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RETENTION OF STRONTIUM 85 IN RATS

II. Effect of various barium sulphate preparations as influenced by soluble sulphates, carrier strontium and by the physiologic state of animals

by

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Considerable decrease in the retention of ^{85}Sr given orally can be achieved if the administration is shortly followed by a mixture of barium and sodium or magnesium sulphates (VOLF & ROTH 1965). Conditions during precipitation are especially important in the preparation of the barium sulphate; the resultant particles may be of different size and shape and the physico-chemical properties may also differ (LIESER & FABRIKANOS 1959, SUITO & TAKIYAMA 1954). The authors have therefore determined the ability of various barium sulphate preparations alone, or in the presence of soluble sulphates, to bind radiostrontium in vitro and in vivo.

The effect of the isotopic carrier and of certain physiologic factors (presence of food in the gastrointestinal tract, maturity of animals) has also been studied.

Methods

Barium sulphate. Barium sulphate (preparation I) precipitated from boiling 0.5 M solutions of barium hydroxide and sulphuric acid was used as in the

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Table 1

The chemical contents of Czechoslovak bitter mineral waters

Mineral water	Evaporation residue (mg/l)	CO_2 (mg/l)	Cations (mg/kg)		
			Na	K	Sr
Zaječická hořká (Middle Bohemian Springs)	36027	—	2159	81	3
Šaratica (Moravian-Silesian Springs)	36220	103	7040	49	—

previous experiments (VOLF & ROTH 1965). The possibly disturbing influence of further ions during precipitation was thus avoided; sulphuric acid was added in excess and the precipitate was repeatedly washed and tested for free barium and sodium ions.

Barium sulphate (preparation II) was prepared in the same way, only barium chloride was used instead of barium hydroxide and the precipitate was very thoroughly boiled. The contrast medium Skiabaryum (Slovakofarma, ČSSR), as well as the barium sulphate used in its preparation, were tested; this preparation III complies with the regulations of the Czechoslovak pharmacopoeia on chemical purity.

In vitro experiments. The sorptive capacity of the above barium sulphate preparations was tested, carrier-free ^{85}Sr chloride solution being added to 100 ml of 0.4 % water suspension of the sorbent. The water suspension of sulphate with added ^{85}Sr was shaken at half-hourly intervals three times and then left standing at room temperature. Twenty hours after adding ^{85}Sr, two 1-ml aliquots of supernatant were collected and assayed by a well-type scintillation counter. The decrease of the activity in the solution with the sorbent present was compared with the radiostrontium standard and expressed as a percentage of the added activity. The sorption was followed up on barium sulphate alone, as well as after that the equimolar quantity of sodium sulphate had been added.

Animal experiments. Details of the procedure have been reported previously (VOLF & ROTH 1965). Two hundred male Wister albino rats received orally 1 to 2 μCi of $^{85}SrCl_2$ in 0.1 ml of liquid, and 10 min later 0.8 mM of each sulphate in 2 ml distilled water. Whole body counting was made 15 min after the administration of ^{85}Sr and repeated 24 and 48 hours later, when the animals were sacrificed. The ^{85}Sr in the dissected femurs was determined. The results were expressed as percentages of the ^{85}Sr dose administered.

Table 1 *(cont.)*

				Anions (mg/kg)				
Ca	Mg	Fe	Al	HCO_3	Cl	SO_4	NO_3	H_2SiO_3
371	5483	—	12	1090	359	23828	2642	—
382	2820	0.3	—	117	304	23060	—	21

The isotopic carrier was added either to the radiostrontium or the sulphates. To the sodium sulphate 10 μM of Sr^{2+} ions in the form of strontium chloride were added. No visible precipitation of strontium sulphate appeared in vitro. Ten and 100 μM Sr^{2+} ions were added to the barium sulphate.

The effect of sulphates in fasting and feeding rats (weighing 170 to 200 g) was investigated in two experiments. In the first experiment, half the number of animals were deprived of food 20 hours before and the others were normally fed. In the second experiment food was withdrawn from all the animals. Half the number of rats were fed one hour before the start of the experiment, on a weighed quantity of standard diet which was withdrawn half an hour later.

