New approach for evaluation of Co, Ni, Mo, V, and Ge levels in serum of no Hodgkin lymphoma patients.

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Abstract

This research included detection of five trace elements Co , Ni , Mo , V , and Ge in the serum of 60 patients (35 males with mean age 41±17:07.6SE years and25 female with mean age 31 ±2.31268SE
SE years) with lymphoma and 70 healthy(40 male with mean age 34.6±1.91724SE years and 42 females with mean age 42±3.8223SE years) cancer enrolled in Margin Hospital countryside Babylon governorate /Iraq by using atomic absorption spectrophotometry flam-less .Analysis t-test dose not reflect the true levels of these elements because of wide range of ages and different interferences .These reasons turned the data from atomic absorption spectrophotometry to grapher 5 program ,and the resulted diagrams were divided the level of these elements into new 4 age groups raising 10 years for each, and solution the mean of each 10 years(25 , 35 , 45 , and55 year age) using 2nd order equation to give a new results represented the real serum levels of trace elements, which are lower than healthy for males and females , in agreements with published levels of these elements in addition gave significant results compared with control of age groups by take the mean of these 4 age groups .The new levels of trace elements(µg/l for males and females respectively) are 0.0120582 , 0.0154365 of patients 0.0205877 , 0.152809 of control of Co , and 0.0136302 , 0.011899 of patient 0.0175932, 0.0113087of controls of Ni , and 0.0092995 , 0.0092762 of patients 0.0110997 , 0.145282 of controls of Mo , and 0.0128912 , 0.0072407 of patients 0.033547 , 0.0229725 of controls of V , and the last serum level of Ge trace element is 0.0346395 , 0.0346395 of patients 0.036890 , 0.0612455 of controls .while these results are lower than published , but it's reflected the related with malnutrition's of people in Babylon / Iraq .

الخلاصة

يشتمل هذا البحث على تعين خمسة عناصر نزرة هي Ge, Mo, Ni, Co في مصل دم 60 مريض في مرض اللمفوما (35 ذكور وكان معدل العمر41± SE 17.07 سنة ولناث مع معدل عمر 31 ± SE 2.31268 سنة) مع مقارنة مع 70 عينة اصحاء (40 ذكور بمعدل عمر 34.6 ± SE 1.91724 سنة

واناث بمعدل عمر 42 ± 3.8223 SE سنة) لمرضى السرطان الراقدين في مستشفى مرجان /محافظة بابل/ العراق، وتم تعين تراكيز تلك العناصر باستخدام تقنية الامتصاص الذري اللالهبي.

استخدمت في البحث طريقة التحليل الاحصائي اختبار t– ، ولوحظعلى ان هذا التحليل لايعطي القيم الحقيقية لمستويات تلك العناصر بسبب سعة الفئة العمرية الميتخدمة في الدراسة، واختلاف التداخلات، هذه الاسباب دفعت في نقل هذه المعلومات المحصلة من تقنية المطياف الامتصاص الذري اللالهبي الى استخدامها في برنامج الراسم Grapher 5. 5 ، اعطت نتائج مخططات بعد ان قسمت الى العينات المستخدمة الى مجاميع عمرية لاربعة مجاميع جديدة لكل عشرة سنوات ، وتم حل المعدل لكل عشرة سنوات على اساس عمر (25 ، 35 ، 45 و 55 سنة) باستخدام المعادلة من الدرجة الثانية ، والتي اعطت نتائج جديدة تمثل المستويات الحقيقية لتلك العناصر النزرة في مصل الدم التي هي اقل مستوى مما في الاصحاء الى ان النتائج دلت انسجامها مع النتائج المنشورة لتلك العناصر. بالاضافة لذلك اعطت نتائج دالة مقارنة مع مجاميع السيطرة العمرية التي اخذت كمعدل للمجاميع الاربعة العمرية، المستويات الجديدة للعناصر النزرة (مايكروغرام/لتر) للذكور والاناث على التوالي هي 0.0120582 ، 0.0154365 ,للمرض , 0.0205877 0.152809 لمجموعة السيطرة لعنصر Co 0.0136302، 0.011899 للمرض 0.0175932 ، 0.0113087 لمجموعة السيطرة لعنصر Ni ، و 0.0092995 ، 0.0092762 للمرض 0.0110997 ، 0.145282 لمجموعة السيطرة لعنصر Mo و 0.0128912، 0.0072407 للمرض 0.033547، 0.0229725 لمجموعة السيطرة لعنصر الـ V والمستوى الاخير في مصل الدم لعنصر Ge هو 0.0346395، 0.0346395 للمرض 0.036890 ، 0.0612455 لمجموعة السيطرة ، بينما هذه النتائج هي اقل مما هو منشور في الادبيات لتلك العناصر ، ولكنها تعكس العلاقة مع سوء التغذية للناس في محافظة بابل/ العراق.

Introduction

Cancer diseases are a tumors , it is developed from a single cell with series of mutation with uncontrolled growth rate .Cancers are classified according to the cell or tissue which is arise the disease , Lymphomas which are arise from mesoderm . There are several biochemical markers such as enzymes and cofactors which the serum levels either decrease or increase [1].

Some elements are essential trace elements (acts as a cofactors of enzymes) are present at different concentrations mg/kg or µg/g or g/kg (ng/g) ultimately, there are relationship between the intake of an essential nutrient and the dependent optimal biological function located between deficiency and toxicity[2,3,4]

Trace Element	the references.	Limiting rang and founding
Ni	1- One of the essential ultra trace elements , the deficiency of nickel causes altraration of folate and vitamin C .[1,5] 2-Nickel ions used in the iron transport system a cross small intestine related with ferreitin, thereby cause anemia[5]. 3-Nickel salt is nontoxic, give the same effecting of copper or iron deficiency [1]. 4- The deficiency of nickel are called nickel allergy[1] . 5- It is toxicity more than 100 time of carbon monoxide[1]. 6-The exposure to nickel compounds cause carcinogenic diseases[7.] 7- Ni II selectivity interacted with heterochromatic long arm of the X-chromosome ,because Ni II binding to the histone protein, which is form octahedral or square planer with protein which are more efficient in coordinating nickel complex than high molecular weight of double strand DNA , which is cause chromosomal damage peripheral lymphocyte ,when the worker exposure to the nickel[12,14,15] , also cause mutation for the human workers lunge[14,16] . 8-Nickel deficiency cause in general lipid metabolism of animals by accumulation of hepatic lipid TG, PL, VLDL, and LDL[14]. 9-Nickel deprived reduced the activity of glucose-6-phosphate dehydrogenase, lipogenesis, malic enzyme and fatty acid synthase and impair hepatic lipid secretion into blood[17]. 10-Nickel deficiency had significantly reduced hematological parameter including erythrocyte count; hemoglobin and hematocrit the same variable also have shown to be affected by iron deficiency[17]. 11-Nickel levels correlated with blood sugar, HbA1C, fructosamine, salic acid level and age[8]. 12- Nickel-generated formation of oxygen radicals plays a very important role in nickel carcinogenesis[17]. 13-Lowers requirement for B_{12} causes B_{12} deficiency symptoms[18].	*2.4-1.7 nmol/l in serum [1]. *Another ref. sing the conc. is 1.15±1.89 µg/l[8,9] *Also in another ref. the level in serum 0.3 µg/l with upper limits 1.1 µg/l [5, 10]. * Nickel rich food hems (chocolate, nuts , beans, porridy oats) * Serum nickel levels correlated with in take of the food [6,11,12,13.]

