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Radiological Properties of Some Chemotherapy Drugs for Electron, Proton and Carbon Ion Interactions in the Energy Region 10 keV – 400 MeV

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Abstract

Radiological properties of some chemotherapy drugs such as Doxorubicin, Vincristine, Teniposide, Azathioprine, Etoposide, Cyclophosphamide, Vinblastine and Bleomycin were investigated according to total electron interaction and some heavy charged particle interactions on behalf of effective atomic numbers (Z_{eff}) and electron densities (N_{eff}) for the first time. Calculations were performed for total electron, proton and C ion interactions, commonly used in therapy, in the energy region 10 keV- 400 MeV. Variation of Z_{eff}s and N_{eff}s of given drugs was studied according to the energy of electron or heavy charged particles and significant variations were observed for all types of interaction in the given energy region. The highest values of Z_{eff} were found in the different regions of energy for different particle interactions remarkably and variation in N_{eff} seems approximately to be same with alteration in Z_{eff} for the investigated drugs. Also, Z_{eff} values of all drugs were plotted together and compared with each other for electron, proton and C ion interactions in the continuous energy region. Maximum and minimum values of Z_{eff} were observed in Azathioprine (6.14) and Vinblastine (2.25) for electron interaction and proton interaction in the continuous energy region, respectively. The obtained results were compared with the Phy-X/ZeXTRa program between 10 keV-15 MeV energy region.

Keywords: Charged particles, chemotherapy drugs, effective atomic number, electron density

1. Introduction

Besides photons, electrons, protons and heavy ions became a commonly used instrument in radiotherapy, cancer and diagnostic applications [1]. On the other hand, the effect of ionizing radiation on human body parts, tissues, biomolecules and drugs is characterized by absorbed dose, energy and type of radiation in terms of radiation response. Thus, studies on the interactions of ionizing radiation with industrial materials, drugs or complex molecules are significant in related fields like cancer therapy. Chemotherapy is known as a cancer treatment using drugs to break down cancer cells or tumors, and radiotherapy uses X-, gamma rays and charged particles to demolish the cancer cells. Whereas chemoradiation is the treatment in which chemotherapy and radiotherapy are used at the same time for certain types of cancer. Chemotherapy drugs are vital for cancer treatment, thus the interaction of radiation with the drugs is significant in terms of radiation response or distinguishable especially in chemoradiation.

Mass attenuation coefficient and stopping power are diverse parameters characterizing the materials in terms of radiation response for photons and charged particles such as electrons, protons and heavy ions. Also, Z_{eff} and N_{eff} are useful physical properties both photons and others in health, biophysics, dosimetric applications, medical and particle physics. A multi-element material can be characterized via a term Z_{eff} to obey equivalence since a single number cannot characterize the multi-element material for the energy of a photon as revealed by Hine [2]. It also relies on photon energy. In addition, it is significant for calculating other properties like absorbed dose in health. Because the dose in medical physics is being utilized for radiological aims such as diagnosis and therapy. N_{eff} designates the number of electrons per unit mass of a material. Because Z_{eff} and N_{eff} are exclusive properties utilized to characterize different types of materials, this makes them distinguished properly and, thus drugs are better distinguished from each other in the continuous energy region.

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In addition, if it is estimated how the radiation response of the material is, the damage to healthful tissues or drugs will be minimized due to the fact that these drugs can have various physiological effects on life regimes [3].

There are some studies about drugs with regard to Z_{eff} and N_{eff} in literature. Mass attenuation coefficient, effective atomic numbers and electron densities of some narcotic drugs were investigated for total and partial photon interactions in the energy range 1 keV - 100 GeV [4]. The mass attenuation coefficient and effective atomic number of the active pharmaceutical ingredients were calculated for total and partial photon interactions in the energy range from 1 keV to 100 GeV and some significant variations were observed in the effective atomic numbers of drugs [5]. Effective atomic numbers, electron densities, energy absorption and exposure buildup factors of some anti-inflammatory drugs were computed in a 0.015–15 MeV energy region up to a penetration depth of 40 mfp (mean free path) and variations of these parameters of drugs were evaluated in the continuous energy region [6]. Effective atomic numbers, electron densities and photon buildup factors of some chemotherapy drugs, used simultaneously with radiation therapy for cancer treatments, were calculated in a 0.015–15 MeV energy region [7-9].

