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Investigation of Radiation Interaction Parameters of Anti-Human Immunodeficiency Virus Drugs in Wide Energy Region

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Abstract: Human Immunodeficiency Virus (HIV) positive patients are exposed to radiation therapy for the treatment of various types of cancer. During these treatments, it is inevitable that radiation will interact with the antiviral drugs used. Determining the radiation attenuation parameters of drugs used in HIV treatment is, therefore, considered essential. In this context, the radiation attenuation capabilities of the HIV drugs were analyzed based on the parameters mass attenuation coefficient (MAC), atomic cross section (ACS), electronic cross section (ECS), effective atomic number (Z_{eff}), exposure build-up factor (EBF) and energy absorption build-up factor (EABF). The values were investigated in the 0.015-15 MeV range using the Phy-X/PSD software. The build-up factors were also analyzed using the geometric progression (G-P) method up to a penetration depth of 40 mean free path (MFP). Based on the results, Efavirenz and Indinavir were found to have the highest and lowest radiation attenuation capacities, respectively. It is believed that these findings can be used to make medical processes more beneficial.

Anti-İnsan İmmün Yetmezlik Virüsü İlaçlarının Geniş Enerji Bölgesindeki Radyasyon Etkileşim Parametrelerinin İncelenmesi

Anahtar Kelimeler
Anti-HIV ilaçlar, Radyasyon zayıflaması, Radyasyon-madde etkileşimi, Kanser tedavisi, Phy-X/PSD yazılımı

Öz: İnsan İmmün Yetmezlik Virüsü (HIV) taşıyan hastalar, çeşitli kanser türlerinin tedavisi için radyasyon tedavisine maruz kalmaktadır. Bu tedaviler sırasında radyasyonun kullanılan antiviral ilaçlarla etkileşime girmesi kaçınılmazdır. Bu nedenle HIV tedavisinde kullanılan ilaçların radyasyon zayıflatma parametrelerinin belirlenmesi elzem kabul edilmektedir. Bu bağlamda, HIV ilaçlarının radyasyon zayıflatma yetenekleri kütle zayıflatma katsayısı (MAC), atomik zayıflatma tesir kesit (ACS), elektronik zayıflatma tesir kesit (ECS), etkin atom numarası (Z_{eff}), maruz kalma birikim faktörü (EBF) ve enerji soğurma birikim faktörü (EABF) parametreleri temel alınarak analiz edilmiştir. Değerler Phy-X/PSD yazılımı kullanılarak 0.015-15 MeV aralığında incelenmiştir. Ayrıca birikim faktörleri 40 ortalama serbest yol (MFP) penetrasyon derinliğine kadar geometrik ilerleme (G-P) yöntemi kullanılarak analiz edilmiştir. Sonuçlara göre, Efavirenz ve Indinavir ilaçlarının sırasıyla en yüksek ve en düşük radyasyon azaltma kapasitelerine sahip oldukları bulunmuştur. Bu bulguların tıbbi süreçleri daha faydalı hale getirmek için kullanılabileceğine inanılmaktadır.

1. INTRODUCTION

Ionizing radiation is a widely used therapeutic instrument in the field of medicine. Radiation, especially in low doses, has become indispensable for modern medical practices. Low-dose ionizing radiation is used in the treatment of different cancers, infections, inflammations, autoimmune and neurodegenerative diseases, traumatic brain injuries, and damaged parts of the brain after cerebral palsy. In addition, radiation in imaging systems

used in the diagnosis phase before treatment is quite common [1-3]. Life expectancy in HIV-positive patients has increased significantly with effective antiretroviral treatments. As life expectancy increases, the incidence of cancer in HIV-positive individuals has also increased. As it is known, the incidence of various types of cancer increases with the weakening of the immune system in HIV-positive patients. In other words, individuals with HIV infection and AIDS have a high risk of cancer. The most common cancer types in these patients include cervix cancer, anal and oropharyngeal cancers, liver cancer associated with hepatitis B infection, Lung cancer, Kaposi's sarcoma, and non-Hodgkin lymphomas [4, 5]. In this context, HIV-positive patients are likely to be exposed to ionizing radiation during cancer treatments, especially due to chemotherapy applications. There is a high probability that antiretroviral drug treatments and cancer treatments will be used together in the treatment processes of these patients. Detecting the interactions of drugs used in HIV treatment with ionizing radiation may be useful in terms of treatment processes.

