Qualitative Analysis of Pharmaceutical Drugs by X-ray Transmission Method: A Non-destructive Technique

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Abstract. Prime importance is given to the analysis of the pharmaceutical drugs manufactured by different pharma laboratories through determination of mass attenuation coefficient (MAC) by x-ray spectrometric technique (nondestructive technique). MAC were determined at low energies ranging from 8 keV to 44 keV x-rays using High Purity Germanium (HPGe) detector for the samples of different forums with similar Active Pharma Ingredient (API). Obtained results were compared with the theoretical WinXCom values. Hence evaluation of different laboratories on the basis of particle size effect on the MAC is also discussed in this paper.

INTRODUCTION

Once the qualitative and quantitative analyses are carried out by the pharmacists, pharma drugs are dropped into the markets. But these analyses are very critical and necessary or integral part of the pharma business. Hence, analytical methods as well as the involved analytical tools assume prime importance in the pharma business. Several well known analytical tools viz., HPLC, GC, IR, UV-Vis, atomic absorption spectrophotometer etc., are available to a pharmaceutical analyst. A non destructive testing/ technique (NDT) has an important role in the applied physics/medicine/industry. It has multiple applications in the field of qualitative analysis or quality control of industrial products, radioactive materials control, diagnostics of tissue and organs etc. The main task of this method is to determine the technical characteristics and properties of the controlled objects being examined. It is vitally necessary not only to provide enhanced tools for scientific and technological investigation, but to meet current needs for improved protection, safety and health of civil populations. Now a day, a strong interest has been developed to determine the quality control of the products with respect to overall composition without destructing. Single product is manufactured by different forums which may or may not be maintaining the quality and quantity (especially in the drugs). There are different drugs in the market for particular disease with different brand names.

This article attempts to depict merits of the mass absorption spectrometer in estimation of quality assurance of the pharmaceutical products. Hence, in this approach Diclofenac Sodium tablets were chosen as the model drug for the study. The drug chosen for the study has a great importance due to its large clinical applications especially for the cases of arthritis, including both osteoarthritis and rheumatoid arthritis. Many researchers have carried out studies in determining the composition and concentration levels of diclofenac sodium in various commercially available tablets and are destructive one. Here, the paper describes the product analysis non-destructively by determining the mass attenuation coefficient which is one of the basic parameter in the x-ray spectrometric technique.

MASS ATTENUATION COEFFICIENT (MAC)

Mass attenuation coefficient is a measure of the average number of interaction between incident photons and the matter that occur in a given mass per unit area thickness of the substance. Hence, the importance of mass attenuation coefficient have been found in different /verities of fields viz., radiation shielding, agricultural, medical fields, aeronautical engineering, photon transport, space research, military, security checking purposes (most important now-a-days) and research and development etc,. Hence, in view of the above applications verity of experimental investigations have been performed to determine the mass attenuation coefficient values on the various types of materials such as elements [1], compounds [2], tissue equivalent compounds [3], mixtures (different percentage of elements) [4], alloys [5-6], building materials [7], etc. at different photon energies to study the quality of the material under consideration.

A series of photon interaction (Photoelectric, Compton and pair production) with any compound or a mixture is the contribution of each element to the mass attenuation coefficient and is given by Bragg's additivity law.

$$\frac{\mu}{\rho} = \sum_i \alpha_i \left(\frac{\mu}{\rho}\right)_i \tag{1.}$$

where $(\mu/\rho)_i$ is the mass attenuation coefficient for the ith element and ω_i, is its weight fraction of the ith element. The experimentally determined mass attenuation coefficient is compared with the theoretical (WinXCom) data and the percentage deviation is calculated by the relation;

$$Percentage\ Deviation = \frac{\left[\left(\frac{\mu}{\rho}\right)_{expt} - \left(\frac{\mu}{\rho}\right)_{thr}\right]}{\left(\frac{\mu}{\rho}\right)_{thr}} X100 \tag{2.}$$

SAMPLE DESCRIPTION

Non-steroidal anti-inflammatory drugs (NSAIDs) have been selected for the qualitative analysis. NSAIDs are usually prescribed for the treatment of acute or chronic conditions where pain and inflammation are present. These are generally suggested for the symptomatic relief of Rheumatoid arthritis, Osteoarthritis, renal colic, mild-to-moderate pain due to inflammation tissue injury etc. Diclofenac sodium is one of the NSAIDs pharma drugs which is opted for the present study. The diclofenac sodium manufactured by different pharma laboratories with similar active pharmaceutical ingredient (API) have been chosen viz., diclofenac sodium (50 mg) in combination with paracetamol (500 mg). This drug is taken to reduce headache, body pain, and dental pain, sports and accident injuries, rheumatism, arthritis, lumbago, bursitis and sciatica. Four branded drugs of diclofenac sodium manufactured by different laboratories in India have been selected viz., Diclomol and Dynapar from Uttarakhand, Diclogesic and Voveran Plus from Solan (HP) and Karnataka respectively.

