MedAppSci
Journal of Medicine and Applied Sciences

Original Article
J Med App Sci, 2022; 2(2): 29-36

Ionizing electromagnetic radiation interaction properties of some antihypertensive drugs

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Received: *23 April 2021*
Revised: *10 July 2021*
Accepted: *12 August 2021*

ABSTRACT

In the present work, the mass attenuation coefficient (MAC), half value layer (HVL), mean free path (mfp), effective atomic number (Z_{eff}), electron densities (N_{el}), exposure and absorption build-up factors (EBF and EABF) of sixantihypertensive drugs (Fisonopril, Captopril, Losartan Potassium, Irbesartan, Ramipril, Telmisartan) have calculatedusing EpiXS program as a function of gamma-ray energy. Losartan Potassium has larger MAC, Z_{eff} and N_{el} values and lower HVL and mfp values than the other studied drugs. The smallest EBF and EABF values are observed for Losartan Potassium for all of the penetration depths. As a result, it can be said that losartan absorbs more photon radiation than the other drugs.

Keywords: Antihypertensive Drug, Photon interactions paramaters Mass attenuation coefficient, Exposure build-up factor

INTRODUCTION

Hypertension, defined as high blood pressure, is a public health problem associated with significant morbidity and mortality. Chronic high blood pressure leads to hypertensive heart disease as it causes an increase in the workload on the heart with the structural and functional changes it creates in the left ventricle, left atrium and coronary arteries. Hypertensive heart disease is the clinical reflection of all conditions including left ventricular hypertrophy (LVH) and related systolic or diastolic heart failure, conduction arrhythmias, atrial fibrillation and coronary artery disease (CAD) risk [1,2].

Heart disease and cancer are leading causes of morbidity and death worldwide. More than 50% of cancer patients receive radiotherapy during treatment[3]. Radiotherapy is the intense application of high-frequency electromagnetic waves to cancerous tissue. Patients receiving radiotherapy may also have hypertensive diseases and may use antihypertensive drugs concurrently with radiotherapy. Angiotensin converting enzyme (ACEIs) inhibitors (fosinopril, captopril, ramipril, etc.) and angiotensin receptor blockers (ARBs) (irbesartan, telmisartan, losartan, etc.) are among the drug groups indicated in hypertension [4,5]. These drugs are taken at least once a day, although they vary with the doctor's advice. Studies have found that the combination of ACE inhibitor and ARB is more effective in the treatment of cardiovascular diseases compared to their use alone[6,7].

Ionizing electromagnetic radiation is used in the diagnosis and treatment of many diseases in the field of health. These radiations (gamma and X-rays) can interact with atoms and molecules in tissues, causing free radicals that break chemical bonds [8]. When a compound is exposed to ionizing radiation, different interactions occur with the electrons of the atoms of the compound. Depending on the energy of the photon radiation, three different photon-matter interactions are observed. These interactions can be listed as follows: i) Photoelectric absorbing effect, ii) Compton scattering effect, iii) pair production event. There are some studies on drug-radiation interaction in the literature. Akman and Kacal (2018) investigated the photon attenuation parameters such as mass attenuation coefficient, linear attenuation coefficient, half-value layer, mean free path, and effective atomic number for chemotherapeutic drugs namely Lomustine, Cisplatin, Carmustine, and Chlorambucil [9]. Gounhalli et al. (2012) calculated total and partial photon interactions for a few narcotic drugs (ND) (Heroin (H), Cocaine (CO), Caffeine (CA), Tetrahydrocannabinol (THC), Cannabinol (CBD), Tetrahydrocannabivarin (THCV)) by the direct

method in the wide energy range of 1 KeV-100 GeV using WinXCOM [10]. Akbaba et al (in press) investigated the radiation interaction properties of several HIV drugs, with the purpose of determining the interaction parameters, mass attenuation coefficient (MAC), atomic cross-section (ACS), electronic cross-section (ECS), effective atomic numbers (Z_{eff}), and effective electron density (N_{eff}) in the range of 0.015-15 MeV [11]. Kavaz et al. (2015) computed photon energy absorption and exposure of build-up factors using the five-parameter geometric progression (G-P) fitting formula for some chemotherapy drugs in the energy range 0.015–15 MeV [12].

