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# Excretion of Metals into the Rat Intestine

SIEGFRIED G. SCHÄFER AND WOLFGANG FORTH*

*Institut für Pharmakologie und Toxikologie, Medizinische Fakultät, Ludwig-Maximilians-Universität, D-8000 München 2, Nussbaumstr. 26, West Germany*

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## Abstract

The acute excretion of metals across the intestinal wall and by bile was investigated in vivo within 2 h after iv administration in rats. Heavy metals of biological interest, such as copper and zinc, and of toxicological importance, such as cobalt, cadmium, mercury, lead, and bismuth, as well as rubidium and strontium as examples of the alkali and alkali-earth metals were chosen. Most of the metals were excreted along a concentration gradient from blood into the intestinal lumen. Rubidium is the only metal excreted against a concentration gradient from blood into the lumen of both the small and large intestines. For all metals investigated, excretion into the small intestine exceeds that into the large intestine. Metal excretion by bile also occurred mainly along a concentration gradient from liver to bile, e.g., cobalt, zinc, mercury, rubidium, and lead, which is chosen as example of this group. Copper and strontium are excreted against a considerable concentration gradient from blood into bile. This holds true also for cadmium and bismuth in low doses.

**Index Entries:** Metals, excretion into the intestine; heavy metals, Co, Cu, Zn, Cd, Hg, Bi, Pb, excretion across the intestinal wall, excretion by bile; alkali metal, rubidium, excretion across the intestinal wall, excretion by bile; earth alkali metal, strontium, excretion across the intestinal wall, excretion by bile.

## 1. Introduction

Excretion of metals by the intestine is often claimed in literature (*1–7*). Reliable data, however, can be found only scarcely. In most of the studies published, only fecal and/or biliary excretion has been determined (*1–15*). Using these methods, one cannot discern the amounts of metals excreted across the intestinal epithelium from that eliminated by bile. Furthermore, the importance of the different parts of the intestine cannot be evaluated. Therefore, the excretion of radioactively labeled


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metals from blood into the lumen of the gastrointestinal tract (GIT) was investigated directly. Heavy metals of biological interest, i.e., copper and zinc, and of toxicological importance, i.e., cobalt, cadmium, mercury, lead, and bismuth, were chosen. Strontium and rubidium were studied as examples of alkali-earth and alkali metals. The method of pendular perfusion (*16*) has been used; this allows the investigation of different sections of the GIT simultaneously, e.g., of the jejunum and the colon.

## 2. Materials and Methods

### *2.1. Animals*

Adult Wistar rats (260–300 g body weight) purchased from Wiga (Sulzfeld, FRG) were fed a standard diet (Höveler, Langen-Immigrath, FRG) and had free access to water. Food was withdrawn about 16 h before starting the experiments.

The chemical compounds and the radioactive nuclides used in these experiments were of analytical grade and commercially available (Table 1).

### *2.2 Preparation of the Intestinal Segments of Rats for Pendular Perfusion*

Detailes of the method of pendular perfusion of intestinal segments in vivo on anesthetized rats can be found elsewhere (*16*). Briefly, the rats were anesthetized (urethan 1.25 g/kg body wt, im). Body temperature was maintained at 37°C. The jugular vein and the carotic artery were cannulated with PVC tubes. PVC tubes were inserted into the jejunum at the flexura duodenojejunalis and 5 cm distal of this point and connected with thermostatized storage vials. The colon was prepared in the same manner starting at the valvula ileocoecalis and 5 cm proximal of this point. The intestinal segments were filled with 4 mL (jejunum) and 4 or 5 mL (colon) of saline containing 0.1% polyethylenglycol-4000 (PEG-4000) labeled with $^{3}H$ or $^{14}C$, respectively, depending on the possibility of a simultaneous measure-

TABLE 1
Radioactively Labeled Metal Salts, and the Simultaneously Used Unabsorbable Markers

| Metal salts | Unabsorbable marker |
|---|---|
| $^{60}Co$,($CoCl_2$) | $^{14}C$-PEG-4000 |
| $^{64}Cu$,($CuCl_2$) | $^{3}H$-PEG-4000 |
| $^{65}Zn$,($ZnCl_2$) | $^{14}C$-PEG-4000 |
| $^{85}Sr$,($SrCl_2$) | $^{3}H$-PEG-4000 |
| $^{86}Rb$,(RbCl) | $^{3}H$-PEG-4000 |
| $^{115m}Cd$,($CdCl_2$) | $^{3}H$-PEG-4000 |
| $^{203}Hg$,($HgCl_2$) | $^{14}C$-PEG-4000 |
| $^{207}Bi$,($BiCl_3$) | $^{3}H$-PEG-4000 |
| $^{210}Pb$,[$Pb(NO_3)_2$] | $^{14}C$-PEG-4000 |

ment of the radioactively labeled metals (cf. Table 1). Because of the poor solubility of $BiCl_3$ in water the segments were filled in this case only with an isotonic sodium tartrate solution; all other metals were dissolved in saline. The two batteries of storage vials could be moved up and down against the platform. Thus, the perfusion medium was able to flow back and forth through the lumen of the intestinal segments using the gravity as driving force. The pendular frequency was 5/min.

