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DETERMINATION OF THE SODIUM, ALUMINIUM, POTASSIUM, MANGANESE, MAGNESIUM, BROMINE, CADMIUM AND CHLORINE CONCENTRATION VALUES IN THE WHOLE BLOOD SAMPLES OF HUMAN CANCER USING NEUTRON ACTIVATION ANALYSIS FACILITY OF THE SECOND EGYPTIAN RESEARCH REACTOR

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Neutron activation analysis (NAA) using the Second Egyptian Research Reactor (ETRR-2) has been utilized to analyze whole blood samples. The National Cancer Institute of Egypt provided us with 18 blood samples (11 breast, 2 prostate, 2 colon, 1 pancreatic, 1 ovarian) and a random sample of normal person to estimate the concentration values of Sodium, Aluminium, Potassium, Manganese, Magnesium, Bromine, Chlorine. The pneumatic irradiation rabbit system (PIRS) built in the vertical thermal column of the ETRR-2 reactor is used for short time irradiation at constant power. Elemental concentrations were estimated from measurements of the gamma-ray spectra of the product short lived isotopes in the samples. The calculated thermal to epithermal neutron flux ratio was found to be 196 at irradiation position. The tabulated concentrations were calculated by using k_0-neutron activation analysis (k_0NAA) standardization method.

Keywords: whole blood, k_0-standardization, neutron activation analysis, cancer.

Introduction

The essential function of the hematology laboratory is to provide information which can help in diagnosis and clinical management of patients. NAA is an accurate and rapid method for multi-element analysis [1 - 4] due to the possibility to determine a lot of elements in one sample without any chemical preparation. The k_0-NAA method allows measuring the elemental concentrations using Au as a single comparator without the need to use multi-elements standard samples. The present work is done to check the feasibility of using the k_0-NAA technique to perform hematological analysis in human being using the PIRS at the ETRR-2. This paper gives some information about the change in elemental concentration levels in some blood samples of some patients suffering from different kinds of cancer diseases.

Elemental concentration of ρ_a in NAA by k_0-standardization can be calculated from the following equation (1).

According to the k_0-standardization of NAA the concentration of an element in a sample is obtained as:

$$\rho_a(\mu g/g) = \frac{\left(\frac{N_p/t_c}{SDCw}\right)_a}{A_{sp}} \frac{1}{k_{0,m}(a)} \frac{f+Q_{0,m}(\alpha)}{f+Q_{0,a}(\alpha)} \frac{\varepsilon_{p,m}}{\varepsilon_{p,a}} 10^6, \quad (1)$$

where ρ_a - concentration of analyte a (in μg/g); m - co-irradiated neutron fluence rate monitor; N_p - measured net peak area, corrected for pulse losses [dead time, random coincidence (pulse pile-up), true coincidence (cascade summing); t_c - counting time; $S = 1 - \exp(-\lambda t_{irr})$ - saturation factor, where t_{irr} - irradiation time and $\lambda = (\ln 2)/T_{1/2}$ with $T_{1/2}$ - half lifetime; $D = 1 - \exp(-\lambda t_d)$ - decay factor, with t_d - decay time (from end of irradiation to start of counting); $C = [1 - \exp(-\lambda t_c)]/\lambda t_c$ - counting factor, corrected for decay during counting; w - sample mass (in grams); $A_{sp} = (N_p/t_c)/SDCw$, the specific count rate, with w - mass of the monitor element (in grams); $k_{0,m}(a)$ - experimentally determined k_0 factor of analyte a versus monitor m, defined as $k_{0,m}(a) = (M_m \theta_a \sigma_{0,a} \gamma_m)/(M_a \theta_m \sigma_{0,m} \gamma_a)$, with M-molar mass; θ - isotopic abundance; σ_0 - (n, γ) cross section at 2200 $m.s^{-1}$ and γ-absolute gamma intensity; $f = \varphi_{th}/\varphi_{ep}$ - the thermal (sub-cadmium) to epithermal neutron fluence rate ratio;

$$Q_0(\alpha) = \left\{ \frac{Q_0 - 2(E_0/E_{cd})^{1/2}}{(E_r)^\alpha} + \frac{2(E_0/E_{cd})^{1/2}}{(2\alpha+1)(E_{cd})^\alpha} \right\} (1\text{ eV})^\alpha.$$