The present study aims to investigate the mass attenuation coefficient (MAC), half-value layer (HVL), mean free path (mfp), effective atomic number (Zeff), electron densities (Nel), exposure and absorption build-up factors (EBF and EABF) of six antihypertensive drugs (Fisonopril, Captopril, Losartan Potassium, Irbesartan, Ramipril, Telmisartan) using EpiXS program as a function of gamma-ray energy in the wide energy range of 1 keV to 100 GeV.

METHODS

Calculations of MAC, Z_{eff}, N_{el}, EBF and EABF

The probability of a electromagnetic radiation (EMR) interacting in a particular way with a exposed material, per unit path length,is called the linear attenuation coefficient (LAC), and it is of great importance in radiation-matter interaction [13].The mass attenuation coefficient (MAC) is the ratio of the LAC value to the density of the material (μ/ϱ).Half Value Layer (HVL) is the thickness of the absorbingmatter, which gives radiation flux rate of the half intensity [14].While the atomic number or average atomic number takes a single value for elements, compounds and mixtures, Hine (1952) mentioned that the effective atomic number cannot be expressed with a single number for materials composed of different elements [15].The effective electron density, N_{el}, stated in the number of electrons per unit mass is closely related to the Z_{eff} value [16].The build-up factors (EBF and EABF), which are important in radiation dosimetry applications, can be defined the ratio of the total value of a given amount of photon radiation any point in a medium to its radiation value reach the same point without collision [17].

The absorbing and scattering parameters of ionized electromagnetic radiation (EMR) passing through a mattercould be computed theoretically using EpiXS code. EpiXS is a new code with embedded EPDL2017 of ENDF/B-VIII and EPDL97 of ENDF/B-VI.8 libraries designed for EMR attenuation calculations. This code can provide the MAC (partials, total), as well as other fundamental EMR attenuation parameters including cross-sections (partials, total, electronic), linear attenuation coefficients, mean free paths (mfp), half-value layers (HVL), effective atomic numbers (Z_{eff}), effective electron densities (N_{el}), equivalent atomic numbers, and build-up factors (EBF and EABF) at photon energies between 1 keV and 100 GeV[18].

RESULTS AND DISCUSSION

The theoretical values of the mass attenuation coefficient (MAC), half-value layer (HVL), mean free path (mfp), effective atomic number (Zeff), electron densities (Nel), exposure and absorption build-up factors (EBF and EABF) of six antihypertensive drugs (Fosinopril, Captopril, Losartan Potassium, Irbesartan, Ramipril, Telmisartan) computed using EpiXS program as a function of gamma-ray energy in the wide energy range of 1 keV to 100 GeV. At the same time, the graph of MAC values versus energy is plotted in Fig.1. From the figure it can be seen that MAC values of studied drugs decrease as photon energy increases. This result shows that thesedrugs have a high absorbing capacity of low energy EMR and the absorbing capacity gradually decreases as EMR energies increase.Another important observation made while examining the same graph is that the MAC is dependent on the chemical formula of the drugs under investigation.Losartan potassium is the most radiation absorbing drug.When the studied drugs are evaluated among themselves, Losartan potassium contains K (Z=19) element with the highest atomic number.In the low energy region (1 keV-100 keV), where the probability of photoelectric absorption effect is high, MAC values are biggest in this energy region, since the cross section of the photoelectric absorption effect depends on the atomic number as Z^{4-5} [19].

Atintermediate energy zone (100 keV-10 MeV), it is observed that there is a decrease in the values of MAC due to the linear dependence between the cross-section of Compton scattering and atomic number Z. At high energy zone (10 MeV and beyond) the probability of pair production is increasing, and the MAC values increases as its probability is proportional to Z^2.

Fig.2. and Fig.3. illustrate the change in mfp and HVL values (respectively) depending on EMR.The results show that the Losartan Potassium has the lowest HVL and mfp values.This means that this drug absorbs more EMR than the others.The changes of Z_{eff} and N_{el} with EMR energy for the drugs were illustrated in Figs. 4-5.It was seen from these figures that, the highest value of $Z_{eff}$and N_{el} were found in the

low energy zone, as the Z^{4-5} dependence of photoelectric effect cross-section provides a extra contribution to the Z_{eff} of drugs.When evaluating MAC values, the same comments made for energy zones apply to $Z_{eff}$and N_{el}.

