Selcuk Dental Journal 12/1 (Nisan 2025): 144-148

Review / Derleme

Zebrafish, A Model Organism For Research in Dentistry

Zebra Balığı, Diş Hekimliği Araştırmalarında Model Organizma

Simge MEŞELİ[α], **Dilek TAĞTEKİN**[α], **Ebru EMEKLİ ALTURFAN**[β]

[α]Marmara University, Faculty of Dentistry, Department of Restorative Dentistry, Istanbul, Türkiye
[α]Marmara Üniversitesi, Diş Hekimliği Fakültesi, Restoratif Diş Tedavisi AD, İstanbul, Türkiye
[β]Marmara University, Faculty of Dentistry, Deparment of Basic Medical Sciences, Istanbul, Türkiye
[β]Marmara Üniversitesi, Diş Hekimliği Fakültesi, Temel Tıp Bilimleri Bölümü, İstanbul, Türkiye

ABSTRACT

Zebrafish (Danio rerio) is a tropical freshwater fish, lives in South Asia, India, and Pakistan. The use of zebrafish as a model organism in embryology and genetic studies of vertebrates was first mentioned by George Streisinger. Zebrafish has become a popular vertebrate model organism for biomedical research due to its numerous advantages. Zebrafish genome has homologues of 70% human genes, 80% of which are associated with human diseases. Zebrafish embryos are transparent, developes rapidly, and the development stages can be monitored easily by a stereomicroscope. Due to its various advantages, zebrafish has been preferred in neuroscience, cancer, pharmacology and toxicity research for years. Recently, it has begun to be used as a model organism in dental research. This review aims to provide information on the use of zebrafish in many fields of dental research, dental materials and tooth formation.

Keywords: Zebrafish; Model organism; Dental research; Biocompatibility; Toxicity

ÖZ

Zebra balığı (Danio rerio), Güney Asya, Hindistan ve Pakistan'da yaşayan tropikal bir tatlı su balığıdır. Zebra balığının omurgalıların embriyolojisi ve genetik çalışmalarında model organizma olarak kullanılmasından ilk kez George Streisinger bahsetmiştir. Son yıllarda zebra balığı, sayısız avantajı nedeniyle biyomedikal araştırmalar için popüler bir omurgalı model organizma haline gelmiştir. Zebra balığı genomunun %70'i insan genlerinin homologlarına sahiptir ve bunların %80'i insan hastalıklarıyla ilişkilidir. Zebra balığı embriyoları şeffaftır, hızlı gelişir ve embryoların gelişim aşamaları stereomikroskopla kolaylıkla takip edilebilir. Zebra balığı, çeşitli avantajlarından dolayı nöroloji, kanser, farmakoloji ve toksisite araştırmalarında yıllardır tercih edilmektedir. Son zamanlarda diş hekimliğine ait araştırmalarda model organizma olarak kullanılmaya başlanmıştır. Bu derleme, zebra balığının dental araştırmalar, dental materyaller ve odontogenezis gibi birçok alanda kullanımı hakkında bilgi vermeyi amaçlamaktadır.

Anahtar Kelimeler: Zebrabalığı, Model organizma, Dental araştırma, Biyouyumluluk, Toksisite

INTRODUCTION

Model organisms are considered the guide for toxicity and biomedical studies to investigate the human biology. Many model organisms, such as rat, mice, dog, pig, rabbit or zebrafish are used in studies according their human-like genetic properties and practical advantages.[1]

Zebrafish (Danio rerio), which is a model organism, is used in chemical toxicity studies,[2,3] and recently indicated as "gold standard".[4]

Zebrafish, which is a tropical freshwater fish, lives in South Asia, India, and Pakistan, and belongs to *Cyprinidae* family, in the infraclass Teleost of the class of Actinopterygii.[1]

