

sung der Radioaktivität die mit Jod markierten Kieselgelzonen in Szintillatorröhrchen übergeführt und mit Permablend III (Fa. Packard, 91% PPO, 9% bis-MSB) als Szintillatorlösung versetzt.

Wie die Tabelle zeigt, nimmt die Einbaurate von $^{14}\text{CH}_3$ in die mikrosomale Phosphatidylcholinfraktion Tetrachlorkohlenstoff-vergifteter Rattenlebern im Vergleich zu den Werten der Kontrolle um ca. 40% zu. Gleichzeitig steigt auch der auf die Gesamtphospholipide bezogene Phosphatidyläthanolamingehalt in der Lebermikrosomenfraktion unter der CCl_4 -Intoxikation leicht an. Im Gegensatz zur erhöhten Methylierung von Phosphatidyläthanolamin ist die Änderung der Einbauraten in die Sphingomyelinfraktion deutlich geringer und lässt sich statistisch nicht sichern. Da das Verhältnis der spezifischen Radioaktivitäten der mikrosomalen Gesamtlipide zu mikrosomalen Proteinen bei der CCl_4 -Intoxikation ebenfalls erheblich gesteigert ist, kann gefolgert werden, dass auch die Umsatzraten der durch Methylierung modifizierten Lipide der Lebermikrosomen im Verhältnis zu den Umsatzraten der neu synthetisierten mikrosomalen Proteine nach Tetrachlorkohlenstoffvergiftung zunehmen.

Obwohl im wesentlichen nur die Hexaenspecies von Phosphatidyläthanolamin spezifische Substrate der mikrosomalen Methionin-Phosphatidyläthanolamin-Methyltransferase sind¹⁰, scheint auch zwischen dem mikrosomalen Pool an Gesamt-Phosphatidyläthanolamin und der Einbaurate von $^{14}\text{CH}_3$ in die Phosphatidylcholinfraktion der Lebermikrosomen eine deutliche Beziehung zu bestehen (Figur).

Die bei doppelt reziproker Auftragung der $^{14}\text{CH}_3$ -Einbauraten gegen die entsprechenden Phosphatidyläthanolaminkonzentrationen berechneten Regressionsgeraden des Kontroll- und CCl_4 -Kollektivs erstrecken sich zwar über verschieden grosse Bereiche von 1/S, sind statistisch parallel und differieren in ihren Restvarianzen. Auch bei Berücksichtigung der unterschiedlichen Restvarianzen unterscheiden sich die Schnittpunkte der beiden Geraden $1/V_{\max}$ und $1/K_m$ jedoch statistisch signifikant ($2\alpha < 0.005$). Unter der Voraussetzung, dass die berechneten Regressionsgeraden auch in den nicht erfassten Bereichen

von 1/S gültig sind, nimmt somit die «Affinität» der Phosphatidylcholinmarkierung zum mikrosomalen Gehalt an Gesamt-Phosphatidyläthanolamin nach CCl_4 -Intoxikation deutlich ab, während die «Maximalgeschwindigkeit» dieser Reaktion ansteigt. Dieser Befund ist insofern bemerkenswert, als der Polyensäuregehalt der Leberphospholipide und somit die Konzentration des spezifischen Substrats der Methionin-Phospholipid-Methyltransferase unter der CCl_4 -Intoxikation abnimmt³.

Unsere Ergebnisse stimmen mit den von SHIMIZU⁴ in der Gesamtleber gemessenen Befunden nicht überein. Die Unterschiede dürften zum Teil darauf beruhen, dass wir den radioaktiv markierten «Precursor» nicht i.v., sondern i.p. und in einer kürzeren Zeitperiode vor Töten der mit geringerer CCl_4 -Dosis geschädigten Tiere verabreicht haben. Auch die von FEUER et al.⁵ in vitro bei der akuten CCl_4 -Intoxikation der Ratte registrierte Aktivitätsabnahme der mikrosomalen $^{14}\text{CH}_3$ -Methionin-Phospholipid-Methyltransferase muss unseren in vivo gewonnenen Ergebnissen nicht widersprechen, da den publizierten Daten nicht zu entnehmen ist, zu welchem Zeitpunkt die Aktivität gemessen wurde. Weiterhin ist bisher unbekannt, inwieweit die mikrosomale Methionin-Phospholipid-Methyltransferase für die in-vivo-Methylierung von Phosphatidyläthanolamin geschwindigkeitsbestimmend ist.

