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ABSTRACT

Pollution by alpha emitters is one of the factors harmful to children's health. Drugs are composed of naturally occurring ingredients that contribute to the nuclear radioactivity, this is a concern. As a result, this investigation assessed the presence of alpha emitters (radon-222, radium-226, uranium-238, and Polonium-218) in pharmaceuticals that are commonly utilized by children in Al-Najaf, governorate. Alpha emitters were measured using a CN-85 detector. Additionally, the investigation assessed the annual average internal dose (AAIED) and the probability of increased fatalities per million people (RECFPMP) resulting from alpha emitters found in the samples of the present study. The average radon-222, radium-226, and uranium-238 values were measured at 2.840, 0.173, and 2.830 Bq/kg, respectively. Moreover, the average AAIED and RECFPMP values associated with alpha emitters in all medical plant samples were 55.526 nSv/y and 0.214μ, respectively. Finally, the average levels of (^{218}Po and ^{214}Po) were recorded as 15.926 and 6.716 Bq/m3, respectively. After conducting a thorough examination of the samples and cross-referencing them with the globally accepted and permissible (218Po, 214Po) range, it has been determined that the radiation levels found in the emissions of specific antibiotic medications prescribed for pediatric age groups are entirely natural and fall within the approved range. Consequently, there is no cause for concern regarding the radioactive component of these drugs and their safe consumption by humans.

Keywords: Alpha emitters, anti-inflammatory drugs, children, CN-85 detector and Iraq

1. Introduction

The radiation may have a variety of effects on organisms that are living, including creating molecules that are ionizing inside the cells that comprise the body. Ultimately, this may have a significant impact on human genetic makeup, which is more likely to be passed down to children.

Humans can be adversely affected and placed in danger via different methods depending on their radiation exposure, the length of their exposure, and their body's sensitivity [1]. Alpha particles comprise two protons and two neutrons that are closely associated. They are released from a specific atom's atomic nucleus during the radioactive decay. Alpha particles have a low ability to penetrate and can be stopped by a sheet of paper or human skin. On the other hand, ingestion or inhalation of particles makes it possible for the alpha particles to be concentrated in a few cells and thus provide their energy there. Alpha particle emissions are also a side effect of some pediatric drugs that can have serious effects if not closely monitored [2]. The ionization process caused by alpha particles can damage the DNA in cells, leading to mutations and possibly cancer. This vulnerability is especially true for pediatric patients because they have smaller body sizes and organs that are still developing.

Regarding the ingestion of radionuclides, one of the more serious health outcomes is lung cancer mainly due to alpha particle exposure. Besides that, the uranium, radon, and radium content in plants can increase with consumption by people and cause significant harm as well. As such, it is important to establish how much radioactive isotopes are present in herbal remedies before they are used to keep those who do not want radiation out of their body safe. The regulation in pediatric drug formulation based on alpha particle emission and its effect is indeed significant. The FDA has introduced a draft guidance document "General Clinical Pharmacology Considerations for Research on Pediatric Drugs, Including Biologics," which describes historical aspects, highlights problems that arise when developing pediatric drug formulations, and emphasizes the importance of good practices in this area [5]. The guidance also emphasizes the importance of monitoring alpha particle emission from pediatric medication. The function of the environmental radiation mentor is crucial in maintaining public order and peace of mind. Since a rise in radiation levels may have far-reaching consequences, knowing about it is essential. Especially those associated with harmful effects on one's genes, health, or physical appearance. In this sense, we might say that the rise in background radiation is a kind of radioactive contamination. In this essay, we discuss the effects of alpha particle emission on children. As a result, research into the effects of radiation, the detection of radiation, and the pollution levels associated with it are desperately necessary. As such, several investigations and studies have been conducted, as well as numerous methods for estimating the amount of radioactive material present in different media, including drugs. The necessity of learning how the radioactive substances in these materials affect living things has been recognized. Several studies to study alpha emitters in different types of drugs [6-9]. Alpha particles released from certain anti-inflammatory drugs used by Iraqi children pose potential health risks that require attention and action by various stakeholders. Identifying alpha particle-emitting drugs and analyzing their potential health risks is important to reduce these risks.

