Reduction in the Absorption of Dietary Strontium in Man by Nutritional Factors

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Abstract. Radioactive isotopes of strontium, mainly $^{90}$Sr, may considerably contribute to the total activity of long-lived fission products released into the environment in nuclear accidents. Consequently, the ingestion of strontium radionuclides with contaminated foodstuffs may result in a significant internal radiation exposure of members of the public. The committed radiation dose dependents significantly on the fraction of the ingested activity that crossed the gut wall ($f_1$ value). In controlled tracer kinetic investigations, the influence of black and green tea on the gastrointestinal uptake of strontium was investigated, since tannin, a constituent of tea, is well known for being an inhibitor of gut uptake of some trace metals. In further experiments, the effect of sodium alginate and pectin, which are naturally occurring non-absorbable polyelectrolytes, on the gastrointestinal absorption of strontium was studied in human subjects. The data obtained show that the uptake of ingested strontium from green tea was reduced by a factor of 1.4 in comparison to aqueous solution, whereas administration of black tea had a less pronounced effect on strontium absorption. Addition of alginates in milk resulted in a large reduction of the $f_1$ value by a factor of about 20. Investigations with pectin indicate that this is also a possible inhibitor of strontium uptake. Alginates and pectin therefore seem to be effective nutritional factors to reduce the strontium uptake into the systemic part of the body, which in turn results in a corresponding reduction of the effective dose after ingestion of radionuclides of strontium.

1. Introduction

Strontium-90 from the fall-out of atomic explosions and from accidental release by industrial plants, presents a risk to health. Strontium is absorbed into the human body and deposited in the skeletal tissue in much the same way as calcium, although some biological discrimination against strontium seems to exist, which takes place mainly in the absorptive phase. In view of the possibility of dietary contamination with Sr-90, it is desirable to be able to inhibit the absorption by binding the ingested radionuclide before absorption can occur. It is important, however, that calcium absorption should not be reduced considerably.

Nutritional factors may influence the fractional absorption of strontium from the gastrointestinal tract into the systemic part of the body. A number of factors have been found both in animals and humans to increase absorption, including fasting and low dietary levels of calcium, magnesium and phosphorus [1, 2, 3]. On the other hand, high calcium diets and administration of alginates have been shown to decrease the absorption of ingested strontium [3, 4, 5, 6]. Furthermore, the selective inhibition of radiostrontium uptake by rats following the administration of pectic acid or pectin-like compounds has been reported [7, 8, 9]. Up to now, there exist no similar investigations for pectin in humans. Alginates are structurally carbohydrates consisting of polymerised mannuronic and guluronic acids, which are extracted from brown seaweed. Like alginate, pectin is known as non-toxic and non-absorbable polyelectrolyte and is found in fruit and vegetables and mainly prepared from waste citrus peel and apple pomace. Pectin consists of homopolymeric partially methylated poly-galacturonic acid residues. Both substances are used commercially in the food and drug industries for many purposes, such as gelling agents, emulsifiers and thickeners. Additionally, pectin has been shown to be effective in preventing the gastrointestinal uptake of lead [10].

It is well known that tea, which contains polyphenolic compounds as ingredients, e.g. tanning agents (tannin), have a wide range of effects in vivo and in vitro, including antioxidant and metal-chelating activities. Tea is reported to have the potential to reduce the gut uptake of several trace metals, mainly of iron [11, 12] or other elements, e.g. molybdenum [13]. Black and green teas both contain similar amounts of flavonoids, they differ however in their chemical structure.

In 1965, Hayashi et al. reported about the inhibitory effect of green tea on the gastrointestinal absorption of Sr-90 in rats [14].

This paper deals with the effect of some dietary factors and foodstuffs such as green and black tea as well as the effect of pectin in comparison to alginates on the uptake of ingested strontium in humans.
For $^{90}$Sr, the committed radiation dose after ingestion of contaminated foodstuffs depends significantly on its fractional intestinal absorption, i.e. the $f_1$-value to be used in the dose calculations. Information on the determination of the fractional intestinal absorption of strontium in humans can be obtained by controlled tracer kinetic investigations. The application of radionuclides of strontium to healthy volunteers in such investigations is ethically hardly justifiable, even if the resulting committed radiation doses are small. Stable isotopes used as tracers represent an ethically acceptable alternative for biokinetic investigations, as they are free from any radiation risk for the volunteer subjects [15, 16]. Stable tracers are artificially produced by modification of the natural isotopic composition of the element of interest. Biokinetic investigations can thus be conducted by the administration of one or more tracers in suitable form to volunteer subjects. It is then possible to quantify the tracers in biological samples, e.g. blood or urine, from the measurement of their concentrations, of their isotopic abundances or isotopic ratios, provided that the isotopic composition of the natural element and of the tracer(s) is known (see Table I).

