INAA of Trace Elements in Colorectal Cancer Patients

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ABSTRACT

The concentration of trace elements in samples of both colorectal cancer tumors and normal tissues of a Mexican population were irradiated for 30 s and 4 h and their elemental content were measured by instrumental neutron activation analysis. Ca, Cu, Co, I, Mg, Se, Fe, Zn, Hg, Ba, and Cr were analyzed. Alterations in Co, Fe, I, and Ba were found in tumors with respect to normal tissues.

Index Entries: INAA; trace elements; colorectal cancer.

INTRODUCTION

An important increase in the incidence of colorectal cancer has been detected in the industrial countries. Cancer is the second cause of morbidity in Mexican population (1) and a growing incidence of colorectal cancer has been observed in this population. This fact could be attributed to several causes, namely the diet habits acquired from industrialized countries.

There is a lot of important information involved in molecular studies of different biochemical pathways and different genes in colorectal cancer (2,3). It is known that trace elements and metals are important in the biochemistry of different diseases (4,5) because these elements could be important in the biological mechanisms in normal and cancer tissues. One of the trace elements studied has been selenium (6), whose diminution has been associated with the risk of acquiring cancer. However, this field has not been extensively studied. The aim of this work was to determine the amount of trace elements and some metals in samples of

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colorectal tumors and normal tissues from Mexican patients. The elements were studied by instrumental neutron activation analysis (INNA) (7,8), which consists in irradiating the sample tissues with neutrons and once the activation is produced, the gamma radiation (9) emitted is characteristic of each of the elements in the sample.

MATERIALS AND METHODS

Colectomy specimens from patients aged 30–86 yr with colorectal carcinoma were placed on ice immediately after surgical removal and rinsed with ice-cold phosphate-buffered saline (PBS). Small portions of all carcinomas were snap-frozen and stored in liquid nitrogen until the study was performed. All the specimens were obtained from the Hospital de Oncologia, C. M. N., S. XXI, I. M. S. S. (Mexico City). Patients were surgically treated between 1992 and 1996. Seven samples were from normal tissues and 12 from tumors corresponded to sporadic colorectal adenocarcinomas. After being washed three times with tridistilled water, the samples were dried at 70°C in an oven for 24 h. Then, 50 mg of each sample were put in a high-density polyethylene container.

The samples were irradiated in a TRIGA MARK III Nuclear Reactor with a thermal neutron flux of 9×10^{12} n/cm²/s. In order to detect short half-life time elements, a pneumatic SINCA system was utilized. The samples were irradiated for 30 s and counted for 90 s. The same samples were irradiated for 4 h in the SIFCA position with a neutron flux of 2×10^{12} n/cm²/s and counted for 1 h. A HPGe (EG&G ORTEC coaxial P type) detector was used, connected to the conventional nuclear electronic modules to an ORTEC card as a MCA plus a Maestro II software to analyze the spectra.

RESULTS

The results of the analysis carried out with colorectal tumors and normal tissues show differences in the amounts of Co, Ba, I, and Fe; in contrast, variations in the amounts of Hg, Cr, Cu, Se, Zn, Mg, and Ca were not measured. Table 1 shows the elements of short half-life time and Table 2 shows the elements of long half-life times. Between these two groups, there must be a series of half-life times that escape our measurements. Table 3 shows the average for each element in tumor tissues as well as in normal tissues. The overall differences are shown in Figs. 1–4.

DISCUSSION

The results of this study have shown differences in the amount of Co, Ba, I, and Fe in the tumor tissues compared with normal tissues;

