Original Research Article

Studies on Effective Atomic Number of Some Pharmaceutical Active Ingredients in Drug

ABSTRACT

Mass attenuation coefficient and effective atomic number of the active pharmaceutical ingredients viz, Alprazolam, Amiodar, Amiodarone, Ciprofloxacin, Diclofenac Sodium, Femotidine and Nimesulide have been calculated over a wide energy range from 1 keV to 100 GeV for total and partial photon interactions by using WinXCom. The obtained data results that change in mass attenuation coefficient and electron density are varies with energy and chemical composition of the active pharmaceutical ingredients (API's) in drugs. The results in the variation of photon interaction with energy and effective atomic number of the API's in drug are shown in the logarithmic graphs.

Keywords: API, Pharmaceutical, WiXCom, Absorption edge.

1. INTRODUCTION

The mass attenuation coefficient is a measure of probability of interaction that occurs between incident photons with matter of unit mass per unit area. Accurate values of mass attenuation coefficients are required to provide essential data in diverse fields such as nuclear diagnostics (computerized tomography), radiation protection, nuclear medicine, radiation dosimetry, x-ray fluorescence studies, radiation biophysics and etc. The extent to which the biological system is due to ionizing radiation depends on this mass attenuation coefficient.

The idea of the effective or average atomic number is to assume that a mixture or a compound can for special purpose be regarded as being built up of one kind of particle called atoms with atomic number Z, in other words, a single atomic number is used to represent an element. In composite materials, however, a single number cannot represent the atomic number uniquely across the entire energy region for photon interactions. This unique number in composite material is called effective atomic number, varying with energy. In the literature there has been extensive use of the "effective atomic number" defined in different ways [1-6]. The application of such effective atomic number can be described in two ways (1) the effective can be put into formulas and in this way a compound can be reduced to an ordinary element, if calculation of Z-dependent effects are to be carried out and (2) the effective atomic number can be used to find compound with atomic composition like air or water, etc. Hence, a precise knowledge of effective atomic number can takes a very important role in medical radiation dosimetry, radiation therapy etc. There are many researchers are performed to calculate and to determine the effective atomic numbers of composite materials [7-8], energies close to absorption edges of the elements [9-11].

Hence in the recent years, several experimental and theoretical investigations have been carried out to understand the nature of interaction of different biological molecules viz., amino acids fatty acids, proteins, carbohydrates etc., but there is no reports were found literature survey on the pharmaceutical active ingredients. Active Pharmaceutical Ingredients (API) is the basic functioning product in the drug. But the drug which is available in the market is composition of active and inactive pharmaceutical gradients. Therefore it is necessary to understanding the effective number in the drug. Hence this is the concept which promoted us to calculate total attenuation cross sections as well as the composition dependent quantities such as effective atomic number (Zeff) and effective electron densities (Ne) of active pharmaceutical ingredients. It is, therefore, desirable to have a compete knowledge of the nature of interaction of API over the some energy range.

In the present work, we are computing the effective atomic numbers and electron densities of photon interaction for basic components of pharmaceutical drugs at various energies using WinXCom program developed by Gerward et al. For this computational function we have opted seven active pharmaceutical ingredients for all photon interactions (incoherent, photoelectric and total photon interaction [with coherent]) in the energy range 1keV to 100 GeV. The variations of effective atomic number and electron density with energy are shown graphically for the all photon interactions. The variation of photon mass attenuation coefficient with energy is also show graphically only for total photon interaction.

2. METHOD OF COMPUTATIONAL AND THEORETICAL WORK

A narrow beam of mono-energetic photons in the X- or gamma ray region is attenuated to an intensity I from an incident intensity I0¬ in passing through a material thickness with mass per unit area x, according to the well established Beer-Lambert's exponential law

$$I/I_0 = \exp\left(-\frac{\mu}{\rho}\right)x \tag{1}$$

$$\left(\mu/\rho\right) = x^{-1}\ln\left(I/I_0\right) \tag{2}$$

in which μ/□ is the mass attenuation coefficient and can be obtained from the measured I, I0 and x data. The photon mass attenuation coefficient for any chemical compounds or a mixture can be written as