$Q_0 = I_0/\sigma_0$ with I_0 resonance integral, defined as

$$I_0 = \int_{0.55\text{ eV}}^{\infty} \sigma(E) dE/E,$$

$\overline{E_r}$ = effective resonance energy (eV); α - measure for the deviation of the epithermal neutron fluence rate distribution from the $1/E$ shape, approximated by $1/E^{1+\alpha}$ dependence; ε - full-energy detection efficiency. In equation (1) the co-irradiated monitor

used is ^{198}Au(n, γ)^{198}Au, E_γ = 411.8 keV and k_0 factor ($k_{0,Au}$) is given by

$$k_{0,m}(a) = k_{0,Au}(a) / k_{0,Au}(m).$$

Experimental procedures

1. Collection and preparation of the blood samples. About 20 mg of blood samples of different patients suffering from different kinds of cancer were drawn from the patient's arm at National Cancer Institute and inserted in clean polyethylene vials. The samples were put on ice and then in the refrigerator until the beginning of sample irradiation.

2. Neutron Activation. The PIRS built in the vertical thermal column of the ETRR-2 (Inchass, Egypt) was used for short irradiation time. Blood samples was irradiated for a period of 60 ÷ 180 s at 19 MW in the vertical thermal column. To obtain thermal to epithermal flux ratio *f* a bare gold foil weighing 1.5 mg and another weighing 2.6 mg covered with 0.5 mm cadmium were sealed in polythene vials and irradiated separately at the same position.

Sample Container

3. Determination of neutron flux parameters. The determination of the thermal flux φ_{th}, the epithermal flux φ_{ep}, the flux ratio *f*, and the epithermal flux spectrum shape factor α are necessary for all types of absolute and mono standard methods of neutron activation analysis. The cadmium difference method, using a thin gold foil (^{197}Au) as a neutron flux monitor, has been applied to measure thermal to epithermal neutron flux ratio *f*. The measured *f* value of the irradiation position was found to be 196. At this higher thermal component, α has no significance in concentration calculations [6].

4. Measurements. The measurements of gamma-ray spectra are carried out with P-type coaxial EG&G Ortec HPGe cylinder with 100 % relative efficiency, 1.9 keV FWHM at 1.3325 MeV of ^{60}Co. A Canberra 10 thickness ultra low background lead shield with low carbon steel casing was used in shielding the HPGe detector. A gamma-vision card of 16384 channels ADC was mounted PC for data acquisition. The gamma-vision software is used for energy and efficiency calibrations as well as for spectrum analysis. The counting time for each sample 300 s and decay time about 40 s. In order to reduce the error, nuclide with more than one gamma-line were calculated separately and the average concentration is calculated. Two blood samples from random person are collected, irradiated and counting as well as the patient's blood samples and used to test the technique by comparing the results from the k_0-NAA method with that from the ICP-MS method at the Central Laboratory for Elemental and Isotopic Analysis (Inchass, Egypt).

Results and discussion

Table 1 reported the nuclear constants of the element of interest in the present work. The tabulated ratio Q_0, of the neutron resonance integral I to the thermal neutron capture cross section, at 2200 m/s can be used instead $Q_0(\alpha)$ in equation (1) due to the large value of the flux ratio at the irradiation position *f* = 196.

Table 1.