Mo	1-Assential ultra trace element for humans[1, 14], which have the biological concentration in the tissues[1]. 2-It is important for three enzymes, xanthine oxidase, aldehyde oxidase, and sulfite oxidase[14]. 3-It is nontoxic to human, the high dietary of molybdenum have been linked to elevated uric acid in blood, which is signed to increase of goat[14]. 4-Several diseases which are cause by an imbalance in the concentration of Mo, Cu, and sulpher, then molybdenum is a cofactor disease [4]. 5- Molybdenum disease associated with Mo deficiency, including goat with including accumulation of uric acid and cancer[17, 19, 20]. 6- It is toxic when exposure to high Mo conc., the toxicity as antagonist to copper[18]. 7- Erythrocyte molybdenum is more sensitive for the detection of deficiency in patients[20]. 8- Molybdenum is modulates calcium, magnesium, copper metabolism[18]. 9- Molybdenum has some effects on the synthesis of vitamin C in plants , which inhibit synthesis of nitroso compounds in the human body[21] .Mo has protective action against the induction of cancer in rats by organic N- nitroso compounds when treated with sodium molybdate (cited in [22]) . 10- Lack of molybdenum in the environment may obviously influence nitrogen fixation and transformation of soil nitrates as well as compound formation, and that Mo deficiency is definitely related to high mortality rate of gastric cancer in local inhabitants [21]. 11- Lack of molybdenum in the human body indicated of the causes of gastric cancer [21] 12- Leu *et al* studied (cited in [21]) the effect of molybdenum on the activities of P- 450 and demethylase in rate liver and found that small dose of molybdenum could speed up detoxification of carcinogens. Molybdenum's key is as a facilitator of liver detoxification. It is also vital for the function of several enzymes in the body, one of which regulates urinary excretion[23]. Mo is a mineral that is used as a supplement for sulfite sensitivity, cancer preventation , asthma , cavity preventation , allergies, and Wilson's disease (cited in [24]) .	*Range intake is 50 -100 µg/l[17] * Detection limit in serum is 0.06 µg/l[17]. * Serum molybdenum contents of patients were lower than those of healthy controls 21.84 µg/l ±7.49µg/l and 25.38 µg/l± 8.58µg/l respectively[21].

Co	1-Is an essential element for human, as apart of vitamin B12 (coblamin) – micro flora of the lumen intestine[1,] There are radio and non radio active, non radioactive is stable. [20, 25, 26 ,27] 2-Cobalt is more toxic in the presence of oxygen than in its absence[6]. 3- Increasing of cobalt concentration of diet is effected on blood glucose, hemoglobin and weight; these results from research investigated on rats[25]. 4- Cobalt – activated cyclase is absent from the sera of health subjects and from patients with liver cirrhosis, obstructive jaundice or chronic hepatitis. It's activity however appears invariably in serum during the early stage of acute viral hepatitis (with toxic hepatitis which help in the diagnosis of this disease) [28]. 5- There are relationships between total homocysteine and serum concentration of cobalt, and related with homocysteine production, assessed in human peripheral mononuclear cells[30]. 6-It's toxic in high concentration in erythrocyte[, 17, and 31]. 7- Cobalt has correlated with changes in levels of total cholesterol anti-collagen type IV antibodies and essential hypertension in children[36]. 8-Exposure to large amounts of radioactive cobalt can damages cells, and exposure to high levels of cobalt radiation can cause changes in the genetic materials with in cells and may result in development of some types of cancer[31].	
V	1-Vanadium is an essential ultra trace mineral[1, 33]; it is a heavy metal, its toxic [17]. 2- Vanadium has pentavalent anion, as phosphate anion[33]. 3- Vanadium affects on ATPase, alkaline phosphate and act as activator of 5-aminolevenlinic acid transaminase and cardiac adenylate cyclase, and monoamine oxidase[1]. 4- Vanadium has lead symptoms including growth retardation, determination healthy bones, teeth, and infertility[33]. 5- Vanadium toxicity has resulted in skeletal abnormality, it's toxic effects from its ability to interfere with biological function of amino acids, peptides, nucleotides, ATP and carbohydrates[20, 34]. 6- Erythrocytes vanadium appears to be more sensitive index to detect deficiency[15]. 7- It's highly redox active transition metal as oxidative, it's elevated in diabetes is known to contribute the secondary complication of diabetes[17]. 8- Vanadium is associated with greater insulin sensitivity and influencing the glucose/insulin system which is associated with aging[1].	*Concentration of vanadium in serum is 0.014-0.23 µg/l (0.27-4.5 nmol/l). *Another ref. detected the limit of vanadium is 0.03µg/lof serum[19]. * Another refs. Serum vanadium is 0.018-0.076µg/l[35,40], at normal range correlated with cytosolic blood presser and inversely correlated with red blood cell