Table I: Natural [17] and enriched stable isotope abundances (as certified by Chemotrade GmbH, Düsseldorf, Germany)

<table>
<thead>
<tr>
<th>Mass number</th>
<th>$^{84}$Sr</th>
<th>$^{86}$Sr</th>
</tr>
</thead>
<tbody>
<tr>
<td>84</td>
<td>0.56</td>
<td>76.40</td>
</tr>
<tr>
<td>86</td>
<td>9.86</td>
<td>4.64</td>
</tr>
<tr>
<td>87</td>
<td>7.00</td>
<td>1.96</td>
</tr>
<tr>
<td>88</td>
<td>82.58</td>
<td>17.00</td>
</tr>
</tbody>
</table>

2. Materials and methods

Two solutions of strontium, one enriched with the stable isotope $^{84}$Sr, the other enriched with $^{86}$Sr, were purchased as strontium carbonates from Chemotrade GmbH, Düsseldorf, Germany. The metal isotopes $^{84}$Sr or $^{86}$Sr were brought into solution as follows: An aliquot of 30 mg of $^{84}$Sr or $^{86}$Sr was dissolved in 0.30 ml of hydrochloric acid (15%) and the solution was filled up to the desired concentration with deionised water (MilliQ). For oral applications, a stock solution of $^{86}$Sr with concentration of 1g Sr/l was prepared. For intravenous application, the $^{84}$Sr solution contained approximately 42 mg Sr/l and was made isotonic by adding adequate amounts of sodium chloride and sodium citrate, whereby the pH value was adjusted between 6 and 7 by adding sodium hydroxide (30%). Aliquots of 10 ml were filled into glass ampoules, melted tight and sterilized at 120°C within 20 min. Sterility of samples was checked according to German European Pharmacopoeia.

The isotope ratios of strontium were determined by means of a thermal ionisation mass spectrometry (TI-MS). For that purpose, a thermal ionisation source with dual filament technique and mass separation by a sector field magnet (Finnigan MAT262; Bremen, Germany) was used.

Kinetic data were attained by means of a double tracer technique [18, 19]. Applying this method, a defined amount of $^{86}$Sr isotope is administered orally, while a solution of $^{84}$Sr is simultaneously injected intravenously. The double-isotope method provides an accurate estimate of fractional absorption and is a convenient technique in that only a single sample of blood (or urine) needs to be collected.

Human investigations were conducted on healthy volunteers in accordance with the Helsinki Declaration and according to the protocol approved by the Ethics Committee of the Medical Faculty, Technical University Munich, Germany. The participants were given oral and written information
about the study and written consent was obtained before their participation in the study. A total of 35 tracer kinetic investigations were carried out on ten human volunteers (six males/four females, see Table II), aged between 24 and 61 years (mean ± SD: 41.1 ± 12.4).

Table II: Characteristics of volunteer subjects

<table>
<thead>
<tr>
<th>Volunteer</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Weight (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 T.H.</td>
<td>38</td>
<td>m</td>
<td>75</td>
</tr>
<tr>
<td>2 M.R.</td>
<td>39</td>
<td>f</td>
<td>62</td>
</tr>
<tr>
<td>3 E.P.</td>
<td>50</td>
<td>f</td>
<td>60</td>
</tr>
<tr>
<td>4 F.R.</td>
<td>33</td>
<td>m</td>
<td>70</td>
</tr>
<tr>
<td>5 E.W.</td>
<td>59</td>
<td>m</td>
<td>85</td>
</tr>
<tr>
<td>6 U.L.</td>
<td>61</td>
<td>m</td>
<td>75</td>
</tr>
<tr>
<td>7 A.L.</td>
<td>35</td>
<td>m</td>
<td>82</td>
</tr>
<tr>
<td>8 J.B.</td>
<td>24</td>
<td>f</td>
<td>65</td>
</tr>
<tr>
<td>9 B.M.</td>
<td>28</td>
<td>f</td>
<td>78</td>
</tr>
<tr>
<td>10 J.B.</td>
<td>44</td>
<td>m</td>
<td>77</td>
</tr>
</tbody>
</table>