Product radio-isotopes	Half lifetime	Main gamma-ray energies, keV	k_{0Au}	Q_o
^{24}Na	14.95 h	1368.6	$4.68 \cdot 10^{-2}$	0.59
^{27}Mg	14.950 h	843	$2.53 \cdot 10^{-4}$	0.64
^{28}Al	2.13 min	1778.9	$1.75 \cdot 10^{-2}$	0.71
^{38}Cl	37.21 min	1642.4	$1.97 \cdot 10^{-3}$	0.69
^{56}Mn	2.57 h	846	$4.96 \cdot 10^{-1}$	1.053
^{41}K	12.36 h	1524.7	$9.46 \cdot 10^{-4}$	0.87
^{80}Br	17.68 min	616.3	$6.92 \cdot 10^{-3}$	12.1

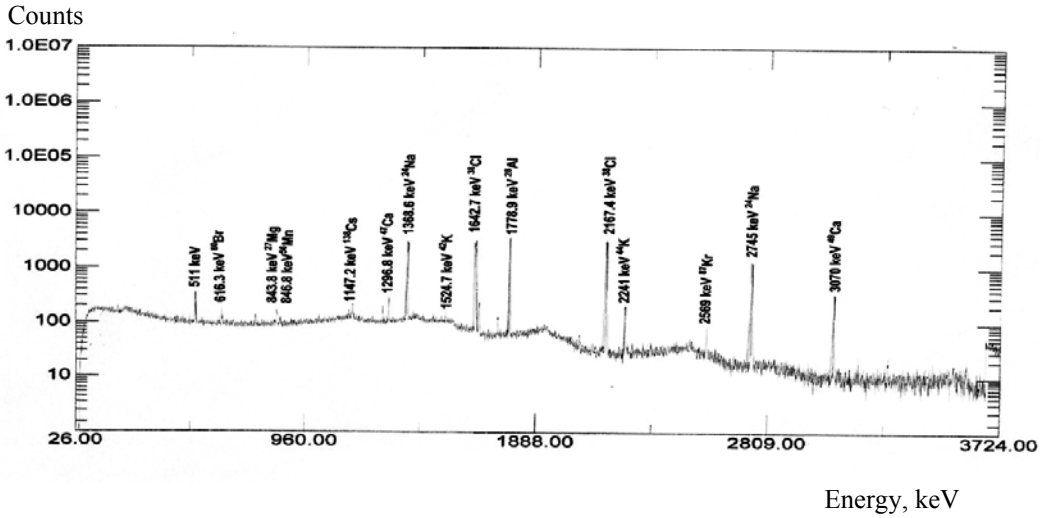
The elemental concentration of one blood sample from random person is calculated using short irradiation neutron activation technique and the same sample is analyzed using ICP-MS technique. The results are shown in Table 2. The results show a good agreement. Table 2 shows the elemental

concentration of random blood samples using k_0-NAA and ICP-MS techniques and compared by some previous work for normal whole blood samples which deal with the present work. The interference of 846.8 keV of ^{56}Mn and 843.8 ^{27}Mg is not present due to the good resolution of the used detector.

Table 2.

Elements	Concentration (k_0-NAA), mg/kg	Concentration (ICP-MS) ± 1 %, mg/kg	Previous works for normal blood
Na	1632 ± 22	1600	1480 - 2006 [1]
Mn	0.03 ± 0.006	Not detected	0.03 [8]
Al	2.2 ± 0.41	Not detected	
Mg	35 ± 0.42	50	
Cl	1834 ± 26	1820	1720 [10], 2540 - 3500 [1]
K	1466	Not detected	1480 - 2060 [9], 1310 - 1890 [1]
Br	1.6 ± 0.16	1.7	1.48 [8]
Ca	442 ± 6	450	

The Figure shows the gamma-ray spectrum of one of the breast cancer samples. The elemental concentration of Sodium, Aluminium, Magnesium, Bromine, Chlorine, Potassium, and Manganese are determined and tabulated.



The gamma-ray spectrum of the breast cancer blood samples measured for 300 s, following 30 cooling time post 180 s irradiation using PIRS of the ETRR-2.

Table 3 shows the elemental concentration (mg/kg) of 11 blood samples from breast cancer patients.

Table 3.

