ISTITUTO NAZIONALE DI FISICA NUCLEARE

Sezione di Milano

INFN/TC-91/11
25 Novembre 1991

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A PRELIMINARY STUDY ON Te INTESTINAL ABSORPTION WITH STABLE TRACERS

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ABSTRACT

An investigation on Tellurium metabolism by administration of tellurium stable isotopes was performed.

Fractional intestinal absorption was determined in a male rabbit by the double tracer technique. The investigated subject was given an enriched solution of Te–124 orally and few minutes later an enriched solution of Te–126 intravenously. Blood samples were drawn at different times following the tracer administration. The Te–124 and Te–126 contents in plasma samples were determined by proton nuclear activation.

The described methodology offers a means for the study of tellurium metabolism in humans without radiation risk.

1.–INTRODUCTION

We developed a method based on proton nuclear activation (PNA) to study the metabolism of oligoelements with stable tracer administration; this method prevents radiation exposure for the subject under study and consequently fit well the need of studies in humans even in particularly radiosensitive groups of population.

The methodology was applied at first to iron metabolism studies both in animals and in humans[1,2] and then to molibdenum metabolism studies in animals[3].

In this paper we present a study concerning tellurium intestinal absorption in animals based on the double tracer technique.

2.–METHODOLOGY

2.1.– Double tracer method

The double tracer technique consists in the administration to the investigated subject of two isotopes of the element under study, one given orally and the other intravenously. The determination of the intestinal absorption may be performed by measuring the concentrations of both isotopes in plasma samples withdrawn at different times after the administration of the tracers.

In fact, an oral administration of a tracer is equivalent to continuos intravenous injection of a tracer in plasma at variable rate B(t). It follows that the function G(t), which represents the fractional quantity of the orally given tracer present in plasma at time t after administration, is obtained by the convolution integral:

$$G(t) = \int_0^t B(x)F(t-x)\,dx \qquad (1)$$

where F(t) is the function describing the fractional quantity in plasma of the injected tracer.

Since the functions G(t) and F(t) are experimentally determined, the initial entry fraction B(x) can be calculated and utilized for the evaluation of the intestinal absorption.

2.2.– Proton nuclear activation method

The PNA method, extensively described in previous works [4–6], essentially consists in the bombardment of the sample with a proton beam of appropriate energy to induce predominantly (p,xn) reaction on the nuclei of the target.

The measurement of the intensities of the gamma rays emitted by the radioactive nuclei obtained from the stable isotopes allows the analysis of the sample content. The choice of the particular (p,xn) reaction is determined by the characteristics of the decay and by the mean life of the residual radioactive nucleus obtained from the isotope of interest.

For the quantitative analysis the internal reference method is used. Each sample is doped with a known quantity of a suitable reference element, and a standard sample is prepared, which contains also a known amount of the isotope under study. After irradiation the ratio between the intensities of the two gamma–ray transitions, one identifying the trace isotope and the other identifying the reference element is compared to the same ratio obtained from the standard sample. With this procedure the isotope content is determined

3.– DETERMINATION OF STABLE TELLURIUM ISOTOPES BY PNA

The natural isotopic composition of tellurium is shown in Tab.1. On the basis of the possible nuclear reactions induced by proton on the Te stable isotopes and of the decay characteristics of the radioactive isotopes obtanaible from such reactions, (p,n) reactions on the stable Te–124 and Te–126 resulted to be the most convenient for our aim: indeed, as shown in Tab.2, the obtained radioisotopes have mean lifes long enough to allow an off–line detection of

gamma–rays and a significant reduction of the matrix background and have gamma line emissions with energy and intensity suitable for detection.

Vanadium was chosen as reference element for quantitative analysis.

In order to optimize the condition of measurement, the proton energy corresponding to the maximum yield of the chosen reactions was determined. With this aim a sandwich of thin targets enriched with the isotope of interest, separated by aluminium foils of appropriate thickness, was irradiated by a proton beam. Because of the energy degradation along the stack, each target was irradiated at different proton energy but with the same beam flux.