	9- Vanadium , recently , it has been shown that sodium vanadate, an inhibitor of (Na^+/K^+)- activated adenosine triphosphate , has pointed natriuretic effecting in the rate , because vanadium is naturally occurring trace element and is exerted by kidney[34] . 10- Its highly toxic element to human and animals, accumulated in the tissue[37]. 11- The raised CK levels are consistent finding with vanadium exposure and may be related to its role in catalyzing the transfer of high energy phosphate bond from adenosine triphosphate to creatine in resting muscle and reversed when contracts muscle. Vanadium is known to interfere with energy transduction mechanisms, which suggest effective participation of vanadium in the energetic coupling and transport of ATPase carbohydrate41. 12- Vanadium helps the body to achieve healthy sugar levels; it may promote healthy glucose levels in people with a lack of sensitivity to insulin by increasing the sensitivity because vanadium compounds have been termed "insulin mimetic " and promote healthy cellular replication in the body[33]. 13- Vanadium, required for glucose tolerance factor, the deficiency causes hypoglycemia, diabetes[37].	count and Hb [36, 37, 38]. Normal concentration from other laboratory is 1 ng/mL[39] Biomarkers[46] Hb/gl^{-1} 80-140. Lymph/10^9 l^{-1}2.5-7.7. Mono/10^9l^{-1}0.03-0.84. Serum of workers exposure to vanadium dust the V, conc. 225-± 83nmol/l [36] Serum vanadium level in chronic hemodialysis patients before hemolysis is 18.4 - +/-7.6 ng/ml.[40] Certificate concentration 0.068± 0.017SD, µg/l [42].
Ge	1-Germanium is an essential trace element, non-metallic element, [43] micro mineral[45]; Ultra traces elements[44]occurring in di/ tetra- valance states, refers to ionic germanium[43]. 2- Cancer patient are often low in Ge level[43]. 3- May be involved in carbohydrate metabolism[43]. 4-No deficiency disease has been described[43]. 5-Inorganic forms of germanium compounds are more toxic than organic [43] .The inorganic form has no nutritional value[45]. 6-Germanium causes specific toxic effect on kidney, muscles and nervous system[43]. 7-Fatel renal failure by Ge increased in urea nitrogen and serum creatine levels[46]. 8-Organic nutrient is known as (Ge-ox-132) used to treat cancer (anticancer) [45, 46] and their forms of degenerative disease produced during aging, by free radical damage. Anther way for this compound can to reduce or eliminate cancer cell, in the body is by creating the level of oxygen at the cellular level[46]. 9-Germanium has 32 electrons, 4 of which are in the outer shell. These 4 electrons are easily gained by other	* Ge is present in low conc. In food including beans, tomato juice , tuna and Garlic[43] * Ge conc. In serum after 5 month cessation of the Ge intake is 0.0578mg /l[44]. * It is found in all plant and animals tissues[43].

	molecule, such as a singlet oxygen molecule or oxidized protein[48]. 10- Germanium -132 may be protective against such toxic heavy metals as mercury and cadmium .since it can bind and discharge hydrogen ions , thereby increase the level of oxygen ,Ge -132 raises the level of reduced glutathione ,(free radical scavenger)[48].	

Aim of study

1-To predict the true levels of trace elements (Vanadium, Cobalt, Molybdenum, Nickel and Germanium) for age groups (the medium for 10 years of each group are 25, 35, 45, and55ages), in the patients and healthy peoples.

2-To show the importantance of the above trace elements as biochemical markers (tumor markers) in lymphoma cancer disease.

Experimental

Patients and Methods:

This study was included a random samples of patients with lymphoma cancer whose admitted to MerjianTeaching Hospital in Babylon governorate/ Hilla city .(for the period 2002, patients were enrolled their cancer diagnosis into different estimations of clinical biochemistry analysis and others clinical identification .) , they account are sixty. Sixty patients (35 males with mean age 34.666 ±10.145 and 25 females with mean age 31.11.792±1) , compared with levels of trace elements in the sera of 70 healthy as a control (40 males with mean age 40.051 ±19.294 , and 30 female with mean age 42.125±18.725) .

Instrumentation

Sera were digested with nitric acid , injected into auto sample cup of Shimadzu AA-670/G U-7 flam atomic absorption spectrophotometer and flame less Graphite furnace with deuterium lump are background correction system were used in successfully to reduce the background to an acceptable levels .

Statistical analysis & mathematic treatments

The results were expressed by the following statistical analysis:

meain ± SE of trace elements (Co, V, Mo, Ni and Ge), range (min. and max.) , students (t) test, and P values as in table 1.

Mathematical treatments

1- Using trace elements values with Grapher 5 program (prepared by golden software company) the results 4 curves are two for healthy and other for patients.

2- Using second order equation for treatment the values of trace elements for healthy and patients, solutes (modulating) the results into new values as in tables 2.

Results

Table1: concentration of trace elements in serum of patients (with non Hodgkin lymphoma) and healthy people in addition to the statistical results.

elements	Mean µmol/L	±SE µmol/L	Study values Lower-upper µmol/L	P value	significant
Males(M) 40controls 35patients Females(F) 30controls(con.) 25patients(pat.)	41.05128 years 34.66667 42.125 years 31.32	17:07.6 years 1.91724 3.8223 years 2.31268	4- 60 years 13- 70 years	0.085735 0.021046	
Co M,con. M,pat. F, con. F, pat.	 0.011667 0.021083 0.0112 0.0316	 0.000547 0.00183 0.000517 0.002657	 0.007- .018 0.007-0.019	 0.000276 0.001306	 Sign. Sign.
Ni M, con M, pat. F ,con F, pat.	 0.014462 0.022125 0.013147 0.010125	 0.001053 0.01037 0.000776 0.000295	 0.008- 0.025 0.008- 0.022	 0.509915 0.000786 7	 Nonsign.* Nonsign.*
Mo M, con. M, pat F,con F, pat.	 0.009619 0.010909 0.0098 0.0119	 0.00034 0.000513 0.00037 0	 0.008- 0.013 0.007- 0.017	 0.050932 0.242709	 Nonsign.* Nonsign.
V M, con. M, pat. F, con. F, pat.	 0.010185 0.009 0.011033 0.0105	 0.0004 0.0004631 0.000388 0.0005	 0.008- 0.013 0.005- 0.013	 0.070382 0.471425	 Sign*. Sign.*
Ge M, con. M,pat. F, con. F, pat.	 0.032432 0.043833 0.035222 0.058	 0.0023 0.00764 0.001423 0.00737	 0.016- 0.072 0.016- 0.052	 0.172456 0.014875	 Nonsign. Sign.*