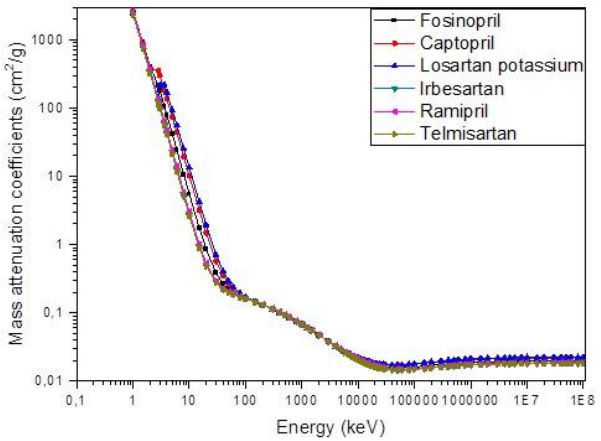

Figure 1. The theoretical values of MAC for studied drugs.

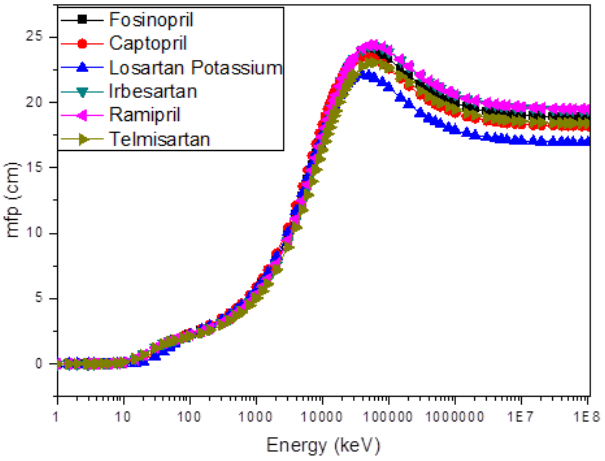

Figure 2. The theoretical values of mfp for studied drugs.

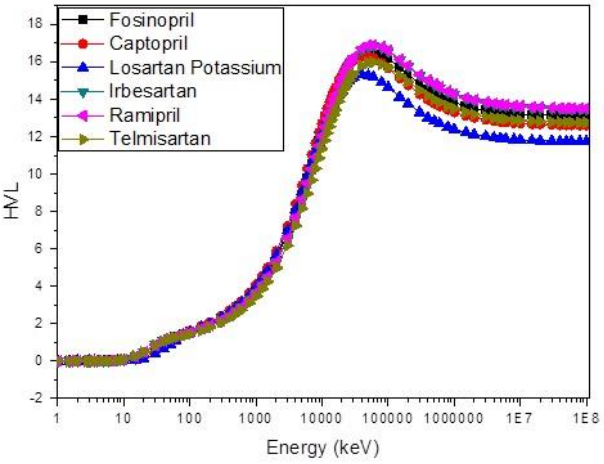

Figure 3. The theoretical values of HVL for studied drugs.

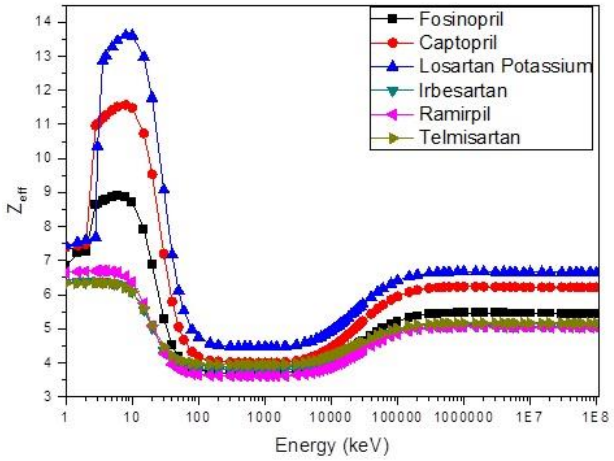

Figure 4. The theoretical values of Z_{eff} for studied drugs.