2. Materials and methods

2.1. Collection of samples

Fifteen samples of antibiotics commonly used by different age groups of pediatrics were collected from different pharmacies in the Iraqi market from November to December of 2023. The name of the sample, its scientific name, and the symbol associated with it are enumerated in Table (1).

Table (1): Name, nation, and antibiotic sample manufacturers

No.	Sample name	Sample code	Manufacturers	Country
1	somaxime	F1	Samarra	Iraq
2	E-mox	F2	Eipico	Egypt
3	Azithro	F3	Biotech	India

4	Amoxicillin	F4	Company	Iraq
5	pumoxyi	F5	Microlabs	India
6	Azithro	F6	Riva pharma	Egypt
7	TRicef	F7	Ilko	Jordan
8	sefarin	F8	Pharma	Turkey
9	AuDiciav	F9	Aqualab	India
10	omnicef	F10	JPL	Saudi Arabia
11	Azithro	F11	Denk	Germany
12	Jamox	F12	AI Jazeera	Iraq
13	cefix	F13	Pharma	Turkey
14	septrin	F14	Aspen	Ireland
15	Azithro	F15	Pioneer	Iraq

2.2. Preparation samples

Once the samples have been gathered, they are transferred to a plastic container and labeled with their respective sample codes before being transported to the nuclear laboratory at the University of Kufa. All of the samples of antibiotics in this study were composed of powdered substance, uniformity, and were dried. Samples were collected directly without being pre-prepared.. The respective net weights are measured and recorded with a highly sensitive digital weighing balance with a percentage of ±0.01%. Next, 20 g (thickness of 2 cm) of powder samples were placed in plastic containers with diameter (5cm) and length (7 cm). Then, the CN-85 detector reagent was securely affixed to the top of a plastic container filled with the samples from the ongoing study.

2.3. Technical measurement

It employed the integrated passive dosimeter to gauge the concentration of alpha emitters in medical samples of drugs in this research from various local pharmacies of Iraq, these included solid state detectors CN-85 that measured 222Rn with a (1 × 1) cm^2 configuration for 90 days (the duration of the radiation period). The CN-85 (cellulose nitrate) detector has a thickness of (12µm), this is part of the distribution system of Kodak, France. The chemical formula for CN-85 is $C_6H_8O_9N_2$ which is widely used to detect alpha emitters ranging from (0.5-8) MeV to measure radon levels in different samples [10]. After the end of the irradiation period, the detectors were extracted from the containers and underwent chemical etching (NaOH) which was done using a water bath (Type HH-420, Germany). The best conditions for chemical etching in CN-85 were NaOH (2.5N), time (90 min), and temperature (60° C) [11]. Next, tracks were counted using an optical microscope with a magnified 400x [12].

2.4. Alpha Emitter Calculations

Alpha emitters (radon the airspace of tube C, radon within the sample C_{Rn}, ^{226}Ra activity within the sample C_{Ra}, uranium concentrations C_U, as well as radon daughters (^{218}Po and ^{214}Po) deposited ($D_{218_{Po}}$ *and* $D_{214_{Po}}$) on the detector chamber walls (POW) and face (POS)) were determined using equations from (1) to (6), respectively [13-17]:

$$C\left(\frac{Bq}{m^3}\right) = \frac{\rho}{K\,T} \qquad (1)$$

$$C_{Rn}\left(\frac{Bq}{m^3}\right) = \frac{C\,\lambda_{Rn}\,h\,T}{L} \qquad (2)$$

$$C_{Ra}\left(\frac{Bq}{kg}\right) = \frac{C\,h\,A}{M} \qquad (3)$$

$$C_U(ppm) = \frac{M_U}{M} \quad (4)$$

$$POW = D_{218_{Po}} = D_{214_{Po}} = \frac{C_{Rn}}{4} r \left(\frac{r}{r+h}\right) cos\theta_C \quad (5)$$