It was first mentioned in the study of George Streisinger that zebrafish could be used as a model organism in embryology and genetic studies of vertebrates.[5] Kimmel researched detailed genetics, developmental characteristics and nervous system of zebrafish.[6,7] By the 1990's, zebrafish became a widely used model organism in developmental genetics and toxicity studies.[8]

Although zebrafish is anatomically different from mammals due to the lack of some organs, they have similar molecular and physiological characteristics. Zebrafish genome has homologues of 70% human genes, 80% of which are associated with human diseases.[9]

The zebrafish embryo develops rapidly, and has a short generation time of 3-4 months. All of its major organs appear within 36 hours postfertilization and are functional on the 5th day. The fertilization of zebrafish happens externally and it allows to manipulate the embryos during development stage. Zebrafish embryos are transparent and one of the main advantages of zebrafish is the visualization of the development of embryos by using a stereomicroscope (**Figure 1**). There isn't a placental barrier, so applying toxins to zebrafish embryos by adding to the water is easy than other model organisms in toxicology studies.[1,10] Large numbers of zebrafish can live in small tanks, and maintance of research is relatively more efficient because of the rapid reproduction of zebrafish compared to other mammals.[11]

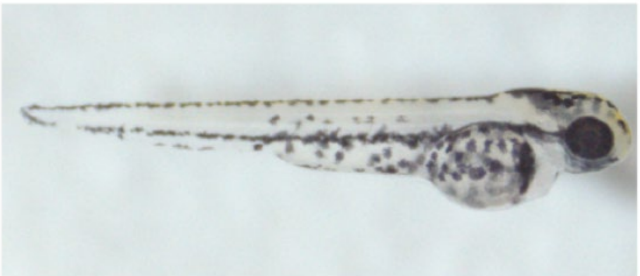

Figure 1. Representative image of a zebrafish embryo taken by a stereomicroscope at 72 hours post fertilization (hpf)

Due to all these advantages, zebrafish has been preferred in neuroscience, cancer, pharmacology and toxicity research for years.[12-14] In recent years, it has begun to be used as a model organism in dental research.

Zebrafish is a polyphyodont organism, replacing teeth throughout its life, has no teeth in oral cavity, instead it has 22 pharyngeal teeth.[15] The teeth of zebrafish have similar structure with human teeth. In zebrafish, dental pulp contents odontoblasts, dental nerves and blood vessels. It is covered by dentin, which has no tubules. Like the human tooth embryogenesis, tooth crown of zebrafish is produced from dentin, and it is covered by enameloid. Enameloid is a hypermineralized layer and has both epithelial and mesenchymal

Gönderilme Tarihi/Received: 2 Mart, 2024
Kabul Tarihi/Accepted: 11 Eylül, 2024
Yayınlanma Tarihi/Published: 21 Nisan, 2025
Atıf Bilgisi/Cite this article as: Meşeli S, Tağtekin D, Emekli Alturfan E. Zebrafish, A Model Organism For Research in Dentistry. Selcuk Dent J 2025;12(1): 144-148 Doi: 10.15311/ selcukdentj.1446275

Sorumlu yazar/Corresponding Author: Simge MEŞELİ
E-mail: dtsimgemeseli@gmail.com
Doi: 10.15311/ selcukdentj.1446275

origins. There is no cementum layer is found in zebrafish (**Figure 2**).[1,16,17] Sculze et al. declared that zebrafish is a good model organism to study odontogenesis.[18] Accordingly, in recent years, zebrafish and their embryos have begun to be used in dental research, in order to analyze the biocompatibility and toxicity of biomaterials, as well as to examine the effect of dental x-ray devices used for diagnosis on embryo development, and in research in the field of periodontology (**Figure 3**).[19-44]