Tumor Sample	µg∕g Zn	μ <i>g/g</i> Fe	μ <i>g/g</i> Co	μ <i>g/g</i> Ba-	μg/g Cr	μ <i>g/g</i> Hg
1*	1.12±7.8%	157.07±2.5%	0.01±13.2%	0.11±18.3%	0.46±12.1%	0.01±26.2%
2	7.15±8.2%	124.00±3.1%	0.03±14.2%	0.27±15.7%	0.70±11.5%	0.04±21.3%
3	16.26±6.9%	76.54±4.3%	0.05±15.4%	0.24±18.2%	0.68±11.8%	0.07±20.6%
4	1.90±9.4%	50.15±5.1%	0.04±15.4%	0.07±18.9%	0.69±11.4%	0.01±26.8%
5	8.72±5.4%	57.16±5.3%	0.04±16.8%	0.08±17.9%	0.37±14.1%	0.03±28.4%
6*	4.48±6.8%	62.23±4.8%	0.02±14.8%	0.09±14.5%	0.17±20.1%	0.02±24.8%
7*	13.22±7.6%	212.61±2.0%	0.01±15.9%	0.12±15.3%	1.10±10.4%	0.02±27.6%
8	6.6 4±8 .6%	125.01±2.6%	0.01±15.9%	0.18±15.5%	0.59±15.4%	0.04±24.8%
9	3.00±6.9%	236.19±3.1%	0.02±15.7%	0.12±14.3%	1.36±10.8%	0.03±26.4%
10	10.20±8.7%	181.53±3.5%	0.02±14.8%	0.31±15.6%	0.62±12.4%	0.02±27.6%
11 [*]	4.09±9.1%	77.62±5.1%	0.01±15.6%	0.08±183%	0.28±14.8%	0.01±28.4%
12	4.76±10.2%	38.03±6.4%	0.01±16.2%	0.17±16.5%	0.59±16.4%	0.01±24.5%
13 [*]	10.86±5.8%	236.88±3.1%	0.02±14.9%	0.13±11.5%	0.61±16.4%	0.02±26.8%
15	4.88±7.5%	116.72±2.1%	0.01±16.8%	0.18±16.8%	1.64±12.7%	0.04±26.3%
16	12.35±6.5%	231.57±3.6%	0.01±15.9%	0.29±16.4%	0.70±16.5%	0.01±27.8%
17	9.87±5.6%	82.23±3.5%	0.01±16.4%	0.09±17.5%	0.22±14.5%	0.02±24.5%
18*	8.83±6.5%	90.27±3.8%	0.01±15.6%	0.05±16.4%	0.39±15.4%	0.01±28.9%
19 [*]	10.14±8.6%	83.47±4.2%	0.01±18.6%	0.10±17.1%	0.23±16.3%	0.03±24.7%

 Table 1

 Quantification of Short Half-Life Time Elements in Colorectal Cancer

* Samples corresponding to normal tissue.

Qualitification of Long Hair-Life Time Elements in Colorectal Cancer						
Tumor	Mg μg/g	Ι μ <i>g/g</i>	Se µg/g	Ca µg/g	Cu μg/g	
Sample						
- t						
1	$24.01\pm3.4\%$	1.23±5.4%	0.78±15.2%	3.13±8.2%	$0.45 \pm 15.2\%$	
2	19.71±3.8%	0.93±6.1%	0.53±15.9%	4.74±6.2%	0.05±16.1%	
3	30.99±3.4%	3.52±5.6%	2.44±16.1%	32.99±8.4%	0.01±14.5%	
4	11.97±4.3%	3.02±5.4%	1.66±15.4%	20.17±9.1%	1.92±13.8%	
5	22.92±3.8%	4.05±5.0%	3.48±17.4%	10.10±10.4%	0.21±16.5%	
6*	29.78±3.0%	3.42±5.9%	3.08±15.8%	5.50±9.5%	1.99±12.8%	
7*	14.39±5.5%	0.65±6.4%	1.36±15.6%	16.11±10.2%	0.23±15.7%	
8	3.50±4.6%	1.50±6.2%	1.29±16.4%	8.487±8.4%	0.02±16.5%	
9	31.33±3.6%	5.14±5.4%	0.83±17.1%	44.95±9.2%	0.09±15.4%	
10	30.13±3.8%	2.06±5.7%	0.79±16.4%	2.91±12.0%	0.03±14.3%	
11*	29.64±3.9%	2.09±5.8%	0.50±15.4%	12.81±7.9%	0.01±13.6%	
12	15.85±4.2%	1.60±4.9%	1.64±16.8%	2.229.2%	0.06±14.8%	
13*	21.95±4.6%	2.42±5.6%	1.90±16.1%	33.37±8.6%	0.05±16.1%	
14	19.31±5.8%	2.19±6.1%	1.61±17.0%	16.10±6.8%	0.03±16.4%	
16	28.68±4.6%	3.48±6.4%	1.59±18.1%	5.15±8.9%	0.30±15.7%	
17	14.53±3.5%	2.63±6.9%	1.17±15.6%	4.03±7.5%	0.04±17.9%	
18*	10.11±3.4%	2.51±5.2%	0.80±16.2%	3.04±11.0%	0.02±16.4%	
19 [*]	8.43±4.1%	1.31±5.4%	0.78±18.1%	4.32±8.9%	0.05±14.8%	

Table 2	
Quantification of Long Half-Life Time Elements in Colorectal Canc	er

* Samples of a normal tissue.