### *2.3. Preparation of the Ductus Choledochus*

In a second series of experiments in anesthetized rats (urethan), the proximal part of the bile duct was cannulated with a PVC tube (1.0 mm id). In these experiments the blood supply of the kidneys was also tied-off.

### *2.4. Dosage of Metals*

In order to limit the number of experiments, the metals were administered on two doses only, i.e., $3.7 \times 10^{-6}$ and $3.7 \times 10^{-10}$ mol/kg body wt. Since limited amounts of the radioactively labeled metals $^{64}Cu$ and $^{210}Pb$ were available, only the higher dose was administered.

### *2.5. Analytical Design*

*2.5.1. Measurement of Fluid Movement Across the Epithelium and the Concentration of the Metals in the Plasma and the Perfusion Fluid* Blood samples (0.3 mL) were taken from the carotic artery and centrifuged immediately (4000 rpm) for 5 min. The concentration of the metals were determined in 0.1 mL plasma and 0.1 mL of the perfusion fluid. Samples were taken 10, 20, 30, 40, 60, 90, and 120 min after iv administration of the metal. The concentration of radioactively labeled metals as well as of $^{3}H$- or $^{14}C$-PEG-4000, respectively, were measured simultaneously. Radioactively labeled PEG-4000 was added as an unabsorbable marker of the volume (*17*) in order to calculate the actual volume of the perfusion fluid. $^{3}H$- or $^{14}C$-PEG-4000 was chosen depending on the energy spectrum of the metal nuclide used in the experiments (cf. Table 1).

*2.5.2. Determination of Biliary Excretion of Metals* Samples of the bile were collected in periods of 20 min for 2 h. The excreted radioactively labeled metals were measured in the bile fluid.

*2.5.3. Measurement of Radioactivity* Aliquots of plasma, perfusion fluid, or bile (0.1 mL) were added to 9 mL of a modified Bray solution on dioxane basis. The concentration of the radioactivity was measured in a liquid scintillation counter (β-Scint 5000, Berthold-Friesecke, Wildbad, FRG) with exception of $^{85}Sr$ and $^{207}Bi$. The concentrations of these nuclides in the samples (0.1 mL) were determined in a γ-ray analyzer (Packard, Type Armac). When necessary, the results were corrected for quench by a computer program.

### *2.6. Statistics*

Statistical evaluation for paired and nonpaired data was made by Student's *t*-test.

## 3. Results and Discussion

For simple methodological reasons, the experimental design results in two series of experiments: (a) the transepithelial intestinal excretion of metals, and (b) the biliary excretion of the metals.

### *3.1. Intestinal Excretion of Metals*

After iv injection, the time courses of metal excretion into the intestine may be discerned in two groups:

(a) Metals that move from blood into the intestinal lumen along the concentration gradient; as an example lead (Pb) will be discussed in detail.

(b) Metals that are excreted against a concentration gradient from blood into the intestinal segments; as an example rubidium will be presented more intimately.

The amounts of the metals excreted into the perfusion fluid varied in a wide range (Table 2). The excretion of metals into the lumen of the small intestine always exceeds that in colonic segments. Most of the metals were excreted across the mucosal layer of the intestine according to the chemical gradient between blood and lumen, e.g., zinc, cadmium, mercury, lead, bismuth, cobalt, copper, and strontium. It appears to be noteworthy that an excretion of zinc against a concentration gradient into the lumen could not be confirmed (*5*). This holds true also for strontium. An excretion of this alkali earth metal against a concentration gradient across ileal segments as reported by Wassermann (*18*) could not be found.

In the following a more detailed description of the excretion of lead and rubidium (Rb) is presented. Lead is an example of a metal moving along the concentration gradient from blood into the lumen, and rubidium is, as were thallous ions (*16, 19, 20*), excreted against a concentration gradient.