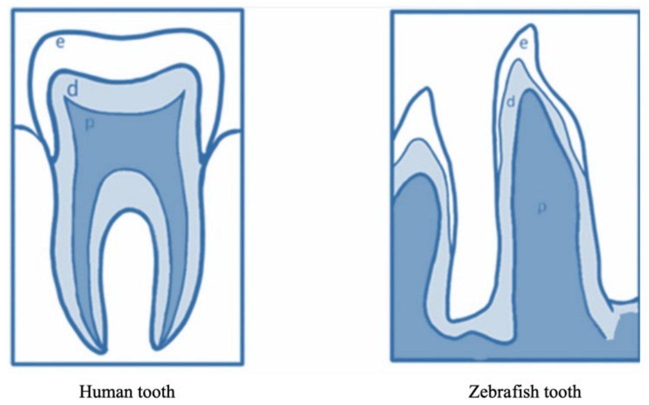

Figure 2. The shape of human tooth and zebrafish tooth e: enamel, d: dentine, p: pulp

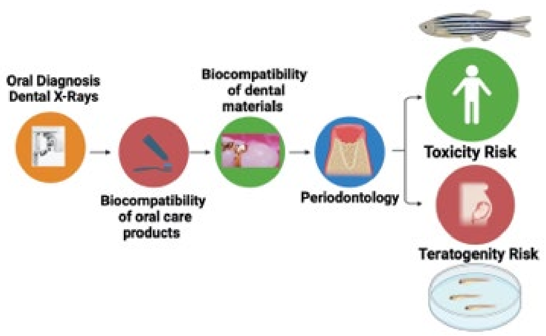

Figure 3. Zebrafish and their embryos are used in dental research to analyze the biocompatibility and toxicity of biomaterials, to examine the effect of dental x-ray devices used for diagnosis on embryo development, and in research in the field of periodontology. Created with BioRender.

CLINICAL and RESEARCH CONSEQUENCES

1. Studies on Toothpaste Ingredients:

Toothpaste contains many chemical components. Some studies have been conducted with zebrafish embryos on the biocompatibility of these components. Meşeli et al. compared a herbal toothpaste with a conventional toothpaste, the hatching and mortality rates of the herbal toothpaste were found to be similar to the control group. While the hatching rate of conventional toothpaste was found to be lower than the control group, the mortality rate was found to be significantly higher than the control group.[19]

Fluoride content in toothpastes can be found in the forms of sodium monofluorophosphate (SMFP), sodium fluoride (NaF), amine fluoride (AmF), and stannous fluoride (SnF_2).[20] Zhang et al. applied to zebrafish embryos various doses of fluoride to induce dental fluorosis in odontogenesis stage and found minor cystic-like changes after fluoride treatment.[21] Barlett et al. exposed zebrafish to different concentrations of NaF and after fluoride treatment they found pits and increased organic components in zebrafish teeth.[22]

In the study investigating the effect of NaF on the zebrafish reproductive system, it was found that NaF exposure with different doses for 30 and 60 days, significantly affected ovarian development, disrupted reproductive hormones, and caused apoptosis in the zebrafish ovary.[23] It has also been stated that fluoride not only affects the ovary, but also can disrupt the testicular structure and affect sex hormone synthesis in zebrafish.[24]

Sodium lauryl sulfate (SLS) is the most commonly used detergent in toothpastes due to its antibacterial and cleansing effects. Meşeli et al. examined the biocompatibility of low-dose and high-dose SLS on zebrafish embryos. The results of this study showed that there was no significant difference between low dose SLS and the control group. The survival rate in the high dose SLS group was found to be significantly lower than the control group.[13] In a recent study, the effect of toothpastes with different detergent contents (SLS and cocamidopropyl betaine (CAPB) on the odontogenesis of zebrafish embryos were examined.[25] As a result of this study it is declared that SLS and CAPB content significantly affected the development parameters of zebrafish embryos and the expression of genes affecting tooth development.

