Progress in Nuclear Energy 100 (2017) 297–308

Contents lists available at ScienceDirect

Progress in Nuclear Energy

journal homepage: www.elsevier.com/locate/pnucene

# Assessment of radio-protective properties of some anti-inflammatory drugs

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ARTICLE INFO

*Article history:*
Received 8 November 2016
Received in revised form
14 May 2017
Accepted 6 July 2017

*Keywords:*
Radioprotective
Buildup factor
Geometric-progression method
Anti-inflammatory drugs
Effective atomic number

ABSTRACT

When ionizing radiations are exposed to humans, numerous deleterious health effects including cancer may occur. Recently, radioprotective agents with a novel mode of action have drawn strong interest. Radioprotective agents are able to palliate, to prevent, or to handle radio-induced side-effects. In this study, in the parliamentary procedure to investigate the radioprotective effects of some pharmacological compounds, we have estimated the effective atomic number ($Z_{eff}$) and electron density ($N_e$) of six analgesic and anti-inflammatory drugs for total photon interaction in the energy range of 1 keV −100 MeV using WinXCom. In addition, and by Geometric-Progression (G-P) method, the energy absorption (EABF) and exposure buildup factors (EBF) for incident photon energy 0.015 MeV to 15 MeV up to penetration depths of 40 mean free paths (mfp) were estimated. It has been observed that EABF and EBF posses maximum values in the intermediate energy region, where Compton scattering is the dominant photon interaction process. Among the selected compounds, Etodolac (ET) has the largest EABF and EBF, while the minimal values of EABF and EBF were recorded for Meloxicam (ME). The present work could be useful to develop novel pharmacological compounds used in radioprotection, medical diagnostics, and radiation therapy.



## 1. Introduction

Ionizing radiation is high-energy radiation like X-ray and gamma ray causes hurtful effects within living cells, tissues and organisms. The fast technological advancement has multiplied people's exposure to ionizing radiations greatly. Widespread applications of radiation in different fields such as manufacturing, agriculture, space explorations, medical imaging, radiation therapy, nuclear war, scientific research and other scientific and technological fields require that humans be protected against unnecessary exposures. However, in some conditions, it is difficult to avert radiation exposure, such as in medical diagnosis and therapy or accidental exposure to high radiation levels. For this reason pharmacological intervention; which is nontoxic, rapidly absorbed, economically cheap, and orally administrable would probably be the most prudent approach to minimize or prevent humans towards the hazardous outcome of ionizing radiations. The pharmacological approach to radiation protection seeks to develop different drugs or chemical products having the ability to get rid of or scale down the damaging effects of ionizing radiation (Jagetia, 2007). Radio protective agents have been separated into four primary groups: (a) thiol compounds, (b) other sulfur compounds, (c) pharmacological agents (anesthetic drugs, cholinergic drugs, dopamine, hormones, anti-inflammatory, tranquilizers, etc.) and (d) other radioprotective agents (cyanide, sodium fluoroacetate, melting, erythropoietin, etc.) (Veranda and Tavares, 1998). Nonsteroidal anti-inflammatory drugs (NSAIDs) are one of the most commonly used medications worldwide for their antipyretic, analgesic and anti-inflammatory properties (Ungprasert et al., 2015). Furthermore, new evidence suggests that NSAIDs are anticancer agents (Verdoodt et al., 2017). NSAIDs can be classified based on their chemical structure or mechanism of action into different chemical groupings; enolic acid (e.g.meloxicam, piroxicam), salicylates (aspirin), Propionic acid (ibuprofen), acetic acid (indomethacin), Coxibs (celecoxib, rofecoxib) and Sulfonanilides (Nimesulide) (Mattana et al., 1997).