The Te–124 enriched targets, and likewise the Te–126 enriched targets, were prepared adding a Te–124, or Te–126, enriched solution with a gel substance to obtain, after drying, a thin layer of the order of 2 mg/cm^2 with a concentration of Te isotope of about 2 μg/mg. Nine targets, obtained from the so prepared layer, and accurately controlled in thickness, were piled up with a 0.05 mm Al foil between one and the other. The energy of the incident proton beam was 18.5 MeV and the energy incident on each successive target was calculated on the basis of the energy loss table by Williamson et al.[7].

TABLE 1. NATURAL ABUNDANCE OF Te ISOTOPES

isotope	abundance %
Te–120	<0.1
Te–122	2.5
Te–123	0.9
Te–124	4.6
Te–125	7.0
Te–126	18.7
Te–128	31.7
Te–130	34.5

TABLE 2. MAIN NUCLEAR DATA OF REACTIONS INVOLVED

reaction	E_{th} (MeV)	half life(d)	main emission(keV)	rel. intensity
$^{124}Te(p,n)^{124}I$	4.0	4.2	602.7	62.0
			722.8	10.0
$^{126}Te(p,n)^{126}I$	3.0	13.0	388.6	35.0
			666.3	32.0
$^{51}V(p,n)^{51}Cr$	1.6	27.7	320.0	90.0

In Fig.1 the intensities of the 602.7 keV gamma–line from I–124 decay and the 666.3 keV gamma–line from I–126 decay, measured using the same geometry and the same collecting time for each target, are given as a function of the corresponding proton energy. From the figure we

can estimate that the maximum yields for the production of I–124 and I–126 are obtained for proton with energies of 9–10 MeV and 8–9 MeV respectively. We therefore chose an incident proton energy in order to have 9 MeV in the median plane of the plasma sample, the composition of which is considered nitrogen equivalent from the point of view of energy loss.

Possible nuclear reactions on the nuclei of the plasma sample, which can produce the same radioisotopes emitting gamma–rays as those of interest or different radioisotopes emitting gamma–rays interfering with gamma rays utilized for the analysis, were considered. For what is concerning the determination in plasma of Te–124 and Te–126, Tab. 3 shows the interfering reactions which in principle could contribute to the production of the radioisotopes of interest and the corresponding threshold energies. However, it must be emphasized that the content in plasma samples of tellurium isotopes different from those used as tracers , is undoubtely non significant (no values of Te content in plasma are known in literature) and so the related nuclear reactions interfere negligeably.

The content of iodine (I–127, 100% natural abundance) in plasma as given in literature is in the range 38–60 ng/ml [8]; by considering the chosen irradiation energy and the threshold energy of this interfering reaction, only a part of iodine contained in plasma sample contributes to the production of I–126. Taking also in account the low value of the cross–section (<2 mb as evaluated from Muenzel et al.[9]), we have estimated that the interfering reaction on I–127 gives a contribution within 1% to the determination of a Te–126 amount of 10 ng, and a decreasing contribution for Te–126 increasing amount.

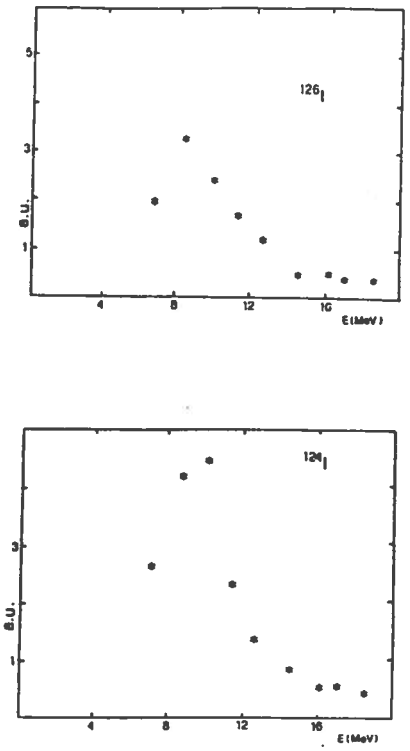

FIG. 1 – Intensity of the gamma–lines.

For the determination of Te–126 in plasma, the 662.3 keV gamma–line was taken into consideration instead of the most intense 388.6 keV gamma–line, due to the interference with the 388.4 keV gamma–line from Y–87 (half–life = 80.3 hrs.), which is produced via a (p,n) reaction (E_{th} = 2.7 MeV) on Sr–87 (7% natural abundance and about 0.1 μg/ml content in plasma).