The effect of sulphates in rats of various ages (which has been estimated according to their bodyweight — Table 6) was studied in three experiments. Doses and volumes have been adjusted according to the difference in bodyweight, so that young and adult animals each received the same quantity of ^{85}Sr and sulphates per kg bodyweight. In the first experiment 3.8 mM of barium sulphate (preparation II), in the second and third 8.9 mM and 7.6 mM of barium sulphate (preparation III), respectively, with equimolar doses of sodium sulphate, were administered per kg bodyweight.

Two Czechoslovak natural mineral waters (see Table 1) containing a considerable amount of sodium and magnesium sulphates, alone and in combination with barium sulphate (1.6 mM per dose) were also tested. One dose (3 ml) of mineral water contained about 0.7 mM of sodium and magnesium sulphates.

Results

Various barium sulphates. Examination with an electron microscope (Figs 1 and 2) proved that the particles of preparation II are considerably larger than those of preparation I, so that it can be assumed that the inner surfaces

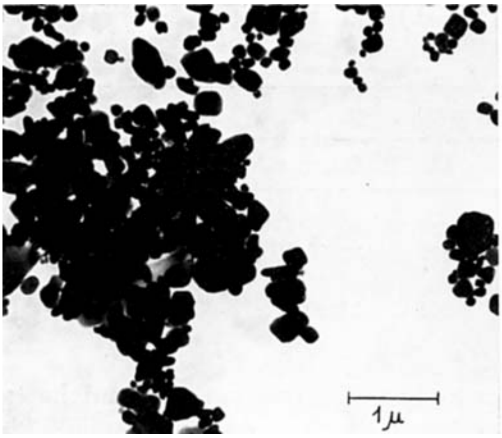

Fig. 1. Barium sulphate (preparation I) in water suspension.

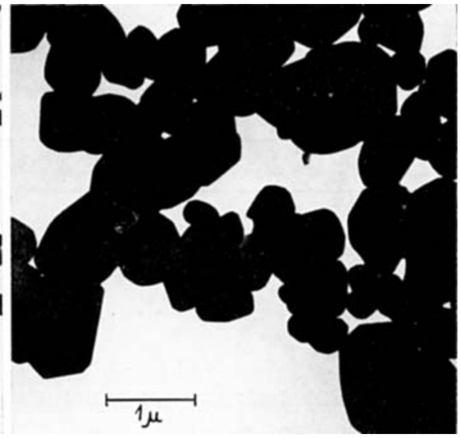

Fig. 2. Barium sulphate (preparation II) in water suspension.

of both samples also differ. Figs 3 and 4 show preparation III and Skiabaryum; conglomerates of particles of the latter are larger than in preparation III; in addition, hazy spots, probably particles of higher solubility, are evident in Fig. 4.

It is seen from Table 2 that the sorptive capacity of various barium sulphate preparations in vitro differed, but in the presence of an excess of the sulphate ions it always increased considerably.

The results given in Table 3 indicate that after the administration of preparation I to rats, the average retention of ^{85}Sr in the whole body, as well as the content of ^{85}Sr in the skeleton, after 24 and 48 hours were markedly lower (by about 60 %) than after the administration of preparation II.

Different barium sulphate preparations are compared in Table 4, on the basis of the calculated ratios of their effect in vitro as well as in vivo. In estimating the effectiveness in vivo, the degree of decrease in the skeletal ^{85}Sr retention in rats after the oral administration of 0.8 mM barium sulphate, or its combination with 0.8 mM sodium sulphate, 10 min after contamination with ^{85}Sr (experiments reported above and in our previous communication), was taken into account. The less effective means are shown in the upper half of the table, and it is evident that marked difference in the effect in vitro is necessary in order for them to appear in vivo as well. The more effective means in the lower part of the table prove that the more they differ from each other in vitro the more obvious their difference in vivo. The difference in the effect of the same preparation is usually more marked in vivo than in vitro.

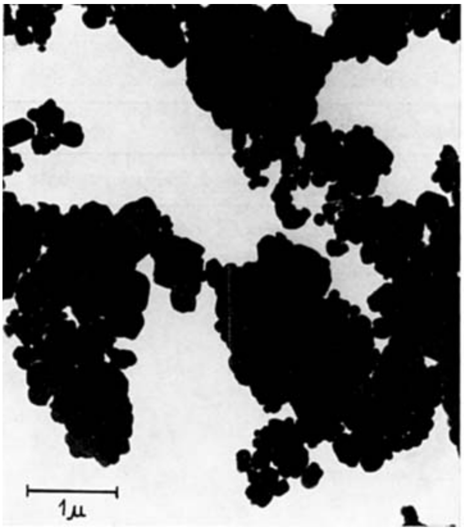

Fig. 3. Barium sulphate (preparation III) in water suspension.

