# Role of Some Trace Elements in Breast Cancer Receiving Chemotherapy

**Article** *in* International Journal of PharmTech Research · June 2016

CITATIONS
16

READS
417

**3 authors:**

Abdulsamie H. Alta'ee
University of Babylon
**68** PUBLICATIONS **187** CITATIONS
SEE PROFILE

Mufeed Ewadh
University of Babylon
**61** PUBLICATIONS **208** CITATIONS
SEE PROFILE

Zainab Kamil
University of Babylon
**4** PUBLICATIONS **20** CITATIONS
SEE PROFILE

International Journal of PharmTech Research
CODEN (USA): IJPRIF, ISSN: 0974-4304, ISSN(Online): 2455-9563
Vol.9, No.5, pp 381-386, 2016

# Role of Some Trace Elements in Breast Cancer Receiving Chemotherapy

**Abdulsamie H. Alta'ee[1]*, Mufeed J. Ewadh[1], Zainab H. Kamil[2]**

[1]College of Medicine, University of Babylon, Hilla, P.O. Box 473, IRAQ.
[2]College of Dentistry, University of Babylon, Hilla, P.O. Box 473, IRAQ.

**Abstract :** This study aim to examine changes in serum concentration of trace elements; cobalt (Co), germanium (Ge), molybdenum (Mo), nickel (Ni), vanadium (V), and magnesium (Mg) in breast cancer patients and control group, in addition to establish of databases in the Iraqi population. The study was included 40 patients with breast cancer and 50 healthy subjects. Serum concentrations of trace elements were measured by flame atomic absorption spectrophotometer. Statistical analysis of data demonstrated significant decrease ($p<0.001$) in Co, Ge and Mg concentrations in patients with breast cancer when compared with healthy. The study showed a significant increase ($p<0.001$) in Ni and V concentration in patients with breast cancer when compared with healthy. The results showed no change in concentration of Mo in breast cancer patients as compared to healthy. In conclusion, essential elements Mg and trace elements Co, Ge, Ni and V may play a central role in the pathogenesis of breast cancer.
**Key words:** Trace elements, Mg, Co, Ge, Ni, V breast cancer, , atomic absorption spectrophotometer.

## Introduction

The specialized cancer agency of the World Health Organization; the International Agency for Research on Cancer (IARC) released on 12 December 2013 the latest data on cancer statistics worldwide. The IARC's database, take about 14.1 million new cancer cases and 8.2 million cancer deaths in 2012[1].

Cancer is a significant and a major health problem all over the world. Iraqi reports found that at least 350 people in Babylon province/Iraq alone were affected by cancer every year[2]. Cancer is a cellular disease caused by mutation or abnormal activation of cellular genes responsible in control cell growth and mitosis[3], with different types that vary from one another[4].

Breast cancer is the most common cancer detected in women throughout the world[2]; and a second most common cancer in the world-wide with 1.7 million new cases per year which represent 11.9% of cancer cases[1].

Breast cancer is caused by genetic factors (about 5-10% of breast cancer are hereditary) or hormonal factors (prolonged estrogen exposure) and many other risk factors such as late first pregnancy, obesity in postmenopausal women (about 50%) and alcohol intake[5]. Other environmental carcinogens included radiation, organic chemical (tobacco smoke) pollutants like exposure to metals, dust, nickel, uranium and others[3, 4].

The immunity of the human body is the natural mechanism that protects against cancer. Trace elements represent vital processes in human health and disease in contributing in cellular and subcellular function, including immunoregulation by both humoral and cellular immunity[6]. In addition, trace elements considered

anticarcinogenic agents by its antioxidant potential dependent enzyme, induction metallothionien, DNA repair and alteration of carcinogen metabolism[7].

Cobalt (Co) is nutritionally essentially metal as a part of vitamin $B_{12}$ or cobalamin[8]. It is found in very low levels (less than 0.1mg/kg) in food, the highest in nuts and yeast extract. Since it is a fundamental part of cobalamin, a deficiency of these rare elements (0.001% of the lithosphere) probably causes pernicious anemia[9]. Co is necessary for the synthesis of thyroid hormone and beside iodine and other chemical elements found to influence thyroid goiters and then cancer[10]. Physiological concentration of Co acts as cardioprotective while high dosage of Co may cause cardiac failure[11]. Co could be carcinogen; the mechanism of gene mutation by Co is DNA breaks and inhibition of DNA repair[12].