$$POS = D_{218_{Po}} = D_{214_{Po}} = \frac{C_{Rn}}{4} r \left(\frac{r}{r+h}\right)\left(cos\theta_C \frac{r}{R_\alpha}\right) \quad (6)$$

where, ρ is the density of the track, k is the coefficient of variation (0.28±0.043Track.cm^{-2} /Bq.m^{-3}.day), t is the time exposure (90 days), λ_{Rn} is the decay constant for ^{222}Rn, h is the distance between the sample and the detector, L is the thickness of the plastic cup's sample, A is the area of the sample and M is its weight.

For the estimation of the health risk parameters associated with alpha-emitting radiation, such as the annual average internal dose (AAIED) and the probability of a fatality associated with an excess number of cancer cases per million people. (RECFPMP), the equations (7) and (8) were used, respectively [15,18]:

$$AAIED\left(\frac{nSv}{y}\right) = A \times I \times CF \quad (5)$$

$$RECFPMP = AAIED \times DL \times RF \quad (6)$$

where, A is the activity in units Bq/kg for radon-222, radium-226, and uranium-238, I is the daily consumption rate, CF is the conversion factor for radon-222, radium-226, and uranium-238 ingestion by people, Dl is the duration time (70 year), and Rf is the conversion factor.

3. RESULTS AND DISCUSSION

Table (2) presents the results for alpha emitters (^{222}Rn, ^{226}Ra, and ^{238}U) found in specific anti-inflammatory medications. The data reveals and Figure (1) that (C_{Rn}^{a}) concentrations ranged from 22.887 Bq/m^3 to 142.224 Bq/m^3, with an average of 59.396 Bq/m^3. Similarly, the concentrations of (C_{Rn}^{s}) varied from 934.116 Bq/m^3 to 5804.864 Bq/m^3, with an average of 2424.254 Bq/m^3. Additionally, the concentrations of ($C_{Rn}^{s,ac}$) ranged from 1.057 Bq/kg to 6.202 Bq/kg, with an average of 2.840 Bq/kg. The values for ^{226}Ra ranged from 64.730 mBq/kg to 379.905 mBq/kg, with an average of 173.938 mBq/kg. Furthermore, the U(ppm) concentrations ranged from 0.085 ppm to 0.500 ppm, with an average of 0.229 ppm. Lastly, the concentrations of ($C_{U}^{s,ac}$) varied from 1.053 Bq/kg to 6.180 Bq/kg, with an average of 2.830 Bq/kg. Variations in the levels of radon gas can be attributed to various factors. Throughout history, medicinal substances were primarily extracted from natural sources, including plants, animals, fungi, and other organisms. Radon gas can also contribute to radiation pollution by absorbing radionuclides present in the atmosphere. The absorption of radionuclides by plants differs from one plant to another, affecting the plants and the earth's crust and fertilizers. Consequently, this leads to reduced radiation exposure within the system.

The concentrations of radon found in the samples of certain anti-inflammatory medications used for children in this study were lower than the acceptable action levels, which have a lower limit of 200 Bq/m3, according to the International Commission on Radiological Protection (ICRP) [19]. These values were also lower than the recommended values set by the World Health Organization (WHO), which suggests a limit of 100 Bq/m^3 for radon gas in the air [20]. It is important to note

2 that the radon parent (radium) was detected within the samples rather than in the tube airspace. The reported values for radon gas concentration in certain anti-inflammatory medication samples of this study were all below the recommended values according to the WHO. The global allowed for other alpha emitters like radium-226 in the present study was 30 Bq/kg according to UNSCEAR [21]. Additionally, the levels of uranium concentrations in the present study were 2.8 ppm, as guided by UNSCEAR [21], and were also found to be below the recommended levels in the medical samples of certain anti-inflammatory drugs.