*3.1.1. Lead* In Figs. 1a and 1b the time course of the $^{210}Pb$ concentration in the plasma (a) and the perfusion medium of jejunal and colonic segments (b) is shown. The decrease of plasma concentration of iv administered lead can be fitted by a first-order kinetic ($p < 0.01$) with a half time ($t_{1/2}$) of 48 min. At the end of the experiment the ratio between $^{210}Pb$ concentrations in the intestinal lumen and plasma was 0.019 (jejunum) and 0.0017 (colon), suggesting an excretion along the concentration gradient between blood and perfusion fluid. The concentration of $^{210}Pb$ in the jejunal and colonic lumen increased linearly throughout the experiment ($p < 0.01$). In other words, there was no close correlation between the $^{210}Pb$ concentration in the plasma and the perfusion medium. As demonstrated in Fig. 1b, there was a significant difference ($p < 0.01$) between the concentrations of $^{210}Pb$ in the perfusion medium of jejunum and colon increasing with time to a maximal ratio of about 10 after 120 min. At the end of the experiment, a total of 0.034% and 0.005% of the dose was excreted into the jejunal and the colonic segments, respectively. The data suggest that intestinal excretion of $^{210}Pb$ mainly results from an excretion across the mucosal epithelium of the jejunum, whereas the colonic excretion is of secondary importance. It must be taken into consideration

TABLE 2
Excretion of Metals Across the Mucosal Epithelium of the Jejunal and Colonic Segments and by Bile After iv Administration in Rats

| | Dose | | | | | |
|---|---|---|---|---|---|---|
| | $3.7 \times 10^{-10}$ mol/kg % of the dose ($\bar{x} \pm$ SEM) $n = 5 - 9$ | | | $3.7 \times 10^{-6}$ mol/kg % of the dose ($\bar{x} \pm$ SEM) $n = 5 - 9$ | | |
| Metal | Jejunum, 5 cm | Colon, 5 cm | Bile | Jejunum, 5 cm | Colon, 5 cm | Bile |
| $^{60}Co$ | 0.046 ± 0.014 | 0.019 ± 0.009 | 1.610 ± 0.120 | 0.003 ± 0.001 | 0.001 ± 0.001 | 3.550 ± 0.370 |
| $^{64}Cu$ | — | — | — | 0.008 ± 0.002 | 0.011 ± 0.003 | 1.151 ± 0.092 |
| $^{65}Zn$ | 0.017 ± 0.006 | 0.007 ± 0.002 | 0.216 ± 0.033 | 0.031 ± 0.006 | 0.021 ± 0.006 | 0.322 ± 0.049 |
| $^{85}Sr$ | 0.131 ± 0.017 | 0.161 ± 0.011 | 9.275 ± 0.713 | 0.110 ± 0.023 | 0.106 ± 0.015 | 0.855 ± 0.072 |
| $^{86}Rb$ | 0.188 ± 0.031 | 0.423 ± 0.044 | 0.105 ± 0.008 | 0.205 ± 0.023 | 0.356 ± 0.059 | 0.116 ± 0.009 |
| $^{115m}Cd$ | 0.005 ± 0.003 | 0.005 ± 0.004 | 0.423 ± 0.042 | 0.009 ± 0.003 | 0.014 ± 0.006 | 0.592 ± 0.093 |
| $^{203}Hg$ | 0.021 ± 0.005 | 0.033 ± 0.026 | 0.468 ± 0.038 | 0.034 ± 0.006 | 0.008 ± 0.003 | 0.318 ± 0.022 |
| $^{207}Bi$ | 0.055 ± 0.017 | 0.032 ± 0.007 | 2.801 ± 0.609 | 0.059 ± 0.012 | 0.041 ± 0.012 | 0.654 ± 0.100 |
| $^{210}Pb$ | — | — | — | 0.033 ± 0.011 | 0.005 ± 0.002 | 0.877 ± 0.078 |