Germanium (Ge) is ultra trace element found naturally in very low concentration in food, especially meats and described as an antioxidant and anticancer agent[13]. Its rich sources are wheat bran, vegetables and leguminous seeds. Ge occurs mainly in the human body in the bone (9µg/g), liver (0.3µg/g) and pancreas (0.2µg/g) and it has been considered non-essential trace element as its molecules of biological importance is none identified[14]. Ge has believed to drop blood pressure and excite immunity to inhibit rheumatoid arthritis[15]. Lück *et al*.[13] mentioned that intake of Ge compounds causes renal failure, liver dysfunction and anemia.

Molybdenum (Mo) is nutritionally essentially metal accumulated in the human body in liver, kidney, bones and skin[14]. Several enzymes contain Mo including xanthine oxidase and xanthine dehydrogenase; necessary for the uric acid formation, and involved in purine degradation[9]. All foods and beverages (even water) contain Mo[9,14]. Mo deficiency could be a reason for forming esophageal cancer[6,16], development of thyroid goiters and cancer and associated with sexual impotency and tooth decay[10]. Mo is considered as anti-cancer[16].

Nickel (Ni) is a trace metal with potential advantage effects[8] which has the ability to bind to many organic compounds of biological concern, including amino acids; especially histidine and cysteine, and protein mainly albumin[9,14]. Ni levels in food are low and can be seen in dried tea leaves, cacao beans and nuts[9]. Ni mainly found in the adrenal glands, bones, kidney and thyroid. It has a role as a cofactor in the metabolic pathway of vitamin $B_{12}$ and folic acid[14], and involved in the regulation of methionine-folate cycle[17]. Ni has been considered as important carcinogen[18]. Nickel deficiency status includes a change in skin color, hormone imbalance and abnormal bone growth [15], and low growth and reproductive action[19].

Vanadium (V) is a micronutrient element that has an important and distinctive role in human metabolism, found in cereals, meat, fish, vegetables and milk with daily intake about 10 µg-2mg[9]. High content of V in the body exists in bone, kidney, liver, spleen and testis, V have been believed to use iron transport system and bone is a storage part for excess vanadium[14]. It's important for bone, glucose and cholesterol metabolism and affect thyroid and the dentin of tooth, high dose intake of V could cause vitamin C diminution[15]. It has been mentioned that V can alter the activity of Na/K-ATPases involved in muscle contraction. Deficiency of V has been related to impaired reproduction and altered genesis of red blood cells and iron metabolism[9]. Also, Cesar[8] and Jaryum *et al.*[19] mentioned that V deficiency can cause skeletal deformities and increasing of thyroid weight.

Magnesium (Mg) is an essential major mineral found in the human body as a part of several enzymatic processes in intra- and extra- cellular components[20], about 300 enzymatic reactions involve Mg: it plays an important role in the stabilization of ATP and other molecules, glycolytic cycle, oxidation of fatty acids, protein synthesis[15,21,22] and also plays an important role in carbohydrate metabolism[23]. Mg is important in bone development and maintenance of bone, about 60% of Mg exists in bone[14,21], 38% in the skeletal muscle and liver, and less than 2% is in the extracellular fluid[24]. Mg provides elasticity to prevent injury and act with calcium to assist in muscle contraction, blood clotting and thought to regulate blood pressure[22]. Deficiency of Mg mentioned to be a contributor of tetany, calcium deficiency, and development of cardiovascular disease, diabetes mellitus and hypertension[14,15]. Mg deficiency is more widespread in cancer patients than others[24].

Current study aim to examine changes in serum concentration of trace elements in patients with breast cancer and control group, in addition to establish of data bases in the Iraqi population.

## Materials and Methods

### Materials

This study was approved by the Local Ethical Committee. All persons participated in the present study were agreed to participate and signed an informed consent.