$$\mu/\rho = \sum_i w_i\left(\mu/\rho\right)_i \tag{3}$$

Equation (2) is closely related to the total cross section per atom σtot according to the relation

$$\mu/\rho = \sigma_{tot}\left(N_A/M\right) \tag{4}$$

in which NA is Avogadro's number and M is the atomic weight. The total cross section σtot in turn, can be written as the sum over contribution from the principal of interactions

$$\sigma_{tot} = \sigma_{coh} + \sigma_{incoh} + \tau + \kappa + \sigma_{ph.n.} \quad (5)$$

in which σcoh and σincoh are the coherent (Rayleigh) and incoherent (Compton) scattering cross section, respectively, τ is the atomic photoelectric cross section, κ is the positron-electron pair-production (including triplet) cross section and σph.n.is the photonuclear cross section.

The effective (average) atomic cross section (σa) can be easily determined from the following expression,

$$\sigma_a = \frac{1}{N_A} \sum f_i A_i \left(\mu / \rho \right)_i \quad (6)$$

Similarly, effective electronic cross section (σe) for the individual element is given by the following relation,

$$\sigma_e = \frac{1}{N_A} \sum \frac{f_i A_i}{Z_i} \left(\mu / \rho \right)_i = \frac{\sigma_a}{Z_{eff}} \quad (7)$$

where fi and Zi are fractional abundance and atomic number respectively of constituent element i. Now the effective atomic number can be written as

$$Z_{eff} = \frac{\sigma_a}{\sigma_e} \quad (8)$$

The effective electron density (Ne) (number of electrons per unit mass) can be derived by using the Eqs. (3) and (7),

$$N_{el} = \frac{\left(\mu / \rho \right)}{\sigma_e} = \frac{N_A}{M} Z_{eff} \sum_i n_i \quad (9)$$

The theoretical values of the mass attenuation coefficient can be found in the tabulation by Hubbell and Seltzer (1995) [12]. Jackson and Hawkes [13] were also gave the formula to determine the effective atomic number for mixture or composite materials. A convenient alternative to manual calculations, using tabulated data, is to generate data as needed, using a computer. For this, Berger and Hubbell (1987, 1999) [13] developed a computer program, XCOM, for calculating cross sections and attenuation coefficients for any elements, compounds or mixtures at energies from 1 keV to 100 GeV. The program has since undergone a number of updates and now available in window version. Recently, this well-known and much used program has been developed to the Windows platform [15][16] and the Windows version is being called WinXCom

3. RESULTS AND DISCUSSION

In this work, the variation of mass attenuation coefficient, effective atomic number and effective electron density with photon energy 1keV to 100 GeV for seven active pharmaceutical ingredients were studied and details of the drugs are tabulated in the table 1.

The results obtained are clearly supports the remarks made by Hine (1952) [17] that the effective atomic number varies with energy. The chemical compositions of the seven API drugs are organic elements only but the ratio of content is different. Except in Alprazolm which contains Carbon, Hydrogen, Chlorine, Nitrogen all contains a basic organic elements (C, H, O), since Alprazolam is grouped in the steroidal class of drug and others are Non-steroidal class of drug/Non-Steroidal Anti Inflammatory Class of drug. The Zeff values of seven organic materials composed of H, C, N, and O were calculated according to the equation (1). The obtained results of total mass attenuation coefficient and effective atomic number are shown in logarithmic graphs in fig 1-4.