Table 3Average of the Concentration of Colorectal Tumor and Normal TissueElement $\mu g/g$ Zn $\mu g/g$ Fe $\mu g/g$ Co $\mu g/g$ Ba $\mu g/g$ Cr

Element		µg/g Zn	μ <i>g/g</i> Fe	μ <i>g/g</i> Co	μ <i>g/g</i> Ba	μ <i>g/g</i> Cr
Average Normal tissue	of	7.53±6.7%	131.45±3.2%	0.01±14.5%	0.10±17.4%	0.46±16.4%
Average Tumour tissue	of	8.08±7.4%	120.24±3.4%	0.02±15.1%	0.18±16.6%	0.44±15.8%
Element		Mg μ <i>g/g</i>	Ι μ <i>g/g</i>	Se µg/g	Ca µg/g	Cu µg∕g
Average Normal tissue	of	19.76±3.7%	1.95±5.4%	1.31±15.6%	11.18±8.3%	0.40±15.1%
Average Tumour tissue	of	20.96±3.9%	2.79±6.8%	1.54±16.2%	9.07±9.1%	0.27±15.6%



Fig. 1. Composition of Co, Ba, and Hg.



Fig. 2. Composition of Cr, I, Cu, and Se.



Fig. 3. Composition of Zn, Mg, and Ca.



Fig. 4. Composition of Fe.

however, changes in the amounts of Hg, Cr, Cu, Se, Zn, Mg, and Ca have not been found. Previous studies suggest that iron induces carcinogenesis (10, 11) and colorectal cancer in animals (12) and raises the risk of human colorectal cancer (13,14). It has been reported that the generation of hydroxyl radicals by iron-catalyzed reactions and the iron dietary enrichment enhances the incidence of tumor induction (11).

Interestingly, in this study, it was found that about 9% lower levels of iron as compared to control tissues, suggesting that in this particular type of cancer, this microelement has no influence on the etiology for the development of the disease as it was suggested in colorectal tumours in animals (12) or in other types of cancer (10,13).

The concentrations of barium detected in the analysis of colorectal cancer samples compared with normal tissues were higher in 56%. Whether the alteration in iodine and barium may have a significance in the etiology of this cancer deserves further investigation.

REFERENCES

- 1. T. P. Cheng, Study of the correlation of trace elements, J. Radioanal. Nucl. Chem. 195 (1) (1995).
- A. Mendoza-Rodriguez, I. Morillen, M. A. Cerbon, P. Luna, H. Santiago-Payon, and A. Quintero, Differential expression of c-fos, c-myc and c-Ki-ras oncogenes in colorectal cancer from Mexican patients, *Bol. Est. Mod. Biol. Mex.* 44, 77–79 (1996).
- 3. P. Vaughan, D. Kaye, S. Ball, H. Reeve, and C. Peers, The effect of barium on (3H) noradrenalin release from the human neuroblastoma SH-SY5Y, *Eur. J. Neurosci.* 1, 875–80 (1995).
- 4. L. Xiao, and H. Zhang, INNA of elemental contents in fingernails of esophageal cancer patients, *J. Radioanal.* Nucl. Chem. **195** (1) (1995).
- 5. M. A. Lovell, and J. D. Robertson, Aplication of radioanalytical techniques to biological and biomedical sciences, J. Radioanal. Nucl. Chem. **195** (1) (1995).
- 6. Y. L. Sziklai, and A. Cser, Selenium determination in biological materials, J. Anal. Nucl. Chem. 190 (1) (1995).
- 7. G. Friedlander, J. Kennedy, E. Macias, and M. Miller, Nuclear and Radiochemistry, Wiley, New York (1981).
- 8. J. T. Proudehomme. Texas Nuclear Corporation. USA (1962)
- 9. K. Way and L. Rose, Nuclear Data Tables, Academic, London (1971).
- 10. S. Toyokumi, Iron-induced carcinogenesis: the role of redox regulation, *Free Radical Biol. Med.* **20**, 553–566 (1996).
- 11. P. Reizenstein, Free radicals and cancer, Med. Oncol. Tumour Pharmacother. 8, 229–233 (1991)
- 12. R. L. Nelson, S. J. Yoo, J. C. Tanure, G. Andrianopoulos, and A. Misumi, The effect of iron on experimental colorectal carcinogenesis, *Anticancer Res.* 6, 111–115 (1989).
- 13. P. Knekt, A. Reunanen, H. Takkunen, A. Aromaa, M. Heliovaara, and T. Hakulinen, Body iron stores and risk of cancer, *Int. J. Cancer* 56, 379–382 (1994).
- 14. R. Stevens, B. I. Graubard, M. S. Micozzi, K. Neriishi, and B. S. Blumberg, Moderate elevation of body iron level and increased risk of cancer occurrence and death, *Int. J. Cancer* 1, 364–369 (1994).
- 15. V. Zaichick, A. F. Tsyb, and B. M. Vtyurin, Trace elements and thyroid cancer, *Analyst* **120**, 817–821 (1995).
- Y. P. Zhu, M. Bilous, and S. C. Boyages, Excess iodine induces the expression of thyroid solid cell nests in lymphocytic thyroiditis-prone BB/W rats, *Autoimmunity* 20, 201–206 (1995).