2 Table (2): The Radon, Radium and Uranium concentrations in certain anti-inflammatory medications

No.	Code	^{222}Rn			^{226}Ra	^{238}U	
		(C^{a}_{Rn}) (Bq/m^3)	(C^{s}_{Rn}) (Bq/m^3)	$(C^{s,ac}_{Rn})$ (Bq/kg)	$(C^{s,ac}_{Ra})$ (mBq/kg)	U(ppm)	$(C^{s,ac}_{U})$ (Bq/kg)
1	F1	24.521	1000.839	1.203	73.689	0.097	1.199
2	F2	32.695	1334.452	1.426	87.335	0.115	1.421
3	F3	29.426	1201.006	1.777	108.832	0.143	1.770
4	F4	71.929	2935.793	3.321	203.438	0.268	3.310
5	F5	142.224	5804.864	6.202	379.905	0.500	6.180
6	F6	98.085	4003.355	3.850	235.803	0.311	3.836
7	F7	39.234	1601.342	1.621	99.286	0.131	1.615
8	F8	50.677	2068.400	2.486	152.290	0.201	2.477
9	F9	40.869	1668.064	2.468	151.156	0.199	2.459
10	F10	93.181	3803.187	6.095	373.355	0.492	6.074
11	F11	58.851	2402.013	2.887	176.853	0.233	2.877
12	F12	42.504	1734.787	1.854	113.535	0.150	1.847
13	F13	91.546	3736.464	3.782	231.666	0.305	3.769
14	F14	22.887	934.116	1.057	64.730	0.085	1.053
15	F15	52.312	2135.122	2.566	157.202	0.207	2.557
Min		22.887	934.116	1.057	64.730	0.085	1.053
Max		142.224	5804.864	6.202	379.905	0.500	6.180
Ave		59.396	2424.254	2.840	173.938	0.229	2.830