Fig 1 shows the results of the total mass attenuation coefficients of active pharmaceutical ingredients against the photon energy. In these cases no absorption edge is found in the ciprofloxacin drug. In the case of Femotidine, Amiodar Nimesulide there are two values for mass attenuation coefficients at 2.47 keV due to sulfur K absorption edge. The value 2.19x10+2 cm2/g, 2.21x10+2cm2/g and 2.26x10+2 cm2/g respectively are valid immediately below the absorption edge and 7.47x10+2cm2/g, 3.44x10+2 cm2/g and 4.19x10+2cm2/g respectively are immediately above the absorption edge. Alprazolam at 2.82 keV have the values of mass attenuation coefficients 1.24x10+2cm2/g and 2.91x10+2cm2/g below and above the chlorine K-absorption edges respectively. Diclofenac sodium has two K-absorption edge at 1.07 keV for Sodium and 2.82 keV for chlorine. The values of mass attenuation coefficients are 2.09x10+2cm2/g and 1.63x10+2cm2/g immediately below the sodium and chlorine K-absorption edge and 2.38 x10+2cm2/g and 3.84 x10+2cm2/g immediately above the Sodium and Chlorine K-absorption edges. The interesting property of API drug in which we opted is the Amiodarone which has K, L1, L2, L3 and M1 absorption edges at 33.2keV, 5.19, 4.85, 4.56keV and 1.07 keV. The values of mass attenuation coefficient for these edges are 2.73 cm2/g, 3.13 x10+2cm2/g, 2.75 x10+2cm2/g, 1.19 x10+2cm2/g and 4.28 x10+3cm2/g respectively below the absorption edges and 14.25cm2/g, 3.59 x10+2cm2/g, 3.66 x10+2cm2/g, 3.14 x10+2cm2/g and 4.42 x10+3cm2/g above the absorption edges. The above discussion and graph of mass attenuation coefficient vs. energy notices that there are three processes photoelectric absorption, Compton scattering and pair production processes are dominating on the interacting API in the drug materials. Results of Kaginelli et.al [18] gives that the theoretical/calculated values have not considered the edge effects since the effective atomic numbers are under/over estimated when any elements falls below the absorption edge.

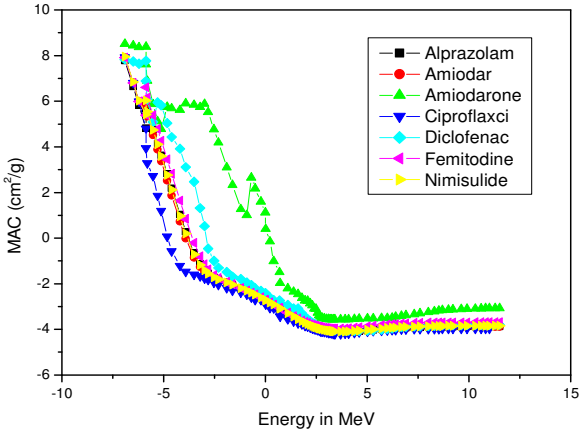
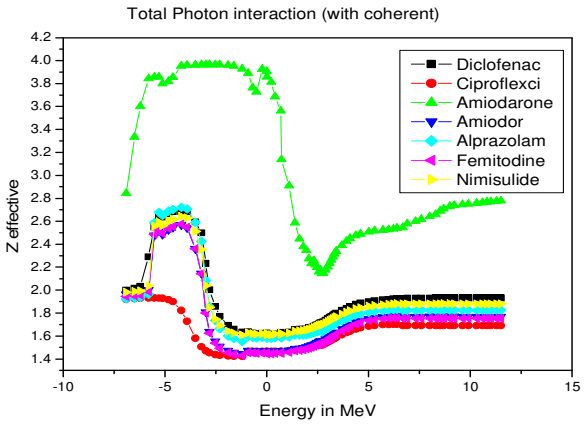


Fig. 1. Variation of Mass attenuation coefficient (MAC) with energy for API in drugs