The investigations started in the morning after an overnight fast of the volunteers. While receiving the tracers, the persons were under permanent medical control. A 24-hour urine sample and one blood sample were collected prior to the tracer application (blank values). The volunteers received an intravenous injection of a sterile isotonic solution of about 0.4 mg $^{84}$Sr. Simultaneously 1 mg of $^{86}$Sr given as strontium chloride in 100 ml of aqueous solution of black tea (Assam), or of green tea (Sencha) was administered orally. For the preparation of tea, a portion (1.5 g) of black tea was infused with 250 ml of boiling water for 5 min, whereas 2.2 g of Sencha tea (green tea) was infused for 2 min with 100 ml water of 70° C. In another series of experiments, 1 mg of $^{86}$Sr mixed in an aqueous solution with pectin (3 g/100 ml, apple pectin from Naturwerk, Hannover, Germany) or in milk with alginate was administered to the volunteers. Pharmaceutically prepared tablets of alginates (Gaviscon, Novartis Consumer Health GmbH, Germany) according to an amount of 3.5-5.0 g of alginic acid were pre-dissolved in 50 ml of water and then mixed with 100 ml of milk [6]. The prepared solutions of pectin and of alginate were rather viscous but drinkable.

After the tracer administration, blood samples were withdrawn via an in-dwelling catheter at given intervals until 24 hours, as well as urinary excretion was collected. Blood plasma was separated from whole blood by centrifugation. Aliquots of 100 ml of urine were mixed with 5 ml of concentrated nitric acid, and thereafter all biological samples were kept frozen until analysis.

TIMS requires thorough sample purification from the biological matrix constituents which could reduce the ionisation efficiency of the trace element and interfere with the signal analysis. In order to get reliable results for the isotope ratios, a number of other elements and molecules have to be separated by an appropriate preparation of the sample for the mass spectrometric analysis, which is described in detail elsewhere[20]. Briefly, an aliquot of 0.25 ml of plasma (or 1.0 ml of urine) was mixed with 1.0 ml nitric acid (65%, subboiling distilled) and wet-ashed in a microwave oven. Strontium was separated selectively from the samples by means of an ion-exchange-chromatography applying Sr.Spec columns (particle size 100-150 µm), which were obtained in a ready-to-use form from ElChrom Industries Inc. (Paris, France) [21]. All procedures related to mineral separation and purification were done in a clean room.

The $f$ value was determined from the ratio of the oral $^{86}$Sr to the intravenously injected $^{84}$Sr in a plasma sample taken 24 h after simultaneous administration, according to the following equation [20]:

$$f = \frac{[\text{oral}]_{86}^{\text{Sr}}}{[\text{intravenous}]_{84}^{\text{Sr}}}$$
\[ f_1 = \frac{z_{86,po}}{z_{84,iv}} \cdot \frac{m_{84,iv}}{m_{86,po}} \quad (1) \]

where

- \( z_{86,po}, z_{84,iv} \): the \(^{86}\)Sr and \(^{84}\)Sr tracer concentrations in blood (or urine);
- \( m_{84,iv}, m_{86,po} \): the amounts of the isotopes \(^{84}\)Sr and \(^{86}\)Sr as administered tracers.
- po, iv: per oral, intravenous

The results are expressed as arithmetic mean values with their standard deviation (mean ± SD) and were analysed with the unpaired Student’s t-test [22]. For the null hypothesis, the mean values of \( f_1 \) for aqueous solution and the other administered solutions were tested for difference.