Charged particles such as electrons and heavy ions are often utilized in medical physics for radiotherapy or diagnosis. So these particles are significant for health in applications [10]. But there is no article showing Z_{eff} and N_{eff} of the drugs for the charged particle interaction. This motivated us to carry out this work. Electrons and heavy ions were used to study the radiological quantities viz. Z_{eff} and N_{eff} of some chemotherapy drugs in the present work for the first time. Z_{eff}s and N_{eff}s of the drugs were calculated for total electron interaction, proton and C ion interactions in the energy region 10 keV-400 MeV. The investigated drugs are shown in Table 1.

Table 1. The chemical formula of chemotherapy drugs.

1	Doxorubicin	$C_{27}H_{29}NO_{11}$
2	Vincristine	$C_{46}H_{56}N_4O_{10}$
3	Teniposide	$C_{32}H_{32}O_{13}S$
4	Azathioprine	$C_9H_7N_7O_2S$
5	Etoposide	$C_{29}H_{32}O_{13}$
6	Cyclophosphamide	$C_7H_{15}Cl_2N_2O_2P$
7	Vinblastine	$C_{46}H_{58}N_4O_9$
8	Bleomycin	$C_{55}H_{84}N_{17}O_{21}S_3$

2. Method

The used method work was adopted for the computation of Z_{eff}s and N_{eff}s for electrons, protons and heavy ions in our last study [11] and some other studies [12-15]. Mass stopping powers of the drugs were firstly determined by the NIST database [16] and the SRIM [17] code for particles. Then, this data was established spanning the lowest and the highest elements present in the investigated materials between 10 keV-10 MeV. And the Z_{eff} has been computed by the logarithmic interpolation procedure:

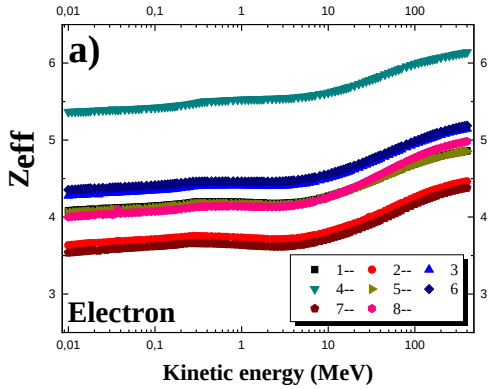
$$Z_{eff} = \frac{Z_1(\log\sigma_2 - \log\sigma) + Z_2(\log\sigma - \log\sigma_1)}{\log\sigma_2 - \log\sigma_1} \quad (1)$$

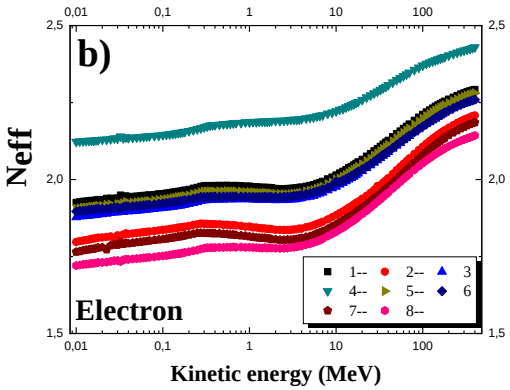
where σ_1 and σ_2 are the stopping cross section (cm^{-1}, expressed per atom) of Z_1 and Z_2 atoms. σ is the stopping cross section of the material that lies between Z_1 and Z_2 elements. This method was utilized to compute the Z_{eff} of the drugs for used particles by replacing the stopping cross section in Eq. 1. Afterthat electron densities (N_{eff}) of the drugs for charged particles have been calculated through the below formula with the mean atomic mass of drugs:

$$N_{eff} = N_A \frac{nZ_{eff}}{\sum_i n_i A_i} = N_A \frac{Z_{eff}}{<A>} \left(\frac{electrons}{g}\right) \quad (2)$$

3. Results and Discussion

Effective atomic numbers of the selected chemotherapy drugs were determined utilizing the mass stopping powers obtained via the NIST and SRIM code in the energy region 10 keV- 400 MeV.