Sample number	Age	Na	Mg	Al	Cl	K	Mn	Br	Ca
18	30	1760 ± 18	41 ± 0.82	9 ± 1.6	1933 ± 48	1606 ± 30	0.02 ± 0.005	1.6 ± 0.16	N.D.[1]
2	37	1906 ± 28	20 ± 0.32	34 ± 0.58	1893 ± 45	1579 ± 9	0.33 ± 0.04	53 ± 5.8	642 ± 10
6	40	1973 ± 29	15 ± 0.16	14 ± 0.15	2126 ± 31	1777 ± 25	0.38 ± 0.03	1.6 ± 0.16	N.D
7	45	1708 ± 27	60 ± 0.84	43 ± 0.65	1756 ± 40	1442 ± 23	0.48 ± 0.07	3.5 ± 0.48	741 ± 9
10	46	1648 ± 19	7.4 ± 0.13	5 ± 0.72	1457 ± 42	1457 ± 15	0.34 ± 0.05	2.8 ± 0.14	N.D.[1]
8	50	1596 ± 17	4.1 ± 0.1	8 ± 0.17	1764 ± 45	1504 ± 25	0.24 ± 0.03	3.9 ± 0.28	N.D.[1]
15	54	1592 ± 19	0.3 ± 0.03	5 ± 0.10	1645 ± 36	1469 ± 30	0.32 ± 0.05	2.1 ± 0.06	N.D.[1]
16	55	1906 ± 28	12 ± 0.19	25 ± 0.68	1492 ± 24	1236 ± 20	0.65 ± 0.1	3.3 ± 0.37	443 ± 7
17	60	1999 ± 24	7.1 ± 0.12	10 ± 0.35	1994 ± 83	1476 ± 12	0.24 ± 0.02	0.94 ± 0.13	N.D.[1]
1	64	2094 ± 33	98 ± 1.6	53 ± 1.76	1846 ± 55	1846 ± 29	0.27 ± 0.03	4.2 ± 0.55	904 ± 13
13	64	2531 ± 24	51 ± 0.61	47 ± 2.16	2284 ± 66	1893 ± 16	0.41 ± 0.01	3.4 ± 0.47	870 ± 12

[1]N.D. - Not detected.

Elemental concentration (mg/kg) of colon cancer samples are determined and tabulated. Table 4 lists the elemental concentration of two blood samples from colon cancer patients.

Table 4.

Sample number	Age	Na	Mg	Al	Cl	K	Mn	Br	Ca
12	56	1864 ± 70	12 ± 1.5	27 ± 0.5	1866 ± 61	1553 ± 36	0.61 ± 0.09	4.7 ± 0.34	494 ± 7
14	58	1351 ± 47	1.6 ± 0.21	28 ± 0.66	1890 ± 46	1114 ± 21	0.41 ± 0.05	1.9 ± 0.31	461 ± 6

Elemental concentration (mg/kg) of prostate cancer samples are determined and tabulated. Table 5 gives the elemental concentration of two blood samples from prostate cancer patients.

Table 5.

Sample number	Age	Na	Mg	Al	Cl	K	Mn	Br	Ca
5	70	3258 ± 114	77 ± 10	15 ± 0.66	3458 ± 86	2875 ± 806	0.44 ± 0.05	7.5 ± 0.87	N.D.[1]
9	73	1766 ± 61	50 ± 6.5	34 ± 0.96	1933 ± 55	1604 ± 52	0.35 ± 0.04	2.9 ± 0.29	667 ± 5

[1]N.D. - Not detected.

Elemental concentration (mg/kg) of pancreatic cancer sample is determined and tabulated. Table 6 shows the elemental concentration of one blood sample from pancreatic cancer patients.

Table 6.

Sample number	Age	Na	Mg	Al	Cl	K	Mn	Br	Ca
11	34	1832 ± 54	34 ± 4	24 ± 5	1772 ± 51	1475 ± 43	0.1 ± 0.01	2.2 ± 0.46	420 ± 6

Elemental concentration (mg/kg) an ovarian cancer sample is determined and tabulated in Table 7.

