EFFECT OF URSODESOXYCHOLIC ACID UPON THE INTESTINAL ABSORPTION OF RIBOFLA- VIN IN GUINEA PIGS

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The effect of bile acid, especially ursodesoxycholic acid, upon the intestinal absorption of riboflavin was investigated on guinea pigs.

TABLE I
Effect of Cholic Acid upon Intestinal Absorption of Riboflavin in Guinea Pigs

No. of intestinal preparation	Composition of the solution injected into the lumen of the intestinal preparation	Riboflavin in the intestinal wall (γ/g)									
		No. 1		No. 2		No. 3		No. 4		No. 5	
		Total	Ester.	Total	Ester.	Total	Ester.	Total	Ester.	Total	Ester.
<i>a</i>	50 γ FR ^a in 1.0 ml H ₂ O + 0.5 ml 0.5% cholic acid in N/50 NaOH	7.20	3.39	8.25	4.27	4.42	3.09	5.98	3.80	5.42	3.21
<i>b</i>	1.0 ml H ₂ O + 0.5 ml 0.5% cholic acid in N/50 NaOH	3.04	2.06	2.79	2.21	3.19	2.52	2.92	2.36	2.54	2.03
Riboflavin absorbed in the intestinal wall $A = a - b$		4.16	1.33	5.46	2.06	1.23	0.57	3.06	1.44	2.88	1.18
<i>c</i>	50 γ FR in 1.0 ml H ₂ O + 0.5 ml N/50 NaOH	6.28	3.15	7.39	3.98	4.22	2.90	4.93	3.17	5.81	3.39
<i>d</i>	1.0 ml H ₂ O + 0.5 ml N/50 NaOH	2.93	2.00	3.27	2.49	2.95	2.37	3.10	2.48	2.90	2.24
Riboflavin absorbed in the intestinal wall $B = c - d$		3.35	1.15	4.12	1.29	1.27	0.53	1.83	0.69	2.91	1.15
Increase or decrease in the riboflavin absorbed in the intestinal wall by adding cholic acid (γ/g) $A - B$		0.81	0.18	1.34	0.77	-0.04	0.04	1.23	0.57	-0.03	0.03
Percentage increase or decrease in the riboflavin absorbed in the intestinal wall by adding cholic acid $= \frac{A-B}{B} \times 100$		23	15	32	59	- 3	7	67	108	- 1	2

The average for $A - B$ in γ/g : total, 0.66 ± 0.82 ; esterified, 0.35 ± 0.46 .

The average for $\frac{A-B}{B} \times 100$ in %: total, 23 ± 31 ; esterified 23 ± 50 .

^a Free riboflavin.

METHODS

The small intestine was isolated from a guinea pig and four parts of the intestine (1, 2, 3 and 4), in the length of 15 cm each, were prepared. Each preparation was washed with the Tyrode solution and ligatured at both ends. The solutions, as listed in Tables I—III, were introduced into the lumen of the prepared intestines, followed by incubating in the Tyrode solution at 38° for 30 minutes with continuous aeration through the solution. The bile acids examined were cholic acid, desoxycholic acid and ursodesoxycholic acid.¹ The riboflavin content of the intestinal wall of each preparation was estimated with a lumiflavin method (2).

RESULTS AND DISCUSSION

On the averages for 5 cases (Nos. 1—5) with an addition of cholic acid, the

TABLE II
*Effect of Desoxycholic Acid upon Intestinal Absorption of
Riboflavin in Guinea Pigs*

No. of intestinal preparation	Composition of the solution injected into the lumen of the intestinal preparation	Riboflavin in the intestinal wall (γ/g)									
		No. 6		No. 7		No. 8		No. 9		No. 10	
		Total	Ester.	Total	Ester.	Total	Ester.	Total	Ester.	Total	Ester.
<i>a</i>	50 γ FR in 1.0 ml of H ₂ O + 0.5 ml of 0.5% desoxycholic acid in <i>N</i> /50 NaOH	7.05	3.42	6.11	3.46	5.25	3.31	4.65	3.23	5.86	3.80
<i>b</i>	1.0 ml of H ₂ O + 0.5 ml of 0.5% desoxycholic acid in <i>N</i> /50 NaOH	2.82	2.08	2.78	1.67	2.58	1.90	3.07	2.54	3.22	2.73
Riboflavin absorbed in the intestinal wall $A = a - b$		4.23	1.34	3.33	1.79	2.67	1.41	1.58	0.69	2.64	1.07
<i>c</i>	50 γ FR in 1.0 ml of H ₂ O + 0.5 ml of <i>N</i> /50 NaOH	6.25	3.35	5.74	3.31	4.63	2.83	4.62	3.16	4.68	3.11
<i>d</i>	1.0 ml of H ₂ O + 0.5 ml of <i>N</i> /50 NaOH	2.53	1.84	2.82	2.38	2.58	2.07	2.86	2.51	3.50	2.88
Riboflavin absorbed in the intestinal wall $B = c - d$		3.72	1.51	2.92	0.93	2.05	0.76	1.76	0.65	1.18	0.23
Increase or decrease in the riboflavin absorbed in the intestinal wall by adding desoxycholic acid $A - B$		0.51	-0.17	1.41	0.86	0.62	0.65	-0.16	0.04	1.46	0.84
Percentage of increase or decrease in the riboflavin absorbed in the intestinal wall by adding desoxycholic acid $\frac{A-B}{B} \times 100$		13	-11	48	92	30	85	-9	6	106	365

