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RETENTION OF ^{85}Sr IN RATS

I. Effect of sodium, magnesium, calcium, strontium and barium sulphates

by

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Barium sulphate has been found to diminish the absorption of radiostrontium from the gastrointestinal tract (BALABUCHA 1959, CATSCH 1956, SEMENOV 1953) and to increase the excretion of absorbed radiostrontium in the faeces in rats (VOLF 1959, 1960). A preparation of barium sulphate was used as 'first-aid' treatment after the accidental inhalation of ^{90}Sr in man and its effectiveness was verified in rats under similar conditions (VOLF 1961). The effect of this preparation on the intestinal absorption and excretion of radiostrontium was also followed up in a clinical study of several cases of carcinoma (VOLF 1963).

MACDONALD et coll. (1952, 1955) described a similar influence of sodium and magnesium sulphates on the absorption of radiostrontium from the intestine. On the other hand, COPP & GREENBERG (1944) reported no substantial decrease in the absorption after the administration of magnesium sulphate, and JONES (1955) doubted the effectiveness of sodium and calcium sulphates.

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RUBANOVSKAIA & USHAKOVA (1957) observed no effects after the repeated administration of magnesium sulphate, and according to TAYLOR et coll. (1962) the absorption of ^{85}Sr from the intestine was not diminished by the administration of sulphate ions.

In view of these contradictory results, the effectiveness of various sulphates on the absorption of ^{85}Sr from the digestive tract of rats was compared under the same experimental conditions. It was borne in mind that although strontium may be bound to barium sulphate mainly by adsorption, it forms the insoluble strontium sulphate with sodium or magnesium sulphates. Whilst barium sulphate is not absorbed from the intestine and passes unchanged, soluble sulphates are partly absorbed and act in the intestine as salinic cathartics.

Combinations of various sulphates were tested in these experiments, considering and also the possibility of increasing the effect of the sulphates as well as of hastening the movement of the intestinal contents, and thus also of the sulphates with bound radiostrontium.

Methods

Experimental animals. In all, 272 male Wistar albino rats, weighing 165 to 205 g, were used. In each experiment, animals with the smallest possible difference in weight (generally 10 to 20 g) were employed. The rats were kept in metabolic glass cages (VOLF 1958), and were given a standard Larsen diet and drinking water ad lib. Food and water were removed before the beginning of the experiment (at 20 and 12 hours respectively) and replaced in the cages two hours later. Radiostrontium and sulphates were given by a stomach tube under light ether anaesthesia. Care was taken to administer equal quantities of liquid to each animal. The rats were sacrificed 48 hours after the administration of radiostrontium.

Radioactive ^{85}Sr chloride was supplied by the Nuclear Science and Engineering Corporation of Pittsburgh, U.S.A., diluted in 0.5 N of hydrochloric acid; radiochemical purity 99 %, total content of 0.1 mg of solids in 0.77 mCi. This stock solution was diluted with distilled water and adjusted to a pH of 6 to 7 with sodium hydrogen carbonate. Each animal was given 1 to 2 μCi ^{85}Sr in 0.1 ml.

Tested substances. The calcium, strontium and barium sulphates were prepared in the laboratory and the sodium and magnesium sulphates were obtained from Lachema, ČSSR. Skiabaryum (Slovakofarma, ČSSR) consists of barium sulphate (86.8 %), talc (10.0 %), bentonite (3.0 %), sodium citrate (0.2 %) and correctives. The preparations were of equimolar strength in all the experiments. The sulphates were administered orally, 0.8 mM in 2 ml of distilled H_2O per dose, in the first experiment immediately after oral contamination with ^{85}Sr, in the other experiments 10 min later. Each dose of Skiabaryum also had to contain 0.8 mM of barium sulphate.

Measurements. The whole-body activity of the rats was determined with the scintillation equipment of the institute. A NaI crystal (Tl) 45 × 25 mm (later 45 × 50 mm), in connection with a photomultiplier, was used for detection. The animals were placed in round aluminium boxes (100 mm in diameter, covered by perforated 3 mm plastic material) and these were put in a lead shielding under the center of the crystal at a distance of 15 cm. The counting efficiency of the equipment was 0.5 to 1%, which is satisfactory for whole-body counting with doses of ^{85}Sr administered in short-term experiments. Counting of the whole-body activity in the rats was started 15 min after the administration of ^{85}Sr and repeated after 24 and 48 hours.