The diagnosis of patients was done according to clinical identification of physician in an Oncology Unit at Merjan Teaching Hospital in Hilla city and clinical analysis.

A random blood samples of 40 patients with breast cancer admitted to the Oncology Unit at Merjan Teaching Hospital in Hilla city in Iraq were collected as well as 50 healthy subjects according to standard procedure and the sera obtained were stored at –20 °C until the day of analysis. Table 1 illustrates the participants number and their mean age.

**Table 1: Number and age of patients and healthy subjects.**

| Mean age (year) | No. | Subjects |
|---|---|---|
| 31.14 ± 9.4 | 50 | **Healthy** |
| 46.1± 5.6 | 40 | **Breast cancer** |

### Treatment Regime

Breast cancer patients treated according to Herdrich and Weinberger[25]. Patients with breast cancer were receiving chemotherapy regimen: doxorubicin 60 mg/m$^2$ or cyclophosphamide.

### Trace element analysis

Serum concentration of Mg, Co, Ge, Mo, Ni and V were measured by using Shimadzu AA-700 atomic absorption spectrophotometer after digestion the sera with concentrated nitric acid and concentrated perchloric acid, then analyzed by instrument according to the procedure described previously[8, 26].

### Statistical analysis:

All data were subjected to t-test: two sample assuming unequal variance to determine the level of significance between healthy and patients with breast cancer, and the value of $p \geq 0.05$ was considered statistically significant. Data are expressed as mean ± standard deviation (±SD).

## Results

### Concentration of trace elements

The results of concentration of trace elements (Co, Ge, Mo, Ni and V) in serum of patients with breast cancers as compared with healthy subjects are presented in Table 2.

**Table 2: Concentration of trace elements in sera of patients with breast cancer and healthy subjects.**

| V (µmol/L) ± SD | Ni (µmol/L) ± SD | Mo (µmol/L) ± SD | Ge (µmol/L) ± SD | Co (µmol/L) ± SD | Subjects |
|---|---|---|---|---|---|
| 0.0090 ± 0.0010 | 0.0106 ± 0.0014 | 0.0104 ± 0.0029 | 0.0512 ± 0.0198 | 0.03955 ± 0.0055 | **Healthy** |
| 0.0107 ± 0.0021 | 0.0125 ± 0.0022 | 0.0100 ± 0.0027 | 0.036 ± 0.0080 | 0.0115 ± 0.0014 | **Breast Cancer** |
| 0.0011 | 0.0009 | 0.061 | 0.0007 | 0.0001 | **p-value** |

**Concentration of Mg**

Table 3 revealed significant increase ($p<0.001$) in a concentration of Mg 12.69 ± 0.01 in patients with breast cancer and as compared with healthy subjects (18.77 ± 2.10 µmol/L).

**Table 3: Concentration of Mg in sera of patients with breast cancers as compared with healthy subjects and.**

| Mg (µmol/L) ± SD | Subjects |
|---|---|
| 18.03 ± 1.42 | **Healthy** |
| 12.69 ± 0.01 | **Breast Cancer** |
| 0.00084 | **p-value** |

## Discussion

The results of this study signify that serum Co concentration were decreased in patients with breast cancer whose receiving chemotherapy which agree with other research by Arooj *et al.*[27]. Deficiency of essential elements Co may cause vitamin $B_{12}$ deficiency since it is part of vitamin $B_{12}$ [9].

The data informed significant decrease in serum concentration of Ge in patients with the breast cancer whose receiving chemotherapy. Ge deficiency could be a risk factor of cancer since Ge represents a powerful antioxidant against cancer by means of its activity to slow down the multiplication process of cancer, hence inhibit tumor growth and enhance natural killer cells to act on[28].

Braverman and Pfeiffer[6] mentioned that deficiency of Mo in the human body could be a proper cause of another type of cancer like esophageal cancer. Mo deficiency seemed to be one of the risks and causative factor of gastric cancer[29]. Mo is thought to prevent body against cancer through augmentation the mechanisms of natural immunological diminution of cancer[6]. Molybdophosphate could be used as anticancer therapy[16].

