



*Pharmaco-kinetics of  $^{87}\text{Sr}$ - and  $^{103}\text{Ru}$ - humic acid complexes*

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The aim of the study was to test: the effect of HUMET<sub>®</sub>-R in male and female Wistar rats of 200-220 g b.w. on

1. the absorption and urinary, respectively faecal elimination rates of  $^{87}\text{Sr}$  and  $^{103}\text{Ru}$  salts (pooled over 24 hrs; groups 1 through 5, 8 and 9; the experiments were finished 96 hours after the administration of the isotopes);
2. the distribution of radioactivity in the organs (groups 6 and 7) 0.25, 0.5, 1, 2, 4, 8, 12, 24, 48, 72 and 96 hrs after  $^{87}\text{Sr}$  and every 24 hrs after  $^{103}\text{Ru}$  (groups 8 and 9).
3. The employed doses were: 250  $\mu\text{g}$  (3.7 MBq) per kg b.w. of the  $^{87}\text{Sr}$  salt, respectively 90.9 mg (1.91 MBq) per kg b.w. of the  $^{103}\text{Ru}$  salt, and 10 ml/kg b.w. of a humic acid solution of 15 g/L.

The respective groups received:

Group 1:  $^{87}\text{SrCl}_2$  aqueous solution orally (n = 3 males and 3 females).

Group 2:  $^{87}\text{SrCl}_2$  - humic acid complex orally (n = 3 males and 3 females).

Group 3:  $^{87}\text{SrCl}_2$  aqueous solution intraperitoneally (n = 5 males).

Group 4:  $^{87}\text{SrCl}_2$  aqueous solution intraperitoneally, then one hour later HUMET<sub>®</sub>-R orally (n = 5 males).

Group 5:  $^{87}\text{SrCl}_2$  aqueous solution intraperitoneally, then HUMET<sub>®</sub>-R orally 1 hour later and every 24 hour (n = 5 males).

Group 6:  $^{87}\text{SrCl}_2$  aqueous solution orally (n = 33).

Group 7:  $^{87}\text{SrCl}_2$  - humic acid complex orally (n = 33).

Group 8:  $(\text{NH}_4)_2^{103}\text{Ru}(\text{H}_2)\text{Cl}_2$  aqueous solution orally (n = 5 males).

Group 9:  $(\text{NH}_4)_2^{103}\text{Ru}(\text{H}_2)\text{Cl}_2$  - humic acid complex orally (n = 5 males).

By using isotope activities, metabolic balance and organ levels were computed.

Conclusions:

- a) Even little concentration differences proved important since metabolization movements (absorption, distribution, elimination) of these heavy metals are slow, low-capacity processes.
- b) Humic acids slow  $^{87}\text{Sr}$  absorption and its incorporation into the animal bone.
- c) Measured by a low background activity device, still measurable micro-levels of  $^{103}\text{Ru}$  could be detected even 96 hours later. At this time, the tissue levels in the humic-acid treated animals were lower than in the untreated controls.

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Report

on the pharmacokinetic studies of  $^{86}\text{Sr}$ - and  $^{103}\text{Ru}$ - humic acid complex, in rats.  
 (Summary)

Nine groups of rats were treated with the test substances according to the schedule presented below. The results are documented in the attached 16 Tables.

Treatment schedule

| group | experiment  | treatment   | results are in         |
|-------|---|---|------------------------|
| 1     | metabolic balance                                     | aqueous sol. of $^{86}\text{SrCl}_2$ ,<br>p.os  | Table 1.               |
| 2     | metabolic balance                                     | $^{86}\text{SrCl}_2$ -humic acid complex,<br>p.os   | Table 2.               |
| 3     | metabolic balance                                     | aqueous sol. of $^{86}\text{SrCl}_2$ ,<br>i.p.  | Table 3.               |
| 4     | metabolic balance                                     | aqueous sol. of $^{86}\text{SrCl}_2$ , i.p.<br>+ after 1 <sup>h</sup> humic acid, p.os                              | Table 4.               |
| 5     | metabolic balance                                     | aqueous sol. of $^{86}\text{SrCl}_2$ , i.p.<br>+ after 1 <sup>h</sup> and every 24 <sup>h</sup><br>humic acid, p.os | Table 5.               |
| 6     | tissue conc.  | aqueous sol. of $^{86}\text{SrCl}_2$ , p.os   | Table 6., 7., 8.       |
| 7     | tissue conc.  | $^{86}\text{SrCl}_2$ -humic acid complex,<br>p.os   | Table<br>9., 10., 11.  |
| 8     | metabolic balance, at<br>96 <sup>h</sup> tissue conc. | aqueous sol. of $^{103}\text{Ru}$ , p.os  | Table<br>12., 14., 16. |
| 9     | metabolic balance, at<br>96 <sup>h</sup> tissue conc. | $^{103}\text{Ru}$ -humic acid complex,<br>p.os  | Table<br>13., 15., 16. |

### Conclusions

1.) The urinary excretion of  $^{85}\text{Sr}$  in rats treated orally with  $^{85}\text{SrCl}_2$ -humic acid complex occurred with half intensity than that in animals treated with only the aqueous solution of the labelled substance ( $1.59 \pm 0.42$  and  $2.87 \pm 0.65$ , respectively,  $p < 0.006$ ). It is most probable that during 96 h less amount of  $^{85}\text{SrCl}_2$  was absorbed from its complex than its solution, in the gastrointestinal tract.

2.) In animals treated with  $^{85}\text{Sr}$ -humic acid complex orally, less quantity of radioactivity was eliminated by the stool in the first 24 h, than in case when the aqueous solution of  $^{85}\text{SrCl}_2$  was administered ( $35.74 \pm 28.04$  and  $78.37 \pm 7.22$ , respectively). During 96 h the difference between the two groups was eliminated. This finding can be due to the constipating action of humic acid.

3.) The oral administration of humic acid to rats (once or repeatedly) did not change the urinary and faecal excretion of intraperitoneally injected  $^{85}\text{SrCl}_2$ . After i.p. treatment nearly equal amount of radioactivity was eliminated by the urine and the stool (7-8 D% or 10-11 D%, respectively).

4.) When rats were treated orally with  $^{85}\text{Sr}$ -humic acid complex less amount of radioactivity was incorporated into the bones (femur, cranial bone), than in the case of  $^{85}\text{SrCl}_2$  administration. The concentrations of radioactivity is low in all of the tissues examined, except in the gastrointestinal tract.

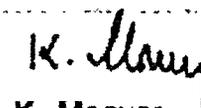
5.) There was no detectable difference in the urinary and faecal excretion of  $^{103}\text{Ru}$  after oral administration of the complex form or the aqueous solution of the radioactive tracer. In the experiments, when  $^{103}\text{Ru}$ -humic acid complex was administered orally, the constipating activity of humic acid in the first 24 h is obvious.

6.) In both groups of rats treated with  $^{103}\text{Ru}$  orally (complex or solution), the tissue concentrations of radioactivity were below the detection limit after 96 h.

except in the kidney and the gastrointestinal tract. With high sensitivity (low background) instrument tissue concentrations can be determined. The results clear that less amount of radioactivity was found in the tissues of animals treated with the complex preparation, than in the controls.

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