. Phospholipase A_2, one of the enzymes, has anti-inflammatory and cytotoxic activity, while hyaluronidase enzyme has a role in the immune system response [95,98].

Cancer development and progression is a multifactorial process accompanied by external factors such as smoking, infectious agents, environmental pollutants, and unhealthy diet, or internal factors such as inherited genetic mutations, hormones, and immune conditions [99]. It continues to be a disease group that affects a large mass in the world and death rates due to cancer are gradually increasing. According to the data of the World Health Organization (WHO), lung, breast, and colorectal cancers were the most frequently diagnosed cancers for both sexes in 2018, while the most deaths were seen in the lung, colorectal, stomach, and liver cancer cases. When we look at the cancer profile of our country, we encounter a similar picture in the world [100,101]. The number of cases, which is 18 million today, will increase to 29 million by 2040, according to the estimates of WHO. This increasing cancer incidence reveals other treatment needs in addition to existing treatment methods such as surgical treatment, radiotherapy, chemotherapy, gene therapy, and hormonal therapy. In addition, the drugs used in current treatments treat the disease, but are not specific to cancer cells, but also damage the normal cells of the body and cause many side effects [102]. For these reasons, the use of biotoxins such as animal poisons as therapeutic agents in cancer treatment has become an important approach. It has also been stated with

current data that bee venom is a potential agent with anti-cancer activity and this activity is due to the peptide called melittin. Melittin, the main biologically active component, is a basic polypeptide consisting of 26 amino acids [94,103]. Anticancer activity mechanisms of Melittin; cell cycle changes, its effect on proliferation and / or growth inhibition, and stimulation of the activation of caspase and matrix metalloproteinases that cause apoptotic or necrotic cell death [104,105]. Various enzymes such as G protein, protein kinase C, adenylate cyclase, phospholipase C, and D shows their effect by stimulating. The lytic effect on the phospholipid layer of the cell membrane by activating the phospholipase A_2 is also one of the important mechanisms [103-107].

Studies on anti-cancer effects of bee venom

With the positive results obtained in studies on the anticancer activity of bee venom, interest in the subject has increased and it has been tried in many types of cancer. In studies on ovarian cancer cells, bee venom caused apoptotic cell death by increasing the expression of death receptors and inhibiting the JAK-STAT (The Janus kinase / Signal transducers and activators of transcription) pathway [108]. JAK-STAT pathway cell proliferation, differentiation, It is a pathway that plays a central role in the survival and embryological processes and may show abnormal activity due to some genetic mutations, polymorphisms, and alter the functioning of the pathway, leading to the development of cancer [109]. In a study conducted in 2017, it was given in combination with cisplatin, which is mostly the first treatment option in ovarian cancer, and a synergistic effect was observed, different results were obtained from the effect of both agents alone. Whether the growth of human cervical tumors was inhibited by bee venom on mice was investigated and it was found that tumor growth was inhibited as a result of the inhibition of nuclear factor kappa B (NF-κB) by increasing death receptors [110]. It has revealed the effect of bee venom by inhibiting the NF-κB pathway in prostate cancer cells as well as apoptotic cell death [111]. In a study conducted on human leukemia cells in 2020, it was stated that melittin induced apoptosis in leukemia cells and could be a therapeutic agent in the treatment of leukemia [112]. The anticancer activity has been demonstrated in the human lung cancer cell line by inducing apoptosis and inhibiting the expression of cyclooxygenase-2 [113]. In a study conducted in 2018 to examine the effects of bee venom on colon cancer, it was shown that apoptosis was induced and colon cancer cell growth was inhibited by activation of death receptors and inhibition of NF-κB [114].

As seen from studies, lung, liver, colon, prostate, ovarian cancer cells are targets for the anti-cancer activity of bee venom and Melittin. For each cancer whose incidence is increasing, bee venom will continue to attract the attention of scientists and be the subject of studies as a more preferred and future preferred product compared to other apitherapy products. More clinical studies are needed for the development of this field and the increase of the applications in this field in our country.

CONCLUSION

Interest in apitherapy, one of the traditional and Complementary Medicine practices, is increasing day by day. In this context, it has become one of the popular products of recent times, as it has been known since ancient times and is used by the public as a healing source and with the support of scientific research on bees and their products [115]. In addition, patients are not satisfied with the applications made with synthetic drugs in the treatment of chronic, difficult to heal, and time-consuming diseases, especially cancer, they want to stay away because of their side effects and the promising results in the researches have led to an increase in the demand for the use of these products. In order to strengthen this area in our country, the production of quality, effective and reliable products must be ensured.

In this review, the effects mentioned for bee products vary according to the content of the product. It should not be forgotten that the content

of the product varies according to the plant source and geographical conditions. Organic bee products produced naturally have therapeutic efficacy for humans and should be supported by scientific research in order to reveal their functions. The biological activities of apitherapy products are very diverse as shown collectively in Table 2, and there are cases that can be treated without encountering adverse situations such as side effects, non-drug effects, or situations that strengthen the effect of existing treatments in the treatment of diseases. Although interest in apitherapy products has increased in our country since 2014, it is not at the desired level. More studies should be conducted on this subject, and our country, which is a natural rich source of bee and bee products, should take its place in the literature in this field.

Although honey, propolis, pollen, bee bread, apilarnil and bee venom are all valuable products, recently scientific studies have focused on bee venom. With its anti-cancer activity coming to the fore, it is the most important agent that has been more involved in studies compared to other apitherapeutic products. It attracts the attention of people as it is a natural product. As mentioned, its effects on many cancer cells have been investigated and will continue to be investigated. The results of the studies are promising for cancer, which is the most common disease group globally. Bee venom can be applied on its own as a chemotherapeutic agent or it can be used together with other available chemotherapeutic agents to create a synergistic effect. Thus, by ensuring the use of each agent in lesser amounts, the negative effects of the agents on the body are reduced. By increasing the number of clinical studies, the application dose, route, and side effects will be determined and it will be inevitable to be used in treatments as an anti-cancer agent in the future. The issue to be considered is that the application of bee venom is done by the doctor who has the Apitherapy Expertise certificate. It should be determined whether there is an allergy before the application. It should not be applied to those with allergies and hypersensitivity.

REFERENCES

1. Yeşilada E. *[Apiterapi Arıyla Gelen Şifa]*. 1 ed. İstanbul: Hayykitap; 2015.
2. Schmidt JO. Bee Products. In: Mizrahi A, Lensky Y, eds. *Bee Products: Properties, Applications, and Apitherapy.* Boston, MA: Springer US; 1997:15-26.
3. Enstitüsü TS. TSE 3036 Bal Standardı. In. Ankara2010.
4. Commission CA. Revised codex standard for honey. *Codex Stan.* 2001:12-1981.
5. Ferreira IC, Aires E, Barreira JC, Estevinho LM. Antioxidant activity of Portuguese honey samples: Different contributions of the entire honey and phenolic extract. *Food Chemistry.* 2009;114(4):1438-1443.
6. da C Azeredo L, Azeredo M, De Souza S, Dutra V. Protein contents and physicochemical properties in honey samples of Apis mellifera of different floral origins. *Food chemistry.* 2003;80(2):249-254.
7. Iglesias MT, De Lorenzo C, Polo MdC, Martín-Álvarez PJ, Pueyo E. Usefulness of amino acid composition to discriminate between honeydew and floral honeys. Application to honeys from a small geographic area. *Journal of agricultural and food chemistry.* 2004;52(1):84-89.
8. Bogdanov S, Jurendic T, Sieber R, Gallmann P. Honey for nutrition and health: a review. *Journal of the American College of Nutrition.* 2008;27(6):677-689.
9. Escuredo O, Míguez M, Fernández-González M, Carmen Seijo M. Nutritional value and antioxidant activity of honeys produced in a European Atlantic area. *Food Chemistry.* 2013;138(2):851-856.
10. Escuredo O, Dobre I, Fernández-González M, Seijo MC. Contribution of botanical origin and sugar composition of honeys on the crystallization phenomenon. *Food chemistry.* 2014;149:84-90.
11. Cuevas-Glory LF, Pino JA, Santiago LS, Sauri-Duch E. A review of volatile analytical methods for determining the botanical origin of honey. *Food Chemistry.* 2007;103(3):1032-1043.
12. Ulusoy E. Bal ve apiterapi. *Uludağ Arıcılık Dergisi.* 2012;12(3):89-97.
13. Efem S. Clinical observations on the wound healing properties of honey. *British journal of Surgery.* 1988;75(7):679-681.
14. Ali A, Chowdhury M, Al Humayyd M. Inhibitory effect of natural honey on Helicobacter pylori. *Tropical gastroenterology: official journal of the Digestive Diseases Foundation.* 1991;12(3):139-143.
15. Mandal MD, Mandal S. Honey: its medicinal property and antibacterial activity. *Asian Pacific journal of tropical biomedicine.* 2011;1(2):154-160.

16. Cianciosi D, Forbes-Hernández TY, Afrin S, Gasparrini M, Reboredo-Rodriguez P, Manna PP, Zhang J, Bravo Lamas L, Martínez Flórez S, Agudo Toyos P. Phenolic compounds in honey and their associated health benefits: A review. *Molecules.* 2018;23(9):2322.
17. Al-Mamary M, Al-Meeri A, Al-Habori M. Antioxidant activities and total phenolics of different types of honey. *Nutrition Research.* 2002;22(9):1041-1047.
18. Gheldof N, Wang X-H, Engeseth NJ. Identification and quantification of antioxidant components of honeys from various floral sources. *Journal of agricultural and food chemistry.* 2002;50(21):5870-5877.
19. Erejuwa OO, Sulaiman SA, Ab Wahab MS. Honey: a novel antioxidant. *Molecules.* 2012;17(4):4400-4423.
20. Poljsak B, Šuput D, Milisav I. Achieving the balance between ROS and antioxidants: when to use the synthetic antioxidants. *Oxidative medicine and cellular longevity.* 2013;2013.
21. Molan PC. Potential of honey in the treatment of wounds and burns. *American journal of clinical dermatology.* 2001;2(1):13-19.
22. Gómez-Caravaca A, Gómez-Romero M, Arráez-Román D, Segura-Carretero A, Fernández-Gutiérrez A. Advances in the analysis of phenolic compounds in products derived from bees. *Journal of Pharmaceutical and Biomedical Analysis.* 2006;41(4):1220-1234.
23. Estevinho L, Pereira AP, Moreira L, Dias LG, Pereira E. Antioxidant and antimicrobial effects of phenolic compounds extracts of Northeast Portugal honey. *Food Chem Toxicol.* 2008;46(12):3774-3779.
24. Alvarez-Suarez JM, Tulipani S, Romandini S, Bertoli E, Battino M. Contribution of honey in nutrition and human health: a review. *Mediterranean Journal of Nutrition and Metabolism.* 2010;3(1):15-23.
25. Shambaugh P, Worthington V, Herbert J. Differential effects of honey, sucrose, and fructose on blood sugar levels. *Journal of manipulative and physiological therapeutics.* 1990;13(6):322-325.
26. Castaldo S, Capasso F. Propolis, an old remedy used in modern medicine. *Fitoterapia.* 2002;73:S1-S6.
27. Semiramis KUTLUCA FG, Ali KORKMAZ. PROPOLİS. In: Samsun: T.C. SAMSUN VALİLİĞİ İl Tarım Müdürlüğü; 2008.
28. Doğan H, Silici S, Ozcimen AA. Biological Effects of Propolis on Cancer. *Turkish Journal of Agriculture-Food Science and Technology.* 2020;8(3):573-579.
29. Burdock GA. Review of the biological properties and toxicity of bee propolis (propolis). *Food Chem Toxicol.* 1998;36(4):347-363.
30. Bankova VS, de Castro SL, Marcucci MC. Propolis: recent advances in chemistry and plant origin. *Apidologie.* 2000;31(1):3-15.
31. Dobrowolski JW, Vohora S, Sharma K, Shah SA, Naqvi S, Dandiya P. Antibacterial, antifungal, antiamoebic, antiinflammatory and antipyretic studies on propolis bee products. *Journal of ethnopharmacology.* 1991;35(1):77-82.
32. Banskota AH, Tezuka Y, Kadota S. Recent progress in pharmacological research of propolis. *Phytotherapy research.* 2001;15(7):561-571.
33. Sforcin JM, Bankova V. Propolis: is there a potential for the development of new drugs? *Journal of ethnopharmacology.* 2011;133(2):253-260.
34. Villanueva MO, Marquina AD, Serrano RB, Abellán GB. The importance of bee-collected pollen in the diet: a study of its composition. *International Journal of Food Sciences and Nutrition.* 2002;53(3):217-224.
35. Bogdanov S. Pollen: Collection, Harvest, Compostion, Quality. 2016.
36. Pascoal A, Rodrigues S, Teixeira A, Feás X, Estevinho LM. Biological activities of commercial bee pollens: Antimicrobial, antimutagenic, antioxidant and anti-inflammatory. *Food Chem Toxicol.* 2014;63:233-239.
37. Güneş M.E. OHH. Arı Ürünleri, Arı Sokması ve Veteriner Apiterapi. In: Doğanay A. AL, ed. *Bal Arısı: Yetiştiriciliği, Ürünleri, Hastalıkları.* 1 ed. Bursa: Dora Yayınevi; 2017:170-171.
38. Nogueira C, Iglesias A, Feás X, Estevinho LM. Commercial bee pollen with different geographical origins: a comprehensive approach. *Int J Mol Sci.* 2012;13(9):11173-11187.
39. da Silva GR, da Natividade TB, Camara CA, da Silva EMS, dos Santos FdAR, Silva TMS. Identification of sugar, amino acids and minerals from the pollen of Jandaíra stingless bees (Melipona subnitida). *Food and Nutrition Sciences.* 2014;2014.
40. Denisow B, Denisow-Pietrzyk M. Biological and therapeutic properties of bee pollen: a review. *Journal of the Science of Food and Agriculture.* 2016;96(13):4303-4309.
41. Ulbricht C, Conquer J, Giese N, Khalsa KP, Sklar J, Weissner W, Woods J. An evidence-based systematic review of bee pollen by the Natural Standard Research Collaboration. *J Diet Suppl.* 2009;6(3):290-312.
42. Komosinska-Vassev K, Olczyk P, Kaźmierczak J, Mencner L, Olczyk K. Bee pollen: chemical composition and therapeutic application. *Evidence-based complementary and alternative medicine : eCAM.* 2015;2015:297425-297425.
43. Campos MGR, Frigerio C, Lopes J, Bogdanov S. What is the future of Bee-Pollen. *Journal of ApiProduct and ApiMedical Science.* 2010;2(4):131-144.