According to the results of this study, serum concentration of Ni were significantly increased in breast cancer patients receiving chemotherapy. This is supported by previous studies[30] which were found increased serum Ni concentration in patients with bladder cancer. Ni level in saliva of oral cancer patients was high as a contrast with healthy people[7]. Ahmed *et al.*[18] mentioned increased Ni concentration in esophageal cancer patients may play some role in carcinogenesis in preventing the intracellular communication and induces DNA deletion. In addition to Ni, V was significantly increased in breast cancer patients receiving chemotherapy. V possibly exert an effect on oncogenesis since it is also interfering with proper chromosome arrangement during cell division[12].

Mg is essential major mineral in the human body as a part of 300 enzymatic processes[15,21,22]. The data of this study showed significant decrease in serum concentration of Mg in patients with breast cancer who's receiving chemotherapy which agree with another previous research in thyroid cancer patients[31]. Koyama[7] found significant reduction in the Mg level in saliva of oral cancer patients. In addition to cancer effect on Mg, anticancer drugs, especially cause hypomagnesemia in cancer patients[24]. Therapy with cytotoxic drugs may have impaired renal tubular reabsorption of Mg causing its loss in urine[32]. Mg deficiency may trigger carcinogenesis by increasing membrane permeability of cancer cells, high level supplemented Mg inhibits carcinogenesis[28].

## Conclusions

Trace elements are essential in the human body and play important roles in many enzymatic metabolism. In conclusion, the decrease in Ge levels which act as antioxidant, increases oxidative stress that in turn may lead to cancer. The decrease in the Mg level leads to increase membrane permeability of cancer cells that may trigger carcinogenesis. The decrease in Mo leads to decrease in immunity of the body which may lead to cancer, as well as compound of Mo act as anticancer. The decrease in Co levels leads to $B_{12}$ deficiency anemia that associate with cancer and one of cancer consequence. Whereas, the increase in Ni levels induces

DNA deletion which leads to cancer. Also, the increase in V levels increases oncogenesis due to interferes with proper chromosome arrangement during cell division that may lead to cancer. Figure 1 summarizes conclusions of the present study.