The dissected femur was placed in a test tube, dissolved in 1 ml concentrated nitric acid and scintillation counting was performed with a well-type NaI crystal (Tl). The counting efficacy was between 30 and 40 %, sufficient counts being taken to keep the statistical counting error within 2 %.

Evaluation of results

All values are expressed as a percentage of the administered dose. For the total retention of ^{85}Sr, the number of counts per minute obtained with each rat during the initial whole-body measurement was considered to be 100 %. For the ^{85}Sr retained in the bones, 100 % of the administered dose was determined by means of standards prepared by injecting one ^{85}Sr dose into a known volume of carrier strontium solution. The amount of ^{85}Sr retained in the whole skeleton was calculated by multiplying the percentage of the ^{85}Sr dose detected in one femur by an empirical factor of twenty.

The arithmetic means as well as their 95 % confidence level were calculated (standard errors of the means multiplied by the corresponding t-values were added to and subtracted from the arithmetic means). The average values were compared with the help of Duncan's test (DUNCAN 1957) of simultaneous evaluation of many averages, modified to various variances of each group compared. Where the average of the experimental values differed significantly from the control values, the effectiveness of various factors in influencing the metabolism of ^{85}Sr was calculated and expressed in the form of a percentage of the control values.

The appendix gives detailed information regarding the methods of statistical evaluation.

Table 1

Effect of Skiabaryum and various sulphates administered orally in doses of 0.8 mM immediately or 10 min after oral contamination with ^{85}Sr

Substances tested	Time of adminis-tration	Number of animals	Percentage of ^{85}Sr administered: Whole body, After 24 hours, $\bar{x} \pm ts_{\bar{x}}$ **	Percentage of control	Whole body, After 48 hours, $\bar{x} \pm ts_{\bar{x}}$	Percentage of control	Skeleton*, After 48 hours, $\bar{x} \pm ts_{\bar{x}}$	Percentage of control
Controls	Immedi-	18	28.8 ± 6.1	100	20.6 ± 4.8	100	19.0 ± 4.5	100
Na_2SO_4	ately after	6	20.1 ± 3.2	n.s.***	12.8 ± 1.7	n.s.	10.4 ± 2.3	55
$MgSO_4$	^{85}Sr	6	25.1 ± 14.5	n.s.	13.9 ± 4.5	n.s.	12.7 ± 3.5	n.s.
$CaSO_4$		6	35.3 ± 14.2	n.s.	15.7 ± 10.4	n.s.	10.5 ± 1.8	55
$SrSO_4$		6	22.0 ± 17.3	n.s.	16.4 ± 10.4	n.s.	12.8 ± 11.4	n.s.
$BaSO_4$		6	22.5 ± 10.4	n.s.	8.5 ± 3.5	41	4.9 ± 3.3	26
Skiabaryum		6	22.0 ± 16.2	n.s.	12.9 ± 7.2	n.s.	11.0 ± 5.7	58
Controls	10 min	12	48.3 ± 9.4	100	35.0 ± 6.7	100	32.4 ± 6.7	100
Na_2SO_4	after ^{85}Sr	5	31.2 ± 23.4	65	25.0 ± 16.8	71	20.4 ± 12.9	63
$MgSO_4$		6	52.9 ± 13.6	n.s.	22.6 ± 5.6	64	18.6 ± 5.5	57
$CaSO_4$		6	25.4 ± 8.8	44	14.2 ± 5.7	40	12.6 ± 7.9	39
$SrSO_4$		6	45.4 ± 19.1	n.s.	25.5 ± 8.4	73	21.9 ± 7.8	68
$BaSO_4$		6	32.4 ± 9.5	67	19.4 ± 3.2	55	14.7 ± 1.7	45
Skiabaryum		6	31.3 ± 13.2	65	22.1 ± 8.4	63	18.9 ± 7.1	58
Controls	10 min	12	55.1 ± 15.6	100	35.8 ± 6.8	100	24.2 ± 4.5	100
Na_2SO_4	after ^{85}Sr	6	29.3 ± 10.5	53	16.1 ± 6.5	45	11.7 ± 5.0	48
$MgSO_4$		6	31.4 ± 10.3	57	16.0 ± 4.0	45	9.9 ± 2.9	41
$CaSO_4$		6	41.4 ± 21.3	n.s.	16.0 ± 5.0	45	10.8 ± 3.1	45
$SrSO_4$		6	36.1 ± 10.2	66	25.4 ± 7.1	71	18.3 ± 4.7	76
$BaSO_4$		5	34.9 ± 27.3	53	10.6 ± 6.6	30	7.4 ± 4.6	31
Skiabaryum		6	46.5 ± 19.5	n.s.	16.9 ± 5.3	45	11.0 ± 4.0	45