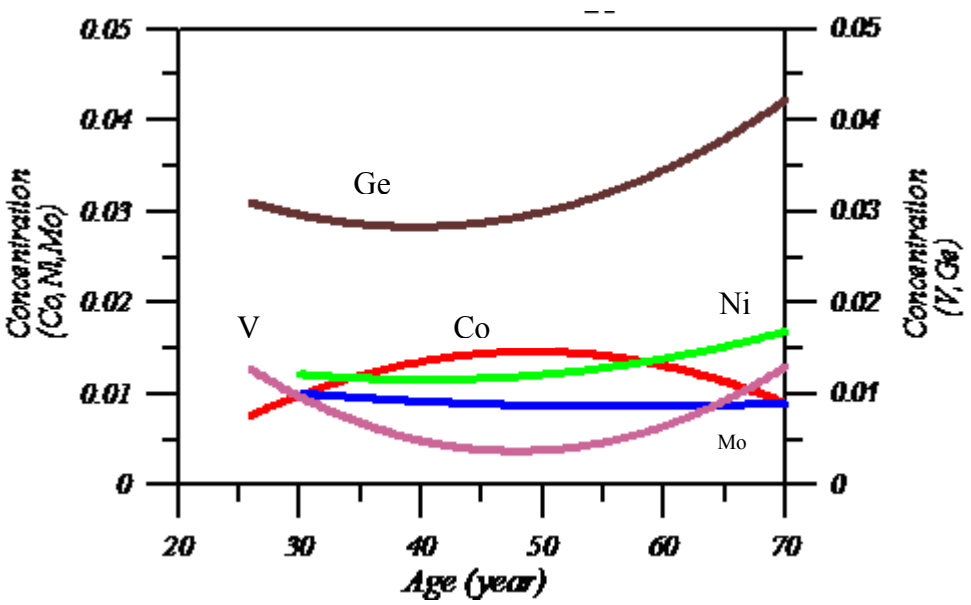

Fig. 1, the relationship between concentration of trace elements and mean age for healthy female (as control) of different ages.

By the application of second order equation , the values of trace elements (as age group each group represents a range of 10 years , from the curve 1 of healthy female for each trace elements, Co, Ni, Mo, V, and Ge , these results represented the new approach concentration of these trace elements .

The general second order equation is:

$Y = a + b\,x + c\,x^2$

When ,a , b , c , are constants for each equation , for each values of trace elements , are resulted after solution the second order equation when substituted x , with the values of trace elements levels of mean age groups for each 10 years , from fig. 1 , Y, represented the new value of trace elements.

The following equation for healthy female.

Y Ge = -0.02897910375 + 0.005740685236 * Age - 8.081276644E-005 *(power) Age^2

YV= -0.006374923794 + 0.0007336923389 * Age

YMo = -0.007256144176 + 0.001112545001 * Age - (1.316950193E-005 * power)Age^2

Y Ni = 0.002067025713 + 0.0004908902339 * Age - 6.025453172E-006 *(power) Age^2

Y Co = 0.3591953255 - 0.02847704508 * Age + 0.0006118530885 *(power) Age^2

Table2: Represented the new values of trace elements (Co, Ni , Mo, V, and Ge) in the healthy females after solution the second order equation with mean age group from fig. 1 .

Ge	V	Mo	Ni	Co	Age of-mean group ,for helthy femeal
0.06403	0.011967	0.012327	0.010573	0.029677	25
0.072949	0.019304	0.01555	0.011867	0.112019	35
0.065706	0.026641	0.01614	0.011956	0.316731	45
0.0423	0.033978	0.014096	0.010839		55

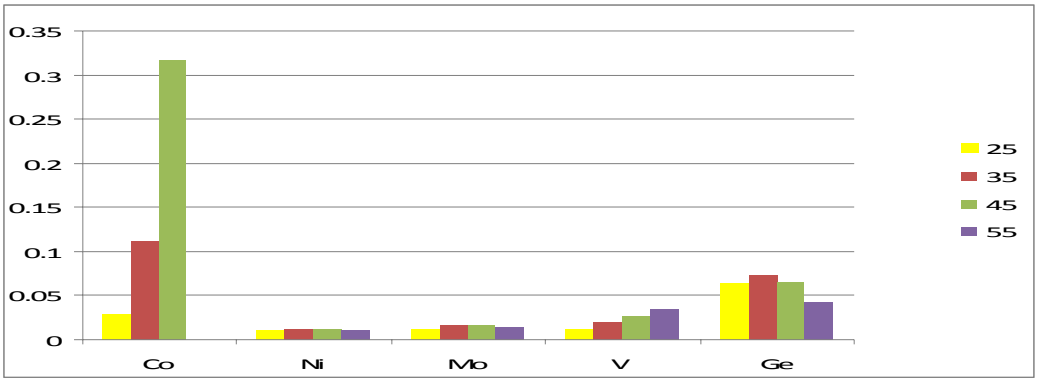

Figure: 2, Represent relationship between concentration and mean ages for each element separately of healthy females which are gated from table2(the concentrations of elements which are obtained from solution of second order equation) .

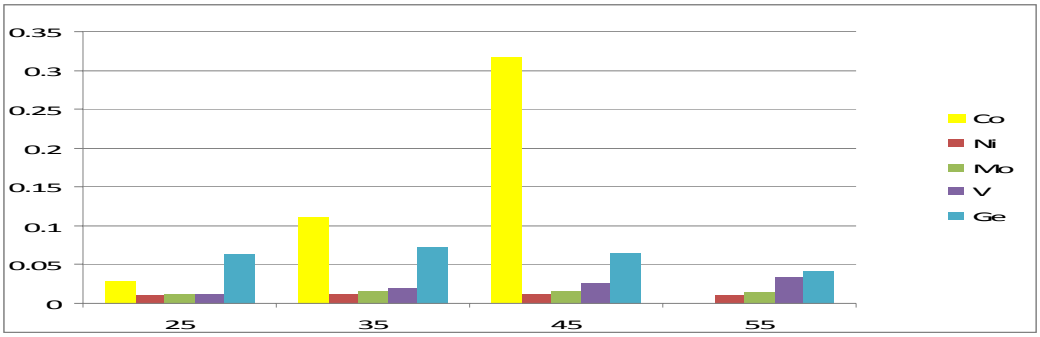

Figure 3: The relationship between the concentration of trace elements obtanied from table2(concentration from solution of second order equation) with age groups.