44. Küpeli Akkol E, Orhan DD, Gürbüz I, Yesilada E. In vivo activity assessment of a "honey-bee pollen mix" formulation. *Pharm Biol.* 2010;48(3):253-259.
45. Yakusheva E. Pollen and bee bread: physico-chemical properties. Biological and pharmacological effects. Use in medical practice. *Theoretical and Practical Basics of Apitherapy.* 2010:84-97.
46. Campos MG, Bogdanov S, de Almeida-Muradian LB, Szczesna T, Mancebo Y, Frigerio C, Ferreira F. Pollen composition and standardisation of analytical methods. *Journal of Apicultural Research.* 2008;47(2):154-161.
47. Rzepecka-Stojko A, Stojko J, Kurek-Górecka A, Górecki M, Kabała-Dzik A, Kubina R, Moździerz A, Buszman E. Polyphenols from bee pollen: structure, absorption, metabolism and biological activity. *Molecules.* 2015;20(12):21732-21749.
48. Ares AM, Valverde S, Bernal JL, Nozal MJ, Bernal J. Extraction and determination of bioactive compounds from bee pollen. *Journal of Pharmaceutical and Biomedical Analysis.* 2018;147:110-124.
49. Bogdanov S. Pollen: nutrition, functional properties, health: a review. *Bee Product Science.* 2011:1-34.
50. Mutsaers M. *Bee products: properties, processing and marketing.* Agromisa Foundation/Technical Centre for Agricultural and Rural Cooperation …; 2005.
51. Khalifa SAM, Elashal M, Kieliszek M, Ghazala NE, Farag MA, Saeed A, Xiao J, Zou X, Khatib A, Göransson U, El-Seedi HR. Recent insights into chemical and pharmacological studies of bee bread. *Trends in Food Science & Technology.* 2020;97:300-316.
52. Havas LJ. Effect of bee venom on colchicine-induced tumours. *Nature.* 1950;166(4222):567-568.
53. Bogdanov S. Royal jelly, bee brood: composition, health, medicine: a review. *Lipids.* 2011;3(8):8-19.
54. Giroud B, Vauchez A, Vulliet E, Wiest L, Buleté A. Trace level determination of pyrethroid and neonicotinoid insecticides in beebread using acetonitrile-based extraction followed by analysis with ultra-high-performance liquid chromatography–tandem mass spectrometry. *Journal of Chromatography A.* 2013;1316:53-61.
55. Ivanišová E, Kačániová M, Frančáková H, Petrová J, Hutková J, Brovarskyi V, Velychko S, Adamchuk L, Schubertová Z, Musilová J. Bee bread-perspective source of bioactive compounds for future. *Potravinarstvo Slovak Journal of Food Sciences.* 2015;9(1):592-598.
56. Nagai T, Nagashima T, Myoda T, Inoue R. Preparation and functional properties of extracts from bee bread. *Food/nahrung.* 2004;48(3):226-229.
57. Baltrušaitytė V, Venskutonis PR, Čeksterytė V. Antibacterial activity of honey and beebread of different origin against S. aureus and S. epidermidis. *Food Technology and Biotechnology.* 2007;45(2):201-208.
58. Abouda Z, Zerdani I, Kalalou I, Faid M, Ahami M. The antibacterial activity of Moroccan bee bread and bee-pollen (fresh and dried) against pathogenic bacteria. *Research Journal of Microbiology.* 2011;6(4):376.
59. Sobral F, Calhelha RC, Barros L, Dueñas M, Tomás A, Santos-Buelga C, Vilas-Boas M, Ferreira IC. Flavonoid composition and antitumor activity of bee bread collected in northeast Portugal. *Molecules.* 2017;22(2):248.
60. National Health Commission of the People's Republic of China. Notice on diagnosis and treatment of novel coronavirus pneumonia (Trial Version 7) [EB/OL] (2020-03-03) . https://med.sina.cn/article_detail_103_1_78534.html (in Chinese).
61. Šimúth J. Some properties of the main protein of honeybee (Apis mellifera) royal jelly. 2001.
62. Crane E. The past and present status of beekeeping with stingless bees. *Bee world.* 1992;73(1):29-42.
63. Takenaka T. Nitrogen components and carboxylic acids of royal jelly. *Chemistry and biology of social insects.* 1987:162-163.
64. Vecchi M, Sabatini A, Grazia L, Tini V, Zambonelli C. Il contenuto in vitamine come possibile elemento di caratterizzazione della gelatina reale. 1988.
65. Viuda-Martos M, Ruiz-Navajas Y, Fernández-López J, Pérez-Alvarez JA. Functional properties of honey, propolis, and royal jelly. *J Food Sci.* 2008;73(9):R117-124.
66. Ramadan MF, Al-Ghamdi A. Bioactive compounds and health-promoting properties of royal jelly: A review. *Journal of Functional Foods.* 2012;4(1):39-52.
67. Xue X, Wu L, Wang K. Chemical Composition of Royal Jelly. In: Alvarez-Suarez JM, ed. *Bee Products - Chemical and Biological Properties.* Cham: Springer International Publishing; 2017:181-190.
68. Tamura T, Fujii A, Kuboyama N. [Antitumor effects of royal jelly (RJ)]. *Nihon Yakurigaku Zasshi.* 1987;89(2):73-80.
69. Fujiwara S, Imai J, Fujiwara M, Yaeshima T, Kawashima T, Kobayashi K. A potent antibacterial protein in royal jelly. Purification and determination of the primary structure of royalisin. *J Biol Chem.* 1990;265(19):11333-11337.
70. Tokunaga KH, Yoshida C, Suzuki KM, Maruyama H, Futamura Y, Araki Y, Mishima S. Antihypertensive effect of peptides from royal jelly in spontaneously hypertensive rats. *Biol Pharm Bull.* 2004;27(2):189-192.
71. Salazar-Olivo L, Paz-González V. Screening of biological activities present in honeybee (Apis mellifera) royal jelly. *Toxicology in vitro.* 2005;19(5):645-651.
72. Vucevic D, Melliou E, Vasilijic S, Gasic S, Ivanovski P, Chinou I, Colic M. Fatty acids isolated from royal jelly modulate dendritic cell-mediated immune response in vitro. *Int Immunopharmacol.* 2007;7(9):1211-1220.

73. Melliou E, Chinou I. Chapter 8 - Chemistry and Bioactivities of Royal Jelly. In: Atta ur R, ed. *Studies in Natural Products Chemistry.* Vol 43. Elsevier; 2014:261-290.
74. Guendouz M, Haddi A, Grar H, Kheroua O, Saidi D, Kaddouri H. Preventive effects of royal jelly against anaphylactic response in a murine model of cow's milk allergy. *Pharm Biol.* 2017;55(1):2145-2152.
75. Ahmad S, Campos MG, Fratini F, Altaye SZ, Li J. New Insights into the Biological and Pharmaceutical Properties of Royal Jelly. *Int J Mol Sci.* 2020;21(2).
76. Bălan A, Moga MA, Dima L, Toma S, Elena Neculau A, Anastasiu CV. Royal Jelly-A Traditional and Natural Remedy for Postmenopausal Symptoms and Aging-Related Pathologies. *Molecules (Basel, Switzerland).* 2020;25(14):3291.
77. Kunugi H, Mohammed Ali A. Royal Jelly and Its Components Promote Healthy Aging and Longevity: From Animal Models to Humans. *Int J Mol Sci.* 2019;20(19).
78. Bărnuțiu L, Mărghitaș L, Dezmirean D, Bobiș O, Mihai C, Pavel C. Physico-chemical composition of apilarnil (bee drone larvae). *Lucrări Științifice-Universitatea de Științe Agricole Și Medicină Veterinară, Seria Zootehnie.* 2013;59:199-202.
79. SİLİCİ S. Chemical Content and Bioactive Properties of Drone Larvae (Apilarnil). *Mellifera.* 2019;19(2):14-22.
80. Matsuka M, Watabe N, Takeuchi K. Analysis of the food of larval drone honeybees. *Journal of Apicultural Research.* 1973;12(1):3-7.
81. Balkanska R, Karadjova I, Ignatova M. Comparative analyses of chemical composition of royal jelly and drone brood. *Proteins.* 2014;16(1.29):14.65-18.33.
82. MARGAOAN R, MARGHITAS LA, DEZMIREAN DS, BOBIS O, BONTA V, CATANA C, URCAN A, MURESAN CI, MARGIN MG. Comparative study on quality parameters of royal jelly, Apilarnil and queen bee larvae triturate. *Bulletin of University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca Animal Science and Biotechnologies.* 2017;74(1):51-58.
83. Ghosh S, Jung C, Meyer-Rochow VB. Nutritional value and chemical composition of larvae, pupae, and adults of worker honey bee, Apis mellifera ligustica as a sustainable food source. *Journal of Asia-Pacific Entomology.* 2016;19(2):487-495.
84. Sawczuk R, Karpinska J, Miltyk W. What do we need to know about drone brood homogenate and what is known. *Journal of Ethnopharmacology.* 2019;245:111581.
85. Doğanyiğit Z, Okan A, Kaymak E, Pandır D, Silici S. Investigation of protective effects of apilarnil against lipopolysaccharide induced liver injury in rats via TLR 4/ HMGB-1/ NF-κB pathway. *Biomedicine & Pharmacotherapy.* 2020;125:109967.
86. Park D, Jung JW, Lee MO, Lee SY, Kim B, Jin HJ, Kim J, Ahn Y-J, Lee KW, Song YS, Hong S, Womack JE, Kwon HW. Functional characterization of naturally occurring melittin peptide isoforms in two honey bee species, Apis mellifera and Apis cerana. *Peptides.* 2014;53:185-193.
87. Kolayli S, Keskin M. Chapter 7 - Natural bee products and their apitherapeutic applications. In: Atta ur R, ed. *Studies in Natural Products Chemistry.* Vol 66. Elsevier; 2020:175-196.
88. Hider RC. Honeybee venom: a rich source of pharmacologically active peptides. *Endeavour.* 1988;12(2):60-65.
89. Rady I, Siddiqui IA, Rady M, Mukhtar H. Melittin, a major peptide component of bee venom, and its conjugates in cancer therapy. *Cancer Letters.* 2017;402:16-31.
90. Banks B, Brown C, Burgess G, Burnstock G, Claret M, Cocks T, Jenkinson D. Apamin blocks certain neurotransmitter-induced increases in potassium permeability. *Nature.* 1979;282(5737):415-417.
91. Shuba M, Vladimirova I. Effect of apamin on the electrical responses of smooth muscle to adenosine 5′-triphosphate and to non-adrenergic, non-cholinergic nerve stimulation. *Neuroscience.* 1980;5(5):853-859.
92. Varanda E, Tavares D. Radioprotection: mechanisms and radioprotective agents including honeybee venom. *Journal of Venomous Animals and Toxins.* 1998;4(1):5-21.
93. Raghuraman H, Chattopadhyay A. Melittin: a membrane-active peptide with diverse functions. *Biosci Rep.* 2007;27(4-5):189-223.
94. Chen J, Guan S-M, Sun W, Fu H. Melittin, the major pain-producing substance of bee venom. *Neuroscience bulletin.* 2016;32(3):265-272.
95. Son DJ, Lee JW, Lee YH, Song HS, Lee CK, Hong JT. Therapeutic application of anti-arthritis, pain-releasing, and anti-cancer effects of bee venom and its constituent compounds. *Pharmacol Ther.* 2007;115(2):246-270.
96. Jim SY, Wittkowski KM. Inflammatory role of two venom components of yellow jackets (Vespula vulgaris): a mast cell degranulating peptide mastoparan and phospholipase A1. *International archives of allergy and immunology.* 2003;131(1):25-32.
97. Shkenderov S, Koburova K. Adolapin-a newly isolated analgetic and anti-inflammatory polypeptide from bee venom. *Toxicon.* 1982;20(1):317-321.
98. Ye M, Chung H-S, Lee C, Yoon MS, Yu AR, Kim JS, Hwang D-S, Shim I, Bae H. Neuroprotective effects of bee venom phospholipase A2 in the 3xTg AD mouse model of Alzheimer's disease. *Journal of neuroinflammation.*