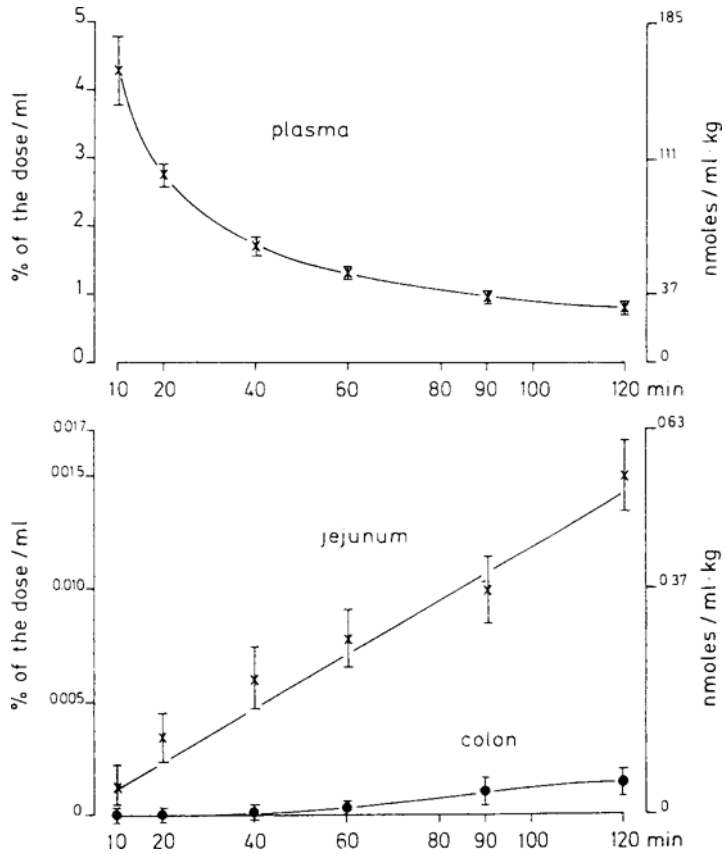


Fig. 1a and 1b. Concentration of $^{210}Pb$ in the plasma and in the perfusion medium of jejunal and colonic segments of anesthetized rats. Intestinal segments (5 cm of length) were perfused by 4 mL (jejunum) or 5 mL (colon) of an isotonic saline (pendular perfusion). The perfusion fluid contained radiolabeled $^{14}C$-PEG-4000 as a marker of the volume. Pb dose iv: $3.7 \times 10^{-6}$ mol/kg as $^{210}Pb$-$[Pb(NO_3)_2]$. The symbols represent the mean of 9 experiments ($\bar{x} \pm$ SEM); $r = 0.7921$; $n = 46$; $p < 0.001$.

that the blood supply of the kidneys was tied-off. Therefore the experimental conditions may favor an excretion of the metals into the GIT.

*3.1.2. Rubidium* In Fig. 2 the time course of the $^{86}Rb$ concentrations in the perfusion medium of the jejunal and colonic segments as well as in plasma of rats is shown. $^{86}Rb$ ions are distributed rapidly after iv injection in the organism (*21, 22*). Already 10 min. after injection the plasma concentration is nearly constant. In the perfusion fluid of the jejunal segments, the $^{86}Rb$ concentration reaches that in plasma 10 min after administration. After 40–60 min the concentration of $^{86}Rb$ ions in the jejunal perfusion medium increases to its maximum value exceeding the plasma concentration by a factor of 3.1, suggesting a net secretion of $^{86}Rb$ similar to that of thallous ions (*16, 20*). After 60 min, the concentration of $^{86}Rb$ ions in the