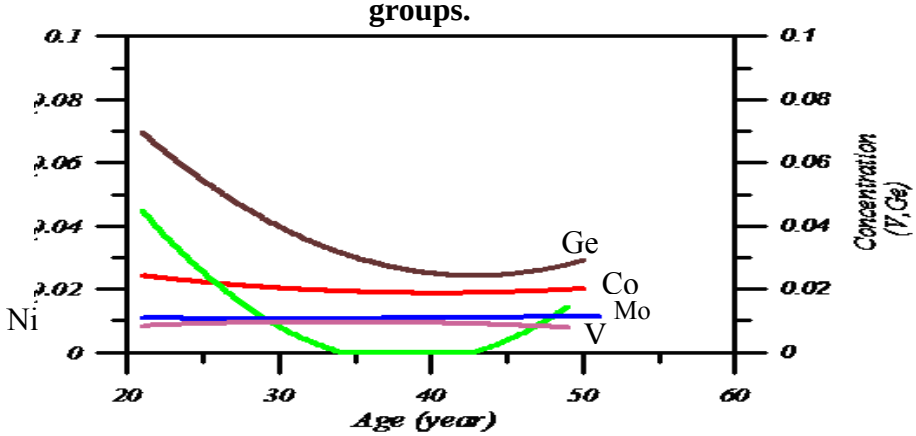

Fig 4, the relationship between concentrations of trace elements with mean age for healthy females (as control)

Table 3: The new values of trace elements (Co, Ni , Mo, V, and Ge) in the healthy males after solution the second order equation with mean age group obtained from fig.4

Ge	V	Mo	Ni	Co	Age-of mean groups helthyy men
0.054463	0.009073	0.010721	0.02541	0.02221	25
0.03006	0.009629	0.010716	0.001047	0.019169	35
0.024696	0.008665	0.011097	0.003841	0.019067	45
0.038371	0.00618	0.011865	0.040075	0.021905	55

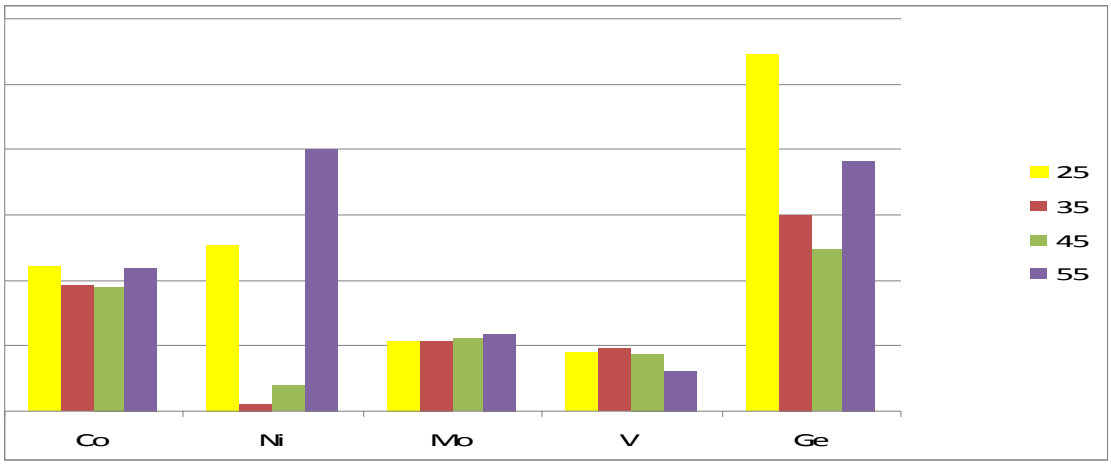

Figure5: The relationship between concentration and mean ages for each element separately of healthy males which are obtained from table3 (the concentrations of elements which are obtained from solution of second order equation).

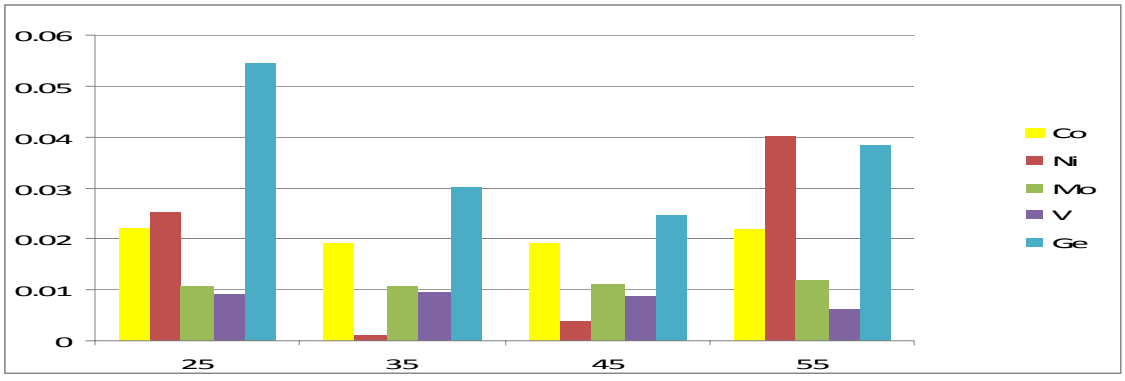

Figure 6: The relationship between the concentration of trace elements obtanied from table3(concentration which are gated obtained from solution of second order equation) with age groups for healthy meals.

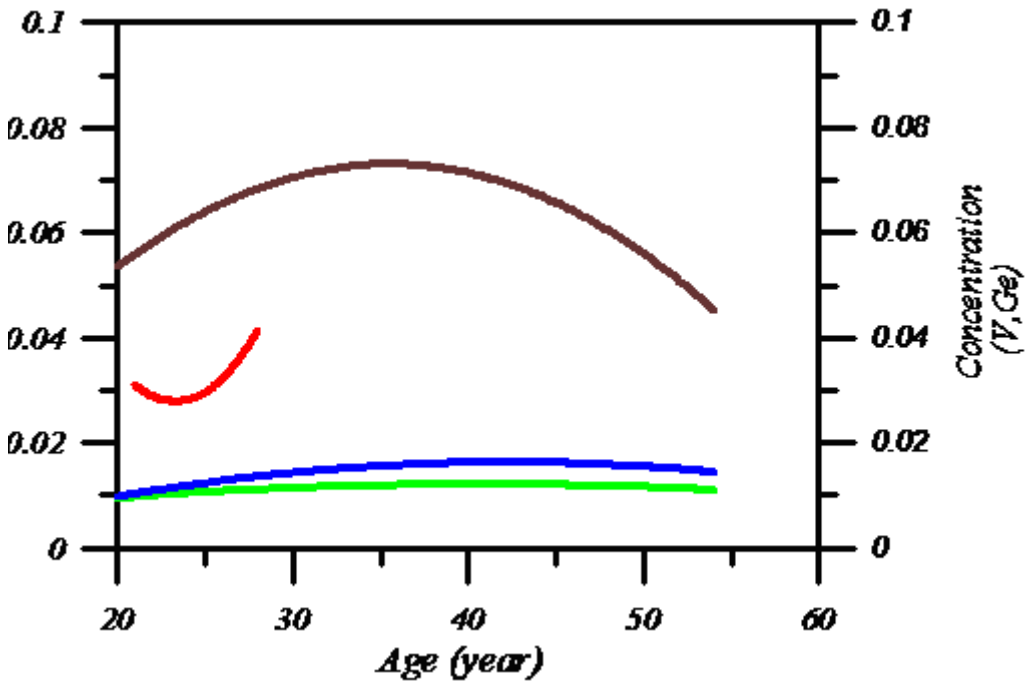

Fig.7, the relationship concentration of trace elements with mean age for females' patients with cancer.