Many studies aim to determine the radiation attenuation parameters of drugs that treat different diseases. These studies are particularly focused on cancer drugs. Lomustine, Cisplatin, Carmustine, and Chlorambucil are drugs in the alkylating agent class most commonly used in chemotherapy. The radiation attenuation parameters of these drugs have been calculated theoretically in the range of 1 KeV-100 GeV. The parameters examined are MAC, linear attenuation coefficient (LAC), half-value layer (HVL), mean free path (MFP), and Z_{eff}. As a result of the investigations, it was determined that the changes in these values differ depending on the energy range of the radiation. The highest MAC, LAC, and Z_{eff} parameter values were reached in the low-energy region. Cisplatin, the drug with the highest physical density and molecular weight, was determined to have the best radiation attenuation feature [6]. Again, in a study examining the radiation attenuation parameters of cancer drugs, the Z_{eff} and electron density (N_{el}) of Anastrozole, Epirubicin, Gemcitabine, Ifosfamide, Methotrexate, and Paclitaxel were calculated theoretically in the energy region of 1 keV to 100 GeV. Energy absorption buildup factors (EABF) and exposure buildup factors (EBF) for these chemotherapy drugs were also examined by applying the Geometric Progression (GP) fitting method. It has been observed that Z_{eff} and N_{el} values depend on photon energies. It has been determined that buildup factors depend on photon energy, the chemical composition of the drug, and MFP. For the drug Ifosfamide, which has a high radiation attenuation capacity, the highest deposition factors were calculated at 15 MeV and the lowest buildup factors at 0.015, 0.15, and 15 MeV energy values [7].

Radiation attenuation parameters of some molecules used in chemotherapy drugs were examined. The investigations were carried out using the XCOM program in the energy range of 1 keV to 100 GeV, using the parameters of Z_{eff}, effective electron density (N_{eff}), and mass attenuation coefficient (μ/ρ). Z_{eff} and N_{eff}'s values were calculated for the drugs Cisplatin, Carboplatin, Oxaliplatin, Ifosfamide, Gemcitabine, Fluorouracil, Pemetrexed, Etoposide, Vincristine, Tamoxifen, and Paclitaxel. Sharp changes in these values have been detected in molecules with high atomic numbers. Especially Cisplatin, Carboplatin, and Oxaliplatin molecules containing the Platinum (Pt) element have the highest Z_{eff} value and showed the best radiation attenuation performance [8].

Antibiotics were also examined in terms of their radiation interaction properties. The study considered the stability, effectiveness, and structural integrity of the relevant drugs under the influence of radiation. The parameters examined are basic parameters such as attenuation coefficients LAC, MAC, N_{eff}, EBF, and EABF, as well as photon transmission factors (TF). This modeling study was conducted using MCNPX Monte Carlo simulation. Theoretical calculations were made using the Phy-X/PSD software. The data shows that the properties of antibiotics exposed to radiation change significantly. It has been observed that serious molecular changes occur, especially in antibiotics that accumulate high radiation in terms of MeV/g. Ceftriaxone/Cefotaxime is the drug with the highest accumulation. These data may be considered in terms of the effectiveness and safety of the drug in intense radiation environments [9].

Similar studies have been conducted on radioprotective materials used in radiation therapy. Natural products such as Apigenin, Bergenin, Caffeine, Chlorogenic acid, Coniferyl aldehyde, Curcumin, Delphinidin, and Quinic acid, which have low toxicity, are the most commonly used radio protectants. The radiation interaction mechanisms of these radioprotectors with gamma and neutron radiation were investigated. The research was conducted on MAC, Z_{eff}, equivalent atomic number (Z_{eq}), N_{eff}, EBF, and EABF parameters. According to the data obtained, Z_{eff} values were determined to be higher in low-energy regions. These results indicate that radio shields are suitable for shielding low-energy gamma radiation. Quinic acid showed the best radioprotective properties for thermal and fast neutrons among the radio protectants examined [10].

As seen in the literature review above, many studies have shown the radiation attenuation properties of drugs and molecules used to make drugs. However, studies on HIV drugs are scarce. In a study, the drugs Combivir, Kivexa, Trizivir, Truvada, Tenofovir, Lopinavir, and Nelfinavir used in the treatment of HIV were examined. Examination: 0.015–15 MeV via MAC, ACS, ECS, Z_{eff} and N_{eff} parameters, Phy-X/PSD software program made with. In addition, EBF and EABF values were determined with the G-P method up to a penetration depth of 40 MFP. The data shows that Combivir has a high content of heavy elements and has the best radiation attenuation ability [11]. In this study presented in this context, other drugs used by HIV-positive patients have been examined in terms of their radiation attenuation abilities. Examined drugs are Tipranavir, Efavirenz, Nevirapine, Atazanavir, Darunavir, Fosamprenavir, Indinavir and Ritonavir. The review was conducted on the parameters MAC, ACS, ECS, Z_{eff}, N_{eff}, EBF, and EABF. EBF and EABF parameters were analyzed up to 40 MFP penetration

depth. The motivation of the presented study is to provide more comprehensive data on the radiation attenuation parameters of antiviral drugs used by HIV-positive patients. Studying how drugs interact with radiation can provide valuable data for medical applications. This information can be used to adjust the dosage of drugs and radiation to be administered during the treatment process. This insight can be considered an additional motivation for this study.