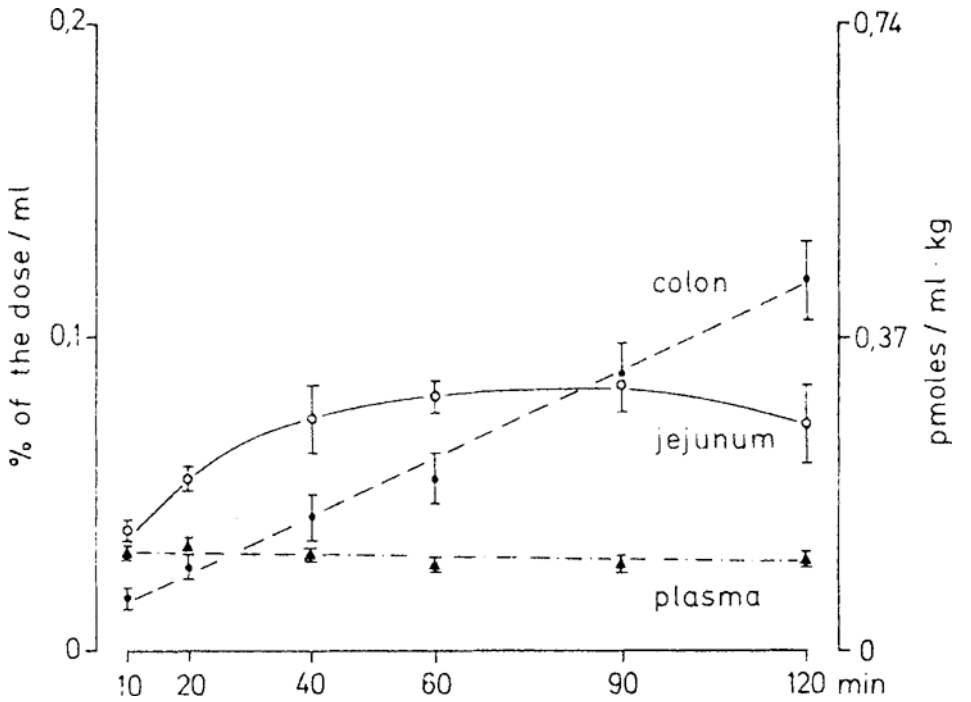


Fig. 2. Concentration of $^{86}Rb$ in plasma and the lumen of jejunal and colonic segments of anesthetized rats. Jejunal and colonic segments of anesthetized rats, about 5 cm of length, were investigated by pendular perfusion. The intestine was perfused by 4 mL (jejunum) or 5 mL (colon) of an isotonic saline, respectively. Perfusion fluid contained radiolabeled $^{3}H$-PEG-4000 as a marker of the volume. Rb dose iv: $3.7 \times 10^{-10}$ mol/kg as $^{86}Rb$-(RbCl). Statistics: 40 min after starting the experiment the rubidium concentration in jejunal and colonic perfusion fluid was significantly higher than in plasma ($p < 0.01$). Mean of 8 experiments ($\bar{x} \pm$ SEM). Ordinate: left, % of the dose/mL; right pmol $mL^{-1}$ $kg^{-1}$. Abscissa: time in min.

perfusate of the jejunal segments remains constant. The time course of the concentration of $^{86}Rb$ ions in the jejunal lumen cannot be interpreted plausibly unless one assumes an enterosystemic circulation of the $^{86}Rb$ ions excreted. This means in other words that the reabsorption of $^{86}Rb$ ions must be in the same order of magnitude as the amount excreted, resulting in an excretion pattern as shown in Fig. 2. Rb ions can be absorbed rapidly from segments of the small intestine or rats, as shown by Pfleger et al. (*22*).

On the other hand, the concentration of Rb ions in the perfusion fluid of the colonic segments increases constantly up to 120 min. At the end of the experiment a considerble concentration gradient has been established between plasma (p) and colonic lumen (cl); ratio cl/p = 4.8.

It also cannot be excluded that the excreted $^{86}Rb$ ions are reabsorbed in colonic segments. The rate of reabsorption, however, must be considerably smaller than that of excretion. Otherwise the time course of the concentration of Rb ions cannot

be linear with time. Since the excretion pattern of $^{86}Rb$ into the intestine after iv administration of the higher dose is very similar to that described above, it is not discussed in detail here.

3.1.2.1. Rubidium Excretion in the Presence of Prussian Blue. The excretion of Rb ions into the jejunal segments was investigated additionally in the presence of Prussian Blue, active as ionophore, which is able to bind Tl(I) ions (*23*), a heavy metal of similar physicochemical properties as the alkali metals potassium or rubidium. The binding of these metals by Prussian Blue may be caused by the rather similar ionic radii of potassium (1.33 Å), rubidium (1.48 Å), and thallium (1.40 Å) (*24*). In the presence of Prussian Blue the excretion of Rb ions increases from 0.21% of the dose in controls to 0.32% of the dose, i.e., roughly by 55%. The data suggest that Prussian Blue is able to reduce the enterosystemic circulation of Rb ions in the small intestine, as shown for Tl(I) ions (*16, 19*).

### *3.2. Biliary Excretion of Metals*

In a second series of experiments, the biliary excretion of the same metals was investigated after iv administration of the same doses as mentioned above. The amount of the metals excreted during the experimental time is given in Table 2. After iv injection the time course of metal concentration in bile of most of the metals investigated is rather uniform. As was done for the excretion of the metals across the mucosal layer, metal excretion by bile will also be discussed in two groups:

(a) Metals that follow the concentration gradient from blood into bile, i.e., zinc, mercury, cobalt, rubidium, and lead; the latter will be discussed in more detail as an example for this group. An excretion along the concentration gradient was observed also after administration of the high dose of cadmium and bismuth ($3.7 \times 10^{-6}$ mol/kg body wt).

(b) Metals that are excreted into bile against a concentration gradient such as copper and strontium; the latter will be presented here as an example of this group. An excretion against a concentration gradient was observed after the administration of the low dose of cadmium and bismuth ($3.7 \times 10^{-10}$ mol/kg body wt).

*3.2.1. Lead* In Fig. 3 the time course of the concentrations of $^{210}Pb$ in plasma and bile collected in periods of 20 min is demonstrated. The concentration of $^{210}Pb$ in the plasma decreases according to a first-order kinetic as mentioned above (Fig. 1a). The concentration of $^{210}Pb$ in bile increases during the first 40 min of the experiment, thereafter it declines in parallel to the plasma concentration. $^{210}Pb$ concentration of the plasma exceeds that of bile during the entire experiment. During the second hour of the experiment, the concentration ratio between plasma and bile was 1.6, suggesting an excretion of $^{210}Pb$ along the concentration gradient from blood to bile.

Throughout the experiment the rats excreted by bile a total of 0.88% of the $^{210}Pb$ dose. The data given in Table 3 illustrate that biliary $^{210}Pb$ excretion was 1.7 times greater than that across the mucosal epithelium calculated for the entire length of the intestine.