By applied the equation of second order , the values of trace elements (as mean age group each group represented by 10 years) , from the fig.7 of patient female with cancer represented the new values of these trace elements .

The general second equation is:

$Y = a + b\,x + c\,x^2$

Y Ge = 0.05150802992 - 0.001177583271 * x + 1.491547689E-005 * power(x) ^{2}

YV = 0.04721362216 - 0.001818667133 * x2 + 1.899932246E-005 * power(x) ^{2}

Y Mo= 0.01525768555 - 0.0002365609777 * x2 + 2.088042815E-006 * power(x) ^{2}

Y Ni = 0.02118748899 - 0.0004824354258 * x2 + 6.006275303E-006 * power(x) ^{2}

Y Co = -0.01662313857 + 0.001270671382 * x2 - 1.293025617E-005 * power(x) ^{2}

Table 4: The new values of trace elements (Co, Ni, Mo, V, and Ge) of patient female with cancer after solution the second order equation with mean obtained group from fig.7.

Ge	V	Mo	Ni	Co	Age of patient female
0.031391	0.013622	0.010649	0.012881	0.007062	25
0.028564	0.006834	0.009536	0.01166	0.012011	35
0.028721	0.003847	0.008841	0.011641	0.014373	45
0.03186	0.00466	0.008563	0.012823	0.01415	55

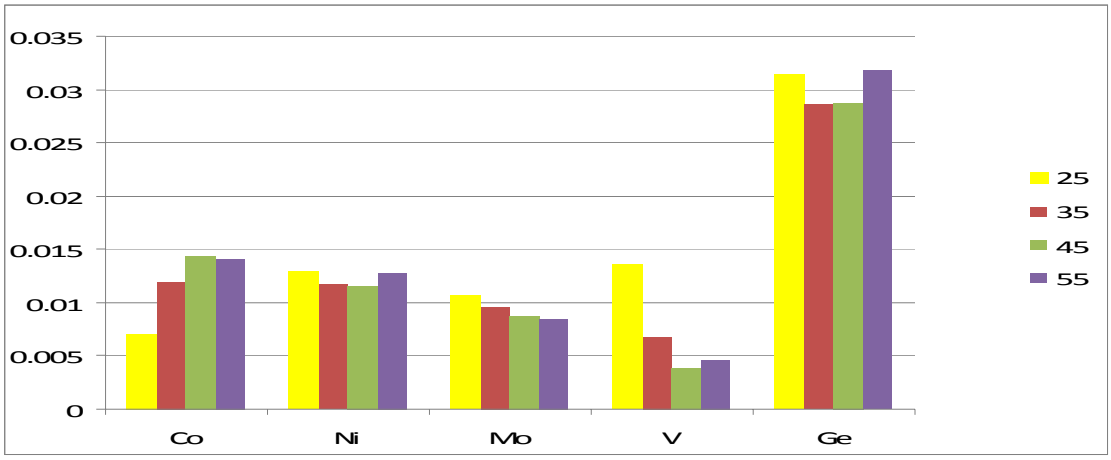

Fig. :5, the relationship between concentration and mean ages for each element separately of patient females with cancer which are obtained from table4(the concentrations of elements which are obtained from solution of second order equation) .

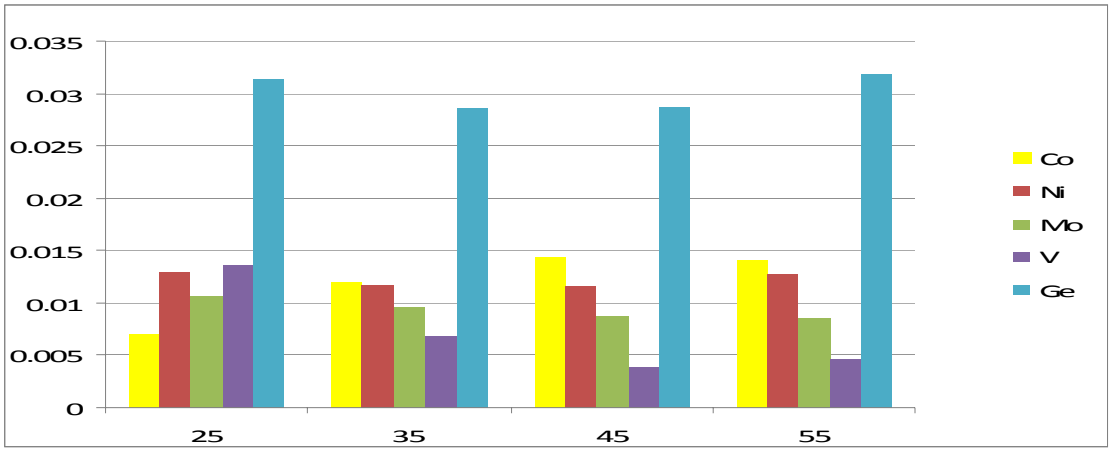

Fig. 9: The relationship between the concentration of trace elements of patient female with cancer resulted from table4 (concentration from solution second order equation).

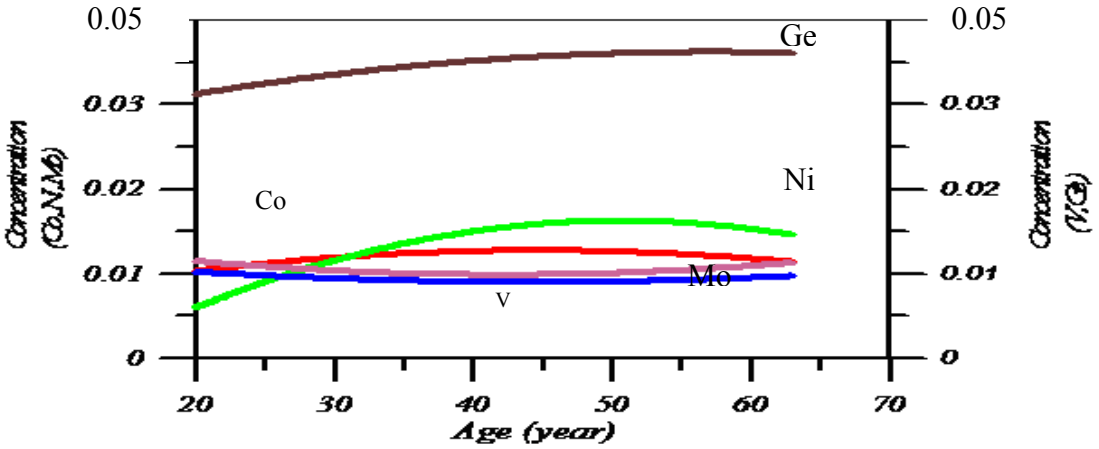

Fig.10, the relationship between concentration of trace elements with mean age for males patients with cancer .