* Content of ^{85}Sr in 1 femur times 20

** Arithmetic mean ± standard error of the mean multiplied by t-value for 95 % confidence level

*** The difference is not statistically significant

Results

Data from three experiments designed to study the effect of equimolar amounts of Skiabaryum and various sulphates upon the intestinal absorption of ^{85}Sr are collected in Table 1. The average whole-body retention 24 hours after ^{85}Sr administration in the treated animals was between 30 and 50% lower as compared with the controls, although this could not always be proved

Table 2

Effect of various sulphates and their combinations administered orally in doses of 0.8 mM 10 min after oral contamination with ^{85}*Sr*

Substances tested	Number of animals	Percentage of ^{85}Sr administered					
		Whole body				Skeleton*	
		After 24 hours		After 48 hours		After 48 hours	
		$\bar{x} \pm ts_{\bar{x}}$**	Percentage of control	$\bar{x} \pm ts_{\bar{x}}$	Percentage of control	$\bar{x} \pm ts_{\bar{x}}$	Percentage of control
Na_2SO_4	10	43.6 ± 11.3	100	30.0 ± 6.3	100	22.4 ± 4.7	100
$MgSO_4$	10	33.1 ± 8.5	n.s.***	22.0 ± 3.9	73	17.8 ± 3.6	n.s.
$CaSO_4$	5	33.8 ± 10.6	n.s.	22.2 ± 7.5	n.s.	18.0 ± 5.9	n.s.
$BaSO_4$	5	54.4 ± 34.2	n.s.	11.5 ± 8.2	38	8.2 ± 4.0	36
$CaSO_4 + Na_2SO_4$	5	28.2 ± 14.3	n.s.	16.3 ± 4.6	54	14.8 ± 5.3	66
$CaSO_4 + MgSO_4$	6	44.0 ± 24.9	n.s.	21.9 ± 9.7	n.s.	16.1 ± 4.3	72
$BaSO_4 + Na_2SO_4$	5	22.7 ± 11.8	52	5.7 ± 2.3	19	3.7 ± 1.6	16
$BaSO_4 + MgSO_4$	6	21.6 ± 7.6	50	6.7 ± 3.0	22	4.4 ± 2.0	19
Controls	12	33.7 ± 9.0	100	24.9 ± 7.7	100	22.4 ± 6.8	100
$CaSO_4$	6	24.3 ± 8.7	n.s.	18.2 ± 6.7	n.s.	15.8 ± 6.4	n.s.
$BaSO_4$	6	19.7 ± 6.8	58	12.0 ± 3.0	48	10.6 ± 3.1	47
$CaSO_4 + Na_2SO_4$	6	21.2 ± 8.4	63	12.5 ± 4.2	50	9.4 ± 3.3	42
$CaSO_4 + MgSO_4$	6	24.6 ± 9.2	n.s.	14.4 ± 6.0	58	10.5 ± 3.5	47
$BaSO_4 + Na_2SO_4$	6	23.4 ± 26.7	n.s.	6.4 ± 2.7	25	4.9 ± 2.5	22
$BaSO_4 + MgSO_4$	6	20.2 ± 12.2	n.s.	8.6 ± 1.6	34	5.4 ± 3.5	24
Controls	8	41.7 ± 12.3	100	17.7 ± 5.3	100	10.7 ± 3.9	100
Skiabaryum + Na_2SO_4	8	39.4 ± 18.8	n.s.	10.2 ± 3.2	57	4.8 ± 1.0	44
$BaSO_4 + Na_2SO_4$	8	17.0 ± 6.5	41	5.5 ± 1.7	31	3.1 ± 0.8	29

