عنوان مقاله:

Influence of quercetin and chrysin on the intestinal permeability of paclitaxel, a substrate of P-glycoprotein and CYP3A4 using in vitro rat gut sacs

محل انتشار:

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خلاصه مقاله:

P-glycoprotein (P-gp) and cytochrome P450 3A4 (CYP3A4) play a significant role in the disposition and elimination of drugs. The objective of this study was to investigate the mechanism underlying the interaction between paclitaxel (substrate of P-gp and CYP3A4) and quercetin and chrysin (known modulator of P-gp and CYP3A4) using everted gut sacs in vitro models. Rat everted and non-everted gut sacs (NEGS) are simple and useful in vitro models to investigate the role of P-gp and CYP3A4 in drug disposition. NEGS were used to evaluate the transport of paclitaxel from mucosal to serosal (M-to-S) side of the intestine. NEGS were loaded with 1mL of modified Krebs-Ringer bicarbonate (KRB) buffer containing paclitaxel (50µg/mL) in the presence or absence of known P-gp and CYP3A4 inhibitors (quercetin and chrysin).The paclitaxel levels in incubated samples were dteremined by UV-spectrophotometer at 227 nm. The same experiment was repeated with everted gut sacs (EGS) to study the transport of paclitaxel from serosal to mucosal (S-to-M) side of the intestine. The apparent permeability coefficient (Papp), efflux ratio and net efflux were determined. In vitro study results showed that the Papp, net efflux and efflux ratio of paclitaxel were significantly increased by quercetin and chrysin. The present study results revealed that quercetin and chrysin enhanced the intestinal absorption of paclitaxel by inhibiting its absorption via P-gp and/or the CYP3A4-mediated biotransformation in intestine.

کلمات کلیدی:

P-glycoprotein, Paclitaxel, Quercetin, Chrysin, Everted Sacs, CYP3A4