2. MATERIAL AND METHOD

In this study, the radiation attenuation parameters of seven drugs (Tipranavir, Efavirenz, Atazanavir, Darunavir, Fosamprenavir, Indinavir, and Ritonavir) used by HIV-positive patients are presented comparatively. The chemical formulas, compositions, and elemental weight percentages of the investigated drugs are given in Table 1.

Table 1. Chemical formulas and compositions of the investigated drugs in weight fraction.

Drug	Chemical Formula	Molecular Weight (g/mol)	C	H	N	O	S	Cl	F	P
Tipranavir	$C_{31}H_{33}F_3N_2O_5S$	602.669	0,6178	0,0552	0,0465	0,1327	0,0532	-----	0,0946	-----
Efavirenz	$C_{14}H_9ClF_3NO_2$	315.676	0,5327	0,0287	0,0444	0,1014	-----	0,1123	0,1806	-----
Atazanavir	$C_{38}H_{52}N_6O_7$	704.869	0,6475	0,0744	0,1192	0,1589	-----	-----	-----	-----
Darunavir	$C_{27}H_{37}N_3O_7S$	547.667	0,5921	0,0681	0,0767	0,2045	0,0586	-----	-----	-----
Fosamprenavir	$C_{25}H_{36}N_3O_9PS$	585.609	0,5127	0,0620	0,0718	0,2459	0,0548	-----	-----	0,0529
Indinavir	$C_{36}H_{47}N_5O_4$	613.803	0,7045	0,0772	0,1141	0,1043		-----	-----	-----
Ritonavir	$C_{37}H_{48}N_6O_5S_2$	720.948	0,6164	0,0671	0,1166	0,1110	0,0890	-----	-----	-----

The MAC value is the most commonly used parameter to evaluate radiation-matter interaction. The well-known Beer-Lambert law states that the relationship between un-attenuated (I_0) and attenuated (I) photon intensities as following formula:

$$I=I_0\, e^{(-\mu t)} \qquad (1)$$

where, μ is the linear attenuation coefficient. In experimental studies, the MAC value can be obtained by dividing the LAC value by the density value of the material. In theoretical studies, the energy-dependent MAC value is obtained by using the elemental content of the material. Many studies in the literature state how these calculations are made [12, 13, 14, 15, 16]. EBF and EABF parameters were calculated using the G-P fitting method. The coefficients (a, b, c, d, and Xk) used in this method were taken from the ANSI database [17, 18]. Theoretical calculations were made in the 0.015-15 MeV range using the Phy-X/PSD software [19]. This software is designed to analyze the interactions of X and gamma rays with matter. It is widely used in fields such as radiation physics, radiotherapy, and radiation protection. The software can perform high-accuracy calculations thanks to detailed physical models and a comprehensive database. It facilitates operations such as shielding design and calculation of interaction cross-sections thanks to its user-friendly interface. It stands out as a reliable tool in scientific research and industrial applications.

3. RESULTS AND DISCUSSION

The MAC is the most fundamental parameter in photon-matter interactions. This parameter presents the interaction cross-section of the incident photons with the target material [13]. This value expresses all interaction processes, including scattering, according to the structure of the absorbing material and the incoming photon energy [14]. The change in MAC values of the drugs examined is presented in Figure 1.

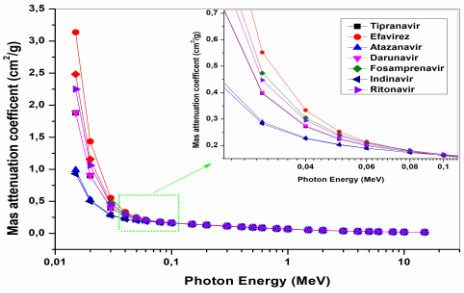

Figure 1. The investigated drugs' MAC values differ from the incoming photon energy.

By looking at the MAC values of the drugs, they can be listed from highest to lowest as Efavirez, Fosamprenavir, Ritonavir, Darunavir =Tipranavir, Atazanavir, Indinavir. It is known that materials with a high abundance of elements with high atomic numbers have a better absorption capacity for excitation photons. Among the analyzed drugs, Efavirenz, which has the composition $C_{14}H_9ClF_3NO_2$, contains 0.5327% Cl element in its structure. Cl element has a higher atomic number and density than other elements such as C, H, and O. The high Cl ratio and density of the drug are the main reasons for the higher MAC value of this drug. The dominant photon-matter interaction mechanism in the low energy range (E<0.2 MeV) is the photoelectric interaction [11]. As is known, this interaction is effective at low energies and occurs when a bound electron completely absorbs the incoming photon. In this interaction, at any given energy value, the entire energy of the incident photon is transferred to an electron of the target material [13]. The dependence of the photoelectric absorption cross-section