### 3. Results and discussion

Table III and fig. 1 present the mean absorption data of uptake of 1 mg of strontium from black or green tea in comparison to aqueous solution, as well as of the data of fractional uptake from the prepared pectin and alginate solutions respectively. The data refer to plasma samples taken 24 hours after tracer administration. The uptake of Sr from aqueous solution was used as reference. In comparison to the data from aqueous solutions, drinking of green tea decreases the mean absorption of Sr from 61\% to 44\%. This represents a reduction of about 30\%. The mean \( f_1 \) value for green tea is statistically significant lower on the level of 1\% (\( p < 0.01 \)). A similar inhibitory effect of green tea (also Sencha tea) against Sr-90 absorption through the intestine was found by using rats [14], when the green tea was administered 30 minutes before the administration of \(^{90}\)Sr, while the simultaneous administration of the tea and \(^{90}\)Sr caused a reduction in absorption of about 18\%, which is statistically not significant. In contrary to this single dose study, studies with tannin on the effectiveness in reducing the retention of chronically ingested radiostrontium in rats showed no beneficial effect in reducing the body burden of radiostrontium [23].

Table III: Fractional intestinal absorption of strontium (\( f_1 \) value) from aqueous solution, green tea, black tea, and pectin and alginate in milk (100-150 ml). Oral \(^{86}\)Sr amount per experiment: 1 mg. Values obtained from plasma taken 24 hours after tracer administration.

<table>
<thead>
<tr>
<th>Experiment with</th>
<th>Number of Experiments</th>
<th>( f_1 ) value (Mean ± SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aqueous solution</td>
<td>10</td>
<td>0.61 ± 0.12</td>
<td>0.40 - 0.78</td>
</tr>
<tr>
<td>Green tea</td>
<td>7</td>
<td>0.43 ± 0.10</td>
<td>0.36 - 0.64</td>
</tr>
<tr>
<td>Black tea</td>
<td>8</td>
<td>0.50 ± 0.21</td>
<td>0.22 - 0.84</td>
</tr>
<tr>
<td>Pectin solution</td>
<td>6</td>
<td>0.23 ± 0.12</td>
<td>0.10 - 0.40</td>
</tr>
<tr>
<td>Alginate/milk solution</td>
<td>4</td>
<td>0.03 ± 0.02</td>
<td>0.02 - 0.06</td>
</tr>
</tbody>
</table>

In the present investigation, drinking of black tea showed a small reduction in Sr absorption from 61\% to 50\% in comparison to aqueous solution, which was determined to be not significant. However, the number of experimental data is still limited and the data showed a considerable variation of \( f_1 \) values (range. 0.22 – 0.84). Probably, the tanning agents in green tea could bind more strontium and therefore reduce the intestinal uptake significantly. Both green tea and black tea come from the leaves of the plant Camellia sinensis, the processing that the leaves undergo however make the final tea different. For black tea (not for green tea), the leaves are fermented (fully oxidized) before drying, which could alter the tanning agents so that they could lose or change their activity.
As expected, the absorption of Sr was inhibited by the polysaccharide solutions. More than 60% less Sr is absorbed from the pectin solution ($f_1 = 0.23 \pm 0.12$) than from aqueous solution of equivalent Sr content. The most striking effect was obtained after administration of the alginate solution (inhibition by about 95%). Both differences in mean values were significant at the 0.1% level ($p < 0.001$).

The data obtained in these controlled human investigations confirm that the uptake of ingested strontium is reduced with high efficiency from 61% to 3% (20-fold) when administrated together with alginates; the polyelectrolyte pectin inhibited Sr uptake by a factor of 2.7. The difference in their effectiveness as strontium binders may depend on their stereochemical configuration, that is, their particular position and reactivity within the sugar units themselves. Administration of green tea resulted in a decrease of the $f_1$ value for Sr by a factor of 1.4. Drinking green tea seems to be of lower effect to reduce the uptake of ingested strontium in humans in comparison to alginate and pectin. Black tea had no significant effect on the uptake of strontium into the human body.

It is concluded that alginates as well as pectin seem to be effective in binding strontium before its uptake into the systemic part of the human body, which in turn results in a corresponding reduction of the effective dose after ingestion of radionuclides of strontium. However, pectin has a higher affinity to Ca ions in comparison to Sr ions as compared with alginates [24]. Therefore, intake of pectin preparations for a long time could disturb the normal calcium uptake into the human body [25]. Alginates, in contrast, do not appear to affect calcium absorption in humans [26].
REFERENCES


Acknowledgements
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