* Content of ^{85}Sr in 1 femur times 20

** Arithmetic mean ± standard error of the mean multiplied by t-value for 95 % confidence level

*** Difference is not statistically significant

statistically. The decrease in the retention of ^{85}Sr was repeatedly significant only with sodium and barium sulphates. Calcium sulphate in one of the experiments was considerably more effective than magnesium and strontium sulphates.

The differences in the average whole-body retention of ^{85}Sr, 48 hours after its administration, were more marked and corresponded roughly with differences observed in the skeletal retention of ^{85}Sr. There was no substantial difference between the effectiveness of the sulphates and Skiabaryum, except in the case of strontium sulphate which in one of the experiments was considerably less effective. It reduced the retention of ^{85}Sr by 29 % at the utmost, this being the lowest effect observed. After barium sulphate, on the other hand, there was always a marked decrease; 70 % was the highest observed efficacy. Yet, regarding the average effect, the barium sulphate group did not show any substantial difference from the other experimental groups.

There was a significant decrease in the skeletal content of ^{85}Sr after the administration of sulphates and Skiabaryum, usually by 40 to 60 %. There was no marked difference in the average effect of the sulphates tested or of Skiabaryum, with the exception of strontium sulphate which decreased the average retention of ^{85}Sr by a maximum of 32 % in comparison with the controls. This represents the lowest effect observed. In one case it was impossible to prove any great decrease in the retention of ^{85}Sr even after magnesium sulphate. Barium sulphate, however, lowered the average skeletal retention by as much as 74 % which is the highest effectiveness observed although the average effect of barium sulphate could not even here be statistically distinguished from the effect of other agents.

The effect of the substances tested, and administered immediately after oral contamination with ^{85}Sr, seems to differ only slightly from the effect of the same substances when given 10 min later.

Data from two experiments, in which a comparison was made of the action of sulphates when administered alone and in combination, are given in Table 2. This table also shows the results of another experiment in which a combination of Skiabaryum with sodium sulphate was tested.

When adding sodium or magnesium sulphate to calcium sulphate, the effect on ^{85}Sr retention improved only slightly, especially as compared with sodium sulphate alone (roughly by 30 %).

A significantly greater effect than with sulphates alone was produced by a combination of barium sulphate with sodium or magnesium sulphate. The average retention of ^{85}Sr after 48 hours in comparison with the controls and with sodium sulphate decreased by about 80 %. These combinations were also more effective: by about 70 to 80 % as compared with magnesium sulphate, by 50 to 60 % compared with calcium sulphate, and by 30 to 50 % when compared with barium sulphate. There was always a more marked decrease in the retention of ^{85}Sr in the skeleton than in the whole organism.

The combination of barium and sodium sulphates was significantly more effective than a similar combination of Skiabaryum with sodium sulphate. The whole body retained 45 % less and the skeleton 35 % less ^{85}Sr after the administration of barium and sodium sulphates than after Skiabaryum. The difference is statistically significant.

Discussion

It is generally accepted that the appearance of ingested radiostrontium in bone is a reliable index of its absorption from the gut when animals are under similar physiologic conditions (WASSERMAN et coll. 1956). The effect on the absorption of ^{85}Sr of the sulphates tested was therefore estimated particularly according to the decrease in the skeletal retention of ^{85}Sr when given orally. Most of the experiments were based on a standard experimental design with equimolar amounts of sulphates administered to fasting rats in single doses, ten minutes after oral contamination with radiostrontium. The sulphates used (0.8 mM per dose) would in man correspond to approximately 100 gram of substance and the volume of liquids to 0.7 l. First-aid in practice could hardly be rendered earlier than 10 min after the accident.