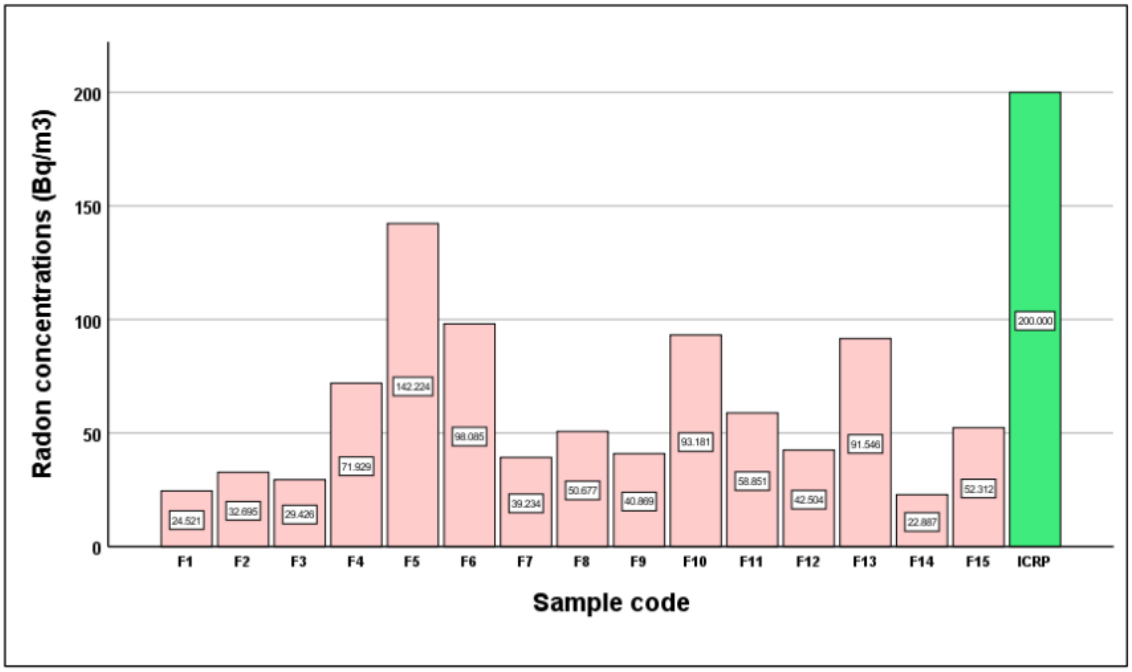

Figure (1): Radon concentration is the airspace above the sample

Figure 2 is the graphic representation of the histogram involved in radon concentration in commonly used antibiotic samples in the present study, which estimates the probability distribution of a continuous variable. From Figure 1, most of the ^{222}Rn results were within the 22 to 142Bq/m^3 concentrations.

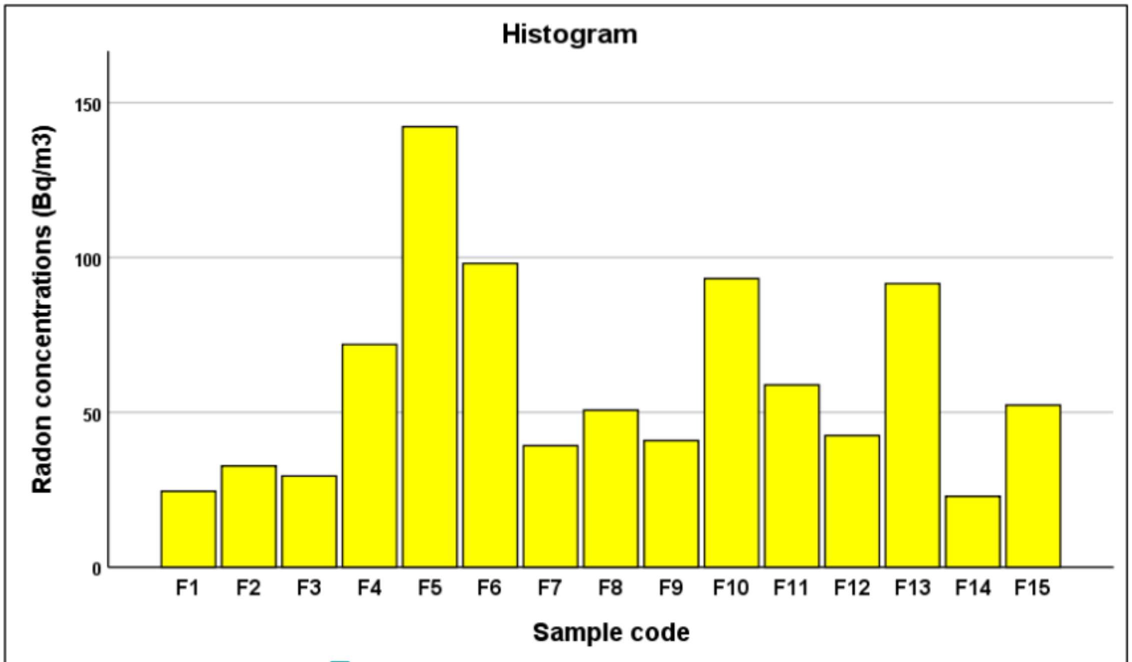

Figure (2): Histogram of Radon concentration in samples of commonly used antibiotic

The current study's box plots of radon concentration in samples are shown in Figure 3, providing a visual depiction of the study's location, variability, and outliers. The Pearson Correlation in Figure 3 confirmed the distribution of the samples to be normal.