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http://dx.doi.org/10.1016/j.pnucene.2017.07.003

In the literature, there are reports of attempts to utilize anti-inflammatory drugs as effective radioprotective agents (Lee and Stupans, 2002; Alok et al., 2013; Juchelková et al., 1998; Hofer et al., 2006; Kozubík et al., 1991; Wallace et al., 1994). In composite material, like NSAIDs it is quite reasonable to deals with some parameters such as effective atomic number ($Z_{eff}$), effective electron density ($N_e$), and buildup factors. These parameters are also convenient parameters that in some cases, viz. designing radiation shielding, calculating absorbed dose, energy absorption and build-up factor, represents photon interaction with matter. In some cases, in order to have an initial information about the chemical composition of a material the $Z_{eff}$ can be utilized. For example, the materials having large $Z_{eff}$ generally correspond to the inorganic compounds and metals, while a small $Z_{eff}$ ($\leq 10$) is an indicator of organic substances. Hence, it might be valuable to analyze the interaction of gamma radiation with NSAIDs in terms of these parameters. The knowledge of how radiation interacts with 'living' matter is hidden in what is called “buildup factors” (Sayyed et al., 2017). The buildup factor has been separated into two types: (a) Absorption buildup factor (EABF) in which the amount of interest is the absorbed or deposited energy in the target and the detector response function is that of absorption in the target material i.e. anti-inflammatory drug. (b) Exposure buildup factor (EBF) in which the amount of interest is the exposure and the detector response function is that of the absorption in air (Sayyed and Elhouichet, 2017). The build-up factor values have been calculated by various codes such as Geometric Progression (G-P) method (Harima et al., 1986), iterative method (Suteau, 2005), invariant embedding method (Shimizu, 2002; Shimizu et al., 2004), and Monte Carlo method (Sandari et al., 2009). American National Standards ANSI/ANS 6.4.3 (ANSI/ANS-6.4.3, 1991) used the G-P fitting method and provided build-up factor data for 23 elements, water, air and concrete at 25 standard energies in the energy range 0.015–15 MeV with suitable interval up to the penetration depth of 40 mean free paths.

Different researchers have used the Geometric Progression (G-P) method to calculate both EABF and EBF for different materials; human organs and tissues (Manohara et al., 2011), glasses (Sayyed et al., 2017), biological samples (Sidhu et al., 2000), thermoluminescent dosimetric materials (Manohara et al., 2010), and human teeth (Kurudirek and Topcuoglu, 2011). This indicates that the G-P fitting method is suitable for the calculation of both EABF and EBF for different materials and compounds. To determine the effectiveness of NSAIDs as Radioprotective agents, in this research article, an attempt has been made to study the gamma-ray interactions with NSAIDs by calculating the effective atomic number ($Z_{eff}$) and electron density ($N_e$) in the photon energy range of 1 keV–100 MeV for six NSAIDs (Meloxicam, Indomethacin, Nimesulide, Celecoxib, Sulindac and Etodolac). Furthermore, we have calculated the EABF and EBFby using the G-P fitting method for the

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

| Drug | Code | Chemical formula | C | H | N | O | S | Cl | F |
|---|---|---|---|---|---|---|---|---|---|
| Meloxicam | ME | $C_{14}H_{13}N_3O_4S_2$ | 0.478516 | 0.037288 | 0.119577 | 0.182118 | 0.182501 | – | – |
| Indomethacin | IN | $C_{19}H_{16}ClNO_4$ | 0.637824 | 0.045074 | 0.039148 | 0.178868 | – | 0.099087 | – |
| Nimesulide | NI | $C_{13}H_{12}N_2O_5S$ | 0.50644 | 0.03923 | 0.09086 | 0.259465 | 0.104004 | – | – |
| Celecoxib | CE | $C_{17}H_{14}F_3N_3O_2S$ | 0.535392 | 0.037 | 0.11018 | 0.083903 | 0.084079 | – | 0.149445 |
| Sulidac | SU | $C_{20}H_{17}FO_3S$ | 0.673985 | 0.048076 | – | 0.134668 | 0.089968 | – | 0.053304 |
| Etodolac | ET | $C_{17}H_{21}NO_3$ | 0.710565 | 0.07366 | 0.048743 | 0.167032 | – | – | – |

**Table 2**
Equivalent atomic number ($Z_{eq}$) and G-P exposure (EBF) and energy absorption (EABF) buildup factor coefficients for Meloxicam (ME).