Summary. Six h after oral administration of carbon tetrachloride, the turnover of $^{14}\text{CH}_3$ from injected Methionine-Methyl- ^{14}C in microsomal lipids is increased in comparison with the turnover in microsomal proteins.

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¹⁰ G. ARVIDSON, Eur. J. Biochem. 4, 478 (1968).

Role of Bile in Intestinal Absorption of ^{203}Pb in Rats

Biliary excretion of lead was studied as early as in the last century. AUB et al.¹ list in their monograph quite a number of authors who had been engaged in the problem. Opinions of those authors on biliary excretion of lead differed however. BLAXTER and COWIE² studied excretion of lead in sheep and found bile to be an important excretion pathway for lead. CASTELLINO et al.³ investigated excretion of lead via bile and via the wall of the gastrointestinal tract in rats and found that the greatest part of lead revealed in stool had been excreted with bile. According to those authors, lead in bile is most probably bound to proteins. In the course of 24 h after a single i.v. administration of ^{210}Pb , an average 6.7% of the dose administered are excreted via bile in rats⁴.

KLAASSEN and SHOEMAN⁵ compared biliary excretion of lead in rats, rabbits and dogs. They established the highest rats of biliary excretion of lead in rats. These authors also studied the enterohepatic circulation (EHC) of lead and came to the conclusion that it was insignificant. The role of bile in the absorption of lead has not been studied.

The present authors studied absorption of ^{203}Pb excreted via bile during 24 h after i.v. administration of

$^{203}\text{PbCl}_2$ on the one hand and absorption of ^{203}Pb administered into the duodenum in the form of $^{203}\text{PbCl}_2$ in rats with both cannulated and non-cannulated bile duct on the other hand. The aim of the study was to evaluate the role of bile in absorption of lead.

Materials and methods. Female Wistar rats (mean weight 200 g) fed on pellet diet were used in the experiments. Rats were starved for 24 h before the study but had free access to water.

The rats were divided into 3 groups: 1. group: Donors (9 rats) were given i.v. $^{203}\text{PbCl}_2$ (in the dose of 125 μg of Pb^{2+} per rat). Bile was collected in donors every 2 h, its radioactivity was measured and the bile obtained

¹ J. C. AUB, L. T. FAIRHALL, A. S. MINOT and P. REZNIKOFF, in *Lead Poisoning* (Williams and Wilkins Publishers, Baltimore 1926).

² K. L. BLAXTER and A. T. COWIE, Nature, Lond. 157, 588 (1946).

³ N. CASTELLINO, P. LAMANNA and B. GRIECO, Folia med. 48, 601 (1965).

⁴ M. CIKRT, Br. J. ind. Med. 29, 74 (1972).

⁵ C. D. KLAASSEN and D. W. SHOEMAN, Toxic. appl. Pharmac. 29, 434 (1974).

Absorption of intraduodenally administered ^{203}Pb in rats

Group	No. of rats	Dose of Pb^{2+} (μg per rat)	Stool + GIT content	Absorption(%)
1. Acceptors	9	10.6	63.1 ± 4.2	36.9 ± 4.2
2. Bile duct non-cannulated	4	10.6	64.4 ± 5.6	35.6 ± 5.6
3. Bile duct cannulated	4	10.6	81.2 ± 2.5	18.8 ± 2.5

Group 1: Acceptors: Biliary excreted ^{203}Pb (from donors) was administered intraduodenally. Group 2: $^{203}\text{PbCl}_2$ was administered intraduodenally. Bile duct non-cannulated. Group 3: $^{203}\text{PbCl}_2$ was administered intraduodenally. Bile duct cannulated. The results are expressed as a percentage of the intraduodenally dose (means and 95% confidence limits of means). GIT = gastrointestinal tract.

was immediately administered to acceptors (9 rats) through a cannula into the duodenum⁶. From acceptors the bile was collected for 24 h. 2. group: 4 rats without bile duct cannulated were given intraduodenally $^{203}\text{PbCl}_2$ every 2 h. 3. group: 4 rats with bile duct cannulated were given intraduodenally $^{203}\text{PbCl}_2$ every 2 h. The dose of lead received by the rats in the 2nd and 3rd group in the course of 24 h was equal to that received by acceptors in donor's bile within the same time interval (10.6 μg of Pb^{2+} per rat).