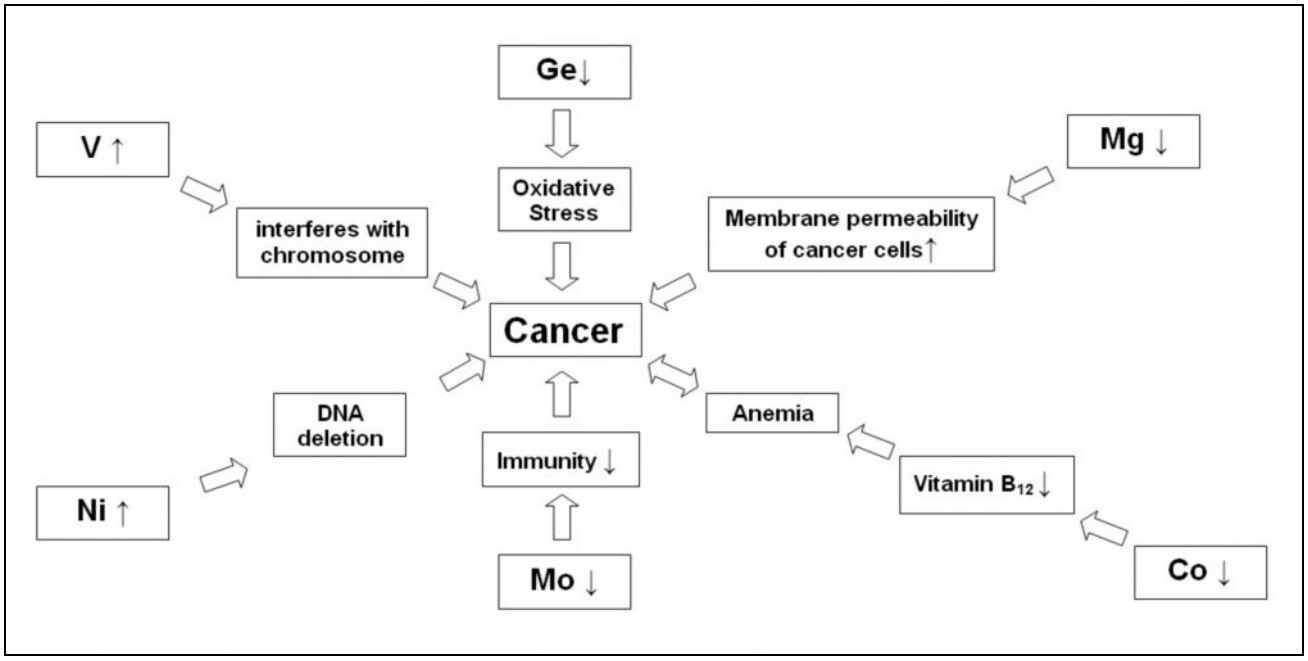


**Figure 1 summary of the role of some trace elements in the pathogenesis of cancer.**
↑ mean increase, ↓ mean decrease.

## Acknowledgements

The authors would like to thank the staff of Oncology Unit at Merjan Teaching Hospital in Hilla city in Iraq due to their facilities to accomplish the task of this study.

### Conflict of Interest

No conflict of interest exists in this study.

## References

1. WHO, The International Agency for Research on Cancer report, PRESS RELEASE N° 223, 2013.
2. Al-Timimi, A.H. and Al-Alawachi,S.F, Study of Malignant Diseases in Babylon Province the period 1990-1999, Univ. Babylon J-Medical Science. 2005; 1, 4, 658-666.
3. Hall, J.E., Guyton and Hall Textbook of Medical Physiology.12th Ed. Saunders of Elsevier Inc. USA, 2011.
4. Mader, S.S. and Windelspecht, M. Human Biology. 12th Ed. McGraw-Hill Companies, New York., 2012.
5. Key, T.J., Schatzkin, A., Willett, W.C.; Allen, N.E., Spencer, E.A. and Travis, R.C., Diet, nutrition and prevention of cancer, Public Health Nutr., 2004; 7, 187-200.
6. Braverman, E.R. and Pfeiffer, C.C., Essential Trace Elements and Cancer, Orthomolecular Psychiatry, 1982; 11, 28-41
7. Alta'ee A H, Hadwan M H, Almashhedy L A, The Balance between Superoxide Dismutase and Catalase Activities in Sera of Obese Iraqi Men, EuroMed Biomed J, 2015; 10: 197-202.
8. Cesar G. F., Relevance, essentiality and toxicity of trace elements in human health, Molecular Aspects of Medicine, 2005; 26: 235–244.
9. Reilly, C., The Nutritional Trace Metals. 1st Ed. Blackwell Publishing, Oxford, UK, 2004.