The average for $A - B$ in γ/g : total, 1.16 ± 1.19 ; esterified, 0.78 ± 0.37

The average for $\frac{A - B}{B} \times 100$ in %: total, 37 ± 95 ; esterified, 107 ± 150 .

¹ Synthesized by Sato *et al.* (1).

² Fiducial limits with a level of significance of 95 per cent

TABLE III
Effect of Ursodesoxycholic Acid upon Intestinal Absorption of
Riboflavin in Guinea Pigs

No. of intestinal preparation	Composition of the solution injected into the lumen of the intestinal preparation	Riboflavin in the intestinal wall (γ/g)									
		No. 11		No. 12		No. 13		No. 14		No. 15	
		Total	Ester.	Total	Ester.	Total	Ester.	Total	Ester.	Total	Ester.
a	50 γ FR in 1.0 ml of H_2O + 0.5 ml of 0.5% ursodesoxycholic acid in N/50 NaOH	6.98	3.70	6.94	3.92	7.40	3.82	6.91	4.40	6.86	4.12
b	1.0 ml of H_2O + 0.5 ml of 0.5% ursodesoxycholic acid in N/50 NaOH	3.23	2.60	3.49	2.60	2.61	1.77	3.11	2.18	3.25	2.53
Riboflavin absorbed in the intestinal wall $A = a - b$		3.75	1.10	3.45	1.32	4.79	2.05	3.80	2.20	3.61	1.59
c	50 γ FR in 1.0 ml of H_2O + 0.5 ml of N/50 NaOH	6.09	3.37	5.59	3.21	5.96	2.83	5.19	3.40	6.27	3.73
d	1.0 ml of H_2O + 0.5 ml of N/50 NaOH	3.19	2.19	3.10	2.42	2.72	1.82	3.02	2.36	3.17	2.66
Riboflavin absorbed in the intestinal wall $B = c - d$		2.90	1.18	2.49	0.79	3.24	0.99	2.17	1.04	3.10	1.07
Increase or decrease in the riboflavin absorbed in the intestinal wall by adding ursodesoxycholic acid $A - B$		0.85	-0.08	0.96	0.53	1.55	1.06	1.63	1.18	0.50	0.52
Percentage of increase or decrease in the riboflavin absorbed in the intestinal wall by adding ursodesoxycholic acid $\frac{A-B}{B} \times 100$		29	-6	38	67	47	107	75	113	16	48

The average for $A-B$ in γ/g : total, 1.16 ± 0.84 ; esterified, 0.82 ± 0.56 .

The average for $\frac{A-B}{B} \times 100$ in %: total, 41 ± 22 ; esterified, 65 ± 55 .

intestinal absorption of total riboflavin was increased by $23 \pm 31^2\%$, and that of esterified riboflavin was increased by $23 \pm 50\%$ (cf. Table I).

On the average for 5 cases (Nos. 6—10) with an addition of desoxycholic acid, the intestinal absorption of the total riboflavin was increased by $37 \pm 95\%$, and that of the esterified riboflavin was increased by $107 \pm 150\%$ (cf. Table II).

On the averages for 5 cases (Nos. 11—15) with an addition of ursodesoxycholic acid, the intestinal absorption of total riboflavin was increased by $41 \pm 22\%$, and that of esterified riboflavin was increased by $65 \pm 55\%$.

These figures showed that a significant increase in the intestinal absorption and riboflavin phosphorylation in guinea pigs were found only in the cases with ursodesoxycholic acid, but not in those with cholic or desoxycholic acid.

Recently Onishi (3), using a perfusion technique in dogs, demonstrated a marked increase in the intestinal absorption and riboflavin phosphorylation in the presence of ursodesoxycholic acid.

SUMMARY

The intestinal absorption and riboflavin phosphorylation was shown to be accelerated significantly by ursodesoxycholic acid in guinea pigs.

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