By applied the equation of second order , the values of trace elements (as mean age group each group represented by averge10 years , from the fig 10 of patient male with cancer represented the new values of these trace elements .

The general second equation is :

$Y = a + b x + c x^2$

Y Ge = 0.02438775466 + 0.0004115336231 * x - 3.599766617E-006 * power(x) ^{2}

YV = 0.01583554312 - 0.0002831677383 * x + 3.352013743E-006 * power(x) ^{2}

Y Mo = 0.01302545017 - 0.0001813161367 * x + 2.0444676E-006 * power(x) ^{2}

Y Ni = -0.01171112536 + 0.001102278515 * x - 1.086943769E-005 * power(x) ^{2}

Y Co = 0.004758246776 + 0.0003567579994 * x - 3.990662685E-006 * power(x) ^{2}

Table 5: The new values of trace elements (Co, Ni , Mo, V, and Ge) of males patients with cancer after solution the second order equation from fig.10.

Ge	V	Mo	Ni	Co	Age-of male patients
0.032426	0.010851	0.00977	0.009052	0.011183	25
0.034382	0.010031	0.009184	0.013554	0.012356	35
0.035617	0.009881	0.009006	0.015881	0.012731	45
0.036133	0.010401	0.009238	0.016034	0.012308	55

Fig. 11, the relationship between concentration and mean ages for each element separately of patient males with cancer which are obtained from table5 (the concentrations of elements which are resulted from solution of second order equation).

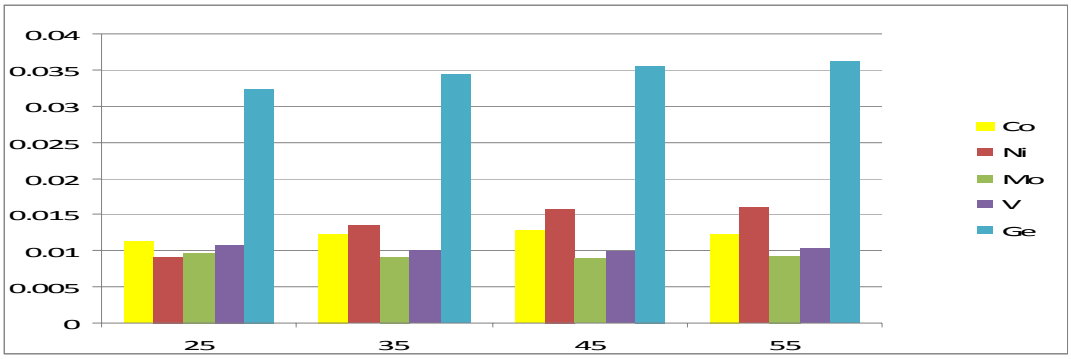

Fig. 12: the relationship between the concentration of trace elements resulted of patient male from table5 (concentration from solution of second order equation).

Table 6: The values of serum trace elements (Co, Ni , Mo , V and Ge) which were collected from tables 1,2,3,4,and 5 , in addition to the references values of these serum trace elements .

Trace elements	Healthy(control) (con.) In µgl/l	Patients of lymphoma cancer (pat.) In µgl/l	Values of trace elements levels after treatments by 2nd order equation, four groups of mean age years, In µgl/l						Levels of trace elements from references
				25 years	35 years	45 years	55 years	40 mean age years	
C Male M Female F	 0.011667 0.0112	 0.021083 0.0316	 M,con Pat. F,con pat	 0.02221 0.011183 0.029677 0.007062	 0.019169 0.012011 0.112019 0.012011	 0.019067 0.012731 0.316731 0.014373	 0.021905 0.012308 0.01415	 0.0205877 0.0120582 0.152809 0.0154365	Serum level, is 0.03 µg/l[29]
Ni M F	0.014462 0.013147	0.022125 0.010125	M,con Pat. F,con pat	0.02541 0.009052 0.010573 0.012881	0.001047 0.013554 0.011867 0.01166	0.003841 0.015881 0.011956 0.011641	0.040075 0.016034 0.010839 0.012823	0.0175932 0.0136302 0.0113087 0.011899	serum 0.3 µg/l [5,10] .
Mo M F	0.009619 0.0098	0.010909 0.0119	M,con Pat F,con pat	0.010721 0.00977 0.012327 0.010649	0.010716 0.009184 0.01555 0.009536	0.011097 0.009006 0.01614 0.008841	0.011865 0.009238 0.014096 0.008563	0.0110997 0.0092995 0.145282 0.0092762	Detection limit in serum is 0.06 µg/l[17].
V M F	0.010185 0.011033	0.009 0.0105	M,con Pat F,con pat	0.009073 0.010851 0.011967 0.013622	0.009629 0.010031 0.019304 0.006834	0.008665 0.009881 0.026641 0.003847	0.00618 0.010401 0.033978 0.00466	0.033547 0.0128912 0.0229725 0.0072407	detected limit of serum vanadium is 0.03µg/l[19]
Ge M.. F.	0.032432 µgl/l 0.035222 µg/l	0.043833 0.058	M,con Pat . F,con Pat.	0.054463 0.032426 0.06403 0.031391	0.03006 0.034382 0.072949 0.028564	0.024696 0.035617 0.065706 0.028721	0.038371 0.036133 0.0423 0.03186	0.0368907 0.0346395 0.0612455 0.0346395	serum after 5 month cessation of the Ge intake is 0.0578mg /l[44]

Discussion

The new evolution of some trace elements (Co,Ni,Mo,V,&Ge) the determination of its levels in serum of healthy and lymphoma cancer in meals and females, were determined by flameless atomic absorption , the values of these levels were listed in table 1 as mean with (± SE) , with P values (by using regression analysis program). These mean levels of patient trace elements were compared with these of control, resulted in significant and nearly significant for all investigated trace elements.