TAB. 3
INTERFERING NUCLEAR REACTIONS WITH THEIR THRESHOLD ENERGY

reaction	E_{th}(MeV)
$^{125}Te(p,2n)^{124}I$	10.6
$^{123}Te(p,\gamma)^{124}I$	0
$^{125}Te(p,\gamma)^{126}I$	0
$^{127}I(p,pn)^{126}I$	9.2

4.–EXPERIMENTAL

For intravenous injection and oral administration Te–124 and Te–126 enriched solutions were prepared. 10 mg and 60 mg respectively of Te–124 and Te–126 enriched metallic tellurium (Techsnabexport, Moscow –USSR) were dissolved in a mixture of HCl and HNO_3 and the solutions were diluted in deionized water to a concentration of 0.51 mg/ml of Te–124 and 0.35 mg/ml of Te–126 respectively.

The compositions of the solutions were: 0.09% Te–122, 0.08% Te–123, 90.00% Te–124, 3.45% Te–125, 4.05% Te–126 and 0.16% Te–3, 0.09% Te–124, 98.40% Te–126 respectively.

Suitable quantities of the enriched solutions were respectively administered intravenously and after about 45 minutes orally, using an intragastric tube to one male rabbit (body weight 2–3 kg). 261 μg of Te–126 were given intravenously and 1.39 mg of Te–124 orally.

Eleven blood samples within 480 minutes after the ingestion were drawn from the rabbit.

Sample preparation for the tellurium isotope determination by PNA did not differ from preparation procedure already standardized for other determinations we made by this method[1–6]. Samples to be analyzed contained 0.8 ml of plasma, measured with an estimated error less than 0.1%. They were doped with 10 μg of V used as reference element, drawn from a standard solution. The standard sample, necessary for the quantitative determination of Te–124 and Te–126 was prepared with the same quantity of plasma as the samples to be analyzed, doped with 20 μg of V, 17.8 μg of Te–126 and 16.3 μg of Te–124, drawn from enriched solutions of these isotopes of the same compositions as those subministered. The accuracy of the pipette used to measure the quantity withdrawn from the various solutions was ± 2%.

Each sample was dried at 35°C, powdered in an agate mortar and compressed to form a 0.9 mm diameter self–supporting disk.

The procedure we followed to prevent introduction of contaminants from environment and from sampling tools and losses of the element during the preparation is described in previous works. Specific controls were performed by PNA to verify that the bidistilled and deionized water used for preparing the standard solutions was not Te–contamined and to ensure that the mylar foils used to protect the samples were not sources of contaminations, due to eventual diffusions of contaminants from mylar to sample during irradiation.

For the irradiation a multi–target chamber with a rotating disk, supporting up to 30 samples, was utilized. Each sample, protected by two aluminized mylar foils, was mounted in a

suitable aluminum frame, screwed up to the disk to have a good thermal contact. With this device each target remains in front of the beam spot just for the time resulting from the rotation speed.

The sample irradiation was performed utilizing the proton beam of the Scanditronix MC40 of the CCR Euratom (Ispra). Typical values were 7 μA for the beam intensity and 8 hours for the irradiation time. The permanence time of each sample in front of the beam was 20 ms per second, corresponding to a total exposition of approximately 4 mC for each sample.

The rotating disk was cooled by circulation in a spiral duct, dug in the disk itself, of a cooling liquid so that during irradiation the temperature of the plasma sample did not exceed 40°C.

We started to collect the gamma spectra from irradiated samples 15–20 days after the end of irradiation, in order to have a reduction of the activity of radioisotopes of shorter mean–life, using a conventional nuclear spectroscopy HPGe detector system. The collecting time of the gamma spectra ranged between 24 and 48 hours for each sample.

5.–RESULTS AND DISCUSSION

The concentrations of the tracers Te–124 and Te–126 in plasma samples withdrawn at different times after tracers administration were detrmined from the analysis of the gamma spectra. A typical gamma spectrum from an irradiated sample is shown in Fig.2, where the gamma–lines due to the decay of I–124, I–126 and Cr–51 are indicated.

Fig. 3 and Fig. 4 show, respectively, the concentration of the injected tracer and of the orally given tracer in plasma samples as a function of time.