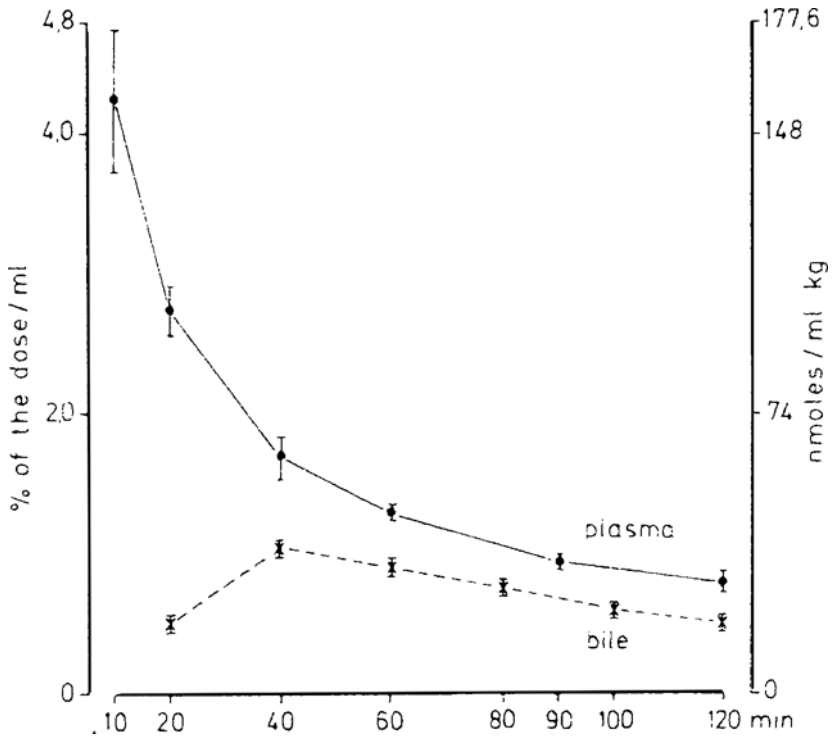


Fig. 3. Concentration of $^{210}Pb$ in plasma and bile of anesthetized rats. Body temperature 37°C; bile was collected in periods of 20 min during 2 h. Pb dose iv: $3.7 \times 10^{-6}$ mol/kg body wt as $^{210}Pb$-$[Pb(NO_3)_2]$. The symbols represent the mean of 7 experiments ($\bar{x} \pm$ SEM). Concentration of $^{210}Pb$ in plasma exceeds concentration in bile during the whole experiment; $p < 0.05$.

*3.2.2. Strontium* Figure 4 illustrates that $^{85}Sr$ concentration in bile exceeds that in plasma during the entire experiment, provided the low dose ($3.7 \times 10^{-10}$ mol/kg body wt) was administered. Already 20 min after iv administration, $^{85}Sr$ concentration in bile exceeds that in plasma by a factor of about 16. The biliary $^{85}Sr$ excretion can be fitted by first-order kinetics ($p < 0.001$) with a half-time of 62 min. During the second hour of the experiment the time course of $^{85}Sr$ concentration in bile and plasma was parallel. In order to test whether the biliary excretion of $^{85}Sr$ follows a saturation-type kinetic, elimination by bile was investigated after injection of two additional doses of the alkali earth metal ($3.7 \times 10^{-9}$ and $3.7 \times 10^{-8}$ mol/kg body wt).

In Fig. 5 the ratios of $^{85}Sr$ concentrations between bile (b) and plasma (p). The ratios b/p were calculated from the results obtained between 60 and 120 min after iv injection. This time was chosen, because the ratio b/p is constant during this interval (cf. Fig. 4). Ratios suggest a nondiffusional transfer from liver to bile. The ratios of $^{85}Sr$ concentrations b/p decreased from 10 to 1 with increasing doses of strontium. The data obtained from biliary excretion of $^{85}Sr$ suggest that in the

TABLE 3
Excretion of Metals Across the Mucosal Epithelium and by Bile After iv Administration in Rats[a]

| Metal | I, small intestine | II, large intestine | Sum I + II | III, bile | Sum, I + II + III |
|---|---|---|---|---|---|
| $^{60}Co$ | 0.05 | 0.01 | 0.06 | 3.55 | 3.66 |
| $^{64}Cu$ | 0.13 | 0.04 | 0.17 | 1.15 | 1.32 |
| $^{65}Zn$ | 0.50 | 0.08 | 0.58 | 0.32 | 0.89 |
| $^{85}Sr$ | 2.01 | 0.38 | 2.39 | 0.86 | 3.25 |
| $^{86}Rb$ | 3.28 | 1.28 | 4.56 | 0.12 | 4.68 |
| $^{115m}Cd$ | 0.14 | 0.05 | 0.19 | 0.59 | 0.78 |
| $^{203}Hg$ | 0.54 | 0.03 | 0.57 | 0.32 | 0.89 |
| $^{207}Bi$ | 0.94 | 0.15 | 1.09 | 0.66 | 1.75 |
| $^{210}Pb$ | 0.53 | 0.02 | 0.55 | 0.88 | 1.43 |

[a]Dose: $3.7 \times 10^{-6}$ mol/kg iv. The excretion of metals was calculated for 2 h. The figures represent percent of the dose administered.