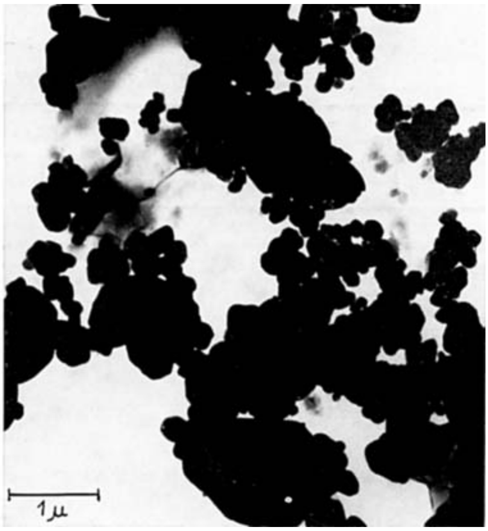

Fig. 4. Skiabaryum in water suspension.

Sulphates and carrier. It may be seen from Table 5 that after the administration of ^{85}Sr and 10 μM carrier strontium, as well as of sulphate without carrier strontium, the variance of the average values of ^{85}Sr retention in the whole body, as well as in the bones, increased. The average effectiveness of barium sulphate after the administration of ^{85}Sr with 100 μM carrier strontium decreased in comparison with the group in which no carrier strontium was added. This decrease is close to the significant value (for $p < 0.05$). There were otherwise no substantial changes in the average effect of sulphates after adding carrier strontium.

The addition of isotopic carrier strontium to ^{85}Sr, or to sodium or barium sulphates, thus tended to decrease the average effect of barium sulphate only when ^{85}Sr with 100 μM carrier (largest carrier dose examined) was administered.

Sulphates in fasting and fed rats. Results of the two experiments are collected in Table 6. Substantially less ^{85}Sr was absorbed from the intestine of feeding than fasting animals. Barium sulphate alone decreased the retention of ^{85}Sr only in the fasting rats; on the others it had no effect. The combination of barium and sodium sulphates decreased the average retention of ^{85}Sr after 48 hours to the same level in both groups. Taking into consideration that the feeding control animals retained significantly less ^{85}Sr than the fasting animals

Table 2

Adsorption of ^{85}Sr on Skiabaryum and various barium sulphate preparations in vitro (solution incubated 20 hours at room temperature with 0.4 % sulphate)

Preparation	Percentage of adsorbed ^{85}Sr	
	Barium sulphate	Barium and Sodium sulphate
Skiabaryum	53.1	79.8
Barium sulphates:		
Preparation I	62.2	95.5
Preparation II	21.8	86.3
Preparation III	40.4	86.6

Table 3

Relative effectiveness of two barium sulphate preparations administered orally in doses of 0.8 mM 10 min after oral contamination with ^{85}Sr

Barium sulphate	Percentage of ^{85}Sr administered[1]	
	Whole body	Skeleton[2]
Preparation I	11.7 ± 3.8	9.9 ± 3.6
Preparation II	29.5 ± 5.7	23.7 ± 4.1

[1] Arithmetic mean ± standard error of the mean multiplied by t-value for 95 % confidence level. Eight animals per group, 48 hrs after administration of ^{85}Sr.
[2] Content of ^{85}Sr in 1 femur × 20.

(by 70 %), there was of course a relatively more marked decrease after the administration of sulphates to the fasting animals (by 80 % and 90 % in the whole body and the skeleton, respectively) than to the others (by 40 % and 50 %, respectively).

Sulphates in young and adult rats. Results of three experiments are summarized in Table 7. The age difference between the groups compared was relatively small, i.e. from 6 to 13 weeks. Although the average retention of ^{85}Sr was repeatedly higher in the younger than in the older rats, the differences observed in the control rats of various ages were significant only in one of the experiments described.

After the administration of barium sulphate (preparation II) in doses of 3.8 mM per kg bodyweight, young animals of 7 weeks of age retained 50 % more ^{85}Sr in their bones than the adult rats of 20 weeks.