The determination of the intestinal absorption by double tracer method involves the measurement of concentrations in plasma samples of both tracers. By linear interpolation of the experimental concentrations of Te–124 and Te–126 we evaluated the functions F(t), fractional quantity of intravenously given tracer, and G(t), fractional quantity of the orally given tracer, every 15 minutes.

The integral (1) was substituted by the sum:

$$G(s) = \sum_{n=0}^{s} B(n)F(s-n)\Delta t \qquad (2)$$

where Δt is a constant interval of 15 minutes. From equation (2) we calculated with an iterative program the values B(n) every 15 min from the moment of oral administration to the time T. Therefore the total fraction of tracer absorbed within the time T is given by:

$$\sum_{n=0}^{T/\Delta t} B(n)\Delta t \qquad (3)$$

We obtained for the fractional intestinal absorption of tellurium the value 0.050±0.008, calculated within 480 min from the oral administration.

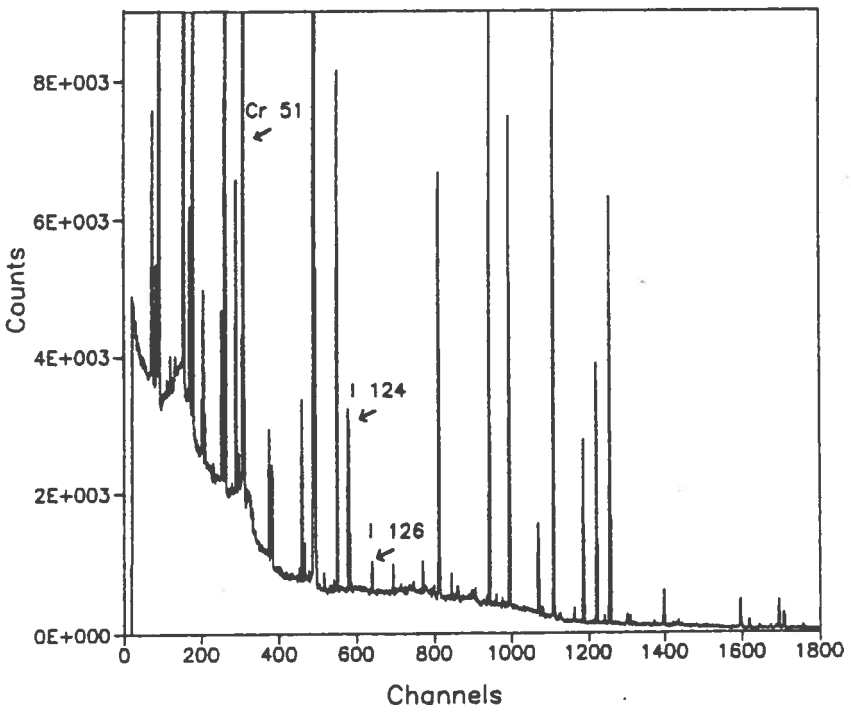

FIG. 2 – Typical gamma spectrum from an irradiated sample.