But P values of Ni males, females of Mo , males and females of V ,and male of Ge were more than 0.05 as in table 1 .which showed in at these levels were faraway of the real values in serum ,where are lead to divided the range of age of patients and control (males and females) in to 4 groups of age for each 10 years interval of range age years (25,35,45,and55) ,as in tables 2,3,4, and5 .

From table 6 (which was represented sum of whole from tables 1, 2, 3, 4, and5 in addition to values of trace elements in serum from references), for comparison the resulted indicates that values from treatments of levels are reflected the true values of levels of these trace elements in serum, and this treatment can used to predicate the levels of serum materials in another like studies.

Results of table 6 : shows the levels of trace elements Co, Ni , Mo, V, and Ge , in the serum of patients of lymphoma cancer detected by flameless atomic absorption spectrophotometry are , 0.021083 , 0.022125 , 0.010909 , 0.009 , 0.043833 , for males , and 0.0316 , 0.010125 , 0.0119 , 0.0105 , 0.058 , for females are higher than the levels of controls serum of males , 0.011667 , 0.014462 , 0.009619 , 0.010185 , 0.032432 , and females , 0.01120 , 013147 , 0.00980 , 011033 , 0.035222 , (data from statistic analysis) , but after solution the serum levels from spectroscopic of these trace elements [by grapher 5 and arranged according to groups of ages 25,35,45, and 55years , and from these years takes the mean values of these levels(which are return to the level of trace elements of 40 years , of mean ages) for patients and controls for male and females] by 2nd order equation (after treatments with grapher 5 program) the new level resulted for these elements are , 0.0120582 , 0.0136302 , 0.0092995 , 0.0128912 , 0.0346395 , for patients male respectively , and , 0.0205877 , 0.0175932 , 0.0110997 , 0.033547 , 0.0368907 , for controls males, according to the sequence of trace elements in table(6) 0.0154365 , 0.011899 , 0.0072407 , 0.030134 , for patients females , are less than the levels of new values of controls , as follows respectively , 0.152809 , 0.0113087 , 0.145282 , 0.0229725 , 0.0612455 µg/l . After compared this new results (results from 2nd order equation) with statistic data , experience the opposite results which are became the values of the levels of serum patients lower than controls , this new results are suitable to the logic , that is reflected the effected of lymphoma cancer by decreased the concentration of these trace elements , in addition to agreements the new results (in the effects of cancer on the decreasing the concentration of these elements) with that published for Co, Ni , Mo , V , and Ge , are 0.03 , 0.3 , 0.06 , 0.03 µg/l , and 0.057 mg/l respectively .[5,10,17,19,29.44]

Cobalt: the result of this study indicated that the levels of cobalt in serum of patients with lymphoma cancer for males and females were ,0.0120582 ,and 0.0154365

,respectively , which are lower than these in serum of controls , 0.0205877 , and 0.152809 , respectively . When compare, these results with these published (0.03 µg/l) [29] , it appears that the depletion depletion of Co in serum of patients is related to vitamin B_{12} as important requirements, it's obtained by meat [25]. We satisfied these results related to levels of salary wages pay to Babylon Iraqi people, after compared these levels of healthy published with healthy controls in this study.

Nickel: In this study the levels of Ni in serum of patients with lymphoma cancer for male and females were , 0.0136302 and 0.011899 respectively , which are lower than levels serum of male/ females of controls , 0.0175932 and 0.0113087 respectively . compared this results of nickel levels both of patients and controls with published values (0.3 µg/l) [5,10] ,it shows high decline in levels of Ni in healthy and patients of this study .In another studies, that shows nickel-exposed worker or confounding factor such as cigarette smoking causes lung cancer because it's damaging the chromosomes , and on molecular basis nickel induce DNA damage (DNA strand breaks and crosslink's infidelity of DNA replication , inhibition DNA repair , and the helical of B-DNA to Z-DNA) by binding nickel to the nuclear protein [14] . These events were reflected the effects of nickel in two states of concentrations , in the statement of exposure to high and the statement of lower serum concentration , tented to causes cancer disease .

Molybdenum: The Mo serum levels of patients are 0.0092995 for male and 0.0092762 for female which are lower than that of control. Male 0.0110997, and0.145282 for males, and 0.145282 for females were lower than the published values of serum molybdenum 0.06 µg/l[17] .It seems there are indications of a relationship between Mo deficiency and is a development of various tumors .[50] sodium molybdenate administrated in drinking water has a protective action against the induction of cancer in rats by organic N – nitroso compounds[22].And another published data pointed out that Mo prevent the carcinogenesis of N –nitroso compound [51] .

Vanadium: The concentration of V in serum of male and female with lymphoma patients are 0.0128912 , 0.0072407 respectively .(these are higher than controls levels of vanadium in serum of this study 0.009073 for males and 0.011967 for females. Related to types of drugs which are taken up by patients may be raised the levels of vanadium in the serum. the low V levels of serum control than it's levels in patients related with malnutrition's people in Babylon / Iraq, when on comparing these results with published data (detected limit of serum vanadium is 0.03µg/l[19] it seems lower of vanadium patient level than the general published values .While we confirm our conclutio through the following A) Vanadium compound used in treatment of diabetic patients , but in optimal maximum dose is become highly toxic elements to man and animals [37] .B) vanadium having an effect on carbohydrate metabolism [2] . C) liquid ionic vanadium mineral raise a new novel drugs effected in fighting cancer cells including breast cancer ,prostate cancer , testicular cancer , ovarian cancer , colon cancer , brain tumors , leukemia and lymphoma[33] .

Germanium: The serum levels of Ge patients (males and females) 0.0346395 , 0.030134 respectively are lower than that of controls (0.0368907 , and 0.0612455) respectively . However in published data some one could sign that the level of germanium

in healthy could not be detected in sera , urine or tissues [46] mean while another study used chronic intake of Ge – lactate – citrate along with the simultaneous onset of multi – organ dysfunction and the exclusion of other systemic diseases led to conclusion that patients suffered from Ge intoxication ., The Ge level even 5 months where are after cessation of Ge intake , the concentration was still elevated to 0.058mg /l in serum [44] . inorganic form of Ge–compound are more toxic than organic compound [43]. Warburg obtained a Nobel Price for his research about organic germanium that can reduced cancer cells in the body is by creating oxygen – rich condition ,hence raising the level of oxygen at the cellular level , causing death for them . Organic germanium basically can supply oxygen into the cell by their transported across the cellular membranes . in another words , the cell can use this additional oxygen to compensate deficiencies in cellular oxygenation that result in patient with cancer (the oxygenation in the cell is oxidative, alternatively germanium act as antioxidant and as anti-cancer molecule [45] .

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