As a considerably lower retention of ^{85}Sr was observed in the control animals given water immediately after radiostrontium (see Table 1), the possibility of a diminution of the ^{85}Sr absorption by transfer of the strontium into distal parts of the intestine was considered. A group of rats, given 2 ml drinking water immediately after oral contamination, exhibited in another experiment significantly lower retention of ^{85}Sr in comparison with another group in which an equal quantity of water was given ten minutes later. The experiment was performed in spring, and again several months later, with as much as 8 ml water given immediately after radiostrontium, without influencing its absorption (unpublished results). This may be explained by the observation of MICHON & QUILLOUX (1959) who, in investigating the normal passage of radiostrontium through the alimentary tract of the rat, noticed a remarkable retardation at the stomach level just in spring when the animals change fur, a considerable amount of swallowed hair was present in the stomach of the rats dissected and absorption of ingested radiostrontium by the hair was presumed. An accelerated passage of radiostrontium through the intestine after the administration of several millilitres of water was also noted.

The decontamination efficacy of the various sulphates tested did not differ substantially, although their mechanism of action was not identical.

Whole-body counting at 24 hours after the administration of radiostrontium indicated no definite effect, probably because faeces containing the unabsorbed ^{85}Sr were not yet excreted. The retention of ^{85}Sr, 48 hours after the administration of sulphates decreased by 30 to 70 % in comparison with the controls.

Barium sulphate, mainly owing to its sorptive properties, minimizes the absorption of radiostrontium. Regarding effectiveness in vivo, it is significant that the solubility of sulphates decreases in the order: calcium sulphate > strontium sulphate > barium sulphate. Barium and strontium sulphate are isomorphous, whereas calcium sulphate is not, neither with barium nor strontium sulphate. Exchange takes place in vitro between the ions of Sr^{2+} from the solution and ions of Ca^{2+} (or Ba^{2+}) from calcium or barium sulphates. The ratio between the ions of Sr^{2+} in solution and on the surface of calcium sulphate (expressed in mole) is approximately 1, while a similar ratio in the case of barium sulphate is approximately 0.1; barium sulphate is therefore substantially more effective (LIESER & HILD 1959).

The present experimental results suggest, however, that in vivo barium sulphate does not differ substantially from calcium sulphate or other sulphates, except strontium sulphate in which the lowest average effectiveness was observed. In this connection it is interesting that strontium was the least effective of the alkaline earth metals (except beryllium) in reducing the intestinal absorption of ^{85}Sr when using in vivo perfusion techniques in rats (MRAZ 1962).

Skiabaryum consists of talc, bentonite and sodium citrate, as well as of barium sulphate. Talc was without effect in the sorption of radiostrontium in decontamination experiments in vitro. The effect of bentonite decreased with increasing acidity (KNAJFL 1962); this also may be the reason why bentonite was without effect in vivo (COPP & GREENBERG 1944, MACDONALD et coll. 1952). Sodium citrate, which could be expected to stimulate intestinal strontium absorption, is present only in negligible quantities; but according to WASSERMAN et coll. (1956) even 0.84 mM of sodium citrate per dose produced no increase in the intestinal absorption of ^{85}Sr in rats.

A comparison of the effect of Skiabaryum and barium sulphate alone in relation to ^{85}Sr disclosed no marked difference. Skiabaryum, combined with sodium sulphate, however, was significantly less effective than a combination of barium and sodium sulphates. It may therefore be assumed that the presence of the other components in Skiabaryum is not desirable for the purposes under consideration.

Sodium and magnesium sulphates are able to dilute the intestinal contents and stimulate their passage by inhibiting the reabsorption of water from the intestine. They form in the presence of stable strontium the less soluble strontium sulphate. It was therefore suggested by SCHUBERT (1955) that after accidental radiostrontium contamination, the treatment of choice would appear to be magnesium sulphate in combination with a laxative and possibly an antacid as well. However, as indicated by WALSER et coll. (1961), unless carrier-strontium is given, the product of strontium and sulphate concentrations in plasma or urine cannot conceivably approach the solubility product of this salt. Hence the result observed in the case of carrier-free strontium may be due to an effect of absorbed sulphate, on urinary excretion of strontium, or due to impaired intestinal absorption of the strontium sulphate complex.