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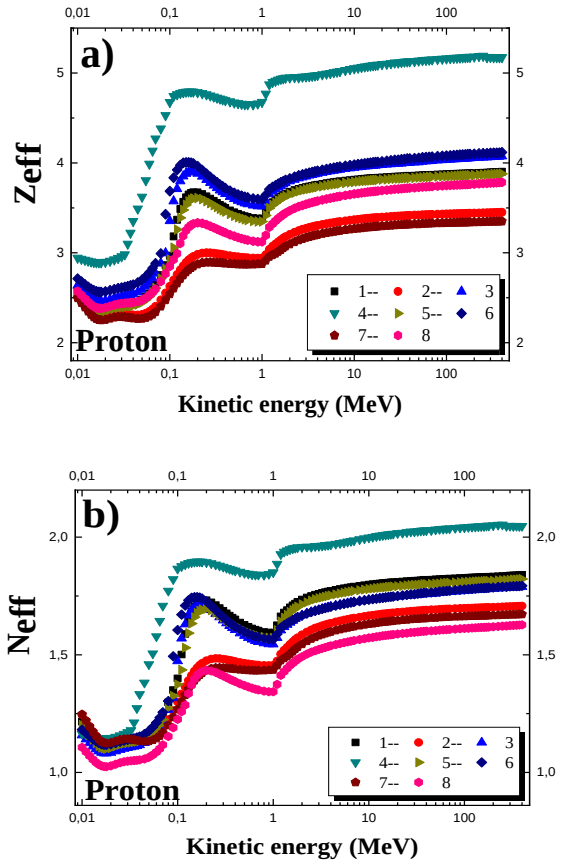
Figures 1. Effective atomic numbers and electron densities of the selected chemotherapy drugs for electron interaction.

The drugs have different chemical formulas, mass stopping powers and elemental cross section. Mass stopping power is used to calculate Z_{eff} especially, therefore changes in Z_{eff} are in accordance with mass stopping power. Figs. 1 show the change in Z_{eff}s and N_{eff}s of the selected chemotherapy drugs for electrons in the continuous energy region (10 keV- 400 MeV).

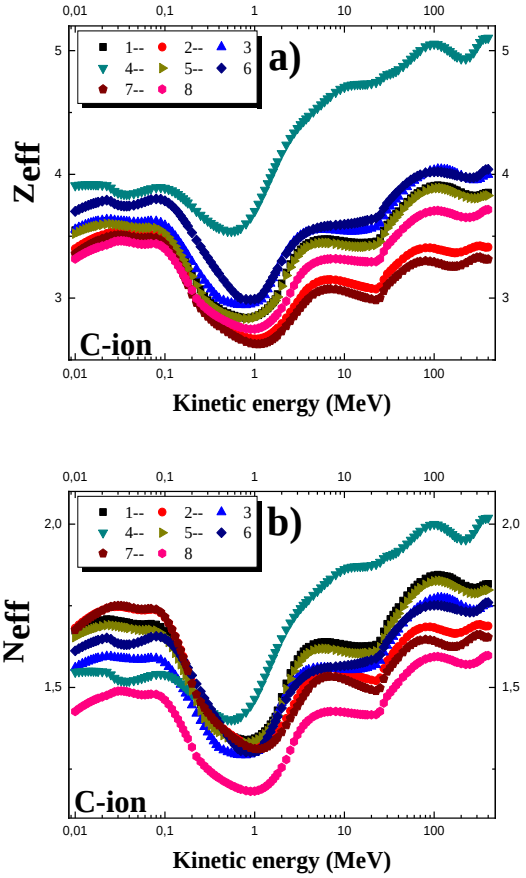
As shown in this Figure 1, the lowest values of Z_{eff} are observed at lower energy values and the highest values are observed at higher energies for all the chemotherapy drugs. On the other hand, the variation of N_{eff}s shows the same energy habituation expectedly as Z_{eff} because N_{eff} is nearly concerned with the effective atomic number as shown in Fig. 1(b) for electron interaction. Effective atomic numbers and electron densities of the selected chemotherapy drugs for proton interaction were shown in graphical form in the energy region 10 keV-400 MeV (Figs. 2).



Figures 2. Effective atomic numbers and electron densities of the selected chemotherapy drugs for proton interaction.

It can be clearly seen from Fig. 2(a), Z_{eff} makes a peak between 0.1-0.2 MeV and it decreases up to around 1 MeV, then it increases up to around 400 MeV for the drugs.