2016;13(1):1-12.
99. Ames BN, Gold LS, Willett WC. The causes and prevention of cancer. *Proceedings of the National Academy of Sciences.* 1995;92(12):5258-5265.
100. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *International journal of cancer.* 2015;136(5):E359-E386.
101. Ferlay J, Colombet M, Soerjomataram I, Mathers C, Parkin DM, Piñeros M, Znaor A, Bray F. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. *Int J Cancer.* 2019;144(8):1941-1953.
102. Zhang Y. Why do we study animal toxins? *Zoological research.* 2015;36(4):183.
103. Orsolic N. Bee venom in cancer therapy. *Cancer Metastasis Rev.* 2012;31(1-2):173-194.
104. Moon DO, Park SY, Heo MS, Kim KC, Park C, Ko WS, Choi YH, Kim GY. Key regulators in bee venom-induced apoptosis are Bcl-2 and caspase-3 in human leukemic U937 cells through downregulation of ERK and Akt. *Int Immunopharmacol.* 2006;6(12):1796-1807.
105. Gajski G, Garaj-Vrhovac V. Melittin: A lytic peptide with anticancer properties. *Environmental Toxicology and Pharmacology.* 2013;36(2):697-705.
106. Raghuraman H, Chattopadhyay A. Melittin: a membrane-active peptide with diverse functions. *Bioscience reports.* 2007;27(4-5):189-223.
107. Premratanachai P, Chanchao C. Review of the anticancer activities of bee products. *Asian Pacific journal of tropical biomedicine.* 2014;4(5):337-344.
108. Jo M, Park MH, Kollipara PS, An BJ, Song HS, Han SB, Kim JH, Song MJ, Hong JT. Anti-cancer effect of bee venom toxin and melittin in ovarian cancer cells through induction of death receptors and inhibition of JAK2/STAT3 pathway. *Toxicol Appl Pharmacol.* 2012;258(1):72-81.
109. Alonezi S, Tusiimire J, Wallace J, Dufton MJ, Parkinson JA, Young LC, Clements CJ, Park JK, Jeon JW, Ferro VA, Watson DG. Metabolomic Profiling of the Synergistic Effects of Melittin in Combination with Cisplatin on Ovarian Cancer Cells. *Metabolites.* 2017;7(2).
110. Lee HL, Park SH, Kim TM, Jung YY, Park MH, Oh SH, Yun HS, Jun HO, Yoo HS, Han SB, Lee US, Yoon JH, Song MJ, Hong JT. Bee venom inhibits growth of human cervical tumors in mice. *Oncotarget.* 2015;6(9):7280-7292.
111. Park MH, Choi MS, Kwak DH, Oh KW, Yoon DY, Han SB, Song HS, Song MJ, Hong JT. Anti-cancer effect of bee venom in prostate cancer cells through activation of caspase pathway via inactivation of NF-kappaB. *Prostate.* 2011;71(8):801-812.
112. Ceremuga M, Stela M, Janik E, Gorniak L, Synowiec E, Sliwinski T, Sitarek P, Saluk-Bijak J, Bijak M. Melittin—A Natural Peptide from Bee Venom Which Induces Apoptosis in Human Leukaemia Cells. *Biomolecules.* 2020;10(2):247.
113. Jang MH, Shin MC, Lim S, Han SM, Park HJ, Shin I, Lee JS, Kim KA, Kim EH, Kim CJ. Bee venom induces apoptosis and inhibits expression of cyclooxygenase-2 mRNA in human lung cancer cell line NCI-H1299. *J Pharmacol Sci.* 2003;91(2):95-104.
114. Zheng J, Lee HL, Ham YW, Song HS, Song MJ, Hong JT. Anti-cancer effect of bee venom on colon cancer cell growth by activation of death receptors and inhibition of nuclear factor kappa B. *Oncotarget.* 2015;6(42):44437-44451.
115. Fratellone PM, Tsimis F, Fratellone G. Apitherapy products for medicinal use. *The Journal of Alternative and Complementary Medicine.* 2016;22(12):1020-1022.

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REVIEW

Plants used in Traditional Treatment for Boils in Turkey

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Abstract
Boils are a painful inflammatory skin disease, often accompanied by swelling and redness of the hair follicle and its surroundings by *Staphylococcus aureus* bacteria. Antimicrobial agents are used in its clinical treatment. In addition to clinical treatment, the treatment applications with herbs continue among the public. In this study, which was prepared by screening of ethnobotanical researches made in Turkey, 171 taxa were recorded in the traditional treatment of boils. Information about scientific and local names, families, used parts and usage patterns of these plants were given. As a result of the research, the biological activities of the genera (*Allium*, *Brassica*, *Malva*, *Plantago*) that are most commonly used in the treatment of boils were evaluated by screening the studies in the literature.
Keywords: Boils, Traditional Treatment, Medicinal Plants, Turkey

INTRODUCTION

Boil known as folliculitis, furuncle, and carbuncle in medicine is a painful inflammatory skin disease (Figure 1) that is mostly caused by *Staphylococcus aureus* type bacteria. It is deeply located in the hair follicle, accompanied by swelling and redness, as a result of the loss of the protective function of the skin [1].

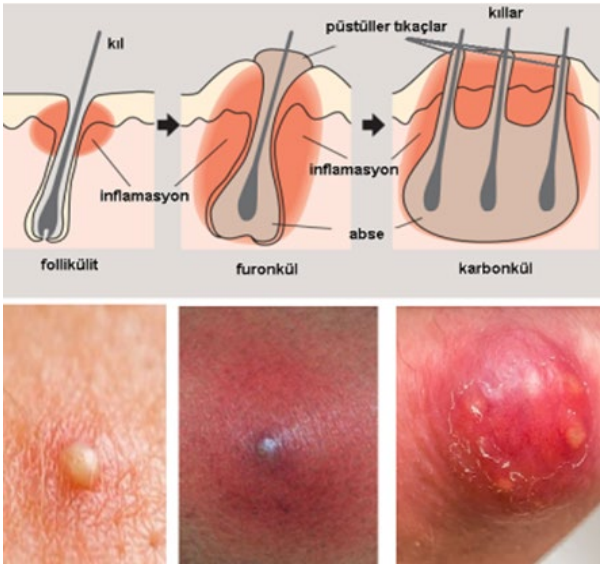

Figure 1. Folliculitis, furuncle & carbuncle *(https://www.hakanbuzoglu.com/images/follikulit/follik%C3%BClit_kil_koku_iltihabi.png)*[2]

Folliculitis is an inflammation of the hair follicle. It is seen as a painful swelling surrounding the hair and sometimes as a pus settle in the middle.

Furuncle is a deep-seated infection of the hair follicle and its surroundings. It mostly occurs with the progression of infection in folliculitis and formation of nodules. It is known among the people as the "kan çıbanı". Lesions first appear in the dermis. It starts as a hard, painful, red nodule and then develops into a painful fluctuating abscess [1].

Carbuncles are deep and large inflammatory lesions that occur in more than one hair follicle. It may occur as a result of the combination of neighboring furuncles. It is more severe than furuncle. It is caused by bacterial infection most commonly with *S. aureus* [3]. It is known among the people as the "aslan pençesi". Lesions are usually located on the neck, back and buttocks. It is observed as painful, erythematous, very hard, large nodules. The lesion is softened by fluctuation and may drain spontaneously. Leukocytosis and systemic symptoms such as pain, fever, malaise may occur. There is a risk of developing bacteremia in long-term infections [1,4].

Clinical treatment for boils

Generally, systemic or topical antimicrobial agents are used for clinical treatment of boils.

In folliculitis, the lesion is cleaned, saline compress is applied, followed by topical antibiotic / antifungal treatment. It heals in 7-10 days without leaving a scar. Applying intermittent hot compresses on the furuncle and carbuncle may facilitate the drainage of the abscess. A single

lesion that drains on its own can heal without the need for additional treatment, but local antiseptic and antibiotic application is necessary to prevent spreading to its surroundings and for faster healing[1]. Large abscesses that cannot drain spontaneously are surgically drained. In such cases, topical and systemic antibiotic treatment is definitely started. Cephalexin, cotrimaxazole, clindamycin and macrolides are used as antibiotics for 10-14 days [4].

Traditional treatment for boils in Turkey

Antibiotics are of great importance in the treatment of infectious diseases, but the increasing number of multi-drug resistant bacteria decreases the effectiveness of antibiotics and increases the frequency of therapeutic failures. For this reason, the continuity of antibacterial drug research is important. Antibiotic treatment is also important in the clinic for boils, which is one of the infectious diseases, but the presence of resistant bacteria may limit the treatment options[1]. At this point, herbs used in traditional treatment among the public have an unlimited potential in search for new drugs. Turkey has a rich flora due to its geographical position [5]. Plants are mostly used in the traditional treatment of many diseases. These plants used in treatment have been revealed by numerous ethnobotanical studies. The purpose of this study is to determine the plants used in the treatment of boils by screening the ethnobotanical studies were carried out in Turkey and evaluate antioxidant, antimicrobial, anti-inflammatory and analgesic activities of the most used genera by screening the studies in the literature.

Plants used for boils treatment in folk medicine are given in Table 1 below with their botanical names, local names, families, used parts and usage.

MATERIAL AND METHOD

This study was prepared screening the MSc and PhD theses in the National Thesis Center of the Council of Higher Education and ethnobotanical studies up to the present conducted in the Turkey with selecting plants used in the treatment of boils.

Then, the most used of these plants, activity studies to support the use of boils were investigated.

RESULT AND DISCUSSION

In this study, the ethnobotanical studies conducted in Turkey were screened and the plants used for the treatment of boils were compiled with their scientific names, local names, parts used and usages and shown in Table 1.

This review also includes studies showing the antioxidant, anti-inflammatory, and antimicrobial activities of the most commonly used species.

171 taxa were recorded in the traditional treatment of boils. *Abies nordmanniana* (Steven) Spach, *Eryngium bithynicum* Boiss., *Papaver triniifolium* Boiss., *Salvia dichroantha* Stapf are endemic.

The most commonly used parts are leaves (70 taxa) followed by aerial parts (34 taxa), fruits (15 taxa), flowers (12 taxa), tubers (11 taxa), roots (8 taxa) and resin (8 taxa) shown in Figure 2.

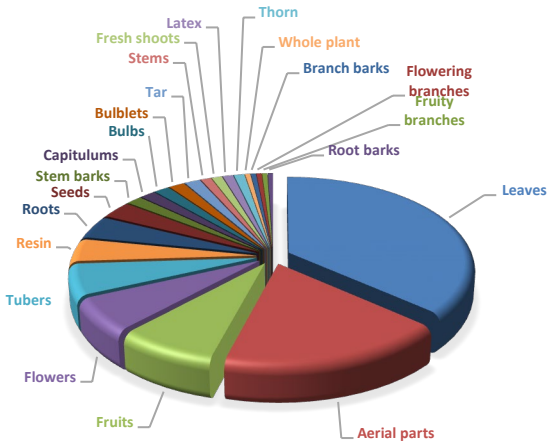

Figure 2. The most used plant parts

The most used plant families in traditional boils treatment are: Asteraceae (17 taxa), Lamiaceae (13 taxa), Fabaceae (10 taxa), Malvaceae (9 taxa), Liliaceae (8 taxa), Polygonaceae (8 taxa), Pinaceae (7 taxa), Rosaceae (7 taxa), Ranunculaceae (6 taxa), Orchidaceae (5 taxa), Plantaginaceae (5 taxa) shown in Figure 3.