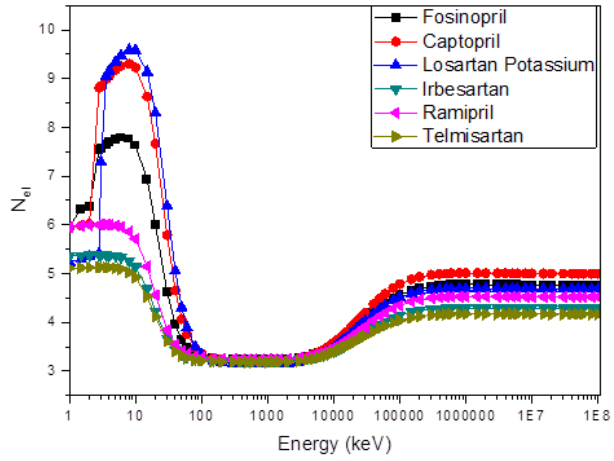

Figure 5. The theoretical values of N_{el} for studied drugs.

There are two types of build-up factors, one is EBF and the other is EABF. EBF is exposure build-up factor. EABF is energy absorption build-up factor. For calculating the build-up factors is used EPIXS 2017 program. The change in the equivalent atomic numbers (Zeq) with incident photon energy for investigated medicines have showed in Table 1. Some parameters such as photon energy and penetration depth have been investigated on both EABF and EBF build-up factors. The EABF and EBF build-up factor parameters a, b, c, d and X_k values of losartan potassium, which show the lowest values in the graphics, are shown in Table 2. To assess the effect of the drugs we plotted EABF and EBF graphs Figures6 and 7 to observe the changes in photon energy penetration depth of energy absorption (EABF) and exposure (EBF) build-up factors. The effect of drugs on EABF and EBF build-up factors with the change of penetration depth at constant energy values (0.015, 1.5 and 15 MeV) are shown in Figure 8 and Figure 9.

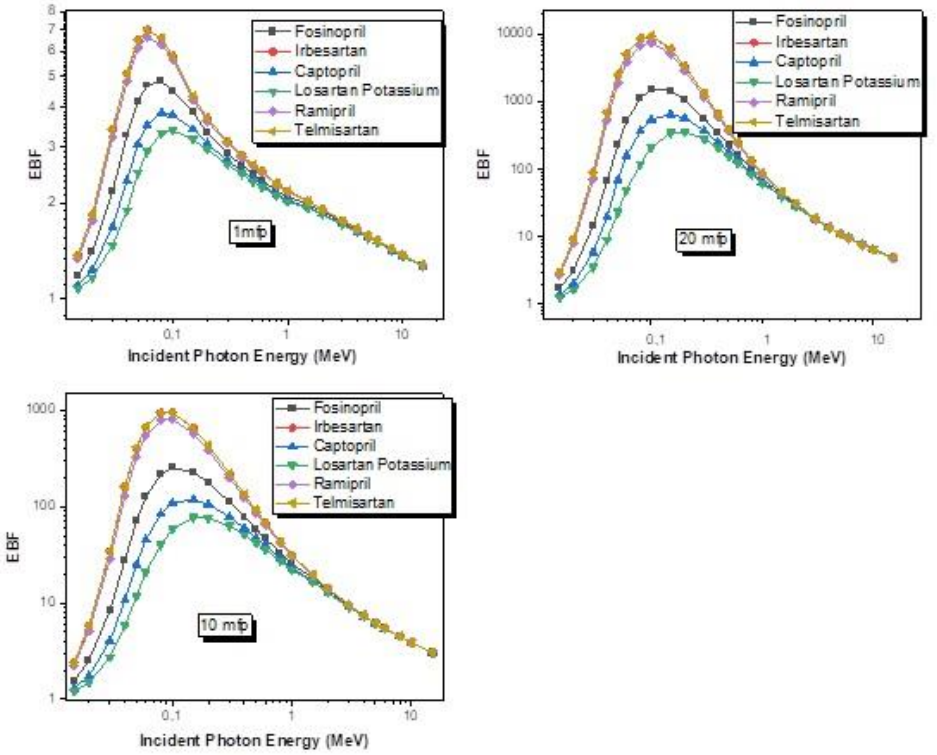

Figure 6. The exposure build-up factor for drugs in the energy region 0.015–15 MeV at 1, 10, 20 mfp.