Another content ***triclosan*** is added to toothpaste due to its antimicrobial effect. Oliveira et al. examined the biocompatibility of triclosan on zebrafish embryos. In this study it is found that triclosan causes acute toxicity, reducing hatching rate, pigmentation and stature.[26]

Gaur et al. conducted a study with ***sodium benzoate***, which is added to toothpastes as a preservative, and found a 100% mortality rate in zebrafish larvae at a dose of 500 ppm.[27]

Calcium carbonate nanoparticles ($CaCO_3$) are one of the widely used abrasives in toothpaste. It was shown safe and don't cause mortality and genotoxicity. Zebrafish treated with $CaCO_3$ developed without developmental abnormality.[28] Another nanoparticle commonly found in toothpaste is ***titanium dioxide***. The doses in specific standards (TiO_2) were biocompatible on zebrafish, however, significantly high doses of TiO_2 showed autophagy and cell necrosis.[20] In the study conducted with ***silica nanoparticles*** added to toothpastes due to their abrasive properties, Yi et al. found that exposure to silica nanoparticles negatively affected the developmental parameters of zebrafish, disrupted the coagulation feature of zebrafish embryos, and triggered thrombolytic activity.[29]

2. Studies on Dental Materials

Biocompatibility may be defined as a material's ability to have a specific functional application providing a suitable host response.[30] It is an emerging need to investigate the biocompatibility of dental materials in contact with human tissues.

Bisphenol A-glycidyl-methacrylate (Bis-GMA) is one of the main components of composite resins used in restorative dentistry.[30] Kramer et al. exposed zebrafish embryos to different concentrations of Bis-GMA (1 μM and 10 μM) and investigated craniofacial development. They found that exposure to Bis-GMA decreased survival rates, increased variety of morphological defects, and impacted specific features of viscernocranium.[31]

Bioceramics are used especially in endodontic treatments as perforation repair materials, pulp capping agents, and root-end fillings. Biodentine and Mineral trioxide aggregate (MTA) are the widely used Bioceramics in today's dentistry. Makkar et al. examined the biocompatibility of the Bioceramics on the zebrafish embryos. They found morphological malformations and increasing mortality rates with the increasing concentrations. They declared that biocompatibility of Biodentine was higher than MTA.[32] Another one of the bioceramics, widely used in dentistry is hydroxyapatite. Carbonate Hydroxyapatite (CHA) is one of the bioceramic material can be used as dental implant.[33] Pratama et al. examined the biocompatibility of CHA exposed to different concentrations in zebrafish embryos. No morphological defect or change in mortality rate, hatching rate and heart rate was observed in zebrafish exposed to CHA[34]. Another one of the neutral bioceramic metal compound used in dental implants is Zirconia oxide nanoparticles (ZrO_2NPs). Karthiga et al. studied the effect of ZrO2NPs on the embryonic development of zebrafish. In this study it is found that ≥0.5–1 µg/ml of ZrO_2NPs instigated developmental acute toxicity in zebrafish embryos, causing mortality, hatching delay, and malformation. At 1 mg/ml of ZrO_2NPs treatmen<t, they observed the mortality of unhatched embryos as a common phenotype. According to their results, they declared that lower concentrations of ZrO_2NPs nanoparticles are more toxic to zebrafish embryos.[35]

Porcelain to metal fused metal crown (PFM) is a widely preferred restorative material in dentistry. Metal base of crowns may consist of some metal alloys such as titanium, silver palladium (Ag-Pd), gold palladium (Au-Pd), nickel chromium (Ni-Cr), and cobalt chromium (Co-Cr). The metal lines of this restorations are exposed to oral cavity and release ions which are not biocompatible on human epithelial cells.[36] Zhaoa et al. investigated the toxicity of the metal alloys of PFM on the zebrafish embryos. In the study, metal alloys were putted in the artificial saliva for 1, 4 and 7 weeks. After that zebrafish embryos were treated in the artificial saliva solution and investigated for mortality, hatching and heart rates, and malformation and swimming behaviors. They found Ni-Cr alloy had the lowest biocompatibility following the Co-Cr and Ag-Pd alloys. As a result of this study, it is declared that Ti and Au-Pd alloys are biocompatible for crowns and dental materials.[37]