The excretion of the metals in the entire small intestine was calculated on the basis of the jejunal values, obtained experimentally. Length of the duodenum: 10 cm; length of either jejunum and ileum: 35 cm; since the surface of the ileum amounts to half of that of the jejunum (*26*), values of the excretion of metals obtained with jejunal segments were divided by 2. The excretion of the metals into the colon was calculated per 18 cm length (*26, 27*).

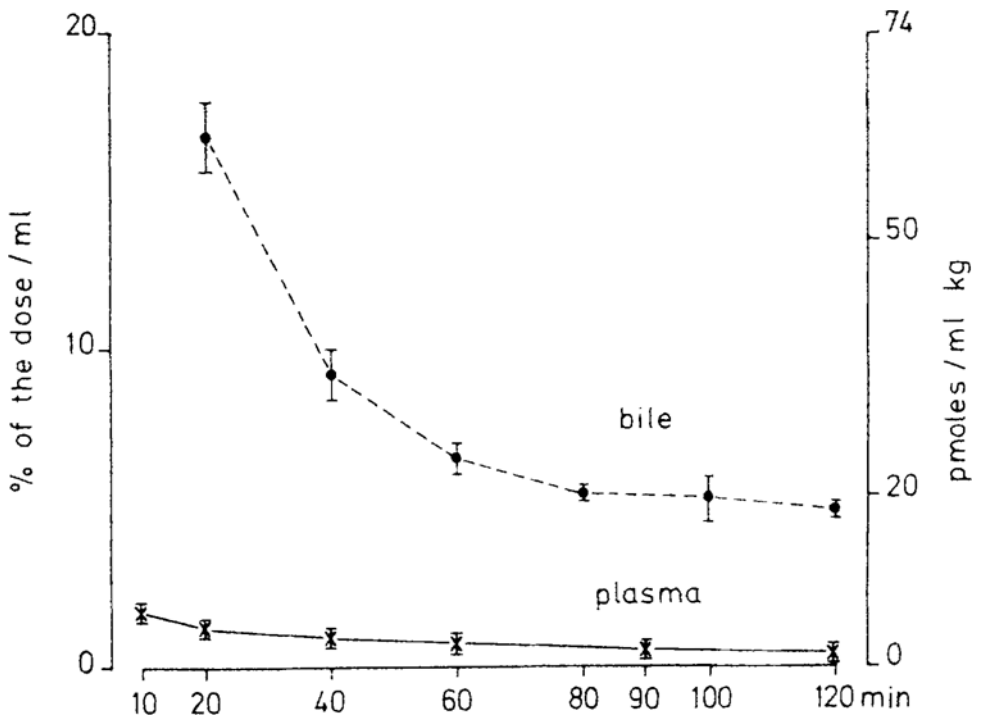


Fig. 4. Concentration of $^{85}Sr$ in the plasma and bile of anesthetized rats. Body temperature 37°C; bile was collected in periods of 20 min during 2 h. Sr dose iv: $3.7 \times 10^{-10}$ mol/kg as $^{85}Sr$-($SrCl_2$). The symbols represent the mean of 8 experiments ($\bar{x} \pm$ SEM).