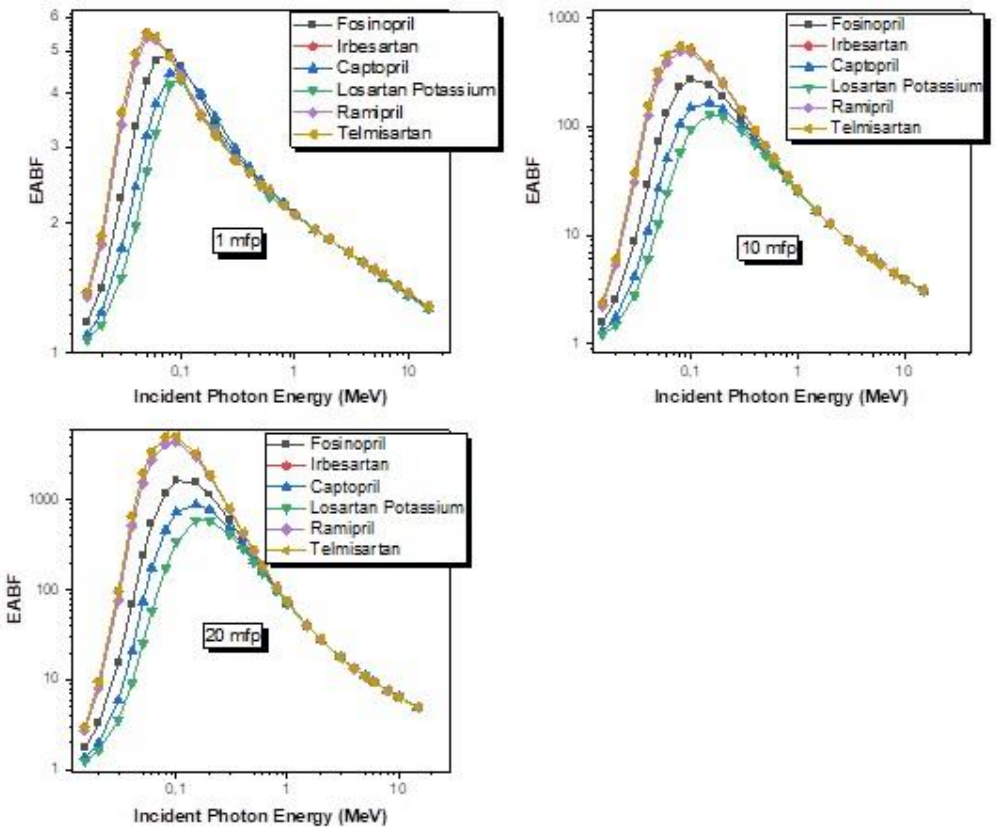

Figure 7. The energy absorption build-up factors for drugs in the energy region 0.015–15 MeV at 1, 10, 20 mfp.