| Energy (MeV) | $Z_{eq}$ | EBF | | | | | EABF | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | b | c | a | $X_k$ | d | b | c | a | $X_k$ | d |
| 0.015 | 9.83 | 1.088 | 0.398 | 0.211 | 12.681 | −0.108 | 1.087 | 0.415 | 0.197 | 12.045 | −0.096 |
| 0.02 | 9.93 | 1.197 | 0.432 | 0.196 | 13.895 | −0.104 | 1.198 | 0.439 | 0.190 | 14.524 | −0.102 |
| 0.03 | 10.08 | 1.571 | 0.545 | 0.151 | 15.085 | −0.079 | 1.613 | 0.523 | 0.162 | 13.827 | −0.081 |
| 0.04 | 10.17 | 2.111 | 0.742 | 0.078 | 15.684 | −0.039 | 2.185 | 0.717 | 0.089 | 15.449 | −0.048 |
| 0.05 | 10.23 | 2.775 | 0.869 | 0.054 | 14.134 | −0.038 | 2.908 | 0.869 | 0.055 | 14.621 | −0.044 |
| 0.06 | 10.27 | 3.218 | 1.050 | 0.008 | 13.373 | −0.018 | 3.509 | 1.063 | 0.004 | 14.235 | −0.014 |
| 0.08 | 10.32 | 3.596 | 1.324 | −0.052 | 13.602 | 0.011 | 4.324 | 1.358 | −0.060 | 12.070 | 0.019 |
| 0.1 | 10.37 | 3.594 | 1.494 | −0.081 | 14.257 | 0.023 | 4.531 | 1.563 | −0.096 | 13.425 | 0.036 |
| 0.15 | 10.42 | 3.306 | 1.658 | −0.106 | 14.671 | 0.032 | 4.024 | 1.795 | −0.132 | 13.677 | 0.052 |
| 0.2 | 10.46 | 3.024 | 1.701 | −0.113 | 14.535 | 0.034 | 3.574 | 1.838 | −0.138 | 13.812 | 0.054 |
| 0.3 | 10.50 | 2.689 | 1.679 | −0.113 | 14.132 | 0.033 | 3.006 | 1.799 | −0.134 | 13.904 | 0.050 |
| 0.4 | 10.55 | 2.500 | 1.618 | −0.106 | 14.973 | 0.032 | 2.712 | 1.721 | −0.125 | 14.142 | 0.046 |
| 0.5 | 10.50 | 2.368 | 1.573 | −0.102 | 14.764 | 0.033 | 2.529 | 1.651 | −0.117 | 14.254 | 0.043 |
| 0.6 | 10.38 | 2.273 | 1.523 | −0.095 | 15.219 | 0.030 | 2.396 | 1.585 | −0.107 | 14.514 | 0.039 |
| 0.8 | 9.91 | 2.139 | 1.457 | −0.088 | 14.872 | 0.031 | 2.223 | 1.485 | −0.093 | 14.703 | 0.035 |
| 1 | 8.91 | 2.073 | 1.397 | −0.079 | 14.809 | 0.030 | 2.107 | 1.413 | −0.083 | 14.421 | 0.032 |
| 1.5 | 8.01 | 1.929 | 1.265 | −0.057 | 14.447 | 0.023 | 1.943 | 1.261 | −0.056 | 14.309 | 0.022 |
| 2 | 7.92 | 1.839 | 1.165 | −0.036 | 15.293 | 0.014 | 1.839 | 1.168 | −0.037 | 14.571 | 0.015 |
| 3 | 7.91 | 1.712 | 1.053 | −0.011 | 12.970 | 0.002 | 1.710 | 1.052 | −0.011 | 14.203 | 0.002 |
| 4 | 7.88 | 1.625 | 0.990 | 0.004 | 19.922 | −0.007 | 1.622 | 0.985 | 0.006 | 13.129 | −0.007 |
| 5 | 7.88 | 1.554 | 0.946 | 0.016 | 14.325 | −0.011 | 1.557 | 0.941 | 0.018 | 13.306 | −0.013 |
| 6 | 7.88 | 1.506 | 0.915 | 0.026 | 15.275 | −0.022 | 1.505 | 0.909 | 0.028 | 15.316 | −0.025 |
| 8 | 7.87 | 1.418 | 0.891 | 0.033 | 12.224 | −0.019 | 1.413 | 0.893 | 0.032 | 12.295 | −0.017 |
| 10 | 7.86 | 1.358 | 0.872 | 0.039 | 14.020 | −0.025 | 1.357 | 0.867 | 0.041 | 13.958 | −0.027 |
| 15 | 7.85 | 1.266 | 0.842 | 0.050 | 15.031 | −0.038 | 1.261 | 0.847 | 0.048 | 14.786 | −0.036 |