3. Studies on Oral Radiology

Panoramic imaging is one of the most used extraoral dental radiographic technique to visualize maxilla, mandible and the surrounding structures. Although patients are exposed to relatively low doses of radiation with panoramic imaging, it appears that it may be hazardous to health considering lifetime exposure. It has been reported that repeated dental x-rays increase the risk of several types of cancers.[38] Karagöz et al. examined the effects of panoramic x-rays at two different exposure times on zebrafish embryos, and focused on developmental parameters. They found that the toxicity effect observed in the development of zebrafish embryos exposed to the high-speed standard panoramic x-rays (5.5 s) were higher than those observed with the pedodontic panoramic x-rays (4.8 s).[39]

As prenatal exposure to various environmental chemicals have been related with the aetiopathogenesis of autism spectrum disorder (ASD), Kollayan et al., (2024) investigated the potential effects of low-dose x-rays from dental diagnostic x-rays on neurodevelopment and molecular mechanisms associated with ASD in developing zebrafish embryos. They found developmental toxicity as evidenced by pericardial oedema, yolk sac oedema and scoliosis, impaired locomotor activity, oxidative stress, apoptosis and alterations in genes associated with neurogenesis and ASD progression.[40] Based on the result of these studies the association between ASD and low-dose ionizing radiation were suggested to be further evaluated.

4. Studies on Periodontology

Periodontitis is a bacteria-induced inflammation, which damages the tissues around the teeth and causes tooth loss. Porphyromonas gingivalis (P. gingivalis) is a strong periodontopathogen, which is related to severe periodontitis. Gingipain (GP) is one of the major endotoxins among the virulence factors of P. gingivalis.[41] Recently, periodontologists are interested in the relationship between metabolic diseases and periodontitis, such as obesity and diabetes mellitus.[42] Gunduz et al. investigated the effects of gingipain injections in overfed zebrafish. They studied with control (C), gingipain (GP), overfeeding (OF) and OF+GP groups. As a result of this study, it is declared that gingipain disrupts the oxidant-antioxidant balance and ALP activity in the intestines due to overnutrition and provided important information on the effects of periodontal pathogens on intestinal health in metabolic diseases.[43] In a recently study, Gunduz et al. examined the effects of gingipain in hyperglycemia-induced zebrafish model by evaluating inflammation, oxidant-antioxidant status, and the cholinergic system. Lipid peroxidation (LPO), nitric oxide (NO), glutathione (GSH), glutathione S-transferase, catalase, acetylcholinesterase (AChE), alkaline phosphatase (ALP), and sialic acid (SA) levels were determined. According the results of this study they declared that gingipains have a role in the increased inflammatory response in hyperglycemia-associated diseases.[44]

CONCLUSION

There are many materials used in dentistry which are in contact with human oral tissues. It is a necessity to investigate the biocompatibility of the chemical dental materials. Zebrafish are used especially in biocompatibility studies due to their rapid reproduction ability, suitability of laboratory conditions, ability of monitoring embryo development, and homology with human genes. Zebrafish can also be preferred in odontogenesis studies because their dental structures are similar to human teeth. Zebrafish studies can be used not only in biocompatibility research but also to search the relationship between periodontopathogen oral pathogenic microorganisms and metabolic diseases.

Değerlendirme / Peer-Review

İki Dış Hakem / Çift Taraflı Körleme

Etik Beyan / Ethical statement

Bu çalışmanın hazırlanma sürecinde bilimsel ve etik ilkelere uyulduğu ve yararlanılan tüm çalışmaların kaynakçada belirtildiği beyan olunur.

It is declared that during the preparation process of this study, scientific and ethical principles were followed and all the studies benefited are stated in the bibliography.