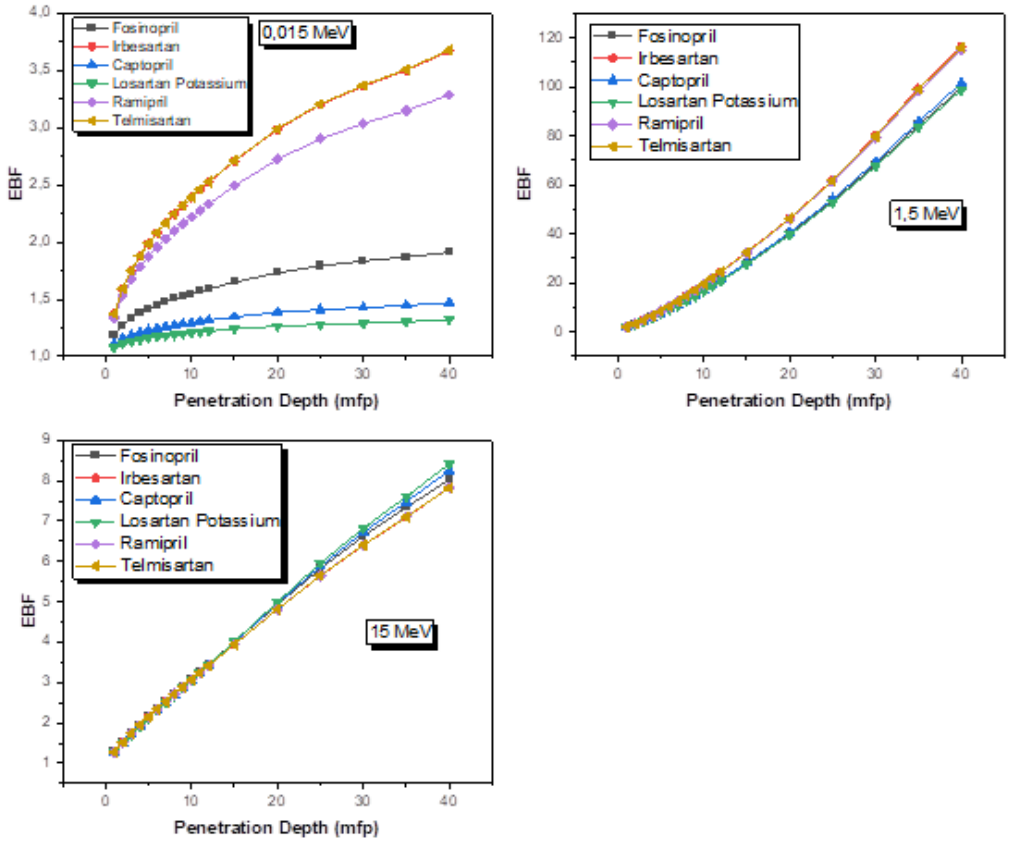

Figure 8. The energy exposure build-up factor for drugs up to 40 mfp at 0.015, 1.5, 15 MeV.

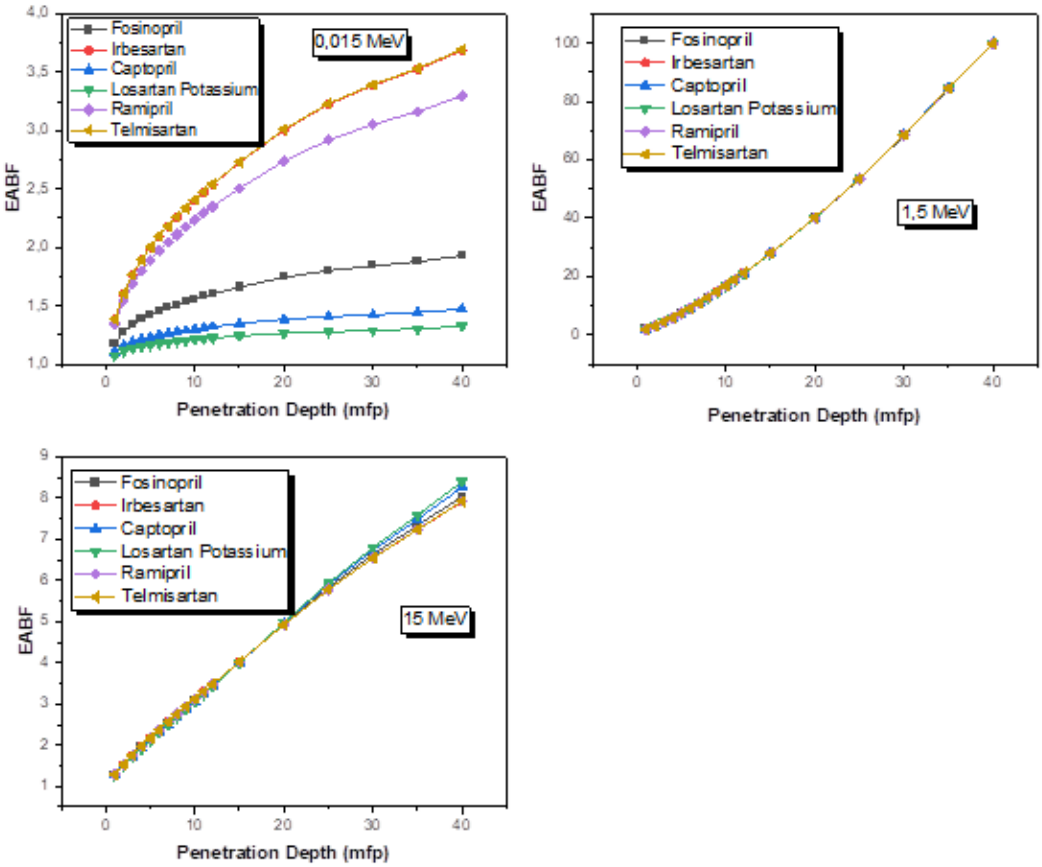

Figure 9. The energy absorption build-up factor for the drugs up to 40 mfp at 0.015, 1.5 and 15 MeV.