Also, Z_{eff} has the lowest values at lower energy values and has the highest values at higher energies for the chemotherapy drugs generally. N_{eff} of the chemotherapy drugs show the same variations as Z_{eff} in the entire energy region as expected for proton interaction (Fig. 2b). As shown in Fig. 3(a), Z_{eff} does not show large variations up to around 0.1 MeV for C ion interaction. After it decreases around 0.7-1 MeV and makes a minimum, then it increases and has the maximum values at higher ion energies (after around 100 MeV). Naturally, N_{eff} shows the same qualitative energy dependence in the studied region for C ion interaction from Fig. 3(b).



Figures 3. Effective atomic numbers and electron densities of the selected chemotherapy drugs for C ion interaction.

Table 2. Mean, minimum and maximum values of Z_{eff} of the given materials for electron, proton and C ion.

Z_{eff}	Mean	Min	Max	Mean	Min	Max
	Electron			**Proton**		
Doxorubicin	4.32	4.08	4.86	3.45	2.37	3.90
Vincristine	3.96	3.65	4.46	3.04	2.28	3.45
Teniposide	4.54	4.28	5.15	3.60	2.46	4.08
Azathioprine	5.63	5.37	6.14	4.62	2.89	5.19
Etoposide	4.30	4.00	4.85	3.42	2.34	3.88
Cyclophosphamide	4.60	4.00	5.19	3.67	2.56	4.12
Vinblastine	3.78	3.54	4.38	2.96	2.25	3.35
Bleomycin	4.30	4.00	4.98	3.30	2.38	3.78
	C-ion					
Doxorubicin	3.46	2.84	3.91			
Vincristine	3.19	2.67	3.53			
Teniposide	3.55	2.94	4.04			
Azathioprine	4.29	3.54	5.10			
Etoposide	3.43	2.83	3.89			
Cyclophosphamide	3.63	2.99	4.04			
Vinblastine	3.13	2.63	3.51			
Bleomycin	3.30	2.75	3.72			

Table 3. Mean, minimum and maximum values of N_{eff} of the given materials for electron, proton and C ion.

N_{eff}	Mean	Min	Max	Mean	Min	Max
	Electron			**Proton**		
Doxorubicin	2.04	1.93	2.29	1.63	1.12	1.84
Vincristine	2.97	1.82	2.21	1.51	1.13	1.71
Teniposide	2.00	1.88	2.26	1.58	1.08	1.79
Azathioprine	2.23	2.12	2.43	1.83	1.14	2.05
Etoposide	2.02	1.88	2.28	1.61	1.10	1.82
Cyclophosphamide	2.00	1.74	2.26	1.60	1.12	1.79
Vinblastine	1.89	1.76	2.19	1.48	1.12	1.67
Bleomycin	1.85	1.72	2.14	1.42	1.02	1.63
	C-ion					
Doxorubicin	1.63	1.34	1.84			
Vincristine	1.58	1.32	1.75			
Teniposide	1.56	1.29	1.77			
Azathioprine	1.70	1.40	2.02			
Etoposide	1.61	1.33	1.83			
Cyclophosphamide	1.58	1.30	1.76			
Vinblastine	1.56	1.31	1.75			
Bleomycin	1.42	1.18	1.60			

The basic statistical information for effective atomic numbers and electron densities of the chemotherapy drugs for the different particle interactions are seen in Table 2 and Table 3, respectively. Azathioprine has the maximum Z_{eff} (6.14, 5.19, 5.10) for electron, proton and C ion interactions respectively (Table 2) due to the heavier elements contributions. But Vinblastine has the minimum Z_{eff} (3.54, 2.25, 2.63) for electron, proton and C ion interactions respectively (Table 2).

In addition, maximum values of Z_{eff} decrease as the weight of particles increases (electron, proton, C respectively). It can be seen that N_{eff}s of the chemotherapy drugs have the same variations for Azathioprine (max: 2.43, 2.05 and 2.02) for electron, proton and C ion interactions respectively (Table 3). Variations in Z_{eff} of the drugs were plotted for all interaction types in Fig. 4.