Benzerlik Taraması / Similarity scan

Yapıldı – ithenticate

Etik Bildirim / Ethical statement

dishekimligidergisi@selcuk.edu.tr

Finansman / Grant Support

Yazarlar bu çalışma için finansal destek almadığını beyan etmiştir. | The authors declared that this study has received no financial support.

Çıkar Çatışması / Conflict of Interest

Yazarlar çıkar çatışması bildirmemiştir. | The authors have no conflict of interest to declare.

Yazar Katkıları / Author Contributions

Çalışmanın Tasarlanması/ Design of Study: SM (%50) DT (%20) EEA (%30)
Veri Toplanması/ Data Acquisition: SM (%50) EEA (%50)
Veri Analizi/ Data Analysis: SM (%60) EEA (%40)
Makalenin Yazımı/ Writing up: SM (%50) DT (%20) EEA (%30)
Makale Gönderimi ve Revizyonu/ Submission and Revision: SM (%100)

REFERENCES

1. Karaman GE, Emekli-Alturfan E, Akyüz S: Zebrafish; an emerging model organism for studying toxicity and biocompatibility of dental materials. *Cellular and Molecular Biology* 2020, 66(8):41-46.
2. He J-H, Gao J-M, Huang C-J, Li C-Q: Zebrafish models for assessing developmental and reproductive toxicity. *Neurotoxicology and teratology* 2014, 42:35-42.
3. Ohashi AS, de Souza Schacher HR, Pizzato CS, Vianna MR, de Menezes LM: Zebrafish as model for studies in dentistry. *Journal of Orthodontic Science* 2022, 11.
4. Jia H-R, Zhu Y-X, Duan Q-Y, Chen Z, Wu F-G: Nanomaterials meet zebrafish: Toxicity evaluation and drug delivery applications. *Journal of Controlled Release* 2019, 311:301-318.
5. Streisinger G, Walker C, Dower N, Knauber D, Singer F: Production of clones of homozygous diploid zebra fish (Brachydanio rerio). *Nature* 1981, 291(5813):293-296.
6. Kimmel CB: Genetics and early development of zebrafish. *Trends in Genetics* 1989, 5:283-288.
7. Kimmel CB: Patterning the brain of the zebrafish embryo. *Annual review of neuroscience* 1993, 16(1):707-732.
8. Lieschke GJ, Currie PD: Animal models of human disease: zebrafish swim into view. *Nature Reviews Genetics* 2007, 8(5):353-367.
9. Howe K, Clark MD, Torroja CF, Torrance J, Berthelot C, Muffato M, Collins JE, Humphray S, McLaren K, Matthews L: The zebrafish reference genome sequence and its relationship to the human genome. *Nature* 2013, 496(7446):498-503.
10. Langheinrich U: Zebrafish: a new model on the pharmaceutical catwalk. *Bioessays* 2003, 25(9):904-912.
11. Saleem S, Kannan RR: Zebrafish: an emerging real-time model system to study Alzheimer's disease and neurospecific drug discovery. *Cell death discovery* 2018, 4(1):45.
12. Ünal İ, Üstündağ ÜV, Ateş PS, Eğilmezer G, Alturfan AA, Yiğitbaşı T, Emekli-Alturfan E: Rotenone impairs oxidant/antioxidant balance both in brain and intestines in zebrafish. *International Journal of Neuroscience* 2019, 129(4):363-368.
13. Meşeli S, Kaplan G, Cansiz D, Üstündağ ÜV, İsmail Ü, Alturfan EE, Yanikoğlu F, Tağtekin D: The biocompatibility of sodium lauryl sulphate on developing zebrafish embryos. *Experimed* 2021, 11(2):67-72.
14. Eryılmaz O, Ateş PS, Ünal İ, Üstündağ ÜV, Bay S, Alturfan AA, Yiğitbaşı T, Emekli-Alturfan E, Akalın M: Evaluation of the interaction between proliferation, oxidant–antioxidant status, Wnt pathway, and apoptosis in zebrafish embryos exposed to silver nanoparticles used in textile industry. *Journal of Biochemical and Molecular Toxicology* 2018, 32(1):e22015.