Table 1. Equivalent atomic numbers of drugs for the energy range 0.015- 15 MeV.

Energy (MeV)	Fosinopril	Irbesartan	Captopril	Losartan Potassium	Ramipril	Telmisartan
0,015	7,63474	6,08396	9,2749	10,19246	6,29689	6,07927
0,02	7,69541	6,09905	9,38629	10,3626	6,31022	6,09296
0,03	7,77488	6,10692	9,52906	10,56774	6,31489	6,10051
0,04	7,82885	6,11018	9,61637	10,69856	6,31627	6,10354
0,05	7,86788	6,11229	9,67624	10,7873	6,31814	6,10554
0,06	7,89636	6,11411	9,72176	10,85402	6,32076	6,10736
0,08	7,93731	6,11671	9,78636	10,95384	6,32569	6,11011
0,1	7,96776	6,11855	9,82901	11,02176	6,32852	6,1119
0,15	8,01408	6,12101	9,90077	11,10586	6,33064	6,11396
0,2	8,03312	6,12242	9,94649	11,15616	6,33348	6,11545
0,3	8,05208	6,12424	9,99335	11,21148	6,3374	6,11743
0,4	8,06341	6,12517	10,01284	11,24158	6,3389	6,11834
0,5	8,07113	6,12539	10,02317	11,25582	6,33932	6,11857
0,6	8,07486	6,12573	10,02858	11,26695	6,33988	6,11891
0,8	8,07945	6,12614	10,0371	11,27525	6,33989	6,11918
1	8,07854	6,12578	10,03581	11,279	6,3409	6,11911
1,5	6,38351	5,66224	7,50144	8,06904	5,73629	5,68896
2	6,2989	5,64747	7,2801	7,68839	5,71541	5,67549
3	6,27898	5,64334	7,23208	7,60323	5,70946	5,6718
4	6,2721	5,64148	7,21603	7,57972	5,70674	5,67008
5	6,26932	5,64161	7,20841	7,56884	5,70648	5,67024
6	6,2664	5,64118	7,20218	7,56072	5,70553	5,66978
8	6,26304	5,64094	7,19662	7,55468	5,70421	5,66953
10	6,26127	5,64066	7,19383	7,55094	5,70351	5,66941
15	6,25755	5,64135	7,18276	7,54072	5,7032	5,66978

Table 2. Taken from EPIXS 2017 programmes exposure and energy absorption build-up factor coefficients for Losartan Potassium in the energy range 0.015 -15 MeV.