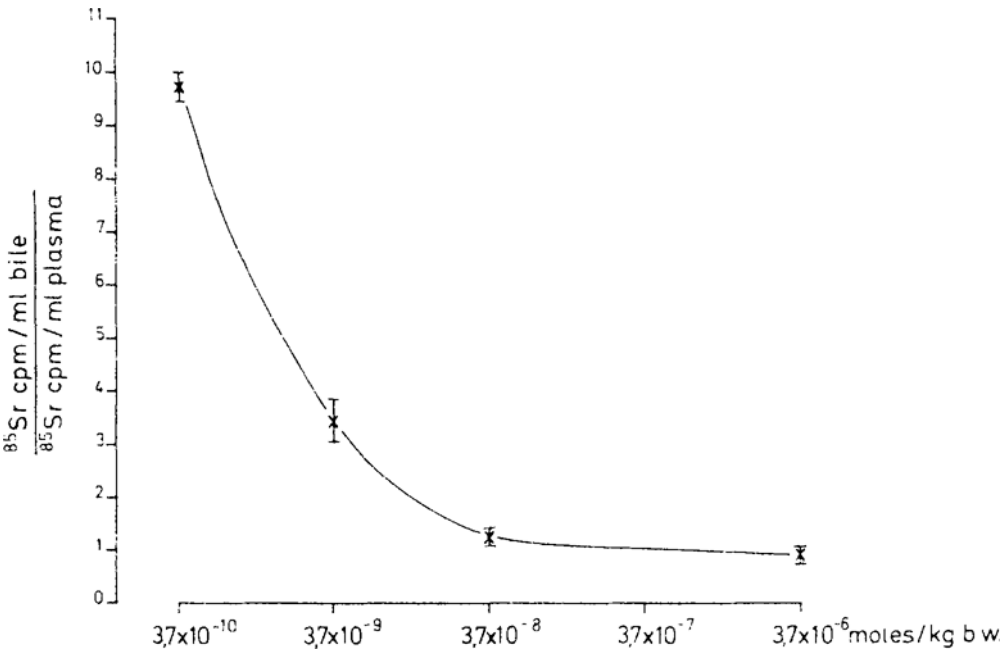


Fig. 5. Bile/plasma ratio of $^{85}Sr$ in anesthetized rats. Bile was collected as described after iv administration of four doses: $3.7 \times 10^{-10}$ to $3.7 \times 10^{-6}$ mol/kg as $^{85}Sr$-($SrCl_2$). The data represent the mean of 3 periods of 20 min in the second hour of 5–8 experiments ($\bar{x} \pm$ SEM). Abscissa: doses administered iv. Ordinate: concentration ratios in $^{85}Sr$ (cpm/mL bile)/(cpm/mL plasma).

presence of small concentrations of $^{85}Sr$ ions in the plasma, the alkali earth metal is moved from blood to bile mainly by a nondiffusional mechanism. With increasing concentrations of strontium in the plasma, the diffusional component becomes predominant over the nondiffusional transfer. In other words, in the liver of rats there may be a transfer system for strontium ions of limited capacity.

## 4. Concluding Remarks

In order to compare the amounts of the metals actually excreted into the small and large intestine with the amounts found in bile, the results presented in Table 2 were calculated for the entire length of both sections of the GIT (Table 3). At least three types of information can be taken from results presented in Table 3:

(1) Heavy metals are excreted into the intestinal tract by either excretion by bile and across the mucosal epithelium.

(2) There exist metals the excretion of which across the mucosal epithelium exceeds that by bile, i.e., strontium, rubidium, and possibly bismuth, whereas at least for cobalt, copper, and cadmium, the biliary excretion exceeds that across the epithelium. For the other metals investigated, i.e., zinc, mercury, and lead, the excreted amount by either route appears to be more or less equal.

(3) The excreted amount of some metals into the intestinal tract, i.e., by bile and across the epithelium, may be at least equal to that which is excreted by the kidneys.

Unfortunately, the literature contains no comparable data on the excretion of metals by the kidneys from short-term experiments of the type carried out here; the urinary excretion of the metals was not measured because of the surgical burden to the animals in addition to the cannulation of the intestinal segments and the bile duct. Since there exist different time courses for the intestinal and the urinary excretion, e.g., for thallous ions (*28*), it was not possible either to extrapolate the data obtained in short-term experiments to the 24 h excretion or to calculate the excretion per hour of metals by the kidneys obtained in long-term experiments. Data on the urinary excretion in long-term experiments are published for cobalt (*25*), copper (*12*), zinc (*5*), strontium (*9*), rubidium (*6*), cadmium (*4*), mercury (*12*), bismuth (*7*), and lead (*1*, *13*).

It appears to be proven that the excretion of bismuth by the kidneys exceeds that into the GIT. For lead both its higher excretion by the intestinal tract compared with that by the kidneys (*13*) and the higher urinary excretion (1) are discussed in the literature. The latter was observed after injection of $^{210}Pb$ in the penis vein so that one may doubt the reliability of the method chosen.

The excretion of thallium into the GIT must be considered a proven method for detoxification in cases of intoxication, provided that the reabsorption of thallous ions is prevented by the presence of unabsorbable Prussian Blue in the GIT as trapping agent (*28–31*). The significance of even small daily losses via the GIT for detoxification has been proven for mercury (*32*). It appears to be worthwhile to discuss the possibility of an additional detoxification of most of the metals presented in Table 3, with exception of bismuth. The prerequisite is, however, that the chemical form of the metals excreted into the GIT is known. There may be differences depending on whether the metals are excreted by bile or across the intestinal wall.

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