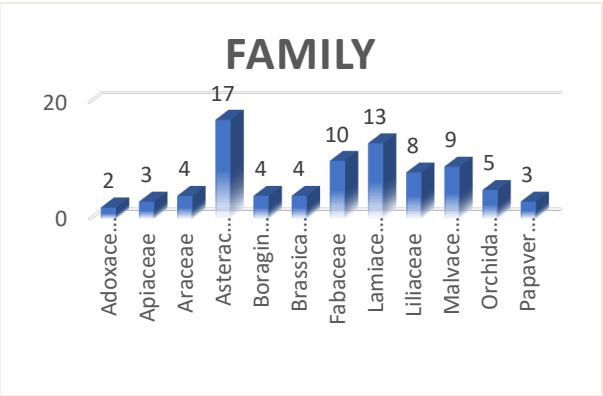

Figure 3. Main families used in traditional boil treatment in Turkey

Table 1. Plants used in the treatment of boil in Turkey

Botanical name	Family	Local name	Plant part used		Usage	Ref.
Abelmoschus esculentus (L.) Moench (Syn. *Hibiscus esculentus* L.)	Malvaceae	Bamya	Fruits	Ext.	Boiled fruits are applied in the painful area and kept for 8-10 hours.	5, 6, 7
Abies cilicica (Antoine & Kotschy) Carrière	Pinaceae	İladin	Resin	Ext.	Resin is applied to the boil.	8, 9
**Abies nordmanniana* (Steven) Spach (Endemic)	Pinaceae	Göknar Köknar	Resin	Ext.	Resin is applied to the boil.	10
Abies nordmanniana subsp. *equi-trojani* (Syn. *Abies bornmuelleriana* Mattf.)	Pinaceae	Künar sakızı	Resin	Ext.	Resin, soap, butter are put into the cavity opened to the onion and heated and the boiled finger is kept in this hole.	11
Acer campestre L.	Sapindaceae	Akça ağaç	Stem barks	Ext.	Ash of stem barks is applied to the boil.	12
Achillea arabica Kotschy (Syn. *Achillea biebersteinii* C.Afan.)	Asteraceae	Ormaderen	Capitulums	Ext.	Crushed capitulums is applied to the boil.	13
Achillea crithmifolia Waldst. & Kit.	Asteraceae	Civanperçemi Mayasıl otu	Aerial parts	Int.	Drink the infusion.	14
Achillea millefolium subsp. *millefolium*	Asteraceae	Civanperçemi	Leaves	Ext.	Crushed leaves are applied to the boil.	15
Alcea apterocarpa (Fenzl) Boiss.	Malvaceae	Hatmi, Gülhatmi	Leaves, Flowers	Ext.	Crushed leaves and flowers are applied to the boil	16
Alcea calvertii (Boiss.) Boiss.	Malvaceae	Hatmi, Gülhatmi	Leaves, Flowers	Ext.	Crushed leaves and flowers are applied to the boil	16
Alcea fasciculiflora Zohary	Malvaceae	Hatmi	Roots	Ext.	Crushed root is applied to the boil.	13, 17
Alcea flavovirens (Boiss. & Buhse) Iljin	Malvaceae	Heru	Roots	Ext.	Crushed root is applied to the boil.	13
Alchemilla minusculiflora Buser	Rosaceae	Deve tabanı Aslan pençesi	Leaves, Flowers	Int.	Drink the infusion.	16
Alkanna tinctoria (L.) Tausch	Boraginaceae	Havacıva otu	Roots	Ext.	Roast the root in butter to obtain an ointment and apply it to a boil.	16
Allium ampeloprasum L.	Liliaceae	Pırasa	Roots	Ext.	The roots of the fresh plant are crushed with butter and milk, then wheat flour is added and cooked. This poultice is applied to the boil.	7
Allium cepa L.	Liliaceae	Soğan	Bulbs	Ext.	-Boiled bulb is applied to the painful area and kept for 8-10 hours. -Grated onion is boiled in milk and then applied to painful area -The grated onion is heated in a pan with soap, milk, beeswax, butter and resin, the resulting ointment is applied to the boil.	6, 9, 11, 18, 19, 20, 21
Allium rotundum L.	Liliaceae	Körmen, Kömüren	Bulblets	Ext.	The onion cooked in embers is crushed and applied to the boil.	5
Allium sativum L.	Liliaceae	Sarımsak	Bulblets	Ext.	Crushed bulb is applied to the boil.	22, 23
Anagyris foetida L.	Fabaceae	Keçigevişi Kokar bakla	Seeds	Ext.	Seeds are crushed with olive oil and applied to the boil.	7
Anchusa azurea Mill.	Boraginaceae	Hımhım Ivveyna	Roots	Ext.	Crushed root is applied to the boil.	24
Arctium minus (Hill) Bernh. (Syn. *Arctium minus subsp. pubens* (Bab.) Arènes)	Asteraceae	Bozpıtrak	Leaves	Ext.	Leaves are heated over fire and applied to the boil.	13, 21
Arctium tomentosum Miller var. *glabrum*	Asteraceae	Toptelli	Leaves	Ext.	Crushed leaves are applied to the boil.	13
Arnebia densiflora (Nordm.) Ledeb.	Boraginaceae	Ellik, Enlik, Eğnik	Roots	Ext.	Crushed roots are mixed with butter and applied to the boil.	25
Arum detruncatum C. A. Meyer var. *detruncatum*	Araceae	Yılan burçağı Yılan yastığı	Tubers, Leaves	Ext.	Fresh tubers and leaves are applied to the boil.	7
Arum elongatum Steven	Araceae	Kabargaç	Tubers, Leaves	Ext.	Poultice is applied to the boil.	20, 26

Arum italicum Mill.	Araceae	Pezük yaprağı	Leaves	Ext.	Fresh leaves are applied to the boil.	21
Arundo donax L.	Poaceae	Kargı, Kamış	Stems	Ext.	Stem is grated and sugar, egg white and some soap grated are added to obtain the ointment and it is applied to the boil.	27
Asteriscus spinosus (L.) Sch.Bip. (Syn. *Pallenis spinosa* (L.) Cass.)	Asteraceae	Nalçeken Dağ nergisi	Flowers	Ext.	The poultice prepared from fresh flowers is applied to the boil.	28
Astragalus ancistrocarpus Boiss. & Hausskn.	Fabaceae	Kuşkonmaz	Aerial parts	Ext.	Aerial part ashes are mixed with olive oil and applied to the boil.	29
Beta vulgaris L.	Amaranthaceae	Pezik	Leaves	Ext.	Fresh leaves are applied to the boil.	18
Brassica oleracea L. (Syn. *Brassica oleracea* L. var *capitata* DC.)	Brassicaceae	Kara lahana Kara kelem	Leaves	Ext.	-The leaf, which is softened by heating in the fire, is applied to the boil and kept for one night. -Fresh leaves are applied to mature and burst the boil.	9, 11, 21, 30, 31, 32
Buxus sempervirens L.	Buxaceae	Şimşir	Leaves	Ext.	Fresh leaves are applied to the boil.	7
Capparis spinosa L.	Capparaceae	Kıbbar, Kebere Kappari	Leaves	Ext.	Crushes leaves are applied to the boil.	33
Capsicum annuum L.	Solanaceae	Acı yeşil biber	Fruits	Ext.	It is cut in half and applied to the boil.	18
Cedrus libani A.Rich.	Pinaceae	Sedir	Tar	Ext.	The onion is cooked in embers and mixed with tar and applied to the boil.	34
Centaurea balsamita Lam.	Asteraceae	Kılıç otu	Leaves	Ext.	Crushed leaves are applied to the boil.	13
Centaurea iberica Trevir. ex Spreng.	Asteraceae	Deve dikeni, Belhok, Çakıldikeni, Deligöz dikeni	Leaves	Ext.	Crushed leaves are applied to the boil.	25
Centaurea pulchella Ledeb.	Asteraceae	Boğa dikeni	Aerial parts	Ext.	Crushed aerial parts are applied to the boil.	9
Centaurea solstitialis subsp. *solstitialis* L.	Asteraceae	Korugoz, Sarıdiken	Capitulums	Ext.	Crushed capitulums are applied to the boil.	35
Centaurea urvillei subsp. *stepposa* Wagenitz	Asteraceae	Çobankaldıran	Leaves	Ext.	Crushed leaves are applied to the boil.	35
Cerastium dubium (Bastard) O.Schwarz (Syn. *Cerastium anomalum* Waldst. & Kit.)	Caryophyllaceae	Cırcamuk	Aerial parts	Ext.	Aerial parts of the fresh plant is kept in olive oil overnight and applied to a boil.	7
Cerasus avium (L.) Moench (Syn. *Prunus avium* (L.) L.)	Rosaceae	Yabani kiraz	Leaves	Ext.	Fresh leaves are applied to the boil.	12
Chelidonium majus L.	Papaveraceae	Kırlangıç otu Temre otu	Latex	Ext.	Latex is applied to the boil.	7
Cichorium intybus L.	Asteraceae	Yabani hindiba Sütlüot, çıtlankuş	Aerial parts	Ext.	Aerial parts are crushed with green lentils and plum seeds and mixed with butter, then applied to the boil.	16
Clematis flammula L.	Ranunculaceae	Acı tefek	Leaves, Flowers	Ext.	Crushed leaves and flowers are applied to the boil.	26
Clematis orientalis L.	Ranunculaceae	Şeytan çubuğu Muşurbaz otu	Aerial parts	Ext.	Aerial parts are chopped finely and applied to the boil.	13, 32, 36
Colutea cilicica Boiss. & Balansa	Fabaceae	Patlangaç Patluk, Patlak	Fruity branches	Ext.	Decoction of fruity branches is applied to the boil.	7
Cornus mas L.	Cornaceae	Kızılcık, ergen	Leaves	Ext.	Leaves are used for boils externally.	26
Coronilla orientalis Miller var. *orientalis* (All.) Vitman	Fabaceae	Yonca	Flowers	Ext.	Crushed flowers are applied to the boil.	7
Cucurbita moschata Duchesne	Cucurbitaceae	Bal kabağı	Fruits	Ext.	Fruit poultice is applied to the boil.	16
Dactylorhiza euxina (Nevski) Czerep.	Orchidaceae	Sahlep	Tubers	Int.	The infusion is prepared	16
Dactylorhiza osmanica (Klinge) P.F.Hunt & Summerh.	Orchidaceae	Sahlep	Tubers	Int.	The infusion is prepared	16
Dactylorhiza umbrosa (Kar. & Kir.) Nevski	Orchidaceae	Sahlep	Tubers	Int.	The infusion is prepared	16
Dactylorhiza urvilleana (Steud.) H.Baumann & Künkele	Orchidaceae	Sahlep	Tubers	Int.	The infusion is prepared	16
Daphne oleoides subsp. *oleoides* Schreber	Thymeleaceae	Ezentene Develik otu Çıtlak	Aerial parts	Ext.	Crushed aerial part is boiled with milk and obtain poultice. This poultice is applied to the boil.	9

Dracunculus vulgaris Schott	Araceae	Yılan burçağı Yılan otu Yılan bıçağı	Leaves, Tubers	Ext.	- Leaves are heated over fire and applied to the boil. - Crushed tuber is applied to the boil.	7
Drimia maritima (L.) Stearn (Syn. *Urginea maritima* (L.) Baker)	Asparagaceae	Ada soğanı	Bulbs	Ext.	It is cooked in embers or some water and applied to the boil.	34
Ecballium elaterium (L.) A.Rich.	Cucurbitaceae	Deli bostan	Leaves	Ext.	Leaves are applied to the boil.	26, 37
Echinops spinosissimus subsp. *bithynicus* (Boiss.) Greuter *(Syn. Echinops viscosus* subsp. *bithynicus* (Boiss.) Rech. fil.)	Asteraceae	Çengel dikeni	Capitulums	Ext.	Warmed and crushed capitulums are applied to the boil.	35
Echium italicum L.	Boraginaceae	Sülük otu	Whole plant	Ext.	The whole plant is boiled in small pieces in water, crushed and applied to the boil.	20, 38
Elaeagnus angustifolia L.	Elaeagnaceae	İğde	Leaves	Ext.	The poultice obtained by crushing *Eleagnus* leaves and ash of *Salix* stem bark is applied to the boil.	20
Erica manipuliflora Salisb.	Ericaceae	Funda süpürge otu püren	Aerial parts	Ext.	Ointment prepared by olive oil is applied to the boil.	26
Erodium cicutarium (L.) L'Hér.	Geraniaceae	İnnelik	Aerial parts	Ext.	Crushed aerial parts are applied to the boil.	39
Eryngium billardierei F.Delaroche	Apiaceae	Gelenk, Boğa dikeni	Roots	Ext.	Crushed roots are applied to the boil.	13, 32
**Eryngium bithynicum* Boiss. (Endemic)	Apiaceae	Şeker dikeni	Aerial parts	Ext.	Aerial parts are boiled with wheat flour to obtaine poultice. Hot poultice is applied to the boil.	9, 19
Eryngium campestre L.	Apiaceae	Boğa dikeni	Flowers	Ext.	Crushed flowers are applied to the boil.	40
Erysimum pycnophyllum J.Gay (Syn. *Erysimum thyrsoideum* Boiss.)	Brassicaceae	Çekme otu	Aerial parts	Ext.	Aerial parts are boiled with wheat flour to obtain poultice and then it is applied to the boil.	40
Ficus carica L.	Moraceae	İncir	Latex, Fruits	Ext.	-Latex is applied to the boil. -Fresh fruit is applied to the boil.	12, 18, 20, 25
Filipendula ulmaria (L.) Maxim.	Rosaceae	Dağ reyhanı	Leaves, Flowers	Ext.	Dried leaves and flowers are powdered and applied to a boil.	41
Frangula alnus Mill.	Rhamnaceae	Banişotu	Stem barks and flowering branches	Ext.	Flowering branch and stem barks are boiled in water, Poultice is prepared by adding barley flour to the water and applied to the boil.	38
Fritillaria pinardii Boiss.	Liliaceae	Mor lale	Bulblets	Ext.	Cut the onion in half, add olive oil, heat it over a low fire and put it on the boil.	25
Galanthus fosteri Baker	Amaryllidaceae	Kardelen, Kar çiçeği	Bulbs	Ext.	Cut the onion in half and put it on the boil.	7
Glaucium grandiflorum Boiss. & A.Huet	Papaveraceae	Boynuzlu gelincik	Fruits	Ext.	Fresh fruits are crushed and applied to the boil.	7
Hedera helix L.	Araliaceae	Duvar sarmaşığı, Orman sarmaşığı	Leaves	Ext.	Fresh leaves are applied to the boil.	42, 43, 44
Hordeum vulgare L.	Poaceae	Arpa	Seeds	Ext.	Poultice prepared by boiling barley flour is applied to the boils.	9, 13
Hyacinthus orientalis L.	Asparagaceae	Sümbül	Tubers	Ext.	Tubers are applied to the boils.	22
Hylotelephium telephium (L.) H.Ohba (Syn. *Sedum telephium* L.)	Crassulaceae	Kalın kaymak bitkisi	Leaves	Ext.	The leaves are kept on a little fire. Then, when we remove the membrane and put it on the inflamed, pimpled or boiled area, it has the ability to dry the inflammation.	45