Table 4

Effect of various barium sulphate preparations in vitro and in vivo

Substances tested:	In vitro		In vivo	
	Percentage of ^{85}Sr adsorbed	Ratio of effect[1]	Percentage of ^{85}Sr in the skeleton[2]	Ratio of effect[3]
$BaSO_4I$	62.2		7.4	
Skiabaryum	53.1	1.2	11.0	1.5 n.s.[4]
Skiabaryum	53.1		7.4	
$BaSO_4III$	40.4	1.3	8.5	1.1 n.s.
$BaSO_4I$	62.2		9.9	
$BaSO_4II$	21.8	2.9	23.7	2.4
$BaSO_4I + Na_2SO_4$	95.5		3.1	
Skiabaryum + Na_2SO_4	79.8	1.2	4.8	1.6
$BaSO_4I + Na_2SO_4$	95.5		4.9	
$BaSO_4I$	62.2	1.5	10.6	2.2
$BaSO_4III + Na_2SO_4$	86.6		2.2	
$BaSO_4III$	40.4	2.1	8.5	3.9

[1] Relation of the percentage of ^{85}Sr adsorbed on the more effective means to the percentage of ^{85}Sr adsorbed on the less effective means.
[2] 48 hours after ^{85}Sr administration — both compared values always result from the same experiment.
[3] Relation of the percentage of ^{85}Sr retained after administration of the more effective means to the percentage of ^{85}Sr retained after administration of the less effective means.
[4] The difference in effect is not statistically significant.

An analogic, but statistically not important, difference was observed after the administration of 8.8 mM barium (preparation III) and sodium sulphates per kg bodyweight to rats 10 and 16 weeks old. When 7.6 mM of barium (preparation III) and sodium sulphates per kg bodyweight were given, young growing rats of 7 weeks retained 55 % more ^{85}Sr in their bones than adult animals of 20 weeks. An analogic difference was apparent in control rats of various ages as far as the retention of ^{85}Sr was concerned.

Mineral waters. The whole body retention of ^{85}Sr decreased after the administration of bitter mineral waters by 40 % to 50 % and the skeletal content by 50 % to 60 % in comparison with the controls. The average effect of both mineral waters was practically the same (Table 8). The retention of ^{85}Sr decreased further (significantly) when barium sulphate suspended in bitter mineral waters was administered (by 80 % to 85 % and by 80 % to 90 % in

Table 5

Influence of carrier strontium on effectiveness of sodium and barium (preparation I) sulphates administered orally in doses of 0.8 mM 10 min after oral contamination with ^{85}Sr

Isotopic carrier ($\mu M\ Sr^{2+}$)		Number of animals	Percentage of ^{85}Sr administered[1]		
			Whole body		Skeleton[2]
^{85}Sr	sulphate		After 24 hours	After 48 hours	After 48 hours
	Sodium				
0	0	6	31.3 ± 8.3	18.6 ± 4.0	13.3 ± 3.7
0	10	6	39.5 ± 14.3	20.6 ± 6.3	14.1 ± 3.8
10	0	6	49.1 ± 23.5	24.2 ± 21.8	15.7 ± 11.5
	Barium				
0	0	6	43.8 ± 28.6	17.7 ± 7.3	12.5 ± 5.5
0	10	5	34.7 ± 10.7	23.3 ± 4.5	17.4 ± 4.4
0	100	5	37.6 ± 10.6	26.6 ± 5.6	17.0 ± 2.4
10	0	5	42.2 ± 13.1	24.5 ± 13.6	18.6 ± 9.1
100	0	5	44.5 ± 33.6	26.8 ± 9.3	19.0 ± 5.1

[1] Arithmetic mean ± standard error of the mean multiplied by t-value for 95 % confidence level.
[2] Content of ^{85}Sr in 1 femur × 20.

the whole body and in the skeleton, respectively, in comparison with controls). The average effect of barium sulphate suspended in 'Zaječická hořká' (Middle Bohemian Springs) was significantly better (by 50 %) than in 'Šaratica' (Moravian-Silesian Springs). (For chemical composition of these mineral waters, see Table 1.)