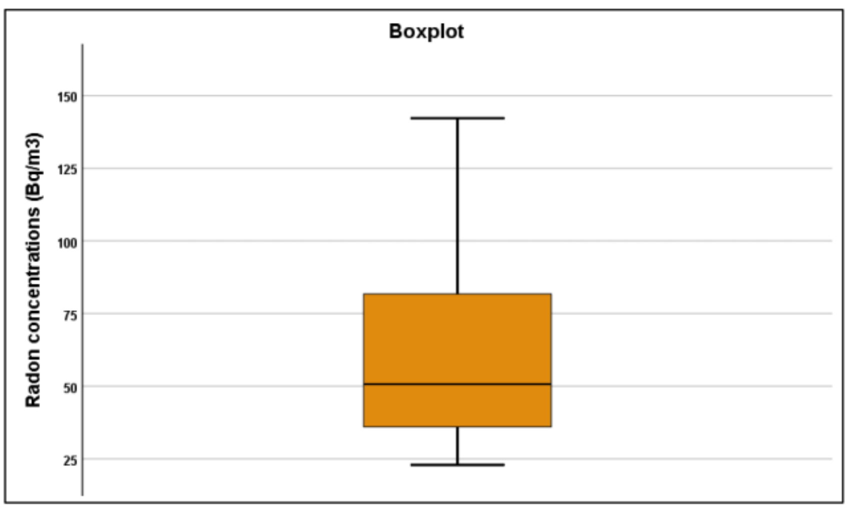

Figure (3): Box Plot of Radon concentration in samples of commonly used antibiotic

Table (3) Shows The results of Polonium (^{218}Po, ^{214}Po) are values average (in Bq/m^3) for ^{218}Po, ^{214}Po, are 15.926, 6.716 respectively. It is considered within acceptable concentrations.

Table (3) Results of Polonium (^{218}Po, ^{214}Po)

No.	Code	Polonium (Bq/m^3)	
		^{218}Po	^{214}Po
1	F1	6.575	2.773
2	F2	8.767	3.697
3	F3	7.890	3.327
4	F4	19.287	8.133
5	F5	38.137	16.082
6	F6	26.301	11.091
7	F7	10.520	4.436
8	F8	13.589	5.73
9	F9	10.959	4.621
10	F10	24.986	10.536
11	F11	15.781	6.655
12	F12	11.397	4.806
13	F13	24.548	10.351
14	F14	6.137	2.588
15	F15	14.027	5.915
Min		6.137	2.588
Max		38.137	16.082
Ave		15.926	6.716

Table (4) and Figure (4) displays the study sample's health risk parameters based on AAIED and RECFPMP. The ranges for AAIED (measured in nSv/year) are as follows: 0.675 to 3.962 for ^{222}Rn, 11.341 to 66.559 for ^{226}Ra, 8.648 to 50.755 for ^{238}U, and 20.664 to 121.277 for total alpha emitters. The average AAIED values (in nSv/year) are 1.814 for ^{222}Rn, 30.474 for ^{226}Ra, 23.238 for ^{238}U, and 55.526 for total alpha emitters. Additionally, Table (4) presents the RECFPMP results, which range from 0.080 μ to 0.467 μ with a mean of 0.214μ. It is important to note that the AAIED results obtained in this study are lower than the global average intake values (0.2 to 0.8 mSv) reported by UNSCEAR [21] and the recommended value of 1 mSv/year by ICRP [19]. The RECFPMP values obtained in this study were also very low across all samples, suggesting they may be disregarded or considered within the normal range.

Table (4): Results of AAIED and RECFPMP

No.	Code	AAIED (nSv/y)			Total AAIED (nSv/y)	RECF x10^{-6}
		^{222}Rn	^{226}Ra	^{238}U		
1	F1	0.768	12.910	9.845	23.524	0.091
2	F2	0.911	15.301	11.668	27.880	0.107
3	F3	1.135	19.067	14.540	34.742	0.134
4	F4	2.122	35.642	27.179	64.943	0.250
5	F5	3.962	66.559	50.755	121.277	0.467
6	F6	2.459	41.313	31.503	75.275	0.290
7	F7	1.035	17.395	13.265	31.695	0.122