on the incident energy and atomic number of the target material is $1/E^{3-5}$ and Z^{4-5}, respectively [6]. Therefore, the target materials exhibit excellent shielding characteristics at such a low energy level. After the energy value of 0.05 MeV, the MAC values of the drugs show a sharp decrease, and the values begin to stabilize. The mechanisms by which photons of medium (0.2 <E< 1 MeV) and high (E>1 MeV, especially E>3 MeV) energy interact with matter are Compton scattering and pair production, respectively [20]. Medium-energy photons interact with matter via Compton scattering. In Compton scattering, electrons in the target material absorb some of the incident photon's energy, and the photon is scattered. At the same time, the interacting electron is scattered in another direction. Again, the scattered photon may undergo multiple scattering in matter. Pair production is the primary photon-matter interaction mechanism when the incident photon's energy is more significant than 1.022 MeV. Here, when the incident photon approaches the atom, it is converted into an electron-positron pair due to the interaction. This phenomenon can be described as the conversion of energy into matter.

The variation of ACS, which represents the interaction cross sections per unit atom, is shown in Figure 2. The ACS value is another radiation attenuation parameter and expresses the probability of interaction of primary photons with atoms in the material. As the likelihood of interaction increases, the ability to attenuate radiation also increases. This interaction is again directly proportional to the presence of heavy nuclei atoms in the target material. The main reason for the difference in ACS values is the different mole percentages of the elements in the target materials. Incident photon energy and atomic content of the target are the factors that directly affect the ACS value. The higher the mole percentage of the heavy element in the material, the higher the ACS value. Thus, the indicator of radiation attenuation ability is a high ACS value. Examining the ACS values in Figure 2 shows that their changes are similar to the MAC values. Again, it is seen that ACS values are high at low energy levels. However, unlike the course of MAC values, the uniformity in values with increasing photon energy started from 0.06 MeV, not 0.04 MeV. When the ACS values of the investigated drugs are examined, the ranking is from the highest value to the lowest value; they are Efavirenz, Fosamprenavir, Ritonavir, Tipranavir, Darunavir, Atazanavir, Indinavir. At 0.015 MeV energy, the highest ACS value is $5.47x10^{-23}$ (cm^2/atom) for the drug Efavirenz, while the lowest ACS value is $1.03x10^{-23}$ (cm^2/atom) for the drug Indinavir. While the ACS value for all drugs is $1.7x10^{-23}$ (cm^2/atom) at 0.06 MeV energy, where convergence begins, this value is determined as $0.033x10^{-23}$ (cm^2/atom) at 15 MeV energy.

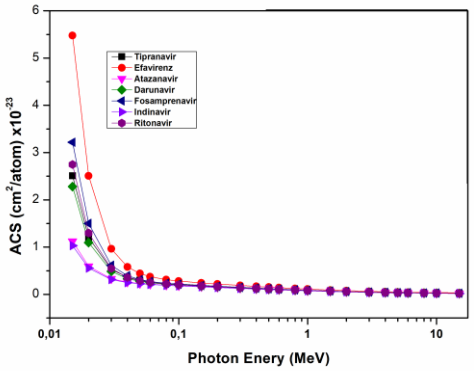

Figure 2. The changes in ACS values of drugs according to incoming photon energy.

Another parameter of drugs that is examined is the ECS parameter. This parameter is critical. It allows the calculation of the adequate atomic numbers of the target materials when evaluated with ACS. The variations in the investigated drugs' ECS values versus the incoming photon energy. The ECS values change according to the incident photon energy, as depicted in Figure 3. The ordering of ECS values is similar to the ordering of MAC and ACS values, as expected. The order is Efavirez, Fosomprenavir, Ritonavir=Tipranavir, Darunavir, Atazanavir and Indinavir. These values show that the drugs examined may have the ability to attenuate incoming radiation at low energies. While there is a difference in the range of 0.015-0.06 MeV, as the energy of the incoming radiation increases, the ECS values of all drugs decrease and become equal at 0.06 MeV. The differentiation at low energies and the decrease in differentiation with increasing energy can be seen more clearly in the inset in Figure 3. The highest ECS value at 0.015 MeV is $5x10^{-24}$ (cm^2/electron) for the drug Efavirenz, while the lowest ECS value is $1.86x10^{-24}$ (cm^2/electron) for the drug Indinavir. At 0.06 MeV energy, where uniformity begins, the ECS value is $0.6x10^{-24}$ (cm^2/electron) for all drugs. The decrease in the ECS value with increasing photon energy is due to the increased possibility of high penetration of high-energy photons in drugs. The ECS value obtained for all drugs at 15 MeV energy is $0.05x10^{-24}$ (cm^2/electron). Contrary to ACS values, it is observed that the uniformity in ECS values begins at lower energies. This is because, as stated before, ACS values depend on the elements' mole percentages, atomic weights, incoming photon energy, and MAC value. In contrast, ECS values are affected by atomic numbers as well as these factors [21].

