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Influence of nutrition factors forming stable mixed micelles on permeation of quinine *in vitro* studied by the everted sac technique

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Oral application as the most widely used way for drug administration bears the risk of interactions with food or food components [1–4]. Bile salts such as glycodeoxycholate influence the dissolution rate and the absorption of drugs by changing the surface tension of the fluid in the gastrointestinal tract or by micellar solubilization. Bile salts facilitate the transfer of drugs across the intestinal wall by affecting the fluid and electrolyte balance, by decreasing the viscoelasticity of the mucos layer, by inducing of mucus secretion and by changing the permeability of the mucosal membrane. Incorporation into mixed micelles consisting of glycodeoxycholate and palmitic acid or palmitic acid and lecithin leads to an enhancement of rectal absorption of poorly absorbable drugs [5–8].

The objective of this work was to study the influence of glycodeoxycholate below and above the critical micelle concentration (CMC) and in addition with fatty acid and/or lecithin on quinine permeation in everted sac-gut from rats [9–12]. Bile salts are able to form stable mixed micelles with fatty acids and/or lecithin [13–15].

A concentration of glycodeoxycholate below CMC (0.5 mM) had no significant effect on the quinine transport, but above (15 mM) CMC a strong inhibition of the quinine transport was observed (Fig.).

Addition of lecithin to the bile salt did not change the transport inhibition of quinine compared to glycodeoxycholate alone.

A combination of glycodeoxycholate and palmitic acid or palmitic acid/lecithin leads to the strongest decrease of the quinine permeation in the everted sac model.

The extend of the transport reduction was similar after 60 min and 90 min.

In conclusion, quinine absorption from the gastrointestinal tract can be influenced by nutrition factors such as bile salts, fatty acids and phospholipids. In this study, the significantly decreased absorption rate of quinine was particularly registered in the presence of glycodeoxycholate above CMC and, particularly, in the presence of stable mixed micelles consisting of bile salt, fatty acids and/or lecithin. Based on this results, the influence of nutrition factors forming stable mixed micelles on the pharmacokinetics of quinine is to be studied.

Experimental

The experiments were carried with a donor concentration of quinine (Caesar & Loretz, Hilden, Germany) of 1.1 mmol/l at pH 7.2 phosphate buffer and gasing with carbogen. Glycodeoxycholic acid, palmitic acid and lecithin from fresh egg yolk (Sigma-Aldrich, Deisenhofen, Germany) were taken. The ileum from rats (male wistar, fasted 20 h) was obtained from the final 8–10 cm of the intestine, just proximal to the cecum [16, 17]. The concentration of quinine was measured in the acceptor medium using HPLC (Kontron, Neufahrn, Germany) with UV-detection.

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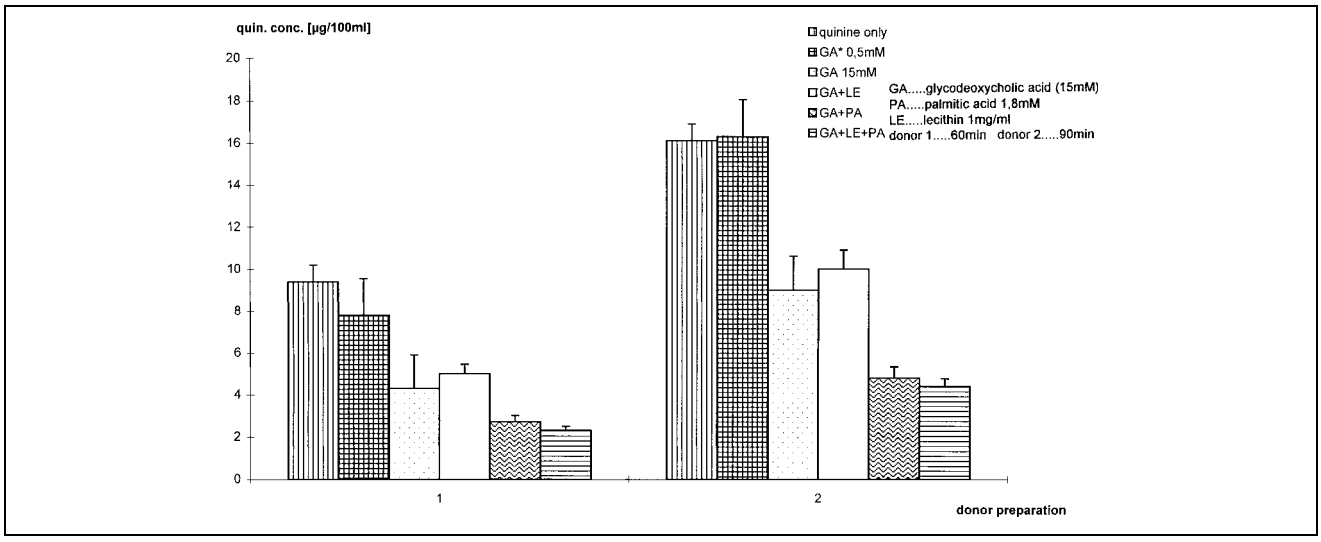

Fig.: Acceptor concentration of quinine after 60 and 90 min