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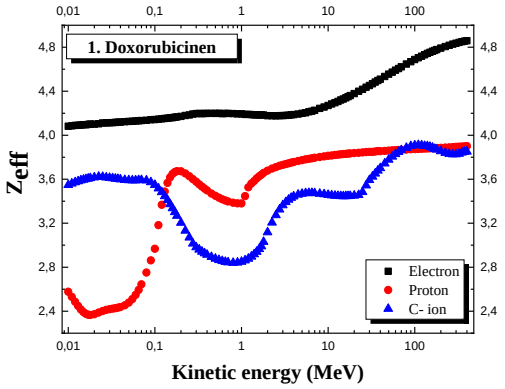

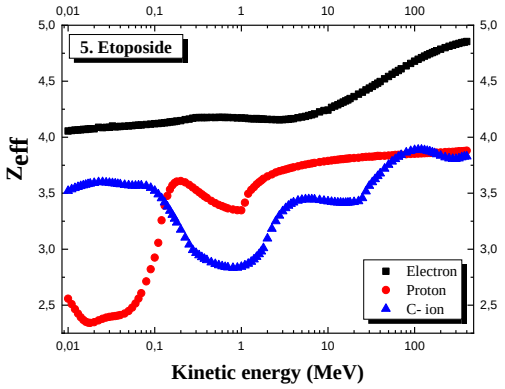

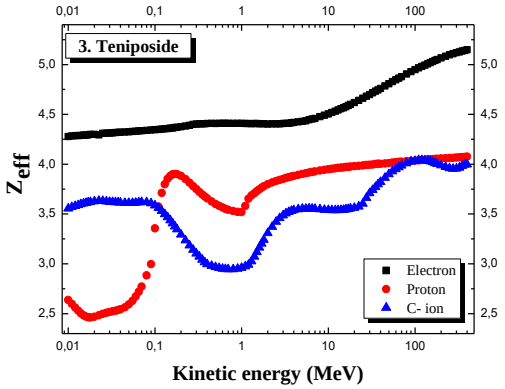

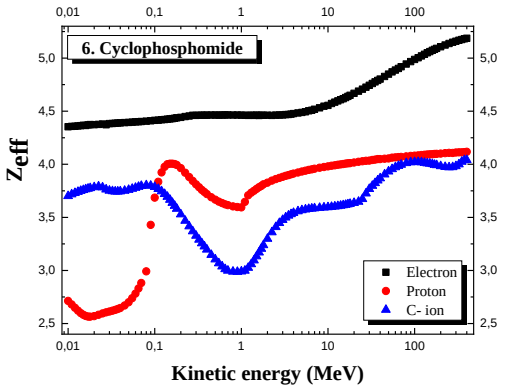

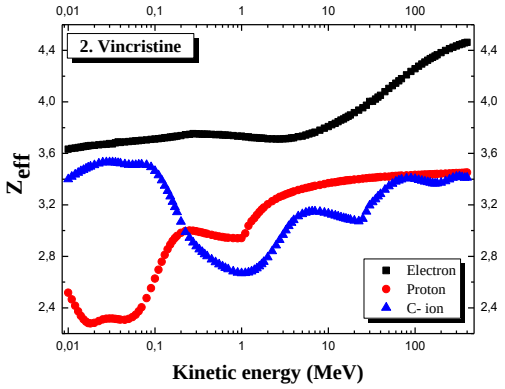

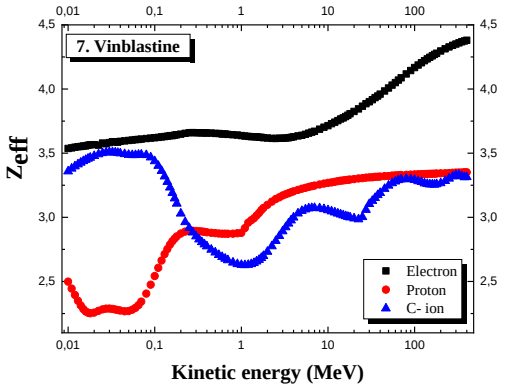

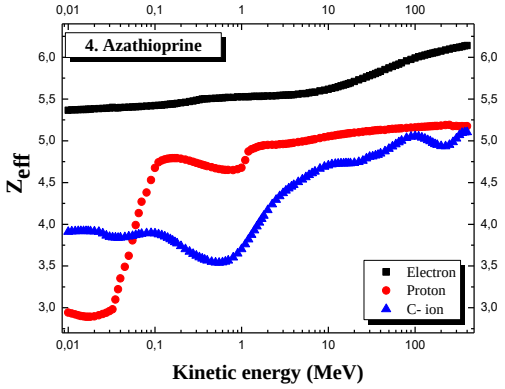

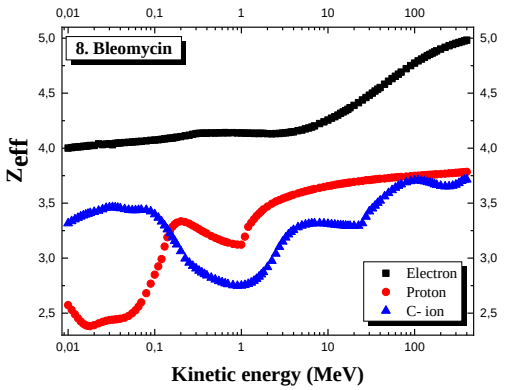

Figures 4. Variations in Z_{eff} for electron, proton and C ion interactions.

It can be obviously seen from the figures, electron interaction has higher values than proton and C ion interaction in Z_{eff}s of the drugs. In addition, differences between proton and C ion interactions are larger at lower energies and the drugs have the same Z_{eff} value between 0.05-0.3 MeV energies for the ions. The differences decrease as ion energy increases and after 50 MeV they get the same Z_{eff} again.

The obtained results were compared with the Phy-X/ZeXTRa program between 10 keV-15 MeV energy region. Phy-X/ZeXTRa program calculates the effective atomic number of different types of materials for photon, electron, proton and C ion between 10 keV – 15 MeV energy region [18]. For comparison differences (%) between the obtained and Phy-X/ZeXTRa results in Z_{eff} were calculated as $diff.(\%) = \left(Z_{eff.ZeXTRa} - Z_{eff.calc} \Big/ Z_{eff.ZeXTRa}\right).100$ in the energy region 10 keV -15 MeV. A minimum difference (0.97%) was observed for electron interaction in the energy region. But a maximum difference (20.30%) was observed for C ion interaction for Vinblastine in the energy region as shown in Fig. 5.

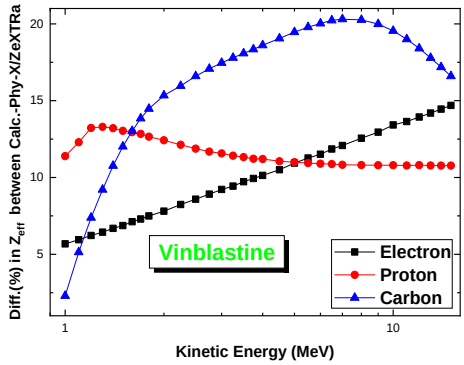

Figure 5. Differences (%) between calculated and ZeXTRa values in Z_{eff} for electron, proton and C ion interactions.

4. Conclusion