Hypericum perforatum L.	Hypericaceae	Kantaron, Yanık otu	Aerial parts	Ext.	Fresh or dried plant is applied to the boil.	46
Hypericum retusum Aucher ex Jaub. & Spach	Hypericaceae	Batof, Bantof, Aran	Leaves	Ext.	The leaves are boiled in water and the poultice is made by adding flour and applied to the boil.	29
Juglans regia L.	Juglandaceae	Ceviz	Fruits	Ext.	Crushed fresh fruits are applied to the boil.	13, 17, 31
Juniperus oxycedrus L.	Cupressaceae	Ardıç	Tar	Ext.	-Tar is applied to the boil - The tar, egg yolk, onion juice and soap grated are fried in a pan and the prepared ointment is applied to the boil.	11, 25
Lamium album L.	Lamiaceae	Ballıbaba Ghiopırçık	Leaves, Flowers	Ext.	It is applied to the boil.	47, 48
Lapsana communis subsp. *intermedia* (M.Bieb.) Hayek	Asteraceae	Tavşan salatası Yabani marul	Leaves	Ext.	The poultice prepared from fresh leaves is applied to the boil.	28
Laurus nobilis L.	Lauraceae	Defne	Fruits	Ext.	The oil obtained from the fruit is applied to the boil.	7
Lavandula stoechas subsp. *stoechas* L.	Lamiaceae	Lavanta	Leaves, Flowers	Int.	The infusion prepared from leaves and flowers is used internally to treat boils.	7
Lepidium sativum subsp. *sativum* L.	Brassicaceae	Tere	Leaves	Ext.	Fresh leaves are used externally to treat boils.	7
Linum usitatissimum L.	Linaceae	Zeyrek	Seeds	Ext.	-The poultice obtained by crushing and boiling the seeds is applied to the boil. - Seeds are crushed, sifted and mixed with yogurt and applied to the boil. - Seeds are crushed, boiled in milk and the resulting poultice is applied to the boil.	9, 11, 20, 21, 49
Liquidambar orientalis Mill.	Hamamelidaceae	Sığala, Günlük	Resin	Ext.	The resin is applied to the boil and kept for 1 night.	34
Lycopersicon esculentum Mill.	Solanaceae	Domates	Fruits	Ext.	The fruits are crushed and applied to the boil.	20, 50
Lysimachia punctata L.	Primulaceae	Horoz ibiği Sivri burun, Karga otu	Aerial parts	Ext.	Take a pinch of the powder obtained from the dried flowered aerial part and mix it with a tablespoon of olive oil. A dressing is made on the boil with a cotton for 1 week.	28
Malva neglecta Wallr.	Malvaceae	Ebegümeci Deve tabanı, Katır tırnağı	Aerial parts	Ext.	- Aerial parts are boiled with water and while it is warm, it is placed directly on the boil. - Aerial parts are crushed, boiled in milk and the poultice is applied to the boil.	9, 11, 17, 18, 20, 32, 40, 51
Malva nicaeensis All.	Malvaceae	Ebegümeci	Leaves	Ext.	The poultice prepared by boiling the leaves is applied to the boil.	52
Malva sylvestris L.	Malvaceae	Büyük ebegümeci	Leaves	Ext.	The poultice prepared from fresh leaves is applied to the boil to maturation.	12, 15, 53, 54, 55
Marrubium vulgare L.	Lamiaceae	Bozkulak, Boz ot Dağ çayı	Aerial parts	Ext.	The aerial parts are boiled and the poultice is applied to the boil.	7
Mirabilis jalapa L.	Nyctaginaceae	Akşam sefası, Akşam sabah çiçeği	Leaves	Ext.	Leaves are applied to the boil.	56, 57
Morus alba L.	Moraceae	Dut	Fruits	Ext.	Dried fruits pulp is applied to the boil.	32, 58
Nepeta nuda subsp. *albiflora* (Boiss.) Gams	Lamiaceae	Pisik otu, Kedi otu	Aerial parts	Ext.	Aerial parts of catnip are boiled and filtered, and the pulp is separated. A small amount of barley flour is added to this pulp and the dough is cooked very little over low heat and the dough is applied to the boil. After waiting one night, it is cleaned and this process is continued for 3 days.	27

Ocimum basilicum L.	Lamiaceae	Reyhan, Fesleğen	Leaves	Ext.	The infusion prepared from the leaves is used externally in the treatment of boils.	7
Olea europaea L.	Oleaceae	Zeytin	Fruit	Ext.	The root of the onion is cooked in embers, olive oil (obtained from the fruit) and soap are added and applied to the boil and left overnight.	34
Orchis mascula (L.) L.	Orchidaceae	Sahlep	Tubers	Int.	Drink the infusion.	16
Ornithogalum umbellatum L.	Liliaceae	Köpek soğanı	Tubers	Ext.	Cut the onion in half and put it on the boil.	59, 60
Paliurus spina-christi Mill.	Rhamnaceae	Karaçalı Öküz gözü	Leaves	Ext.	The poultice obtained by crushing the leaves is applied to the boil.	15, 51
**Papaver triniifolium* Boiss. (Endemic)	Papaveraceae	Kıllı öbük	Aerial parts	Ext.	The aerial parts are crushed and roasted with barley flour to make an ointment and apply it to a boil.	27
Pelargonium zonale (L.) L'Hér. ex Aiton	Geraniaceae	Sardunya	Leaves	Ext.	Fresh leaves are applied to the boil.	9
Petasites hybridus (L.) "G.Gaertn., B.Mey. & Scherb.	Asteraceae	Kabalak, Karakafes	Leaves	Ext.	Fresh leaves are applied to the boil.	12
Phaseolus vulgaris L.	Fabaceae	Fasulye Bakla, Pakla	Seeds	Ext.	Cut the seeds into two halves and applied to the boil.	61
Phlomis kurdica Rech.f.	Lamiaceae	Çay otu Gubel, Şalba	Leaves	Ext.	Fresh leaves are applied to the boil.	25
Phlomis lycia D.Don	Lamiaceae	Çalba, Kızıl çalba Tüylü çalba	Aerial parts	Ext.	Poultice prepared with flour from above ground is used externally in the treatment of boils.	62
Phlomis rigida Labill.	Lamiaceae	Çelbe, it otu	Aerial parts	Ext.	The poultice prepared from aerial part is applied to the boil to maturation.	29
Picea orientalis (L.) Peterm.	Pinaceae	Doğu ladini Sakız ağacı	Resin	Ext.	Resin is used for boils.	63
Pinus brutia Ten.	Pinaceae	Çam, Kızıl kabuk	Resin	Ext.	Resin is used for boils.	9, 61
Pinus nigra subsp. *pallasiana* (Lamb.) Holmboe	Pinaceae	Kara çam	Leaves Resin, Tar	Ext.	- The poultice obtained by boiling the leaves in water is applied on the boil. -Resin or tar is mixed with salt and applied to the boils.	11, 64
Pistacia palaestina Boiss.	Anacardiaceae	Sakızlak meneviş, çıtlık	Resin	Ext.	Resin is used for boils.	65
Plantago lanceolata L.	Plantaginaceae	Damarlı ot Damar otu, Sinir ot, Sinirli ot, Siğilli yaprak	Leaves	Ext.	The poultice prepared from fresh leaves is applied to the boil.	9, 11, 12, 15, 18, 36, 38, 42, 51, 55, 66
Plantago major L.	Plantaginaceae	Sinirli ot Bağ yaprağı Damarlı ot Kırk sinir otu	Leaves	Ext.	Fresh leaves are applied to the boil.	9, 18, 19, 21, 31, 42, 46, 67
Plantago major subsp. *major* L.	Plantaginaceae	Bağ yaprağı Sinirli ot, Siğil otu	Leaves	Ext.	Fresh leaves are applied to the boil.	11, 20, 32, 38, 54, 68, 69
Plantago major subsp. *intermedia* (Gilib.) Lange	Plantaginaceae	Katır tırnağı	Leaves	Ext.	Fresh leaves are applied to the boil.	11, 20, 32, 68, 69
Plantago media L.	Plantaginaceae	Sinir otu Sinirli ot Damar otu	Leaves	Ext.	- Poultice prepared from fresh leaves are applied to the boil. - The leaves are dipped in hot water and removed, then applied to the boil.	16, 23

Platanus orientalis L.	Platanaceae	Doğu çınarı	Leaves Stems and branch barks	Ext.	Purulent boils are washed with decoction and dressing.	44
Plumbago europaea L.	Plumbaginaceae	Serkele, Boya otu Mayasıl otu	Aerial parts	Ext.	Crushed fresh aerial part is applied to the boil.	7
Polygonum cognatum Meisn.	Polygonaceae	Madımak	Leaves	Ext.	Crushed fresh leaves are applied to the boil.	13, 32, 70
Potentilla reptans L.	Rosaceae	Zıbırğut	Leaves, Flowers	Ext.	Crushed fresh leaves and flowers are applied to the boil.	41
Primula acaulis subsp. *acaulis* (L.) L. (Syn. *Primula vulgaris* Huds.)	Primulaceae	Sapsız çuha çiçeği	Leaves	Ext.	Fresh leaves are applied to the boil.	44, 55
Ranunculus arvensis L.	Ranunculaceae	Düğün çiçeği Dövün otu	Aerial parts	Ext.	It is applied to the boil	59, 68
Ranunculus ficaria subsp. *ficariiformis* Rouy & Foucaud	Ranunculaceae	Katır nalı	Leaves	Ext.	Fresh leaves are applied to the boil.	43
Ranunculus illyricus L.	Ranunculaceae	wutsuvoyji	Aerial parts	Ext.	Crushed fresh leaves are applied to the boil (1 hour).	9
Ranunculus neapolitanus Ten.	Ranunculaceae	Sarı çiçek	Aerial parts	Ext.	Crushed aerial parts are applied to the boil	13, 42
Rhamnus lycioides subsp. *oleoides* (L.) Jahand. & Maire	Rhamnaceae	Kördiken	Leaves	Ext.	Poultice made from fresh leaves and barley flour is applied to the boil that do not burst	52
Rhamnus *oleoides* subsp. *graecus* (Boiss. & Reut.) Holmboe	Rhamnaceae	Kördiken	Leaves	Ext.	The leaves are mixed with barley flour and pounded into poultice. It is used as an anti-inflammatory agent by making a compress on boils.	71
Rosa canina L.	Rosaceae	Kuşburnu Köpek gülü	Thorn	Ext.	Used to drain the inflammation of inflamed boils	72
Rubus hirtus Waldst. & Kit.	Rosaceae	Böğürtlen	Leaves	Ext.	Fresh leaves are crushed and left on the boil for 15 minutes.	7
Rubus sanctus Schreb.	Rosaceae	Karamama, Böğürtlen	Leaves, Thorn	Ext.	Boils are bled by drawing with a thorn, and a leaf is placed on the boil and used as an anti-inflammatory.	12, 43
Rumex acetosella L.	Polygonaceae	Küçük labada Kuzu kulağı	Leaves	Ext.	Purulent boils are washed with decoction and dressing.	44, 73
Rumex angustifolius Campd.	Polygonaceae	Evelik, Yağlı pancar	Leaves	Ext.	The leaves are crushed and flour is added and the prepared poultice is applied to the boil.	20
Rumex crispus L.	Polygonaceae	Evelik	Fruits	Ext.	Poultice prepared from decoction of fruit and flour is applied to the boil.	74
Rumex patientia L.	Polygonaceae	Labada, İlabada	Leaves	Ext.	Poultice prepared from leaves is applied to the boil.	26, 55
Rumex pulcher L.	Polygonaceae	Labada, Kuzu kulağı	Leaves	Ext.	Poultice prepared from leaves is applied to the boil.	75
Rumex scutatus L.	Polygonaceae	Kuzu kulağı	Leaves	Ext.	Poultice prepared from leaves is applied to the boil.	51
Rumex tuberosus subsp. *horizontalis* (K.Koch) Rech.f.	Polygonaceae	Kuzu kulağı	Leaves	Ext.	Poultice prepared from leaves is applied to the boil.	51
Ruscus hypoglossum L.	Liliaceae	Tavşan cücüğü Tavşan göbeği Tavşan elması	Fruits	Ext.	Decoction of fruit is applied to the boil.	66
**Salvia dichroantha* Stapf (Endemic)	Lamiaceae	Adaçayı	Leaves	Ext.	Infusion is applied to the boil externally.	7
Salvia multicaulis Vahl	Lamiaceae	Baravine, ikoro bizzeyn	Aerial parts	Ext.	Decoction of aerial part is applied to the boil.	24
Salvia virgata Jacq.	Lamiaceae	Yağlısomra	Leaves	Ext.	The leaves are applied to the boil.	76
Sambucus ebulus L.	Adoxaceae	Mürver, ayı otu	Leaves Fresh shoots	Ext.	The poultice obtained by pounding from leaves and fresh shoots is applied to the boil.	26, 66
Sambucus nigra L.	Adoxaceae	Mürver, kovoksülo, liver, lor, sultan	Fruits Leaves Fresh shoots	Int. Ext.	-Ripe fruits are used in treatment by eating in cases such as wounds or boils in the hand (Internally) - The poultice obtained by pounding from leaves and fresh shoots is applied to the boil.	26, 32, 63