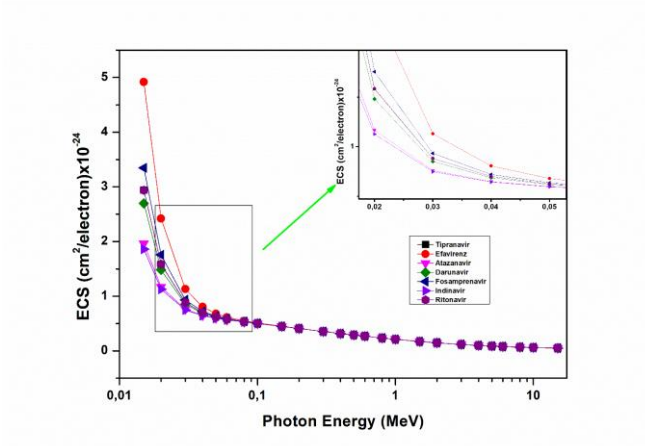

Figure 3. The variations in the investigated drugs' ECS values versus the incoming photon energy.

Z_{eff} value expresses the virtual atomic number of the target material and varies according to the incoming photon energy [22]. This value, shaped by the material's response to incoming photon energy, is an essential indicator of radiation attenuation ability. Z_{eff}, which reflects the complex atomic characteristics of a material containing more than one type of atom, can be used to evaluate the radiation interactions of alloys, compounds, composites, etc. The changes in the Z_{eff} values of the examined drugs in the 15 keV-15 MeV energy range are shown in Figure 4.

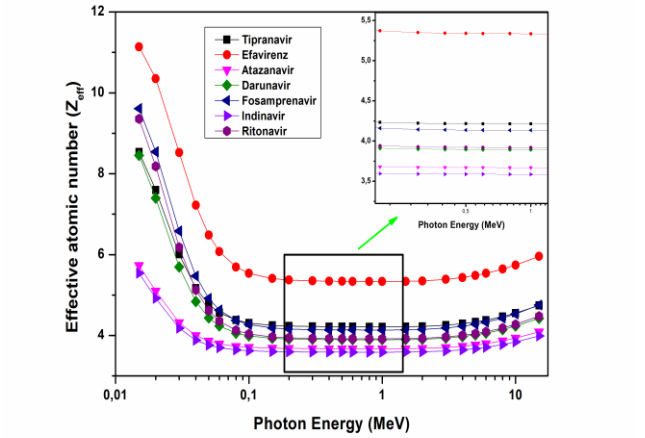

Figure 4. The variations in the investigated drugs' Z_{eff} values versus the incoming photon energy.

As seen in Figure 4, the Z_{eff} values of the drugs are listed from high to low as Efavirenz, Fosamprenavir, Ritonavir, Tipranavir, Darunavir, Atazanavir, and Indinavir. It is observed that Z_{eff} values decrease with increasing photon energy in low-energy regions (0.015-0.15 MeV). In the energy range of 0.2-1.5 MeV, it is observed that the Z_{eff} values of all drugs follow a stable course despite increasing energy. In the range of 1.5-15 MeV, it is observed that there is a slight increase in Z_{eff} values with increasing photon energy. This can be interpreted as drugs' slightly increased radiation attenuation ability in the high-energy region. In the high-energy areas, the incoming photon can turn into an electron-positron pair (pair production). In the range of 1.5-15 MeV, this may become dominant. This can cause attenuation of the incoming photon. The presence of the Cl atom, which has a relatively heavy nucleus, in the content of the Efavirenz drug, which has a high Z_{eff} value, draws attention. The Z_{eff} value of Efavirenz is 11.14 at 0.015 MeV and 5.96 at 15 MeV. The Z_{eff} values of the drug Indinavir, which has the second highest Z_{eff} value, at 0.015 and 15 MeV energies, are 9.61 and 4.74, respectively. The fact that Z_{eff} values of drugs follow a different course compared to MAC, ACS, and ECS values can be considered a reflection of the fact that this value depends more firmly on the energy of the incoming photons and the content and density of the target material. The decrease, stabilization, and slight increase in the Z_{eff} value with increasing energy can be attributed to the change in the dominance of partial photon interaction mechanisms relative to each other according to the incident photon energy. Z_{eff} values are high in the low-energy region where photoelectric interaction dominates. The high Z_{eff} values in low-energy areas can be attributed to the fact that the cross-section of the photoelectric effect is directly proportional to Z^{4-5}. In the medium energy region where Compton scattering is effective, Z_{eff} values of drugs are relatively low and uniform. The reason for observing relatively low and constant Z_{eff} values in the Compton region can be attributed to the fact that the Compton scattering process is proportional to Z. In the high-energy areas where the possibility of pair production is high, the Z_{eff} values of drugs increase slightly since the pair formation mechanism depends on the Z^2 value [20].