Discussion

Barium sulphate preparations bind radiostrontium in vitro to a varying degree and this is reflected in various degrees of decontamination effectiveness in vivo. Many factors during the precipitation of barium sulphate are important; these include the concentration of Ba^{2+} ions in solution, the ratio of Ba^{2+} ions to SO_4^{2-}, the solvent, the age of the solutions used, the presence of foreign ions and other impurities, and the method of precipitation, temperature, and other conditions (LIESER & FABRIKANOS 1959). Barium sulphate precipitates of various forms were obtained in this way by the effect of the concentration of the barium hydroxide and sulphuric acid used for precipitation (SUITO & TAKIYAMA 1954).

The electron microscope photographs of the present investigation are very similar to those of the Japanese authors. The barium sulphate particles are seen to grow, i.e. preparation I < preparation III < preparation II. There

Table 6

Effect of barium sulphate (preparation I) administered orally in doses of 0.8 mM 10 min after oral contamination with ^{85}Sr to fasting and feeding rats

Substances tested	Number of animals	Percentage of ^{85}Sr administered: Whole body, After 24 hours, $\bar{x} \pm ts_{\bar{x}}$[2]	Whole body, After 24 hours, Percentage of control	Whole body, After 48 hours, $\bar{x} \pm ts_{\bar{x}}$	Whole body, After 48 hours, Percentage of control	Skeleton[1], After 48 hours, $\bar{x} \pm ts_{\bar{x}}$	Skeleton[1], After 48 hours, Percentage of control
Controls fasted	4	38.0 ± 32.9	100	27.8 ± 22.0	100	22.2 ± 17.9	100
Controls fed	4	19.0 ± 3.3	n.s.[3]	14.9 ± 2.7	n.s.	9.7 ± 1.5	n.s.
$BaSO_4$ fasted	4	17.4 ± 8.4	n.s.	8.6 ± 7.6	n.s.	7.4 ± 6.7	n.s.
$BaSO_4$ fed	6	20.8 ± 15.4	n.s.	11.5 ± 4.5	n.s.	8.8 ± 3.5	n.s.
Controls fasted	6	45.5 ± 17.6	100	21.9 ± 10.8	100	16.9 ± 10.9	100
Controls fed	6	28.6 ± 5.1	n.s.	6.8 ± 2.9	31	4.6 ± 2.1	27
$BaSO_4$ Na_2SO_4 fasted	6	37.0 ± 14.1	n.s.	4.2 ± 2.2	19	1.7 ± 0.9	10
$BaSO_4$ Na_2SO_4 fed	6	29.8 ± 19.0	n.s.	4.5 ± 1.4	20	2.2 ± 0.7	13

[1] Content of ^{85}Sr in 1 femur × 20.
[2] Arithmetic mean ± standard error of the mean multiplied by t-value for 95 % confidence level.
[3] Difference not statistically significant.

is also a certain difference between preparation III and Skiabaryum, the latter containing additional substances. The microscopic appearances are in accord with the results of the experiments in vitro, as well as in vivo where the effectiveness increases in a reversed sequence in relation to the size of particles, i.e. preparation II < preparation III < preparation I. A somewhat higher percentage of ^{85}Sr is absorbed by Skiabaryum in vitro in comparison with preparation III. This can be explained by the presence of bentonite with a high exchange capacity for radiostrontium in a neutral medium (KNAJFL 1963).

The sorptive capacity of all barium sulphate preparations was considerably improved by adding free sulphate ions. This increase was more marked with the less effective means so that differences between various preparations disappeared. Their effectiveness in vivo in the presence of sodium sulphate also

Table 7

Effect of barium sulphate administered orally, alone or in combination with sodium sulphate, 10 min after oral contamination with ^{85}Sr, followed in rats of various ages