8	F8	1.588	26.681	20.346	48.615	0.187
9	F9	1.576	26.483	20.194	48.253	0.186
10	F10	3.893	65.412	49.880	119.186	0.459
11	F11	1.844	30.985	23.628	56.456	0.217
12	F12	1.184	19.891	15.168	36.244	0.140
13	F13	2.416	40.588	30.951	73.955	0.285
14	F14	0.675	11.341	8.648	20.664	0.080
15	F15	1.639	27.542	21.002	50.183	0.193
Min		0.675	11.341	8.648	20.664	0.080
Max		3.962	66.559	50.755	121.277	0.467
Ave		1.814	30.474	23.238	55.526	0.214

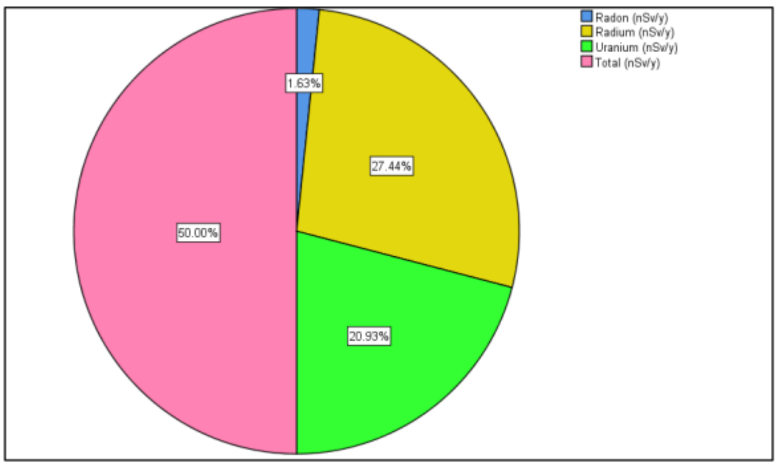

Figure (4): Compares the average annual effective dosage of Radon, Radium, and Uranium

CONCLUSIONS

Results were observed for ^{222}Rn concentrations in the specific anti-inflammatory drugs considered in this study within permissible limits, taking into account WHO and EPA standards. There are also results for ^{226}Ra ^{238}U and 238U in all samples in this work, which are within the range of global recommendations associated with UNSEAR reporting. AAIED's alpha emitter data was also found to be below acceptable levels in all samples Allowable limits for UNSCEAR, ICRP Polonium (^{218}Po, ^{214}Po). Cancer risk factor caused by alpha emission found in all samples Very low, so probably within the normal range. Finally, based on these findings, certain anti-inflammatory drugs may be considered to have no radiation risks.