In a healthy radiation attenuation analysis in non-vacuum environments, scattering in the air must be considered. These effects can be understood by examining EBF and EABF values. These two values can be thought of as values that indicate the amount of secondary scattering produced by the radiation in the material and the medium. The higher these two values are, the greater the scattering in the material and environment. They also indicate the exposure of the target to the scattered radiation and the mechanisms used to transfer energy within the material. A high value of these means too much secondary radiation in the environment. This is undesirable for radiation protection and attenuation [23]. EBF can be defined as the energy accumulation that occurs during radiation propagation within the material, which includes scattering. This value varies depending on the depth of the material and the energy and type of the incoming photon. All factors contributing to the scattering of the incident photon are included in the EBF value [24].

The EABF value is a value that expresses the amount of radiation absorption by the environment and material through which it passes. The amount of radiation absorption may increase depending on the path it follows in the environment or material. Determining these values is essential in examining the material's ability to reduce radiation. In other words, EBF and EABF values are indicators of the ability of the material or medium to absorb and accumulate incoming radiation [25]. The geometric progression (G-P) method was used to calculate these values. This method incorporates the Monte Carlo simulation method with iterative, invariant accumulation properties. Previous studies have stated that

this method is suitable for calculating these two factors [26].

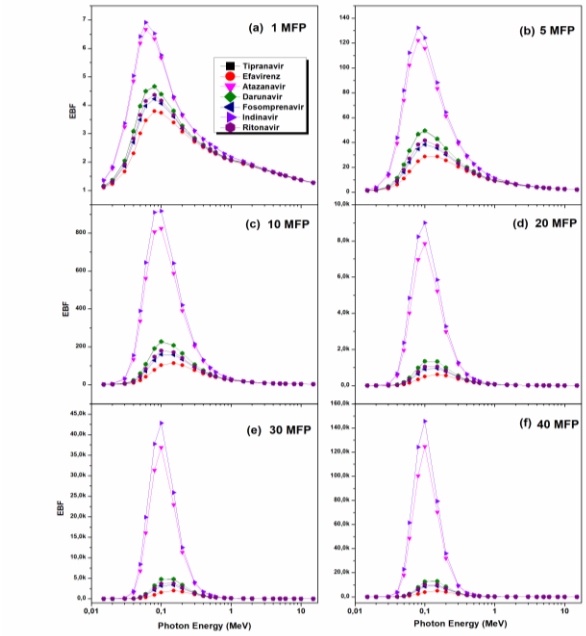

Figure 5. The variations in EBF with photon energy at 1, 5, 10, 20, 30, and 40 MFP for the investigated drugs.

Looking at the general trend in Figure 5, the order of EBF values of the drugs from highest to lowest is Indinavir, Atazanavir, Darunavir = Tipranavir, Ritonavir, Fosamprenavir, and Efavirenz. As expected, this order is the opposite of the MAC values. The uniformity of the EBF values in the low energy region at all depths is related to the high level of photoelectric effect in this region. The activation of Compton scattering explains the high EBF values in the intermediate energy regions. In the case of Compton scattering, the EBF values increase due to the amount of second scattering. In the high energy region, as the cross section for pair production is high, the scattering is reduced, and the EBF values decrease [27].

Efavirenz, which has the highest MAC value, shows the lowest EBF value here. It is an expected result that this drug, which has the highest radiation attenuation according to MAC values, will show the lowest EBF value at all depths due to its chemical content. The graphs are examined in detail; it is seen that the EBF values of the drugs increase in the range of 0.015 MeV-0.1 MeV as the photon energy increases at all depths. At a depth of 1 MFP, the value of Indinavir and Atazanavir drugs reach the highest value with 0.06 MeV, while other drugs reach their peak values with 0.08 MeV. At depths of 5 and 10 MFP, the EBF values of all drugs exhibit a peak at 0.08 MeV energy. At depths of 20, 30, and 40 MFP, the EBF values of all drugs are highest at 0.1 MeV energy. After this energy range, EBF values decrease as energy increases. With increasing penetration depth, the EBF behavior of the drugs becomes similar. This can be expressed in terms of the differences in the content of the drugs becoming insignificant as the depth of penetration increases. Since photoelectric absorption in the low-energy region and pair formation in the high-energy regions are dominant, the photon is completely absorbed in these interaction mechanisms. Consequently, the probability of secondary scattering is decreased, and the values of the scattering factor are low. Compton scattering is dominant in the interaction of the target sample with medium energy photons. Since photon energy cannot be removed entirely in this scattering, secondary multiple scattering is intense. Therefore, high scattering factors are expected [10, 20].