Age group (body weight)	Substances tested (mM/kg b.wt.)	Number of animals	Percentage of ^{85}Sr administered					
			Whole body				Skeleton[1]	
			After 24 hours		After 48 hours		After 48 hours	
			$\bar{x} \pm ts_{\bar{x}}$[2]	Percentage of control	$\bar{x} \pm ts_{\bar{x}}$	Percentage of control	$\bar{x} \pm ts_{\bar{x}}$	Percentage of control
7 weeks	Controls	6	46.3 ± 20.4	100	38.4 ± 17.1	100	35.4 ± 18.7	100
(70 g)	$BaSO_4$II (3.8)	6	36.2 ± 9.2	n.s.[3]	29.8 ± 2.7	n.s.	28.9 ± 8.0	n.s.
20 weeks	Controls	6	50.2 ± 15.4	n.s.	34.2 ± 18.8	n.s.	26.4 ± 15.7	n.s.
(210—225 g)	$BaSO_4$II (3.8)	6	31.7 ± 17.0	n.s.	20.4 ± 9.6	n.s.	14.5 ± 8.4	n.s.
10 weeks	Controls	6	47.3 ± 0.6	100	36.8 ± 6.2	100	29.1 ± 5.4	100
(100 g)	$BaSO_4$III + Na_2SO_4 (8.9)	6	29.2 ± 1.1	62	13.3 ± 5.7	36	10.1 ± 4.8	35
16 weeks	Controls	6	41.0 ± 1.6	100	31.3 ± 12.4	100	26.6 ± 9.4	100
(180—185 g)	$BaSO_4$III + Na_2SO_4 (8.9)	6	20.8 ± 1.0	51	9.5 ± 5.2	30	6.3 ± 3.5	24
7 weeks	Controls	6	68.7 ± 9.9	100	52.4 ± 7.6	100	47.6 ± 5.6	100
(70—80 g)	$BaSO_4$III + Na_2SO_4 (7.6)	6	18.8 ± 5.1	27	11.0 ± 2.2	21	10.5 ± 3.0	22
	Controls							
20 weeks	$BaSO_4$III	6	45.0 ± 17.0	100	30.0 ± 9.6	100	26.1 ± 8.9	100
(210—220 g)	+ Na_2SO_4 (7.6)	6	33.5 ± 9.6	74	7.1 ± 2.9	24	5.1 ± 2.3	20

[1] Content of ^{85}Sr in 1 femur × 20.
[2] Arithmetic mean ± standard error of the mean multiplied by t-value for 95 % confidence level.
[3] Difference not statistically significant.

differed only slightly. Skiabaryum with sodium sulphate was the least effective of all the combinations tested in vitro and in vivo. We assume a disturbing influence of other ingredients in Skiabaryum to be the cause but this could not be confirmed in the experiments.

Many authors pay attention to the influence of a stable isotopic carrier

Table 8

Effect of saline bitter mineral waters and their combinations with barium sulphate (preparation III) administered orally 10 min after oral contamination with ^{85}Sr

Substances tested	Number of animals	Percentage of ^{85}Sr administered					
		Whole body				Skeleton[1]	
		After 24 hours		After 48 hours		After 48 hours	
		$\bar{x} \pm ts_{\bar{x}}$[2]	Percentage of control	$\bar{x} \pm ts_{\bar{x}}$	Percentage of control	$\bar{x} \pm ts_{\bar{x}}$	Percentage of control
Controls	6	51.0 ± 10.4	100	43.9 ± 9.0	100	38.1 ± 8.0	100
Šaratica	5	27.5 ± 11.7	54	21.5 ± 7.5	49	18.7 ± 6.9	49
Zaječická	5	23.7 ± 3.6	46	17.9 ± 3.6	41	14.1 ± 2.9	37
$BaSO_4$ + Šaratica	5	14.0 ± 9.4	27	8.8 ± 4.9	20	7.9 ± 2.9	21
$BaSO_4$ + Zaječická	5	17.5 ± 11.2	34	6.6 ± 2.6	15	4.0 ± 1.4	11

[1] Content of ^{85}Sr in 1 femur × 20.
[2] Arithmetic mean ± standard error of the mean multiplied by t-value for 95 % confidence level.

on the metabolism of radiostrontium. This paper deals only with a carrier administered orally.

Copp & Greenberg (1944) observed that a large dose of carrier strontium (50 mg) had little effect on the intestinal absorption of ^{85}Sr in rats. Whether on stock diet or on a diet low in calcium the animals retained less radiostrontium only when administered simultaneously with carrier. Gross et coll. (1954) administered to rats by stomach tube up to a hundred times the normal daily intake of stable strontium mixed with ^{90}Sr and ^{90}Y daily for seven consecutive days. The amount of stable strontium used did not alter the uptake of ^{90}Sr. Jones (1955), who administered radiostrontium orally in addition to varying amounts of carrier (1—500 μg) per gram bodyweight to fasting rats, observed that the urinary radiostrontium increased threefold after the highest dose; however, the skeletal retention did not change in comparison with the controls. Rubanovskaia & Ushakova (1957) concluded that after the administration of ^{89}Sr by stomach tube, followed immediately by 'treatment' with strontium lactate (50 mg per rat per day) for twelve days, the elimination of ^{89}Sr from the bone as well as from the whole organism was not substantially enhanced. According to Khomutovskii (1959) a previous, four-day oral administration of strontium nitrate (100 mg per diem) does not increase the elimination of ^{89}Sr in rats.