Table 7.

Sample number	Age	Na	Mg	Al	Cl	K	Mn	Br	Ca
19	58	1642 ± 32	17 ± 2	24 ± 5	1761 ± 64	1842 ± 60	0.28 ± 0.03	2.1 ± 0.18	392 ± 7

Elemental concentration ranges (mg/kg) for all samples are summarized, tabulated and compared by previous works is given in Table 8.

Table 8.

Element	Breast	Colon	Prostate	Ovary	Pancreatic	Random sample	Previous works for cancer patient
Na	1592 - 2531	1351 - 1864	1766 - 3258	1642	1832	1664	1930 [4]
Mg	0.3 – 60	1.6 - 12	50 - 70	17	34	35	
Al	5-53	27 - 28	15 - 34	24	24	8	
Cl	1457 - 2284	1866 - 1890	1933 - 3458	1761	1772	1527	2860 [4]
K	886 -2256	900 - 1479	1579 - 2115	1842	1565	1466	
Mn	0.02 - 0.65	0.41 - 0.61	0.35 - 0.44	0.28	0.1	0.04	
Br	0.94 - 53	1.9 - 4.7	2.9 - 7.5	2.1	2.2	1.6	4.58 [2]
Ca	720	477.5	667	392	420	442	

Statistical treatment of the data indicated that many of the elements determined were present in different concentrations in cancer patients as compared with normal samples.

Quantitative study of the Na, Mg, Al, Cl, K, Mn, Br and Ca elements by the NAA using k_0-method shows that the highest concentration values of Na, Mg, Cl, and K recorded in prostate cancer, while the highest concentration values of Al, Br, and Ca recorded in breast cancer. Definite increases in the amount of manganese present in the persons suffering from colon cancer indicated that the use of neutron activation analysis as a diagnostic tool for this condition is clearly feasible**.** Because bromine is toxic to the human body and binds to iodine receptors in the breast. So, the elemental

concentrations of bromine using short lived neutron activation can be used to diagnose the breast cancer.

Conclusion

In the vertical thermal column of the PIRS the thermal to epithermal neutron flux ratio f was found to be 196. The results obtained by k_0-NAA has agreed reasonably with ICP-MS and the normal range for another works, taking into account the different environmental impact on the concentrations of elements from country to another country. This shows the possibility of utilizing the nuclear techniques in diagnostic pathology.

The previous method to analyze liquid samples by using reactor irradiation were carried by immersing a nomination paper by the sample, but in the present work, freezing of samples helps us to keep blood samples for a long time and re-irradiation for some other time and overcome the background due to nomination papers.

From the obtained data, it is shown that there are certain differences in the elemental concentrations in the whole blood samples. By using a FORTRAN or Excel programs and refer to the time optimization established in this experiment to perform the whole blood analysis (irradiation time of $60 \div 180$ s, counting time of 300 s) allowed us to determine the concentrations of several elements in each sample in about half hours or less making this nuclear procedure agile and fast. On the other hand, the short time irradiation and the use of small amounts of biological material 20 mg, reducing the radiation exposure. This experimental techniques using whole blood can be very useful for clinical practices which involves a large number of samples or quantitative analyses of several times. Concentrations of high-value such as Na, Cl, K show that it is possible to establish units within the hospitals which can used closed neutron sources for such analysis. So, the k_0-NAA standardization method using a low power research reactor has proven to be a quick and effective method for monitoring the change in elemental concentrations in human whole blood samples. Moreover, associated with the short time irradiation and with the use of small amount of biological material, it is important to notice that this technique reduces the radiation exposure during the handling process of the active material besides, no treatment have to be made prior to the discarding these materials, which can, after certain time, be treated as regular biohazard or be stored for future reexamination without the need for any specific shielding. Using short-lived neutron activation technique, we can determine Al concentrations with high precision in cancer diseases and as we except in other diseases such as Alzheimer's.

k_0-NAA methods is suitable for studying the elemental concentrations in the biological samples because it simplifies the analysis of bio-samples (no sample preparation) and help in increase the accuracy due to the possibility to analyze samples using single comparator.