Scrophularia libanotica Boiss.	Scrophulariaceae	Kaya çekemi	Aerial parts	Ext.	The plant is beaten with garlic and onion sprouts, and the resulting mash mixture is applied externally.	40
Smilax excelsa L.	Liliaceae	Öz dikeni Gıcır dikeni	Leaves	Ext.	Fresh leaves are applied to the boil.	42
Solanum americanum Mill.	Solanaceae	Köpek sirkeni Göğündürme	Fruits	Ext.	The fruits are crushed and crumbled, applied to the inflamed area and waited for 8-10 hours. Can be repeated every day until the inflammation removes	6
Solanum tuberosum L.	Solanaceae	Patates	Tubers	Ext.	Boiled and crushed tubers are applied to the boil.	7
Syringa vulgaris L.	Oleaceae	Leylak, Elguvan	Leaves	Ext.	Fresh leaves are applied to the boil.	46
Tanacetum balsamita L.	Asteraceae	Bağa yaprağı Kılıç otu	Leaves	Ext.	Fresh leaves are applied to the boil.	32
Teucrium polium L.	Lamiaceae	Mayasıl otu	Aerial parts	Ext.	Boiled aerial parts are applied to the boil.	14
Tribulus terrestris L.	Zygophyllaceae	Çoban çöküren Demir dikeni	Aerial parts	Int., Ext.	Its seeds are prepared as decoction and infusion and drunk. Thorn is burned, powder is mixed with butter and rubbed, the inflammation removes.	77
Trifolium medium L.	Fabaceae	Üçgül, Tırfıl	Aerial parts	Ext.	Crushed aerial parts are applied to the boil.	57
Trifolium rubens L.	Fabaceae	Üçgül	Aerial parts	Ext.	Crushed aerial parts are applied to the boil.	57
Trigonella foenum-graecum L.	Fabaceae	Çemen otu, boyotu	Seeds	Ext.	Poultice prepared from seeds is applied to the boil.	55
Triticum aestivum L.	Poaceae	Buğday	Seeds	Ext.	Wheat flour and Grape molasses are mixed and applied to the boil and left overnight.	34
Tussilago farfara L.	Asteraceae	Bozot Kabarcık yaprağı	Leaves	Ext.	Fresh leaves are applied to the boil.	20, 55
Ulmus canescens Melville (Syn. *Ulmus minor* subsp. *canescens* (Melville) Browicz & Ziel.)	Ulmaceae	Kara ağaç	Roots	Ext.	After the fresh, thin roots are cut into small pieces, it is boiled in milk and filtered and the poultice prepared by adding wheat into milk is used externally in the treatment of boils.	78
Ulmus minor Mill. (Syn. *Ulmus carpinifolia* Gled.)	Ulmaceae	Kara ağaç	Root barks	Ext.	Crushed root barks are mixed with *Malva* sp. aerial part and the poultice is prepared and it is applied to the boil.	32
Ulmus glabra Huds.	Ulmaceae	Kara ağaç	Stem barks	Ext.	Stem barks are boiled in water and applied to the boil.	38
Urtica dioica L.	Urticaceae	Cızlağan	Aerial parts	Ext.	Crushed fresh aerial parts are applied to the boil.	9, 57
Urtica urens L.	Urticaceae	Isırgan	Aerial parts	Int.	Decoction of aerial part is applied to the boils.	7
Verbascum cheiranthifolium Boiss.	Scrophulariaceae	Bozot, yalangı, Kurt kulağı, Sigil otu	Aerial parts	Ext.	It is applied to the boils.	79
Veronica officinalis L.	Scrophulariaceae	Çıban otu Yavşan otu	Leaves	Ext.	Poultice prepared from leaves is applied to the boils.	55
Vicia faba L.	Fabaceae	Kara fasulye	Leaves	Ext.	Fresh leaves are applied to the boil after heated over fire	11
Vigna unguiculata (L.) Walp.	Fabaceae	Börülce	Leaves	Ext.	Leaves are crushed and applied to the boil. Wait overnight until it heals.	34
Viola gracilis Sibth. & Sm.	Violaceae	Hercai menekşe	Flowers	Ext.	After the boiled flowers are crushed and pulped, they are spread on the wound and boil.	76
Viola tricolor L.	Violaceae	Menekşe	Aerial parts	Ext.	The infusion prepared from the aerial part is applied externally to the boil.	7
Vitis vinifera L.	Vitaceae	Üzüm asma, tefek	Fruits	Ext.	- The molasses obtained from the fruit is mixed with flour and applied to boil until it heals and left overnight. - Fresh or dried fruits are crushed and applied to the boil.	9, 26, 57
Ziziphora tenuior L.	Lamiaceae	Nane kekiği Mor kekik	Aerial parts	Ext.	The infusion prepared from fresh or dried herb is used externally for dressing and cleaning boils, burns or wounds	28

Very common to use *Plantago*, *Allium*, *Malva, Brassica* genera.

Although the external use of herbs is common in the treatment of boils, *Achillea crithmifolia*, *Alchemilla minusculiflora*, *Dactylorhiza euxina*, *Dactylorhiza osmanica*, *Dactylorhiza umbrosa*, *Dactylorhiza urvilleana*, *Lavandula stoechas* subsp. *stoechas* , *Orchis mascula* , *Sambucus nigra*, *Tribulus terrestris*, *Urtica urens* taxa are used internally.

In clinical treatment, antimicrobial medicines are used for boils. When the biological activity studies in the literature of the plants used for boils in traditional treatment were examined, it is thought that their healing effects are due to their analgesic, antioxidant, anti-inflammatory, antimicrobial activities of phytochemical compounds such as alkaloid, tannin, saponin, phenolic acid, flavonoid, flavonol, proanthocyanidin, anthocyanin.

When we look at the biological activities of the genera commonly used in treatment;

Allium cepa and *Allium sativum* essential oils were found to have significant antimicrobial activities on *Staphylococcus aureus, Salmomella enteritidis* bacteria *and Aspergillus niger, Penicillium cyclopium* and *Fusarium oxysporum* fungi species[80]. These essential oils also have antioxidant and anti-inflammatory activities[81].

Ethanol extract of *Malva neglecta* flowers showed antibacterial activity on *Bacillus anthracis, Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa* species[82]. In addition, *M. neglecta* also showed antibacterial activity on antibiotic resistant *Staphylococcus aureus* species[83].

In a study investigating the effects of *M. neglecta* aqueous, ethanol and chloroform extracts on bacterial and fungal contaminants causing wound infection, all extracts were found to be effective on *Staphylococcus aureus, Pseudomonas aeruginosa and Proteus vulgaris,* which cause problems with multiple resistant wound infections. It was also found that ethanol extracts showed higher antibacterial activity than others[84].

Aqueous alcohol extract of *Malva sylvestris* leaves showed topical anti-inflammatory activity. Malvidin-3 glycoside was found to be the major compound responsible for this effect[85].

P. lanceolata and M. neglecta species showed high oxygen radical absorbance capacity and total reduction capacity. It has been determined that the major compounds of hydrophilic extracts are phenolic compounds and antioxidant activity correlates with the concentrations of these compounds[86]. In addition, *P. lanceolata* plant has anti-inflammatory activity and accelerating effect on wound healing[87,88].

CONCLUSION

The antibacterial activities of the plants determined by the researches in the literature make their use in traditional boils treatment meaningful. The presence of resistant bacteria and the gradual increase of multi-drug resistant bacteria may limit the treatment options in the clinic and require new drug searches.

We hope that the plants used in the treatment of boils will be researched for the compounds that make them effective in the treatment and they will contribute to the research and development of new drugs.

REFERENCES

1. Gül Ü. Common Bacterial Infections of the Skin. *Ankara Medical Journal*. 2016; 16(1): 98-114
2. https://www.hakanbuzoglu.com/images/follikulit/follik%C3%BClit_kil_koku_iltihabi.png (Date of Access: 01.01.2021).
3. Karaoğlan İ. Deri ve Yumuşak Doku İnfeksiyonlarının Sınıflandırılması ve Etyolojisi. *Yoğun Bakım Dergisi.* 2012; 10(3):109-119
4. Apaydın FE. Deri ve Yumuşak Doku Enfeksiyonları*, The Journal of Turkish Family Physician.* 1998; 2(1): 8-16
5. Baytop T. *Türkiye'de Bitkilerle Tedavi (Geçmişte ve Bugün).* 2. Basım. İstanbul: Nobel Tıp Kitabevleri;1984
6. Kıncal S. Ula (Muğla) ilçesinin etnobotaniği (Tez). Muğla: Muğla Sıtkı Koçman Üniv. 2018.
7. Tuzlacı E. *Türkiye Bitkileri Gelenekel İlaç Rehberi*. 1. Basım. İstanbul: İstanbul Tıp Kitapevi; 2016
8. Demirci S, Özhatay N. An ethnobotanical study in Kahramanmaraş (Turkey); wild plants used for medicinal purpose in Andırın, Kahramanmaraş. *Turkish Journal Of Pharmaceutical Sciences.* 2012; 9(1): 75-92.
9. Sezik E, Yeşilada E, Honda G, Takaishi Y, Takeda Y, Tanaka T. Traditional medicine in Turkey X. Folk medicine in central Anatolia. *Journal of ethnopharmacology.* 2001; 75(2-3): 95-115. https://doi.org/10.1016/S0378-8741(00)00399-8
10. Günbatan T. Çamlıdere (Ankara) halk ilaçları (Tez). Ankara: Gazi Üniv. 2011.
11. Fujita T, Sezik E, Tabata M, Yesilada E, Honda G, Takeda Y, Tanaka T, Takaishi Y. Traditional medicine in