HARRISON et coll. (1957) considered that the amount of radiostrontium absorbed from the alimentary canal after a single dose is approximately proportional to the dose. However, there is a relatively small effect on the retention of an oral dose of radiostrontium because the rate of its urinary excretion increases at the same time; this increase indicates the progression within the range of 2 to 400 μg carrier strontium per gram bodyweight. KAWIN (1959) administered radiostrontium together with increasing doses of stable strontium (0 to 1 263 μg Sr^{2+}) per gram bodyweight. After the oral administration and sufficiently high carrier doses the retention of radiostrontium increased towards, but did not exceed, values obtained following intraperitoneal injection.

The present authors administered 10 μg Sr^{2+} (per 200 gram bodvweight), i.e. approximately 4.5 μg/gram bodyweight. There was also a tenfold addition of carrier with barium sulphate, an amount that, according to HARRISON et coll. (1957) and KAWIN (1959), may influence the absorption and elimination of radiostrontium but not its skeletal retention. BERÁK (1963), when investigating the influence of various ions on the ability of barium sulphate to bind radiostrontium in vitro, obtained the lowest percentage of sorption in preparations contaminated by Sr^{2+}.

The carrier added to ^{85}Sr could consequently, in the presence of sulphates lead to an undesirable effect, especially in the case of barium sulphate where the retention of ^{85}Sr tends to increase with the carrier. It is also possible that ^{85}Sr in the presence of a carrier is adsorbed to a smaller extent on the gastric mucosa and passes to the small intestine where it is better absorbed than carrier-free ^{85}Sr and the possibility of its binding by sulphate is thus decreased.

Fasting animals were often used when attempts were made to influence the intestinal absorption of radiostrontium. The aim was to exclude the effect of a complex of known and unknown factors upon the intestine during the digestion of food. These factors include surface adsorption, the forming of soluble or insoluble complexes, ion exchange etc.

It was apparent from CRAMER's experiments (1959) that previous feeding increased the emptying of stomach and the movement of radiostrontium through the duodenum and jejunum but resulted in longer retention in the ileum. The emptying of the colon also occurred earlier.

Other authors also observed the difference between the radiostrontium retention in feeding and fasting animals. COPP & GREENBERG (1944) report that the absorption in rats, fasting for two days prior to, or following the administration of, strontium increased.

MACDONALD et coll. (1955) administered foods with varying calcium and phosphorus levels immediately after an oral dose of ^{90}Sr to fasting rats. The administration of a standard rat diet (0.75 g in 2 ml distilled water per dose) decreased under these conditions the skeletal retention of ^{90}Sr by 30 % in comparison with the controls. On the other hand, according to JONES (1955) the fact that rats were fasting up to 24 hours before the administration of radiostrontium did not influence its retention. When rats fasted even after that, the absorption doubled. TAYLOR et coll. (1962) reported that in starved as well as fed rats, 6 to 8 weeks of age, the same amount of ^{85}Sr was observed, whereas in older animals (60 to 70 weeks of age) which had been starved for 18 hours before the administration of radiostrontium its absorption increased significantly (by 50 % 7 hours after the administration). Finally, BRUCE (1963) confirmed the results of MACDONALD et coll. (1955) and stated that the retention of radiostrontium decreased threefold when stock diet containing 30 % bone meal was fed immediately after the dose of radiostrontium.

In the present experiments, the ^{85}Sr was administered regularly in the morning. It is probable, owing to the daily cycles in rats, that the intestines were filled at the moment of ^{85}Sr administration when fed ad lib. The fasting animals in one of the experiments were fed with several grams of food immediately before the ^{85}Sr was administered.