Determination of percentage of absorption and measurement of samples were performed in the same way as described formerly⁶. Each animal received about 8 μCi of ^{203}Pb . Carrier-free ^{203}Pb was kindly supplied by the Gustaf Werner Institute, University of Uppsala, Sweden.

Results and discussion. The average cumulative biliary excretion of ^{203}Pb in donors was 8.5% of the administered dose during 24 h. In acceptors (group 1) and in the rats from group 3 excretion via bile during 24 h was $1.6 \pm 0.4\%$ resp. $0.9 \pm 0.4\%$ of the intraduodenally administered dose of ^{203}Pb .

The Table shows the values of ^{203}Pb absorption in separate groups of rats. The results clearly indicate that percentage of absorption in acceptors as well as rats from group 2 (bile duct non-cannulated) is similar (36.9 and 35.6% resp.). The percentage of absorption in the group 3 (bile duct cannulated) is significantly lower —18.8% ($p < 0.05$). It is therefore obvious that absorption of ^{203}Pb administered into the duodenum decreases in rats with cannulated bile ducts. On the other hand, there are no differences between absorption of biliary excreted ^{203}Pb and of ^{203}Pb administered into duodenum in rats without

cannulation of the bile duct. Presence of bile seems to increase absorption of ^{203}Pb from the gastrointestinal tract. Lead probably forms a complex (or complexes) with some of bile components, most probably proteins^{3,7}, perhaps via a non-enzymatic way.

Comparison with results of the study of EHC of ^{52}Mn ⁶ shows that the percentage of absorption of lead excreted via bile is similar to values found in manganese. In case of lead, much lower biliary excretion in comparison with manganese means, however, much smaller importance of EHC in the total turnover of lead in the organism of the rat.

Summary. The author studied absorption of ^{203}Pb after administering intraduodenally ^{203}Pb eliminated with bile. The results obtained were compared with absorption of ^{203}Pb administered into the duodenum as $^{203}\text{PbCl}_2$ in rats forming 2 groups, one with bile ducts cannulated, the other intact. It was found that bile played an important role in absorption of Pb from the gastrointestinal tract. Absorption of Pb^{203} is significantly reduced if the bile is drained off by means of a cannula.

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⁶ M. ČIKRT, Arch. Toxic. 31, 51 (1973).

⁷ M. ČIKRT and M. TICHÝ, Experientia 28, 383 (1972).

Effects of Temperature on the Responses to Noradrenaline, Isoprenaline and Histamine on Isolated Rabbit Mesenteric Artery

In experiments on isolated organs, the responses to β -sympathomimetic drugs were found to be highly sensitive against alteration of temperature, decrease of extracellular H^+ concentration and against metabolic inhibitors. From these observations, it is concluded that the effects of β -adrenoceptor stimulant drugs depend on the metabolic state of an organ^{1,2}. Moreover, using α - and β -sympathomimetic drugs as relaxants on the rabbit ileum temperature elevation reveals a clear cut separation of adrenoceptors into the temperature sensitive β - and the insensitive α -adrenoceptors³.

In order to prove whether this holds true also on the mesenteric artery of the rabbit, the effects of temperature elevation either on the affinity or on the intrinsic activity of α - and β -sympathomimetic drugs were investigated.

It was further of interest to study the effects of histamine under similar experimental conditions.

Helically strips of the mesenteric artery of the rabbit were prepared for isometric recordings. They were suspended under a tension of 2 g in a 50 ml bath containing Krebs-Henseleit solution bubbled with 95% O_2 and 5% CO_2 . The strips were allowed to equilibrate for 60 min prior to application of the drugs at 25° and at 42°C,

¹ H. J. SCHÜMANN, J. WAGNER and D. REINHARDT, Naunyn-Schmiedeberg's Arch. Pharmacol. 275, 105 (1972).

² J. WAGNER, D. REINHARDT and H. J. SCHÜMANN, Archs int. Pharmacodyn. 197, 290 (1972).

³ J. WAGNER, D. REINHARDT and H. J. SCHÜMANN, Naunyn-Schmiedeberg's Arch. Pharmacol. 276, 63 (1973).