The changes in EBF values according to MFP and energy values were examined, and the following figure has been determined.

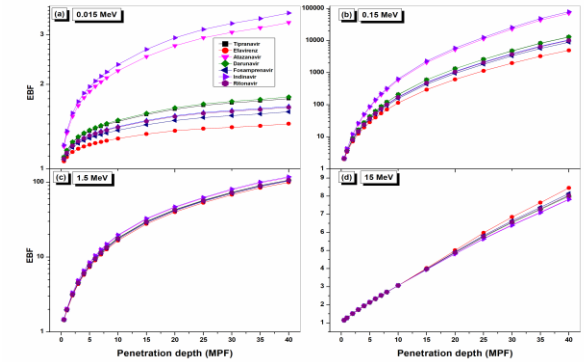

Figure 6. The EBF values for the investigated drugs up to 40 MFP at 0.015, 0.15, 1.5, and 15 MeV.

By examining Figure 6, it is seen that as the depth increases at 0.015 MeV, the EBF values of all drugs increase. Generally, the high to low order is Indinavir, Atazanavir, Darunavir, Tipranavir, Ritonavir, Fosamprenavir, and Efavirenz. The EBF values of all drugs increased with increasing depth at this energy level. After 15 MFP, the increasing values decreased compared to deeper depths. At 40 MFP, Indinavir and Efavirenz have EBF values of 3.58 and 1.44, respectively. The course of EBF values of drugs at 0.15 MeV energy value is similar to the course at 0.015 MeV energy value. However, the difference between them is gradually decreasing. Indinavir 79366 and Efavirenz 4963 show EBF values at 40 MFP at 0.15 MeV energy. Efavirenz has the highest MAC value and the lowest EBF at all depths, which is an expected result. However, the difference between the EBF values of Efavirenz and Indinavir, which showed the highest and lowest attenuation ability at 0.015 MeV, is remarkable. At 0.015 MeV, the percentage difference between the two values is 1.5 %, while at 0.15 MeV, the difference increases to 15 %. At energies below 0.5 MeV, the photoelectric interaction is more dominant. From 0.5 MeV to 1.022 MeV, Compton scattering comes into play, and the scattering rate increases with increasing energy in the photon energy ranges given.

The EBF values of Indinavir and Efavirenz at 0.015 and 0.15 MeV and 40 MFP depth show a difference of 22% and 3.44%, respectively. The difference between the EBF values for Efavirenz, which has a high ability to attenuate radiation at two energies, is more minor. This may mean that the radiation attenuation capacity of the target material, which contains heavy nuclei in its content, follows a more stable course in these two energy ranges. However, in the case of the drug Indinavir, which has the

lowest attenuation, it is seen that the attenuation capacity of the drug decreases more rapidly with increasing energy. At an energy level of 1.5 MeV, although there is an increase in the EBF values of the drugs with depth, the values are close to each other. The drug content is less effective at this energy level than at lower energies. The EBF value of Indinavir is 106, while Efavirenz's is 104 at 1.5 MeV energy and 40 MFP. The difference between the two values in percentage terms is 0.019, which is a minimal difference.

At 15 MeV, the drugs behave differently compared to other energies. The EBF values are the same for all drugs up to 15 MFP, and they differ slightly after this energy level. The order of EBF values in the relevant region, from highest to lowest, is Efavirenz, Fosamprenavir, Ritonavir ≈ Tipranavir ≈ Darunavir, and Indinavir ≈ Atazanavir. Notably, the drug Efavirenz, which has a high ability to attenuate radiation, exhibits the highest EBF value. Efavirenz is expected to have the lowest EBF value when evaluated based on MAC values. Indinavir, on the other hand, shows the lowest EBF values. This can be interpreted as a reduced ability of Efavirenz to attenuate radiation at high energies. Efavirenz has an EBF of 8.45 and Indinavir 7.81 at 40 MFP at 15 MeV. The difference is slight, 0.082%. Based on these results, it can be said that since the radiation-matter interaction mechanism is in the form of pair production rather than scattering, there may be unexpected changes in the radiation attenuation capabilities of the drugs at high energy levels. When the MAC values are analyzed, the decrease and sameness of MAC values with an increase in energy values are compatible with this unexpected situation. Suppose this unexpected situation is analyzed in terms of Z_{eff}. In that case, the slight increase in the Z_{eff} value after 1.5 MeV for all the drugs is related to the rise in the non-scattering interaction mechanisms.

The compositional dependence and the rate at which the EBF increases vary with the incident photon energy. At the energy of 0.015 MeV, the rate of increase of the accumulation factor is lowest, and the effect of the compositional dependence is small. As mentioned, the EBF values of the drugs are maximal at 0.15 MeV. Due to the Compton scattering regime, the importance of the drugs' compositional content is further reduced at this energy. At energies of 1.5 and 15 MeV, the rate of increase of the buildup factor decreases, and the chemical content becomes even less important. This is due to the weak dependence of the Compton scattering cross section on the Z_{eff} value at high energies. In the case of pair production, the cross-section is directly proportional to the square of Z_{eff} [27].