A synergic stimulating action of the absorbed sulphate ions could thus be presumed with both the sulphates; with magnesium sulphate, also from the influence of magnesium ions. CATSCH & MELCHINGER (1959) described a decrease in the skeletal retention of intraperitoneally injected radiostrontium in rats (by 30 to 40 %) if various compounds containing magnesium were administered simultaneously. NELSON et coll. (1963) observed in their experiments with mice that the effect of magnesium sulphate, injected intraperitoneally, on the retention of radiostrontium, was of the same order of magnitude as that of strontium chloride. When CLARK & SMITH (1962) injected magnesium sulphate, the elimination of ^{89}Sr increased in rats that had been given the isotope either one or thirty days before treatment. Oral administration of magnesium chloride increased the urinary excretion of ^{89}Sr although the faecal ^{89}Sr decreased. CLARK & SMITH followed only the elimination of radiostrontium. KROLL (1960) observed an increase in urinary ^{85}Sr, after the intraperitoneal injection of sodium and ammonium sulphates and magnesium chloride by about 15 %, and with magnesium sulphate by 49 %. When sodium sulphate was administered orally but simultaneously with ^{85}Sr, a decrease in the skeletal retention of radiostrontium by 60 %, and a fourfold increase in urinary excretion was described by the same author. He therefore assumed that the intestinal resorption of radiostrontium increased as well and that this might have been the effect of absorbed sulphate ions. In dogs, the rate of urinary radiostrontium excretion during the infusion of sodium sulphate increased several times (WALSER et coll. 1961).

When administering sodium and magnesium sulphates we were unable to differentiate between the results achieved with these and the average effect of other sulphates investigated. Although magnesium sulphate caused diarrhoea in two groups of rats, it was ineffective in one of the experiments. The retention of ^{85}Sr, after the administration of sodium sulphate, decreased by 37 to 52 %, and after magnesium sulphate by 43 to 59 %. This is in agreement with the results of KROLL, and with the observation of MACDONALD et coll. (1952) that the ingestion of magnesium sulphate by rats, immediately following the administration of strontium by stomach tube, decreased its skeletal accumulation from 16 % to 5 %; the effect of sodium sulphate was only slightly lower.

The present results were obtained in rats after administering 0.8 mM per dose of sulphates. MACDONALD et coll. (1955) administered sodium sulphate in a dose four times higher, after oral contamination with ^{90}Sr—^{90}Y, but the resulting decrease in radiostrontium retention was only 34 % in comparison with the controls. JONES (1955), who similarly investigated sodium and calcium sulphates, in doses that have not been indicated in detail, doubted whether the decrease achieved in radiostrontium resorption was significant. RUBANOVSKAIA

& USHAKOVA (1957) administered magnesium sulphate (15 mg per dose) to rats repeatedly for twelve days without any noticeable effect. TAYLOR et coll. (1962) reported that the percentage absorption of ^{85}Sr in rats given orally 300 μg of SO_4^{2}ions did not differ significantly in comparison with the controls. SEMENOV (1953) stated that the skeletal retention of ^{89}Sr, in rats previously fed with barium sulphate, was 1.6 to 1.7 times lower than in the control animals. The administration of the barium sulphate first after the radiostrontium was without substantial effect.

The results of various authors are clearly at variance. This may be explained by the effect of sulphates in relation to their dose (cf part III, to be published later in this journal).

It was assumed in administering a combination of sulphates that the effectiveness of a low-soluble sulphate could be increased by the addition of excess sulphate ions in the form of sodium or magnesium sulphates. It is known that after the addition of a soluble sulphate to barium sulphate in vitro, there is a decrease in the concentration of free Ba^{2+} ions, which compete with the adsorption of Sr^{2+} ions. In this way the total capacity of barium sulphate for the binding of radiostrontium is markedly increased while the rate of adsorption remains unchanged. On the other hand, after the addition of sodium sulphate in a millimolar concentration to a relatively more soluble calcium sulphate, the solubility of the latter remains practically unchanged (BERÁK 1963) and therefore an increase of its effect could hardly be expected.

The results of the experiments carried out in rats are in accordance with this presumption. There was no significant increase in the effectiveness of calcium sulphate after the addition of an equimolar amount of sodium or magnesium sulphates. However, the average effectiveness of barium sulphate was significantly improved by this addition and the variance of the average values of ^{85}Sr retention was also reduced. This means higher effectiveness and reliability in treatment.