EXPERIMENTAL DETAILS

The x-ray spectrometer consists of an n-type x-ray detector of area 500 mm^2 and 10 mm thick high purity Germanium connected to DSA-1000, 16k MCA. The spectrometer is operated by Genie 2000 software. The detector is directly coupled to a preamplifier through a cool FET device, and is mounted over a rigid cryostat accompanied by a Dewar for liquid Nitrogen. DSA-1000 allows independent selection of rise time and flat top selection, which optimizes the performance of the detector, spectral energy, count rate and resolution. HPGe detector along with DSA-1000 has resulted with a resolution of 191 eV at 5.895 keV as against 200 eV by the manufacturers. In the present case live time of the MCA is selected.

The geometrical arrangement adopted is a good geometry [2] and is arranged vertically over the window of the HPGe x-ray detector system as shown in Figure 1. A stand is positioned above the detector to hold the source, specimen and collimators and ensured that the vertical alignment with the help of laser beam. Photons from radioactive sources are collimated by a lead collimator and are incident on the absorber positioned normal to the beam and mid way between source and detector. HPGe detector detects photons after passing through a second lead collimator. The stand is made up of mild steel, which reduces the natural background and also background arises due to scattering from the side walls of the stand, collimators and from the holders. The collimators C_1 and C_2 are 40 mm thick lead discs that collimate the incident and transmitted beam to 6 mm diameter respectively. The scattering acceptance angle equal to the sum of the incident beam divergence and acceptance angle at the detector is found to be ≤ 3 degrees. This thickness of the collimator is sufficient to reduce the intensity of photons of 300 keV by a factor of 10^7.

The variable energy x-ray (VEX) source of 370 MBq (10 mCi) Am-241 is used as the primary source of excitation radiation. The 59.65 keV gamma photons from Am-241 excite the characteristics X-ray energies 8 keV to 44 keV from the six different targets Cu, Rb, Mo, Ag, Ba and Tb respectively. No noticeable impurities were found in these sources when their photon spectrum were analyzed using an HPGe detector. The inner bremsstrahlung intensity from the sources was found to be negligible compared to the x-ray intensity at the region of interest.

The preferred diclofenac sodium tablets from various firms (manufacturer) were grind to a fine powder to pelletize the samples of variable thickness with an area of 1.327 cm^2 using hydraulic pellet machine. The thicknesses of each pellet were determined by taking areal density and ranged from 0.036 to 0.888 g/cm^2. X-rays emitted from the variable energy x-ray source, S passes through the Collimator C1 and are incident on the absorber A (pellets) of different thickness kept normal to the photon beam. The transmitted beam passing through the collimator C2 are detected by a high resolution HPGe x-ray detector system D. To measure the transmitted intensity (Beer-Lambert's law) accurately it is important that the sample is mounted exactly normal to the x-ray beam. The transmitted x-ray spectrum can be recorded using a PC based multichannel analyzer. The obtained mass attenuation coefficients of the samples were compared with the theoretical values using WinXCom software at above energies.

Result and Discussion

The experimental MAC values along with their associated errors, calculated by the least-squares fit are given in the Table 1. The theoretical values of mass attenuation coefficient have been estimated by WinXCom programme [8] which is the successor of program XCOM [9]. The uncertainties involved in the theoretical value are about 1-2%. Since the reproducibility of our experimental value is within 2% and the error contribution from the counting statistics, areal density thickness measurement gives about 2%. An overall experimental discrepancy, i.e., percentage deviation of about 4%, is treated as agreement between experimental and theoretical value, on the other hand percentage deviation greater than 4% should be considered as disagreement between experimental and theoretical value.

From the Table 1, one can also confirm that in the low energy region contribution of photoelectric process is the dominant than the coherent and incoherent process, hence at 8.036 and 13.396 keV deviation is around 73%. But as the energy is increased this percentage deviation will be around 34% only. Hence at 44.476 keV energy, contribution of Compton process to total mass attenuation coefficient becomes more or less equal to the photoelectric process and resolution of the mass attenuation coefficient values of all the laboratories are merged. Particle sizes have been determined by XRD spectrum using Scherrer formula