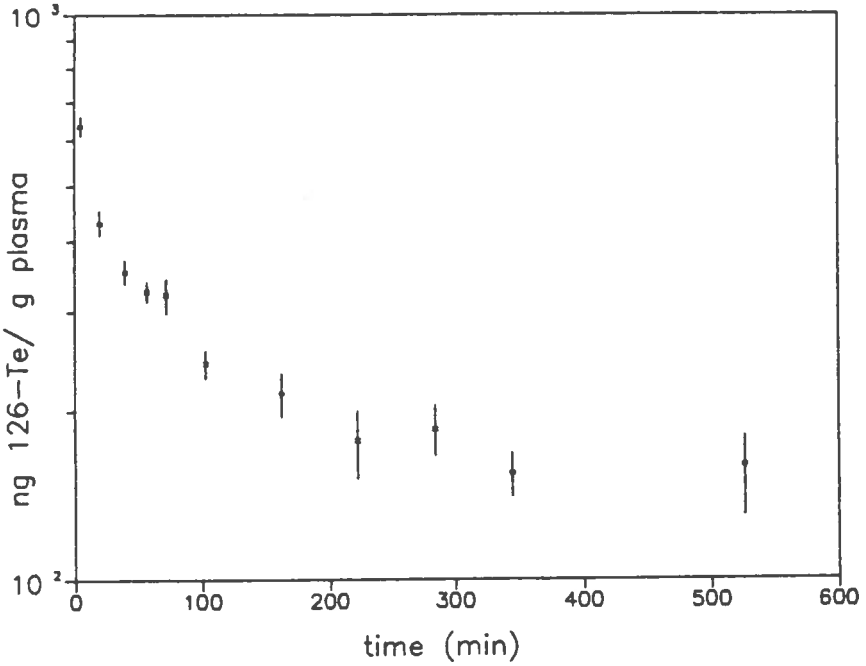

FIG. 3 – Concentration of the injected tracer Te–126.

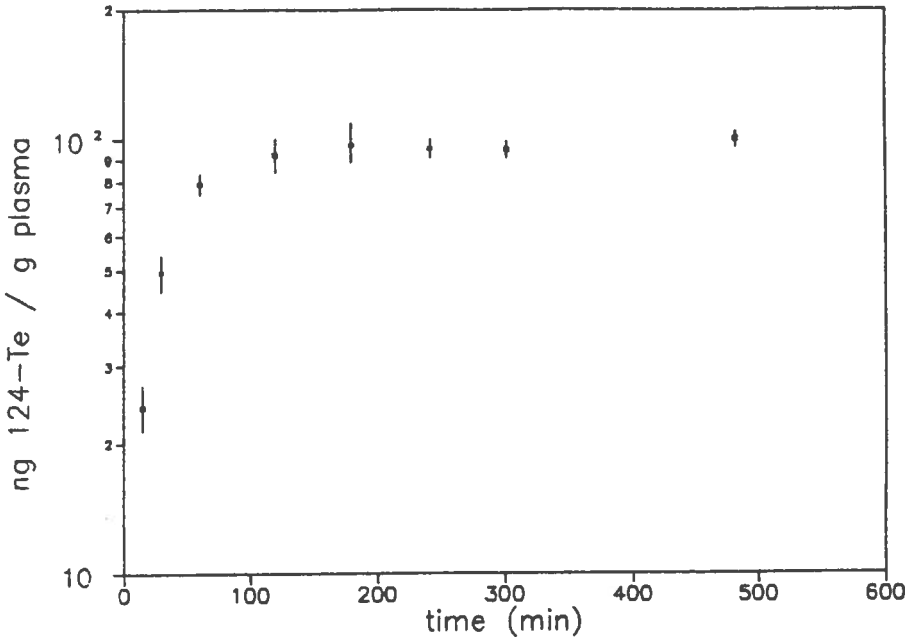

FIG. 4 – Concentration of the orally given tracer Te–124.

REFERENCES

(1) M.C.Cantone, N.Molho, L.Pirola, Ch.Hansen, P.Roth, E.Werner, Med. Phys., **14**, 223–227 (1987)

(2) M.C.Cantone, N.Molho, L.Pirola, G.Gambarini, Ch.Hansen, P.Roth, E.Werner, Med. Phys., **15**, 862–866 (1988)

(3) M.C.Cantone, N.Molho, L.Pirola, G.Gambarini, Ch.Hansen, P.Roth, E.Werner, accepted Med. Phys. October 1991

(4) M.C.Cantone, N.Molho, L.Pirola, Clin. Phys. Physiol. Meas., **3**, 67–77 (1982)

(5) M.C.Cantone, N.Molho, L.Pirola, J. Radioanal. Nucl. Chem., **91**, 1, 197–203 (1985)

(6) M.C.Cantone, G.Gambarini, N.Molho, L.Pirola, J.Radioanal. Nucl. Chem., **111**, 2, 351–357 (1987)

(7) C.F.Williamson, J.P.Boujot, J.Picard, Rapport CEAK 3042 (1966)

(8) Sanz et al., Clin. Chim. Acta,**1**,570 (1956)

(9) K.A.Keller, J.Lange, H.Muenzel, G.Pfenning, LANDOLT–BOERNSTEIN Numerical Data and Functional Relationships in Science and Technology, SPRINGER VERLAG BERLIN, N.Y. 1973