15. Mork L, Crump G: Zebrafish craniofacial development: a window into early patterning. *Current topics in developmental biology* 2015, 115:235-269.
16. Wiweger MI, Zhao Z, van Merkesteyn RJ, Roehl HH, Hogendoorn PC: HSPG-deficient zebrafish uncovers dental aspect of multiple osteochondromas. *PLoS One* 2012, 7(1):e29734.
17. Stock DW: Zebrafish dentition in comparative context. *Journal of Experimental Zoology Part B: Molecular and Developmental Evolution* 2007, 308(5):523-549.
18. Schulze S, Küchler EC, Scariot R, Baratto-Filho F, Carelli J, Proff P, Kirschneck C: Signaling pathways involved in tooth development: why use zebrafish in dental research? *RSBO* 2021, 18(1):86-99.
19. Meşeli S, Üstündağ ÜV, Ateş PS, Ünal İ, Işık Alturfan E: The biocompatibility of a ginger-containing herbal toothpaste on developing zebrafiish embryos. *Journal of Dentistry Indonesia* 2023.
20. Stachurski P, Świątkowski W, Ciszewski A, Sarna-Boś K, Michalak A: A Short Review of the Toxicity of Dentifrices—Zebrafish Model as a Useful Tool in Ecotoxicological Studies. *International Journal of Molecular Sciences* 2023, 24(18):14339.
21. Zhang Y, Zhang Y, Zheng X, Xu R, He H, Duan X: Grading and quantification of dental fluorosis in zebrafish larva. Archives of Oral Biology 2016, 70:16-23.
22. Bartlett J, Dwyer S, Beniash E, Skobe Z, Payne-Ferreira T: Fluorosis: a new model and new insights. Journal of dental research 2005, 84(9):832-836.
23. Li M, Cao J, Zhao Y, Wu P, Li X, Khodaei F, Han Y, Wang J: Fluoride impairs ovary development by affecting oogenesis and inducing oxidative stress and apoptosis in female zebrafish (Danio rerio). Chemosphere 2020, 256:127105.
24. Li M, Cao J, Chen J, Song J, Zhou B, Feng C, Wang J: Waterborne fluoride exposure changed the structure and the expressions of steroidogenic-related genes in gonads of adult zebrafish (Danio rerio). *Chemosphere* 2016, 145:365-375.
25. Karaman GE, Ünal İ, Beler M, Üstündağ FD, Cansız D, Üstündağ Ü V, Emekli-Alturfan E, Akyüz S: Toothpastes for children and their detergent contents affect molecular mechanisms of odontogenesis in zebrafish embryos. *Drug Chem Toxicol* 2024, 47(1):15-25.
26. Oliveira R, Domingues I, Koppe Grisolia C, Soares AM: Effects of triclosan on zebrafish early-life stages and adults. *Environmental Science and Pollution Research* 2009, 16(6):679-688.
27. Gaur H, Purushothaman S, Pullaguri N, Bhargava Y, Bhargava A: Sodium benzoate induced developmental defects, oxidative stress and anxiety-like behaviour in zebrafish larva. *Biochemical and biophysical research communications* 2018, 502(3):364-369.
28. d'Amora M, Liendo F, Deorsola FA, Bensaid S, Giordani S: Toxicological profile of calcium carbonate nanoparticles for industrial applications. *Colloids and Surfaces B: Biointerfaces* 2020, 190:110947.
29. Yi H, Wang Z, Li X, Yin M, Wang L, Aldalbahi A, El-Sayed NN, Wang H, Chen N, Fan C: Silica nanoparticles target a Wnt signal transducer for degradation and impair embryonic development in zebrafish. *Theranostics* 2016, 6(11):1810.