By the XRD analysis Fig 3, one can also confirm that the drugs are crystalline in nature, there is a peak shift towards the higher 2θ value in the Voveran Plus, Dynapar and Diclogesic but there is no peak shift in Diclomol. This peak shift may be attributed due to the location of the stacking fault in extremely small crystals. And the large peak shift occurs when the stacking fault is located in the center of the cube. Hence by this peak shift it can also be concluded that the location of stacking fault in the crystal structure contributes in the measurement of mass attenuation coefficient. As the location of the stacking fault is towards higher 2θ value in the Diclogesic lesser the mass attenuation coefficient and followed by Voveran plus, Dynapar and Diclomol. Due to the increasing vacancy concentration in the Dynapar its intensity is very high but in case of Diclogesic its too less hence the intensity is also less. Particle size of each drug sample also contributes in the determination of mass attenuation coefficient Fig 4. The effect of particle size on the determination of mass attenuation coefficient can be examined very clearly at 8.036 keV low energy region. Difference in the particle size of Dynapar and Diclomol was found to be 0.79 nm and deviation of MAC values between them found to be 2.6 %. But in the case of Diclogesic and Voveran Plus particle size was found to be 4.19 nm hence 3.2 % of deviation.

Conclusion

An average weight of the unpacked tablet were 600- 800 mg but the actual active pharma ingredient will be 550 mg (diclofenac sodium 50 mg and Paracetamol 500 mg), remaining up to 30 % contains inactive pharma ingredients called them as excipients viz., coloring agent to pleasant the eye, taste and buffering etc or in other words contribution of photon interaction with these base materials leads to the large deviation in WinXCom and experimental mass attenuation coefficient values. Therefore, on the basis of experimental result and discussion we can conclude that the technique adopted is the nondestructive, quick to analyze and not much expensive. And particle size of the drug samples affects the determination of mass attenuation coefficient.

Table 1: Mass attenuation coefficient of the drug samples with WinXCom at different energies.

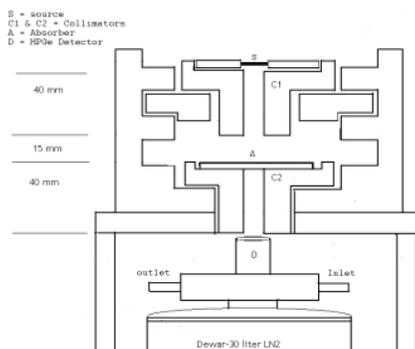| Energy in keV	Diclogesic	Voveran Plus	Dynapar	Diclomol	WinXCom
8.036	7.850±0.024	8.110 ±0.048	8.240±0.020	8.460±0.025	29.695
13.374	1.860±0.019	1.870±0.014	1.940±0.015	2.050±0.015	6.932
17.443	0.946±0.014	0.948±0.003	0.996±0.009	1.030±0.012	3.263
22.103	0.559±0.008	0.559±0.015	0.561±0.003	0.599±0.006	1.705
32.060	0.295±0.002	0.305±0.006	0.299±0.006	0.313±0.005	0.680
44.216	0.223±0.005	0.228±0.007	0.216±0.006	0.241±0.004	0.366

Figure. 1: Experimental setup for the measurement of mass attenuation coefficient for pharma drugs.
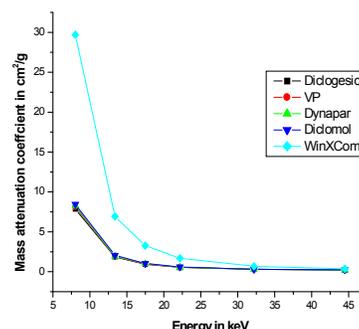

Figure. 2: Variation of mass attenuation coefficient with energy for diclofenac sodium drug of different pharma drug laboratories
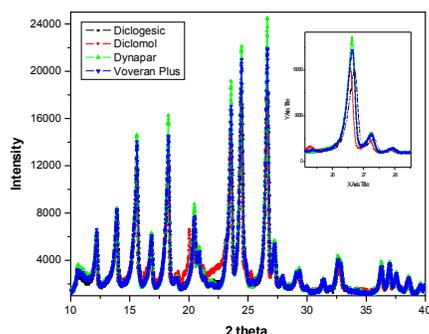

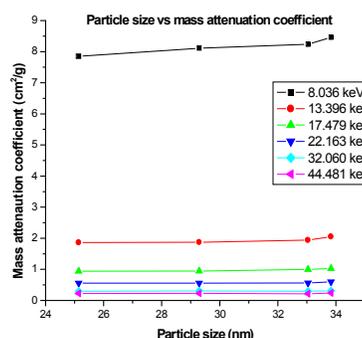Figure 3: XRD spectrum for diclofenac sodium tablets of different laboratories

Figure. 4: Effect of particle size on the mass attenuation coefficient at different energies.

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