The interpretations of variations are being due to photoelectric effect which varies as Z4-5 and less but significantly due to coherent scattering which varies as Z2-3. In the intermediate energy region, where incoherent scattering is dominating process, the mass attenuation coefficient is found to be constant and is due to Z-dependence of incoherent scattering and significant role played by pair production. Singh [19] also found the negligible variation between 150 keV and 5 MeV for biological materials. In the high energy region, significant variation in the mass attenuation coefficient is due to the Z2-dependence of pair production. The variation of Zeff with photon energy for total photon interactions (fig 2) which involves a dominating interacting processes viz., photoelectric, coherent and incoherent processes. The variation of effective atomic number (Zeff) with energy is almost similar in case of Amiodar, Femotidine, Nimesulide and Diclofenac Sodium drugs except in the case of Ciprofloxacin and Amiodarone. The discrimination among the effective atomic numbers for the opted API drugs is due to near absorption edges. There were no edge effect occurs in Ciprofloxacin drug while two Amiodarone has Iodine K, L1, L2,L3 and M1 absorption edges at 33.2, 5.19, 4.85, 4.56 and 1.07 keV respectively. Up to 15-20 keV onwards there is a sharp decrease in effective atomic number and decrease in Zeff with energy upto 150 keV, showing that contribution of scattering processes increases which decreases Zeff. From 150 keV to 3 MeV, Zeff is almost independent of energy. This may be due to the dominant of incoherent scattering in this region. From 3 MeV to 400MeV, there is regular increase in Zeff with photon energy. Hence it is observed that the variation of Zeff also depends on the relative proportion and the range of atomic numbers of the elements of which API drug is composed (fig 2). The Amiodarone has large range of atomic numbers (Z's) from Hydrogen (1) to Iodine (53) than any other API drugs to which the variation in its Zeff with energy is significant in comparison to any other API's. Variation of Zeff with photon energy for photo electric absorption is shown in the fig. 3 which indicates that composition is also very important as explained above. There is a sudden jump occurs in all the cases except in Ciprofloxacin. It has a least range of atomic numbers from 1 (H) to 9 (Fluorine) and hence no absorption edge effect is exist. Diclofenac sodium takes an immediate jump in Zeff at 1.07 keV and 2.82 keV, which are the K absorption edge energies of Sodium (Na) and Chlorine (Cl) respectively. Up to 1 MeV increases sharply and then onwards remains a constant and this is due the fact that photoelectric is the predominant processes in the low energy region (<1MeV) and is for low Z materials. The fig. 3, also confirms that the variation of Zeff in pharmaceutical drugs probably due to more number of elements in Amiodarone and also the API's having edge effect because Ciprofloxacin has no edges in it. Hence in all other active pharmaceutical ingredients, the variation of Zeff is almost independent of energy. This is because of the fact that these API's consists of elements which are same in the number and are of close to the atomic number.



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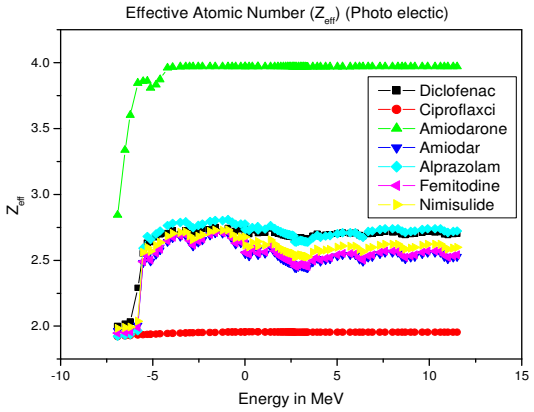
178 **Fig. 2. Variation of Effective atomic number Zeff of API's in drugs with energies for**
179 **total photon interaction**

180 The electron density of the opted API's in drug samples are found to be vary from 2.78 x
181 1023 to 9.04x1023 electrons/g but in the case of Amiodarone it is from 4.93x1023 to
182 29.51x1023 electron/g. Hence electron density is closely related to the effective atomic
183 number and depends on the photon energy and chemical content of the API's in drug
184 samples.



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186 **Fig. 3. Variation of Effective atomic number Zeff of API's in drugs with energies for**
187 **total photon interaction**
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189 **Table 1. Some Common Active Pharmaceutical Ingredients used in the Drugs**
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Sl. No.	API	Name Chemical Composition
01	Alprazolam	$C_{17}H_{13}ClN_4$
02	Amiodar	$C_{22}H_{28}FN_3O_6S$
03	Amiodarone	$C_{25}H_{29}I_2NO_3$
04	Ciprofloxacin	$C_{17}H_{18}FN_3O_3$
05	Diclofenac sodium	$C_{22}H_{19}Cl_2N_2NaO_4$

06	Femotidine	$C_8H_{15}N_7O_2S_3$
07	Nimesulide	$C_{13}H_{12}N_2O_5S$

4. CONCLUSION

The unique number named in the composite materials as effective number and it may plays an important role in pharmacology or pharmaceutical industry by means of determining the quality and quantity of the drug materials in which one can also identify the active and inactive ingredients added during the manufacturing / formulation processes of different firms.

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