The animals in the present experiments absorbed two and a half times more ^{85}Sr when fasting than after feeding on a standard laboratory diet, which is in agreement with results obtained by the previously mentioned authors. The unusually high radiostrontium absorption from the digestive tract observed in a previous clinical study in fasting human subjects could also be explained in this way (VOLF 1963). There is actually no discrepancy with other published data according to which there was much less absorption after the administration of radiostrontium with breakfast. Two cases of accidental ^{90}Sr inhalation in fasting man after several hours of work (VOLF 1961) are recalled. The degree of radiostrontium absorption might of course in other cases be influenced by the presence of food in the intestine.

An important conclusion may therefore be drawn that while after the administration of barium sulphate alone there was no difference between the treated rats and the fed controls, a significant difference appeared after the administration of the same preparation I of barium sulphate combined with sodium sulphate. The skeletal retention of ^{85}Sr then decreased after treatment to approximately the same level in fasting as in the other animals. This means that a sufficiently effective substance might cause a decrease in the intestinal radiostrontium absorption in the presence of various food components; furthermore, less effective means might influence the result to a hardly greater extent than the food alone.

It is known that radiostrontium accumulates in the bones of young growing animals at a higher rate and in greater amounts than in adults. It may be expected that the response to various interferences with the radiostrontium metabolism will also depend on the age of the experimental animal.

WASSERMAN & COMAR (1960) assumed that the effectiveness of dietary calcium in reducing radiostrontium retention may be influenced mainly by the maturity of the animal, apart from the calcium-phosphorus ratio of the diet. In immature rats, elevated dietary calcium levels reduce the body burden of dietary radiostrontium almost proportionally, while in adult rats it is necessary to increase the dietary calcium and phosphorus simultaneously and still the final effect is less marked.

LINIECKI et coll. (1962) also observed that a high strontium diet substantially reduced known differences in the retention of intravenously injected ^{90}Sr in animals of various ages. The whole body retention of ^{90}Sr (80 days after injection) was in comparison with controls five times lower in the group of youngest rats (1 1/2 months of age,) three times lower in the older (7 1/2 months of age), and twice as low in the oldest rats (13 1/2 months of age). MICHON & GOULLOUX (1958), however, observed in short-term experiments, in which radiostrontium was administered in a single dose, that the ion exchangers minimized its intestinal absorption more in adult than in young rats.

The retention of ^{85}Sr in the present experiments was lower in adults than in the young rats in which sulphates were administered in the same quantity per unit of bodyweight. However, when comparing the treated animals with the respective controls, it seems that there is only a slight difference in the relative decrease of ^{85}Sr retention in animals of various ages. In other words it is possible with treatment performed in time to reduce the intestinal radiostrontium absorption to approximately the same extent in young as in adult animals. It must nevertheless be remembered that the final radiostrontium retention will be substantially higher in younger than in older individuals.

Finally the possibility of simple practical applications of the results achieved was investigated with natural mineral waters. 'Zaječická hořká' is a pure bitter mineral water and contains about two and a half times more magnesium ions than sodium ions. 'Šaratica' is on the other hand a concentrated saline bitter mineral water, containing three times more sodium ions than magnesium ions. The total content of sulphate ions is the same in both mineral waters. The effect of bitter mineral waters and their combination with barium sulphate did not differ in principle from results achieved after the administration of various sulphates and their combinations.

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SUMMARY

The average effect of various barium sulphates differed substantially but always increased considerably in the presence of soluble sulphates. The action of sulphates was only slightly influenced by carrier strontium. Barium sulphate in fed animals decreased the retention of ^{85}Sr only in combination with sodium sulphate.

ZUSAMMENFASSUNG

Die durchschnittliche Wirksamkeit verschiedener Bariumsulfate schwankte beträchtlich, aber sie zeigte sich immer stark vergrössert wenn lösliche Sulfate anwesend waren. Die Aktivität der Sulfate war nur begrenzt abhängig von der Anwesenheit von Trägerstrontium. Die Fütterung von Versuchstieren mit Bariumsulfat verminderte die Retention von ^{85}Sr lediglich in Kombination mit Sodiumsulfat.

RÉSUMÉ

L'effet moyen de divers sulfates de baryum sur la rétention de ^{85}Sr chez des rats diffère de façon importante, mais augmente toujours considérablement en présence de sulfates solubles. L'action des sulfates n'est que légèrement influencée par le strontium non radioactif. Chez les animaux qui ont mangé, le sulfate de baryum ne diminue la rétention de ^{85}Sr que s'il est associé à du sulfate de sodium.

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