Turkey VII. Folk medicine in middle and west Black Sea regions. *Economic botany.* 1995; 49(4): 406. https://doi.org/10.1007/BF02863092
12. Genç GE, Özhatay N. An ethnobotanical study in Çatalca (European part of Istanbul) II. *Turkish Journal of Pharmaceutical Sciences*. 2006; 3(2): 73-89.
13. Altundağ E, Öztürk M. Ethnomedicinal studies on the plant resources of east Anatolia, Turkey. *Procedia-Social and Behavioral Sciences*. 2011; 19:756-777. https://doi.org/10.1016/j.sbspro.2011.05.195
14. Tuzlacı E, İşbilen DA, Bulut G. Turkish folk medicinal plants, VIII: Lalapaşa (Edirne). *Marmara Pharmaceutical Journal.* 2010; 14(1): 47-52.
15. Ugulu I. Traditional ethnobotanical knowledge about medicinal plants used for external therapies in Alasehir, Turkey. *International Journal of Medicinal and Aromatic Plants.* 2011; 1(2): 101-106.
16. Korkmaz M, Karakurt E. An ethnobotanical ınvestigation to determine plants used as folk medicine in Kelkit (Gümüşhane/Turkey) district. *Biological Diversity and Conservation.* 2015; 8(3): 290-303.
17. Özgökçe F, Özçelik H. Ethnobotanical aspects of some taxa in East Anatolia, Turkey. *Economic Botany.* 2004; 58(4): 697. https://doi.org/10.1663/0013-0001(2004)058[0697:EAOSTI]2.0.CO;2
18. Gürbüz İ, Özkan AMG, Akaydın G, Salihoğlu E, Günbatan T, Demirci F, Yeşilada E. Folk medicine in Düzce Province (Turkey). *Turkish Journal of Botany.* 2019; 43(6): 769-784.
19. Savran A, Bağcı Y, Kargıoğlu M. Gemerek (Sivas) ve çevresindeki bazı bitkilerin yerel adları ve etnobotanik özellikleri. *Afyon Kocatepe Üniversitesi Fen Ve Mühendislik Bilimleri Dergisi.* 2009; 8(1): 313-321.
20. Yeşilada E, Honda G, Sezik E, Tabata M, Fujita T, Tanaka T, Takeda Y, Takaishi Y. Traditional medicine in Turkey. V. Folk medicine in the inner Taurus Mountains. *Journal of ethnopharmacology.* 1995; 46(3): 133-152. https://doi.org/10.1016/0378-8741(95)01241-5
21. Yeşilada E, Sezik E, Honda G, Takaishi Y, Takeda Y, Tanaka T. Traditional medicine in Turkey IX: Folk medicine in north-west Anatolia. *Journal of Ethnopharmacology.* 1999; 64(3): 195-210. https://doi.org/10.1016/S0378-8741(98)00133-0
22. Metin A. Mut ve çevresinde (Mersin) yetişen bitkilerin etnobotanik özellikleri (Tez). Konya: Selçuk Üniv. 2009.
23. Türkan Ş, Malyer H, Özaydın S, Tümen G. Ordu ili ve çevresinde yetişen bazı bitkilerin etnobotanik özellikleri. *Süleyman Demirel Üniversitesi Fen Bilimleri Enstitüsü Dergisi.* 2006; 10(2).
24. Akgül A. Midyat (Mardin) civarında etnobotanik (Tez). İzmir: Ege Üniv. 2008.
25. Doğan A. Pertek (Tunceli) yöresinde etnobotanik araştırmalar (Tez). İstanbul: Marmara Üniv. 2014.
26. Bulut Y. Manavgat (Antalya) yöresinin faydalı bitkileri (Tez). Isparta: Süleyman Demirel Üniv. 2006.
27. Güneş S. Karaisalı (Adana) ve köylerinde halkın kullandığı doğal bitkilerin etnobotanik yönden araştırılması (Tez). Niğde: Niğde Üniv. 2010.
28. Sargın SA. Alaşehir ve çevresinde (Manisa) tarımsal biyoçeşitlilik ve etnobotanik araştırmaları (Tez). Balıkesir: Balıkesir Üniv. 2013.
29. Balos MM, Akan H. Zeytinbahçe-Akarçay (Birecik, Şanlıurfa) arasında kalan bölgenin etnobotanik özellikleri. *Selçuk Üniversitesi Fen Fakültesi Fen Dergisi.* 2007; 2(29): 155-171.
30. Karcı E. Bafra (Samsun) halk ilaçları (Tez). Ankara: Gazi Üniv. 2013.
31. Tabata M, Sezik E, Honda G, Yeşilada E, Fukui H, Goto, K, Ikeshiro Y. Traditional medicine in Turkey III. Folk medicine in East Anatolia, van and Bitlis provinces. *International Journal of Pharmacognosy.* 1994; 32(1): 3-12. https://doi.org/10.3109/13880209409082966
32. Sezik E, Yeşilada, E, Tabata M, Honda G, Takaishi Y, Fujita, T, Tanaka T, Takeda Y. Traditional medicine in Turkey viii. folk medicine in east Anatolia; Erzurum, Erzíncan, Ağri, Kars, Iğdir provinces. *Economic botany.* 1997; 51(3): 195-211. https://doi.org/10.1007/BF02862090
33. Güzelşemme M. 2014, Antakya'da kullanılan tıbbi bitkiler ile yabani gıda bitkileri (Tez). Hatay: Mustafa Kemal Üniv. 2014.
34. Uysal G. Köyceğiz (Muğla) ilçesinin etnobotaniği (Tez). Muğla: Muğla Üniv. 2008.
35. Bulut G, Haznedaroğlu MZ, Doğan A, Koyu H, Tuzlacı E. An ethnobotanical study of medicinal plants in Acipayam (Denizli-Turkey). *Journal of Herbal Medicine*. 2017; 10: 64-81. https://doi.org/10.1016/j.hermed.2017.08.001
36. Tuzlacı E, Şenkardeş İ. Turkish folk medicinal plants, X: Ürgüp (Nevşehir). *Marmara Pharmaceutical Journal.* 2011; 15(2): 58-68.
37. Bulut G, Tuzlacı E. Folk Medicinal Plants of Bayramiç (Çanakkale-Turkey). *İstanbul Üniversitesi Eczacılık Fakültesi Dergisi.* 2009; 40: 87-99.
38. Han Mİ, Bulut G. The folk-medicinal plants of Kadisehri (Yozgat-Turkey). *Acta Societatis Botanicorum Poloniae.* 2015; 84(2). DOI: 10.5586/asbp.2015.021
39. Furkan MK. Adıyaman ilinde yetişen bazı bitkilerin etnobotanik özellikleri (Tez). Adıyaman: Adıyaman Üniv. 2016.

40. Özkan AM. Pınarbaşı (Kayseri) florası üzerinde farmasötik botanik yönünden araştırmalar (Tez). Ankara: Ankara Üniv. 2002.
41. Behçet L, Arık M. An ethnobotanical investigation in east Anatolia (Turkey). *Turkish Journal of Nature and Science.* 2013; 2: 1-15.
42. Tuzlacı E, Tolon E. Turkish folk medicinal plants, part III: Şile (İstanbul). *Fitoterapia.* 2000; 71(6): 673-685. https://doi.org/10.1016/S0367-326X(00)00234-3
43. Yeşilyurt EB, Şimşek I, Akaydın G, Yeşilada E. An ethnobotanical survey in selected districts of the Black Sea region (Turkey). *Turkish Journal of Botany.* 2017; 41(1): 47-62.
44. Yılmaz YU. Beşikdüzü yöresinde gıda amaçlı kullanılan bitkiler (Tez). Trabzon: Karadeniz Teknik Üniv. 2011.
45. Kayabaşı NP. Manyas ve köylerinde etnobotanik bir çalışma (Tez). Balıkesir: Balıkesir Üniv. 2011.
46. Aktan T. Yenişehir (Bursa) Köylerinin Etnobotanik Özellikleri (Tez). Manisa: Celal Bayar Üniv. 2011.
47. Akan H., Bakır Sade Y. Kahta (Adıyaman) merkezi ve Narince köyünün etnobotanik açıdan araştırılması. *Bitlis Eren Üniversitesi Fen Bilimleri Dergisi*. 2015;4(2). DOI: 10.17798/beufen.47724
48. Sade TB. Kahta (Adıyaman) Merkezi Ve Narince Köyünün Etnobotanik Açıdan Araştırılması (Tez). Şanlıurfa: Harran Üniv. 2014.
49. Ezer N, Avcı K. Çerkeş Çankırı Yöresinde Kullanılan Halk İlaçları. *Hacettepe Üniversitesi Eczacılık Fakültesi Dergisi.* 2004; (2): 66-80.
50. Onar S. 2006. Bandırma (A1(A), Balıkesir) ve çevresinin etnobotaniği (Tez). Çanakkale: Çanakkale Onsekiz Mart Üniv. 2006.
51. Çakılcıoğlu U, Türkoğlu İ, Kürşat M. Harput (Elazığ) Ve Çevresinin Etnobotanik Özellikleri. *Fırat Üniversitesi Doğu Araştırmaları Dergisi.* 2007; 5(2): 22-28.
52. Eşen B. Aydınlar Köyü ve çevresinin (Erdemli/Mersin) etnobotanik özellikleri (Tez). Konya: Selçuk Üniv. 2008.
53. Bağcı Y, Savran A, Dural H. Pozantı (Adana) ve çevresindeki bazı bitkilerin yerel adları ve etnobotanik özellikleri. *Selçuk Üniversitesi Fen Fakültesi Fen Dergisi.* 2006; 2(27): 77-82.
54. Kültür Ş. Medicinal plants used in Kırklareli province (Turkey). *Journal of Ethnopharmacology.* 2007; 111(2): 341-364. DOI: 10.1016/j.jep.2006.11.035
55. Ugulu I, Baslar S, Yorek N, Dogan Y. The investigation and quantitative ethnobotanical evaluation of medicinal plants used around Izmir province, Turkey. *Journal of Medicinal plants research.* 2009; 3(5): 345-367. https://doi.org/10.5897/JMPR.9001216
56. Polat R. Havran ve Burhaniye (Balıkesir) çevresinde tarımsal biyoçeşitlilik ve etnobotanik araştırmaları (Tez). Balıkesir: Balıkesir Üniv. 2010.
57. Sarı AO, Oğuz B, Bilgiç A, Tort N, Güvensen A, Şenol SG. Ege ve Güney Marmara bölgelerinde halk ilacı olarak kullanılan bitkiler. *Anadolu Ege Tarımsal Araştırma Enstitüsü Dergisi.* 2010; 20(2): 1-21.
58. Kolaç T. Konak (Malatya) yöresi halk ilaçları (Tez). Malatya: İnönü Üniv. 2018
59. Deniz L, Serteser A, Kargıoğlu M. Uşak Üniversitesi ve yakın çevresindeki bazı bitkilerin mahalli adları ve etnobotanik özellikleri. *Afyon Kocatepe Üniversitesi Fen Ve Mühendislik Bilimleri Dergisi*. 2010; 10(1); 57-72.
60. Özdemir E, Alpınar K. An ethnobotanical survey of medicinal plants in western part of central Taurus Mountains: Aladaglar (Nigde–Turkey). *Journal of Ethnopharmacology.* 2015; 166: 53-65. DOI: 10.1016/j.jep.2015.02.052
61. Güneş S, Savran A, Paksoy MY, Koşar M, Çakılcıoğlu U. Ethnopharmacological survey of medicinal plants in Karaisalı and its surrounding (Adana-Turkey). *Journal of herbal medicine.* 2017; 8: 68-75.
62. Gürdal B, Kültür Ş. An ethnobotanical study of medicinal plants in Marmaris (Muğla, Turkey). *Journal of Ethnopharmacology.* 2013; 146(1): 113-126. DOI:10.1016/j.jep.2012.12.012
63. Kural K. Trabzon çevresinde yayılış gösteren faydalı bitkiler üzerinde ekonomik botanik yönünden araştırmalar (Tez). İstanbul: İstanbul Üniv. 2012.
64. Alkaç SA. Alaçam dağları (Balıkesir) Bigadiç ilçesi bölümündeki ekonomik önemi olan bazı bitkiler ve etnobotanik özellikleri (Tez). Balıkesir: Balıkesir Üniv. 2013.
65. Yıldırım İH. Alanya ve Gazipaşa (Antalya)' da halk tarafından kullanılan bazı doğal bitkilerin etnobotanik özellikleri (Tez). Afyonkarahisar: Afyon Kocatepe Üniv. 2015.
66. Tuzlacı E, Aymaz PE. Turkish folk medicinal plants, part IV: Gönen (Balıkesir). Fitoterapia 2001; 72(4): 323-343. https://doi.org/10.1016/S0367-326X(00)00277-X
67. Yüzbaşıoğlu E. Reşadiye (A6, Tokat, Türkiye) Ve Çevresinin Etnobotaniği (Tez). Çanakkale: Çanakkale Onsekiz Mart Üniv. 2010.
68. Honda G, Yeşilada E, Tabata M, Sezik E, Fujita T, Takeda Y, Takaishi Y, Tanaka T. Traditional medicine in Turkey VI. Folk medicine in West Anatolia: Afyon, Kütahya, Denizli, Muğla, Aydin provinces. *Journal of*