10. Zaichick, V.Y., Tsyb, A.F. and Vtyurin, B.M., Trace Elements and Thyroid Cancer, Analyst, 1995; 120: 817-821.
11. David A. M., de Lemos J. A., Marc S. S. and Elliott M. A., The Search for a Biomarker of Cardiac Ischemia, Clin. Chem., 2003; 49: 537-539.
12. Fukuda, H., Ebara, M., Yamada, H., Arimoto, M., Okabe, S., Obu, M., Yoshikawa, M., Sugiura, N. and Saisho H., Trace Elements and Cancer, JMAJ, 2004; 47: 391-395.
13. Lück B.E., Mann H. Dunemann L. and Begerow J., Renal and other organ failure caused by germanium intoxication, Nephrol Dial Transplant, 1999; 14,2464-2468.
14. Strain J.J. and Cashman K.D., Minerals and Trace Elements. In: Gibneg, M.J.; Lanham-New, S.A.; Cassidy, A. and Vorster, H.H. (Eds). Introduction to Human Nutrition. Wiley Blakwell. U.K, 2009.
15. Ali H.M. and Al-Zubaidi M.A., Evaluation of Trace Elements in Iraqi Patients with Rheumatoid Arthritis by using Atomic Absorption Spectrophotometer, Iraqi J Pharm Sci, 2012; 21: 77-84.
16. Ewadh M. J., Alta'ee A. H., AL-Mu'min A. S., Mkhlof S. and Renz H., The Behavior of the Plasma Homocysteine and Selenium Concentrations in Patients with Acute Myocardial Infarction, Med. J. of Babylon, 2008; 5: 542-550.
17. Katko M., Kiss I., Karpati I., Kadar A., Matyus J., Csongradi E., Posta J., Paragh G., Balla J., Kovacs B., Varga Z., Relationship between Serum Nickel and Homocysteine Concentration in Hemodialysis Patients, Biol Trace Elem Res, 2008; 124: 195-205.
18. Ahmed B., Ghani H., Azam S., Bashir S. and Begun N., The status of trace elements in lymphoma and esophageal cancer patients: A case study, Afr. J. Biotechnol., 2011; 10: 19645-19649.
19. Jaryum K.H., Dayok O., Daniang I.E. and Longdet I.Y., Trace Element Nutrition in the Developing World: A Review, J. Med. Appl. Bio. Sci., 2010; 2:12-18.
20. Dhandapani S.S., Gupta A., Vivekanandhan S., Mahapatra A.K. and Mehta V.S., Serum ionic magnesium in traumatic brain injury, India J Neurotrauma, 2005; 2: 103-106.
21. Gibney M.J., Lanham-New S.A, Cassidy A. and Vorster, H.H. Introduction to Human Nutrition. 2nd ed. A John Wiley & Sons Ltd., 2009.
22. Poglitsch M., Minerals Elements of Human Nutrition. Learningseed. Chicago, 2009.
23. Khan L.A., Alam A.M.S., Ali L., Goswami A., Hassan Z., Sattar S., Banik N.G. and Khan A.K.A., Serum and urinary magnesium in young diabetic subjects, Am J Clin Nutr, 1999; 69:70-73.
24. Saif, M.W., Management of Hypomagnesemia in Cancer Patients Receiving Chemotherapy, J Support Oncol., 2008; 6: 243-248.
25. Herdrich K. and Weinberger H. Selection Schedules in the Therapy of Malignant Tumors. Part II: Solid Tumor. 7th Ed. Baxter International Inc., 2003.
26. Selvaraju R., Ganapathi R. R., Narayanaswamy R., Valliappan R., Baskaran R., Trace Element Analysis in Hepatitis B Affected Human Blood Serum by Inductively Coupled Plasma atomic Emission Spectroscopy (Icp-Aes),Romanian J. Biophys., 2009;19: 35-42.
27. Arooj B., Ahmed S., Saleem M., Khurshid R. and Zia M., Serum Trace Elements in Diagnosis of Breast Malignancy, J Ayub Med Coll Abbottabad., 2012; 24: 62-64.
28. Singh M., Kumar D., Singh G., Sharma D., and Swami G., Natural Minerals and Cancer. Journal of Applied Pharmaceutical Science, J App Pharmaceutical Sci, 2012; 2: 158-165.
29. Guang-Hui C.A.O., Shi-Ming Y.A.N., Zhao-Kang Y.U.A.N., Lei W.U. and Yan-Fang L.I.U., A study of the relationship between trace element Mo and gastric cancer, World J Gastroenterol, 1998; 4: 55-56.
30. Gecit I., Kavak S., Demir H., Güneş M., Pirinççi N, Çiğdem Ç., Ceylan K., Benli E. and Yildiz I., Serum Trace Element Levels in Patients with Bladder Cancer, Asian Pac J Cancer Prev, 2011; 12: 3409-3413.
31. Al-Sayer H., Mathew T.C., Asfar S. Khourshed M., Al-Bader A., Behbehani A. and Dashti, H., Serum changes in trace elements during thyroid cancer, Mol Cell Biol, 2004; 260: 1-5.
32. Merza W. M., Majid A.Y., Daoud M.S. and Jawad A.M., Serum Magnesium Concentration in Patients with Leukemia and Lymphoma, J Fac Med Baghdad, 2008: 51:101-104.

*****