Reference

[1] Gupta, T. (2013). Radiation, ionization, and detection in nuclear medicine (pp. 451-494). Heidelberg: Springer.
[2] Abojassim, A. A. ., Hashim, R. H. ., & Mahdi, N. S. . (2021). Basics of Nuclear Radiation. Basics of Nuclear Radiation, 1–86. https://doi.org/10.9734/bpi/mono/978-93-5547-140-6.
[3] Kutanzi, K. R., Lumen, A., Koturbash, I., & Miousse, I. R. (2016). Pediatric exposures to ionizing radiation: carcinogenic considerations. International journal of environmental research and public health, 13(11), 1057.
[4] Grzywa-Celińska, A., Krusiński, A., Mazur, J., Szewczyk, K., & Kozak, K. (2020). Radon—the element of risk. The impact of radon exposure on human health. Toxics, 8(4), 120.
[5] Lawi, D. J., Abdulwhaab, W. S., & Abojassim, A. A. (2023). Health risk study of heavy metals from consumption of drugs (solid and liquid) samples derived from medicinal plants in Iraq. Biological Trace Element Research, 201(7), 3528-3540.
[6] Abojassim, A. A., & Lawi, D. J. (2018). Alpha particles emissions in some samples of medical drugs (capsule) derived from medical plants in Iraq. Plant Archives, 18(1), 1137-1143.
[7] Poty, S., Francesconi, L. C., McDevitt, M. R., Morris, M. J., & Lewis, J. S. (2018). α-emitters for radiotherapy: from basic radiochemistry to clinical studies—part 1. Journal of Nuclear Medicine, 59(6), 878-884.
[8] Trujillo-Nolasco, M., Morales-Avila, E., Cruz-Nova, P., Katti, K. V., & Ocampo-García, B. (2021). Nanoradiopharmaceuticals based on alpha emitters: recent developments for medical applications. Pharmaceutics, 13(8), 1123.
[9] Zhang, J., Qin, S., Yang, M., Zhang, X., Zhang, S., & Yu, F. (2023). Alpha-emitters and targeted alpha therapy in cancer treatment. iRADIOLOGY, 1(3), 245-261.
[10] Abojassim, A. A., Abdulwahid, T. A., Hashim, R. H., Abdulshaheed, A. S., & Rajab, H. H. (2022, January). 222Rn, 218Po, and 214Po concentrations in blood samples of cancer patients at Najaf and Kufa cities of Al-Najaf Governorate. In AIP Conference Proceedings (Vol. 2386, No. 1). AIP Publishing.
[11] Ibrahim, A. A., Hashim, A. K., & Abojassim, A. A. (2021). Measurement of Radon-222 concentrations in selected soil samples in Al-Mothafeen Area (Kerbala, Iraq) by using the CN-85 detector. Polish Journal of Soil Science, 54(2), 139-153.
[12] Hashim, A. K., Hatif, A. R., Ahmed, N. M., Wadi, I. A., & Al Qaaod, A. A. (2021). Comparison study of CR-39 and CN-85 detectors to evaluate the alpha radioactivity of some samples of drinks in Iraq. Applied Radiation and Isotopes, 167, 109410.
[13] Hashim, A. K., Mezher, H. A., Kadhim, S. H., & Abojasim, A. A. (2021, March). Annual average internal dose based on alpha emitters in milk sample. In Journal of Physics: Conference Series (Vol. 1829, No. 1, p. 012027). IOP Publishing.
[14] Abojassim, A. A., Hady, H. N., & Kareem, A. H. A. (2016). Radon levels in different types of plants with medicinal properties. Madridge Journal of Food Technology, 1(1), 18-21.
[15] Al-Omari, S. (2015). Radioactivity measurement of 222Rn, 226Ra and 238U in pharmaceuticals and evaluation of cancer risk. International Journal of Low Radiation, 10(1), 61-73.
[16] Kadhim, M. M., Khudhair, M. K., Mraity, H. A. A. B., & Abojassim, A. A. (2022). Cancer Risk estimation in the samples of Iraqi manufactured Medicinal Plants. Journal of Pharmaceutical Negative Results, 1416-1421.

[17] Mohammed, H. A. U., Hussain, H. S., & Abojassim, A. A. (2022, January). Radon and radon progeny concentrations detection for human serum samples in Kerbala governorate. In AIP Conference Proceedings (Vol. 2386, No. 1). AIP Publishing.
[18] Alhous, S. F., Kadhim, S. A., Alkufi, A. A., & Kadhim, B. A. (2020, November). Measuring the level of Radioactive contamination of selected samples of Sugar and Salt available in the local markets in Najaf governorate/Iraq. In IOP conference series: Materials science and engineering (Vol. 928, No. 7, p. 072097). IOP Publishing.
[19] Tirmarche, M., Harrison, J. D., Laurier, D., Paquet, F., Blanchardon, E., & Marsh, J. W. (2010). ICRP Publication 115. Lung cancer risk from radon and progeny and statement on radon. Annals of the ICRP, 40(1), 1-64.
[20] World Health Organization. (2009). WHO handbook on indoor radon: a public health perspective. World Health Organization.
[21] United Nations. Scientific Committee on the Effects of Atomic Radiation. (2000). UNSCEAR... Report to the General Assembly, with Scientific Annexes. United Nations.