Appendix (BY Z. ROTH)

Comparison of the average ^{85}Sr retention in several groups of animals

When comparing the average values of whole-body and the skeletal ^{85}Sr retention among various groups of animals, the analysis of variance could not always be used owing to statistically significant differences regarding the variance in different groups in some of the experiments. This was tested by the Bartlett test according to the formula

$$chi^2 = 2.303\,(f \log s^2 - \sum_{i=1}^{k} f_i \log s_i^2) : c$$

where k is the number of variances compared, s_i^2 the variance in the i-th groups, f_i the degrees of freedom of the variance s_i^2, $f = \sum_{i=1}^{k} f_i$, $s^2 = \left(\sum_{i=1}^{k} f_i s_i^2\right) : f$ and $c = 1 + \left[\sum_{i=1}^{k} (1/f_i - 1/f)\right] : 3(k-1)$. This criterion has $k-1$ degrees of freedom.

The comparison of average values in the various groups was made by Duncan's multiple range test for heteroscedastic groups of data (DUNCAN 1957). Differences between the two means compared were adjusted by a factor K_{ij}, where $K_{ij} = \sqrt{\frac{2}{s^2_{\bar{x}_i} + s^2_{\bar{x}_j}}}$ for i-th and j-th group compared.

When testing differences between the compared means, the Duncan's method had to be modified; the use of the common residual variance as described by DUNCAN was not possible owing to the heteroscedascity of the results. In order to assess the sufficiently correct critical value of Duncan's r_p a method was used, analogic to the procedure of WELCH (1949) for the t-test for two groups of differences of variances. For each pair of means we determined the given p (i. e. the difference in ranks of values compared according to their sizes) and a respective value r_p for the number of degrees estimated according to the formula

$$f = \frac{(s^2_{\bar{x}_i} + s^2_{\bar{x}_j})^2}{\frac{s^4_{\bar{x}_i}}{f_i} + \frac{s^4_{\bar{x}_j}}{f_j}}$$

where f_i and f_j are degrees of freedom of the variance. The test procedure was as follows: when the absolute value of the adjusted difference of both marginal values was lower than the critical value r_p, we determined whether another adjusted difference of two means lying between both marginal values was higher than r_p. The critical value was then taken for the same p but in general not for the same f.

This procedure is not entirely correct but approximately equals the Welch procedure for the t-test. It may be concluded therefore that in cases where a significant difference was found between some pair of means the true significance level does not differ too much from the given test value.

The computed average values were completed by calculation of their 95 % confidence intervals, according to the formula

$$x_{1,2} = \bar{x} \pm t_{0.05}\, s_{\bar{x}}$$

where x_1 and x_2 are limits of the confidence interval for the 95 % confidence level and $t_{0.05}$ the critical value of the Student's t.

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SUMMARY

The average retention of ^{85}Sr given orally decreased when various sulphates were administered immediately or ten minutes later. Excepting strontium sulphate, which proved least effective, there was no substantial difference in their effectiveness. When a combination of barium sulphate with sodium or magnesium sulphates was used the results were significantly better than with each sulphate alone.

ZUSAMMENFASSUNG

Die durchschnittliche Aufspeicherung von Radiostrontium wurde vermindert wenn verschiedene Sulfaten sofort oder 10 Minuten nach der mündlichen Verabreichung von ^{85}Sr gegeben wurden. Ausser Strontiumsulfat, das sich am wenigsten wirksam erwies, war kein grosses Unterschied merkbar. Wenn man Bariumsulfat zusammen mit Natrium- oder Magnesiumsulfat gab, wurden die Resultate aber beachtlich besser als wenn man nur ein Sulfat benutzte.

RÉSUMÉ

La fixation moyenne de ^{85}Sr administré par la bouche diminue quand on administre divers sulfates immédiatement ou dix minutes plus tard. Il n'y a pas de différence dans leur efficacité, excepté le sulfate de strontium qui s'est montré le moins efficace. On obtient des résultats notablement meilleurs quand on emploie une association de sulfate de baryum et de sulfate de sodium ou de magnésium qu'avec chacun de ces sulfates isolément.

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