Chemotherapy drugs are important for cancer treatment. Therefore, it is very important the drugs are distinguished from each other according to Z_{eff} and N_{eff} in the energy region in irradiated application. Some chemotherapy drugs were studied according to Z_{eff} and N_{eff} for the first time in energy region 10 keV-400 MeV for total electron, proton and C ions interaction. Variations of Z_{eff} and N_{eff} have been studied for charged particle interactions with particle energy. The highest and lowest values of Z_{eff} were observed in Azathioprine (6.14) for electron interaction and in Vinblastine (2.25) for proton interaction in the continuous energy region respectively. Z_{eff}s for electron, proton and C interactions have not the same value, but for proton and C ions, it has the same value two or three times in the continuous energy region interestingly.
It can be said that N_{eff}s of the drugs have the same intersections because of the mathematical relation between Z_{eff} and N_{eff}. It can be also concluded that Z_{eff} and N_{eff} depend on ion energy like photon interaction. The obtained results were also compared with the Phy-X/ZeXTRa program, and the maximum difference (%) was observed for Vinblastine as 20.30%. The obtained data should be helpful in developing software programs and chemoradiation when charged particles into these materials as they represent the interaction of particles with these drugs in the continuous energy region.

Author's Contributions

Mehmet Büyükyıldız: Made literature search and experiments, writing - review & editing.
Murat Türemiş: Data curation, investigation, helped in manuscript preparation & editing.

Ethics

There are no ethical issues after the publication of this manuscript.

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