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ВИЗНАЧЕННЯ КОНЦЕНТРАЦІЙ НАТРІЮ, АЛЮМІНІЮ, КАЛІЮ, МАГНІЮ, МАРГАНЦЮ, БРОМУ, КАДМІЮ ТА ХЛОРУ У ЗРАЗКАХ ЦІЛЬНОЇ КРОВІ ОНКОЛОГІЧНИХ ХВОРИХ ЗА ДОПОМОГОЮ УСТАНОВКИ НЕЙТРОННО-АКТИВАЦІЙНОГО АНАЛІЗУ НА ДРУГОМУ ДОСЛІДНИЦЬКОМУ РЕАКТОРІ ЄГИПТУ

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Для аналізу зразків крові застосовано метод нейтронно-активаційного аналізу (NAA) на другому дослідницькому реакторі Єгипту (ETRR-2). Національний інститут раку Єгипту надав для аналізу 18 зразків крові (11 – з легень, два – із передміхурової залози, два – з товстої кишки, один – із підшлункової залози, один – з яєчників) та зразок, взятий за схемою випадкового відбору, здорового пацієнта для визначення величин концентрації натрію, алюмінію, калію, магнію, марганцю, брому, кадмію та хлору. На вертикальному тепловому каналі реактора ETRR-2 було створено пневматичну стрибкову систему опромінення (PIRS) для короткочасного опромінення при постійній потужності дози. Концентрації елементів були одержані з вимірювань гамма-спектрів ізотопів з малим часом життя, що утворилися в зразках. Обчислене відношення термального й епітермального нейтронних потоків становило 196 у точці опромінення. Представлені в таблицях концентрації обчислювались за допомогою стандартного методу k_0-нейтронно-активаційного аналізу (k_0NAA).

Ключові слова: цільна кров, k_0-стандартизація, нейтронно-активаційний аналіз, рак.

ОПРЕДЕЛЕНИЕ КОНЦЕНТРАЦИЙ НАТРИЯ, АЛЮМИНИЯ, КАЛИЯ, МАГНИЯ, МАРГАНЦА, БРОМА, КАДМИЯ И ХЛОРА В ОБРАЗЦАХ ЦЕЛЬНОЙ КРОВИ ОНКОЛОГИЧЕСКИХ БОЛЬНЫХ ПРИ ПОМОЩИ УСТАНОВКИ НЕЙТРОННО-АКТИВАЦИОННОГО АНАЛИЗА НА ВТОРОМ ИССЛЕДОВАТЕЛЬСКОМ РЕАКТОРЕ ЕГИПТА

Н. Ф. Солиман, А. Срур, Л. С. Ашмави, Н. Вели Эль-Дин, Т. Эль Мохамед

Для анализа образцов крови применен метод нейтронно-активационного анализа на втором исследовательской реакторе Египта (ETRR-2). Национальный институт рака Египта предоставил для анализа 18 образцов крови (11 – из легких, два – из предстательной железы, два – из толстой кишки, один – из поджелудочной железы, один – из яичников) и образец, взятый по схеме случайного отбора, здорового пациента для определения величин концентрации натрия, алюминия, калия, магния, марганца, брома, кадмия и хлора. На вертикальном тепловом канале реактора ETRR-2 была создана пневматическая скачковая система облучения (PIRS) для кратковременного облучения при постоянной мощности дозы. Концентрации элементов были получены из измерений гамма-спектров изотопов с малым временем жизни, образовавшихся в образцах. Вычисленное отношение термального и эпитермального нейтронных потоков составило 196 в месте облучения. Представленные в таблицах концентрации вычислялись при помощи стандартного метода k_0-нейтронно-активационного анализа (k_0NAA).

Ключевые слова: цельная кровь, k_0-стандартизация, нейтронно-активационный анализ, рак.

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