Ethnopharmacology. 1996; 53(2): 75-87. DOI:10.1016/s0378-8741(96)01426-2
69. Özgen U, Kaya Y, Houghton P. Folk medicines in the villages of Ilıca District (Erzurum, Turkey). *Turkish Journal of Biology.* 2012; 36(1): 93-106.
70. Oğuz F, Tepe I. Yüksekova (Hakkâri) Yöresinde Halk Tababetinde Kullanılan Bitkiler ve Kullanım Alanları. *Turkish Journal of Weed Science.* 2017; 20(2): 28-37.
71. Saday H. Güzeloluk Köyü ve Çevresinin (Erdemli/Mersin) Etnobotanik Özellikleri (Tez). Konya: Selçuk Üniv. 2009.
72. Koçyiğit M, Özhatay N. Wild plants used as medicinal purpose in Yalova (Northwest Turkey). *Turkish Journal of Pharmaceutical Sciences.* 2006; 3(2): 91-103.
73. Güler B, Manav E, Uğurlu E. Medicinal plants used by traditional healers in Bozüyük (Bilecik–Turkey). *Journal of Ethnopharmacology.* 2015; 173: 39-47. https://doi.org/10.1016/j.jep.2015.07.007
74. Altundağ E., 2009, Iğdır ilinin (Doğu Anadolu Bölgesi) doğal bitkilerinin halk tarafından kullanımı (Tez). İstanbul: İstanbul Üniv. 2009.
75. Öztürk M. Nizip bölgesinin (Aksaray) florası ve etnobotanik özellikleri (Tez). Konya: Selçuk Üniv. 2006.
76. Kızılarslan Ç, Özhatay N. Wild plants used as medicinal purpose in the south part of İzmit (northwest Turkey). *Turkish Journal Of Pharmaceutical Sciences*. 2012; 9: 199-218.
77. Oral DÇ. Konya İlinde Kullanılan Halk İlaçları Üzerinde Etnobotanik Araştırmalar (Tez). Ankara: Gazi Üniv. 2007.
78. Şenkardeş İ. Nevşehir' in güney ilçelerinde (Acıgöl, Derinkuyu, Gülşehir, Nevşehir-Merkez, Ürgüp) etnobotanik araştırmalar (Tez). İstanbul: Marmara Üniv. 2014.
79. Karagöz FK. Suşehri (Sivas) bölgesinin etnobotanik açıdan değerlendirilmesi (Tez). Afyonkarahisar: Afyon Kocatepe Üniv. 2013.
80. Benkeblia N. Antimicrobial activity of essential oil extracts of various onions (*Allium cepa*) and garlic (*Allium sativum). LWT-food science and technology*. 2004; 37(2): 263-268. http://doi.org/10.1016/j.lwt.2003.09.001
81. Wilson EA, Demmig-Adams B. Antioxidant, anti-inflammatory, and antimicrobial properties of garlic and onions. *Nutrition & food science.* 2007; 3: 178-183 DOI 10.1108/00346650710749071
82. Jafari-Sales A, Jafari B, Sayyahi J and Zohoori-Bonab T. Evaluation of antibacterial activity of ethanolic extract of *Malva neglecta* and Althaea officinalis L. on antibiotic-resistant strains of Staphylococcus aureus. *Journal of Biology and Today's World.* 2015; 4 (2): 58-62.
83. Al-Snafi AE. Medical benefit of *Malva neglecta*-A review. *IOSR Journal of Pharmacy.* 2019; 9(6): 60-67.
84. Zare P, Mahmoudi R, Shadfar S, Ehsani A, Afrazeh Y, Saeedan, Niyazpour F, Pourmand BS. Efficacy of chloroform, ethanol and water extracts of medicinal plants, *Malva sylvestris* and *Malva neglecta* on some bacterial and fungal contaminants of wound infections. *Journal of Medicinal Plants Research.* 2012; 6(29): 4550-4552.
85. Prudente AS, Loddi AM, Duarte MR, Santos AR., Pochapski M T., Pizzolatti M G, Hayashi SS, Campos FR, Pontarolo R, Santos FA, Cabrini DA, Otuki MF. Pre-clinical anti-inflammatory aspects of a cuisine and medicinal millennial herb: *Malva sylvestris* L. *Food and chemical toxicology.* 2013; 58: 324-331.
86. Dalar A, Türker M, Konczak I. Antioxidant capacity and phenolic constituents of *Malva neglecta* Wallr. and Plantago lanceolata L. from Eastern Anatolia Region of Turkey. *Journal of Herbal Medicine.* 2012; 2(2): 42-51.
87. Rad NM, Shafie F, Chaghervand MM, Kashfi S, Rashidipour M, Chehelcheraghi F, Mozaffarpur SA, Rasoulian B. The Wound Healing Effect of Plantago Major Leaf Extract in a Rat Model: An Experimental Confirmation of a Traditional Belief in Persian Medicine. *Herbal Medicines Journal.* 2018; 3(1): 26-30.
88. Vigo E, Cepeda A, Gualillo O, Perez-Fernandez R. In-vitro anti-inflammatory activity of *Pinus sylvestris* and *Plantago lanceolata* extracts: effect on inducible NOS, COX-1, COX-2 and their products in J774A. 1 murine macrophages. *Journal of pharmacy and pharmacology.* 2005; 57(3): 383-391.

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CASE REPORT

Treatment of Medical Therapy-Resistant Vestibular Migraine with Cranial Osteopathy: A Case Report

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Abstract
Vestibular migraine is a variant of migraine with episodic vestibular symptoms. Diagnostic criteria were determined in 2012 and the term vestibular migraine was used. Lifetime prevalence in adults is calculated as 1%. The time between the onset of migraine and the onset of vestibular attacks varies among patients. In many patients, migrainous headaches begin before vestibular attacks. Sometimes vestibular attacks can begin years before migraine headaches occur. Vestibular symptoms and attack durations may vary between patients and in different episodes of the same patient. Today, drugs used in the treatment of migraine are generally used in the treatment of vestibular migraine. However, these drugs can sometimes be ineffective or provide short-term improvement. This situation requires -especially for these patients- a treatment scheme that includes different type of holistic medicine approach. In this case report, a vestibular migraine patient who was resistant to medical migraine treatment and was treated with osteopathic treatment method will be discussed.
Keywords: Migraine, Vestibular migraine, Migrainous headache, Osteopathy, Osteopathic treatment, Osteopathic therapy

INTRODUCTION

Today, the relationship between migraine and vertigo has been clearly defined. For the classification of vestibular diseases, the Barany Society Diagnostic criteria for vestibular migraine (VM) and probable vestibular migraine (PVM) have been established [1]. Vestibular migraine prevalence has been reported in various publications as 4.2-29.3% in otolaryngology clinics and 9-11.9% in headache clinics. In elderly patients, especially in postmenopausal women, it has been shown that typical migraine attacks turn into isolated dizziness or vertigo attacks. Vestibular migraine can develop at any age. Average age of onset in adults is reported as 46 years [2]. Rotational or nonrotational vertigo in vestibular migraine can be seen with spontaneous or positional changes. In one study, spontaneous rotatory vertigo was found in 67% and positional vertigo was found in 24%. In vestibular tests, there is no pathognomonic finding for vestibular migraine, but central vertigo must be distinguished. The generally accepted mechanism for migraine is that activation and sensitization of the trigemini-vascular system (TVS) that causes headache [3].

CASE

A 52-year-old female patient had complaints of vertigo attacks that recurred 3-4 times a month for a year. There had been an increase in vertigo in the last 2 months. The complaint of vertigo had been increasing with movements. Recently, there was a throbbing headache that involved the half of the head, accompanied by photophobia and phonophobia that lasts for 3 hours. The patient was known to have hypothyroidism and diabetes, as well as severe migraine. Because of these complaints, she was repeatedly evaluated in ear-nose-throat and neurology clinics, no pathology was found in the examination and laboratory findings, and treatment was started with

levotroxin, metformin hydrochloride, betahistine dihydrochloride and nonsteroidal anti-inflammatory drugs. Despite the long-term treatment, the patient whose complaints continued applied to our clinic again. Cranial MR, MR venography, carotid-vertebral doppler ultrasonography, routine biochemistry and blood analysis findings were normal (Figure 1).

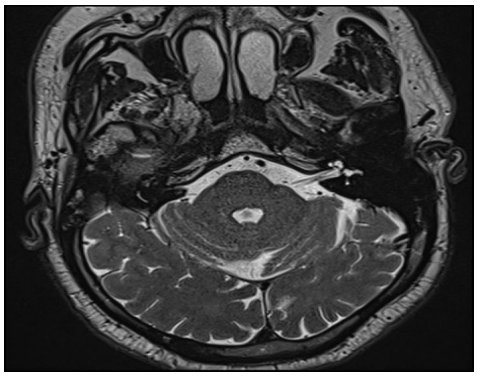

Figure 1. Cranial MR

There was no hearing problem in the audiological examinations of the patient during the attack. Triptans and Selective Serotonin Reuptake Inhibitors (SSRIs) and vestibular rehabilitation treatments were administered to the patient. Despite all these treatments, the patient was referred to an osteopath physician for osteopathic evaluation, since her complaints did not regress. At osteopathic examination (Figure 2) revealed left side bending and rotation dysfunction, defined as physiological dysfunction of the sphenobazillary joint (Figure 3) [4].

Figure 2. Osteopathic examination

The detected dysfunction was manipulated by using the indirect technique (the method of treating the dysfunction by further increasing the dysfunction on the dysfunctional side) [4]. No dysfunction was detected in other cranial osteopathic examinations. The patient was advised to come to her second session a week later and was sent home. The patient stated that her complaints completely disappeared after a week and she did not need a second session; so did not come to the treatment. Communication with the patient continued in the first, third, sixth, ninth and twelfth months. The follow-up was terminated considering that the attacks of the patient, whose complaints disappeared after the osteopathy treatment and did not have any complaints during the 1-year follow-up, were taken under control.

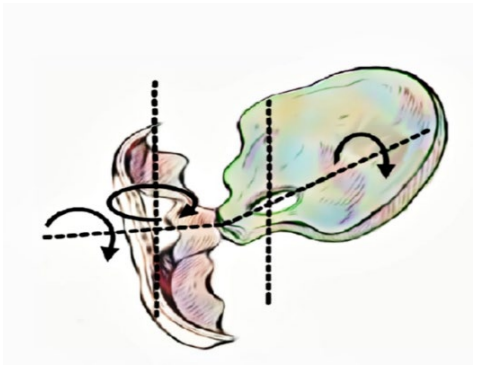

Figure 3. Left side bending and rotation dysfunction

DISCUSSION

Vestibular migraine can occur at any age. It is stated that it is 1.5 to 5 times more common in women than in men. In most patients, migraine occurs earlier. VM is more common in patients with migraine without aura compared to those with aura [5]. Dizziness attack associated with migraine is often manifests itself with; imbalance; movement intolerance with respect to head, eye, and / or trunk; spontaneous attacks of vertigo often accompanied by nausea and vomiting; increased photosensitivity (photophobia), decreased visual focus; tinnitus; ataxia; cervicalgia (muscle pain associated with upper cervical muscle spasms); decreased cognitive functions; spatial disorientation and anxiety/panic symptoms [6]. Vestibular migraine treatment consists of acute attack management and prophylaxis, which also consists of current

protocols for migraine. In a study, migraine prophylaxis protocol was used for vestibular migraine treatment. In vestibular migraine prophylaxis, drugs such as beta blockers, calcium channel blockers, anti-depressants, valproic acid have been used. An improvement in vestibular symptoms was found in 81% of the patients [7]. Johnson et al. found that migraine symptoms and vestibular symptoms decreased in patients who used benzodiazepines, tricyclic antidepressants, beta blockers and SSRIs. Çeliker et al. used valproic acid every day for 3 months in 37 migraine patients. Of the patients, 13 had no vertigo, 13 had no dizziness, and 11 had no vestibular symptoms [8]. Pharmacological therapy does not always work in patients with vestibular migraine. The short effects and insufficient data of pharmacological treatment led clinicians to alternative treatment methods for vestibular migraine treatment. Karen et al. examined the effectiveness of osteopathic manual therapy (OMT) in female patients with migraine. In the study where they evaluated pain, migraine attacks and quality of life, it was stated that OMT reduced pain, decreased the number of days with migraine attacks and improved the quality of life [9].

Although there are a limited number of studies examining the effectiveness of manual manipulation on dizziness, according to the Osteopathic literature and clinical experience of osteopaths, it has been observed that OMT relieves vertigo, especially in cases of peripheral vestibular vertigo [10,11]. The effectiveness of OMT treatment was shown also in our case that had vestibular migraine who was resistant to medical treatment and severely impaired the quality of patient's life. The mechanism of this effect is unknown. Tigeminivestibular reflex mechanisms can cause this. However, in order to understand the mechanism, controlled and randomized clinical studies with sufficient number of cases are needed.

OMT can be preferred as a complementary treatment in individuals with vestibular migraine with medication to improve the severity of dizziness, balance and self-confidence in daily activities.

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REFERENCES

1. Arnold M. Headache classification committee of the international headache society (ihs) the international classification of headache disorders. *Cephalalgia*. 2018;38(1):1-211.
2. Van Ombergen A, Van Rompaey V, Van de Heyning P, Wuyts F. Vestibular migraine in an otolaryngology clinic: prevalence, associated symptoms, and prophylactic medication effectiveness. *Otology & Neurotology.* 2015;36(1):133-138.
3. Espinosa-Sanchez JM, Lopez-Escamez JA. New insights into pathophysiology of vestibular migraine. *Frontiers in neurology.* 2015;6:12.
4. Nicholas AS, Nicholas EA. Osteopathy in the Cranial Field. Atlas of Osteopathic Techniques. 2nd ed. *Lippincott Williams & Wilkins;* 2012: Chapter 18.
5. Johnson GD. Medical management of migraine-related dizziness and vertigo. *The Laryngoscope*. 1998;108(S85):1-28.
6. Brantberg K, Trees N, Baloh RW. Migraine-associated vertigo. *Acta oto-laryngologica.* 2005;125(3):276-279.
7. Salmito MC, Duarte JA, Morganti LOG, Brandao PVC, Nakao BH, Villa TR, Ganança FF. Tratamento profilatico da migranea vestibular. *Brazilian journal of otorhinolaryngology.* 2017;83(4):404-410.
8. Çeliker A, Bir LS, Ardiç N. Effects of valproate on vestibular symptoms and electronystagmographic findings in migraine patients. *Clinical neuropharmacology*. 2007;30(4):213-217.
9. Voigt K, Liebnitzky J, Burmeister U, Sihvonen-Riemenschneider H, Beck M, Voigt R, Bergmann A. Efficacy of osteopathic manipulative treatment of female patients with migraine: results of a randomized controlled trial. *The Journal of alternative and complementary medicine.* 2011;17(3):225-230.
10. Fraix M. Osteopathic manual medicine for vertigo: review of literature, case report, and future research. *J Am Acad Osteopathy.* 2009;2:25-29.
11. Mein EA, Greenman PE, McMillin DL, Richards DG, Nelson CD. Manual medicine diversity: research pitfalls and the emerging medical paradigm. *J Am Osteopath Assoc.* 2001;101(8):441-444.