Energy (MeV)	EBF					EABF				
	a	b	c	d	X_K	a	b	c	d	X_k
0,015	0,21486	1,07618	0,39169	-0,11027	12,3604	0,19724	1,07566	0,41283	-0,09424	11,84942
0,02	0,20263	1,16567	0,41806	-0,1081	13,74806	0,19488	1,16599	0,42724	-0,10587	14,535
0,03	0,16467	1,47184	0,50996	-0,08625	14,82282	0,17194	1,49818	0,49529	-0,0884	14,29346
0,04	0,09141	1,89749	0,69062	-0,04489	16,15173	0,1051	1,96854	0,6605	-0,05556	15,91348
0,05	0,07823	2,49633	0,77464	-0,05069	14,26279	0,07905	2,63513	0,77232	-0,05751	14,88374
0,06	0,03221	2,91042	0,93735	-0,03075	13,29014	0,02729	3,23678	0,94948	-0,0272	14,35979
0,08	-0,02956	3,31958	1,1923	-0,00162	13,57211	-0,03948	4,17922	1,22914	0,0073	11,68707
0,1	-0,06139	3,38151	1,36484	0,01115	14,30322	-0,07832	4,50335	1,44039	0,02559	13,3432
0,15	-0,0928	3,17261	1,56168	0,02466	14,75073	-0,12169	4,05094	1,7147	0,0477	13,50248
0,2	-0,10057	2,94986	1,61242	0,02679	14,85033	-0,12857	3,61967	1,7678	0,04881	13,76542
0,3	-0,10337	2,64509	1,6179	0,02678	14,5227	-0,12781	3,031	1,75477	0,0466	13,93566
0,4	-0,099	2,47001	1,57552	0,02728	15,17988	-0,11975	2,72849	1,68877	0,04243	14,23988
0,5	-0,09562	2,34075	1,53664	0,02882	15,16121	-0,11215	2,5417	1,62496	0,03981	14,3002
0,6	-0,0889	2,24418	1,49111	0,0259	15,38142	-0,1029	2,40586	1,56211	0,03597	14,56551
0,8	-0,07886	2,11217	1,41532	0,02452	15,31066	-0,08886	2,23012	1,46332	0,0319	14,84864
1	-0,06971	2,01753	1,35427	0,02343	15,69712	-0,07642	2,11286	1,38441	0,0278	14,92772
1,5	-0,05678	1,92765	1,26416	0,02332	14,47051	-0,05595	1,94281	1,26078	0,02225	14,30919
2	-0,03719	1,84325	1,16757	0,01483	14,96857	-0,03789	1,83781	1,16968	0,01523	14,42065
3	-0,01214	1,71367	1,05543	0,00303	13,28761	-0,01176	1,70924	1,0539	0,00271	13,65144
4	0,004	1,62683	0,9896	-0,00595	18,53395	0,0064	1,62423	0,98358	-0,007	13,51559
5	0,01683	1,55673	0,9441	-0,01181	14,07148	0,01924	1,56056	0,93744	-0,01363	13,37543
6	0,02711	1,51008	0,91023	-0,02108	14,29508	0,02435	1,50135	0,91827	-0,02154	15,95124
8	0,033	1,41957	0,88928	-0,0179	12,02978	0,03486	1,41915	0,88442	-0,01965	12,20561
10	0,03813	1,3593	0,87243	-0,02386	14,08518	0,0397	1,35946	0,8683	-0,02514	14,08603
15	0,04911	1,26766	0,84156	-0,03657	15,03443	0,04844	1,26476	0,84402	-0,03606	14,86069

When the graphs were examined, it has seen that the changes in the EBF and EABF build-up factors were similar to the changes in the photon energies. When low and high energy photons interact with drug samples, photoelectric, compton and pair formation events are experienced, respectively. As a result of the interaction of photons with drugs, photons are significantly reduced or eliminated. Therefore, the smallest EABF and EBF values occur at low and high energies. The reason for the increase in EBF and EABF values at 0.08 MeV, that is, at medium energy levels, is the compton scattering. When Figures 6 and 7 have examined, it has seen that losarton potassium drug had the lowest EBF and EABF values. The reason for this is that Z_{eq} values are higher than other drugs in all energy ranges. As can be seen clearly, Losartan Potassium has minimum build-up factors values whereas Telmisartan has the maximum build-up factors values. The effect of drugs on EABF and EBF build-up factors with the change of penetration depth at constant energy values (0.015, 1.5 and 15 MeV) are shown in Figures8and 9. At lower energy 0.015 MeV, EABF and EBF values remains nearly constant at all depths of penetration for losartan potassium, whereas for other drugs observed that it increases with increasing penetration depth. The values of all drugs seem close to each other, up to 30 mfp penetration depth at 1.5 MeV and 15 MeV. Since the Compton scattering process is dominant at 1.5 MeV, EABF and EBF values are almost the same for all drugs at all penetration depths.Because of at 15 MeV in which the pair production process starts to be effective, at this transition energy EABF and EBF values do not depend on the content of drugs.

CONCLUSIONS

The present work has been carried out to investigate EMR interaction parameters of six antihypertensive drugs (Fosinopril, Captopril, Losartan Potassium, Irbesartan, Ramipril, Telmisartan).It was observed that the photon interaction parameters changed with photon energy and type of drug.Owing to the element K, Losartan Potassiumwas found to have largest MAC, $Z_{eff}$and N_{el} values and lowest HVL, mfp and build-up factor values.

Conflict of Interest Disclosure

The authors declare no conflicts of interest.

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