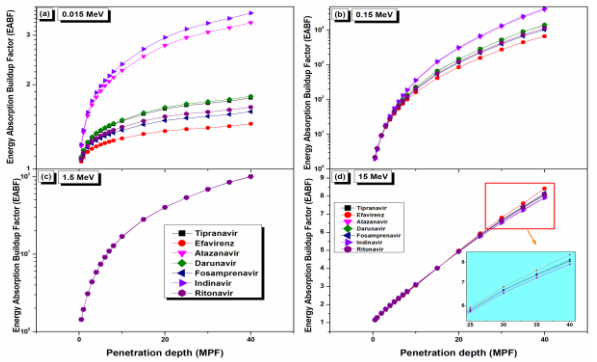

Figure 7. The EABF values for the investigated drugs up to 40 MFP at 0.015, 0.15, 1.5, and 15 MeV.

The results obtained for EABF values are given in Figure 7. These results show that the drugs with an energy value of 0.015 MeV are listed from high to low as Indinavir, Atazanavir, Darunavir, Tipranavir, Ritonavir, Fosamprenavir, and Efavirenz. This ranking is parallel to the EBF values. Although the differences between the behaviors exhibited by drugs for the 0.15 MeV energy value decrease, they are similar to the behaviors they exhibit at 0.015 MeV. However, a complete convergence was observed at 1.5 MeV. For the EABF values, the compositional dependence completely disappears at all depths at this energy value.

As energy increases, the absorption behavior of drugs changes significantly. This change becomes quite evident at 15 MeV, and with increasing depth, the EABF values of the drugs show themselves in a different order, unlike the values in the low-energy regions. At 15 MeV energy value, a slight difference in the values began after 20 MFP depth. The differentiation became more observable after 25 MFP, and the order of the values was from high to low: Efavirenz, Fosamprenavir, Ritonavir ≈ Darunavir ≈ Tipranavir, Atazanavir ≈ Indinavir. Notably, the Efavirenz drug, which has a high MAC value with increasing penetration depth at this energy value, also shows a high EBAF value. In terms of EABF values, other drugs exhibited the opposite behavior in the relevant region to their behavior in the low-energy areas. At 15 MeV, this behavior of the EBF values has the same reasons as that of the EBF values at this energy. At photon energies higher than 0.15 MeV, EABF values decrease due to decreased scattering interactions. At 0.015 MeV, Indinavir has an EABF value of 3.6, while Efavirenz has an EABF value of 1.45.

4. CONCLUSION

This study is an investigation of the radiation attenuation capabilities of several HIV drugs. In the specific case of HIV, this study aims to elucidate the drug-radiation interaction processes. Analyses were performed on the parameters MAC, ACS, ECS, ECS, Z_{eff}, EBF, and EABF. It was found that Efavirenz, the drug with the highest compositional content, had the highest radiation attenuation capacity. Indinavir had the lowest radiation attenuation capacity. It is seen that the radiation attenuation capabilities of the drugs are effective in low-energy regions. If MAC values are analyzed at 0.015 MeV

for the lowest and highest performing drugs, Indinavir and Efavirenz, 0.92 and 3.13 (cm^2/g) values are found, respectively. Z_{eff} values for the same drugs are 5.53 and 11.14, respectively, supporting the results obtained with MAC values. When reviewing the literature on the radiation attenuation capabilities of various HIV drugs, it becomes evident that drugs containing heavy elements with high atomic numbers exhibit greater radiation attenuation capabilities. In a study involving different HIV drugs, it was found that Combivir, with the chemical formula $C_{10}H_{16}N_5O_{13}P_3$, had the highest MAC value. Compared to other elements, the higher atomic number (15) of phosphorus (P) in Combivir contributes to this ability. Furthermore, Truvada, which was administered before HIV and contains sulfur (S) with an atomic number of 16, demonstrated the second highest attenuation capacity [11]. In a study of cancer drugs, Ciplatin, with the chemical formula $Pt(NH_3)_2Cl_2$, showed the highest radiation attenuation ability among the drugs examined [6]. The presence of platinum (Pt), with an atomic number of 78, in Ciplatin is noteworthy. A consistent finding from the reviewed studies indicates that the radiation attenuation ability of these drugs increases, particularly at low energy levels, while this ability decreases at higher energy levels. These findings align with the results of the present study. By identifying the mechanisms of drug interaction with radiation, the effectiveness of drug use can be enhanced. It is hoped that the data obtained in this study will assist in radiotherapy applications and dosimetry calculations for patients who must use HIV drugs.

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