30. Donaruma LG: Definitions in biomaterials, DF Williams, Ed., Elsevier, Amsterdam, 1987, 72 pp. In.: Wiley Online Library; 1988.
31. Kramer AG, Vuthiganon J, Lassiter CS: Bis-GMA affects craniofacial development in zebrafish embryos (Danio rerio). *Environmental Toxicology and Pharmacology* 2016, 43:159-165.
32. Makkar H, Verma SK, Panda PK, Jha E, Das B, Mukherjee K, Suar M: In vivo molecular toxicity profile of dental bioceramics in embryonic Zebrafish (Danio rerio). *Chemical research in toxicology* 2018, 31(9):914-923.
33. Roy M, Bandyopadhyay A, Bose S: Ceramics in bone grafts and coated implants. In: *Materials for Bone Disorders*. edn.: Elsevier; 2017: 265-314.
34. Pratama SF, Ana ID, Retnoaji B: The Effect of Carbonate Hydroxyapatite (CHA) Dental Implant Material on the Early Development of Zebrafish Embryos (Danio rerio). In: *3rd KOBI Congress, International and National Conferences (KOBICINC 2020): 2021*: Atlantis Press; 2021: 307-312.
35. Karthiga P, Ponnanikajamideen M, Rajendran S, Annadurai G, Rajeshkumar S: Characterization and toxicology evaluation of zirconium oxide nanoparticles on the embryonic development of zebrafish, Danio rerio. *Drug and Chemical Toxicology* 2018, 42(1):104-111.
36. Yang H-C, Pon LA: Toxicity of metal ions used in dental alloys: a study in the yeast Saccharomyces cerevisiae. *Drug and chemical toxicology* 2003, 26(2):75-85.
37. Zhao L, Si J, Wei Y, Li S, Jiang Y, Zhou R, Liu B, Zhang H: Toxicity of porcelain-fused-to-metal substrate to zebrafish (Danio rerio) embryos and larvae. *Life sciences* 2018, 203:66-71.
38. Choi J-W: Assessment of panoramic radiography as a national oral examination tool: review of the literature. *Imaging science in dentistry* 2011, 41(1):1-6.
39. Karagöz A, Beler M, Altun BD, Ünal İ, Cansız D, Gündüz H, Alturfan AA, Emekli-Alturfan E, Yalçınkaya ŞE: Panoramic dental X-ray exposure leads to oxidative stress, inflammation and apoptosis-mediated developmental defects in zebrafish embryos. *Journal of Stomatology, Oral and Maxillofacial Surgery* 2023, 124(6):101661.
40. Kollayan BY, et. al., Effects of Low-dose Ionizing Radiation on the Molecular Pathways Linking Nurogenesis and Autism Spectrum Disorders in Zebrafish Embryos. Drug and Chemical Toxicology, 2024. doi.org/10.1080/01480545.2024.2318444
41. Xu W, Zhou W, Wang H, Liang S: Roles of Porphyromonas gingivalis and its virulence factors in periodontitis. *Advances in protein chemistry and structural biology* 2020, 120:45-84.
42. Nibali L, Tatarakis N, Needleman I, Tu Y-K, D'Aiuto F, Rizzo M, Donos N: Association between metabolic syndrome and periodontitis: a systematic review and meta-analysis. *The Journal of Clinical Endocrinology & Metabolism* 2013, 98(3):913-920.

43. Gündüz G, Beler M, İsmail Ü, Cansiz D, ALTURFAN EE, Kose KN: Gingipain Injection Affects Intestinal OxidantAntioxidant Status and Alkaline Phosphatase in Overfed Zebrafish. *Experimed* 2023, 13(2):80-85.
44. Gündüz G, Beler M, Ünal İ, Cansız D, Emekli-Alturfan E, Kose KN: Endotoxin of Porphyromonas gingivalis amplifies the inflammatory response in hyperglycemia-induced zebrafish through a mechanism involving chitinase-like protein YKL-40 analogs. *Toxicological Research* 2023:1-12.