

Table 7 Substrates for MRP2 (cMOAT)

Endogenous compounds	Exogenous compounds
Bile salts	Quinolone antibiotics (grepafloxacin, lomefloxacin)
Cholate-3- <i>O</i> -glucuronide	β -Lactam antibiotics (cefodizime, ceftriaxone)
Taurolithocholate-3-sulfate	HMG CoA reductase inhibitors (pravastatin)
	ACE inhibitors (temocaprilat)
Non bile salts	Methotrexate
Conjugated bilirubin	Camptothecins (topotecan, irinotecan)
Glutathione GSH/GSSG	Bromosulphophthalein
Cysteinyl-leukotrienes	Naphthol-1-glucuronide
2,4-Dinitrophenyl- <i>S</i> -glutathione	Indocyanine green
	Carboxydichlorofluorescein

Source: Information obtained from Refs. 3, 4, 11, 13, 17, 57, 78, 88.

4.2.4. Sinusoidal Efflux of Organic Anions

Organic anion uptake across the sinusoidal membrane is bidirectional, suggesting that sinusoidal membrane transport systems prevent accumulation of toxic bile salts and other cholephilic compounds during conditions of defective canalicular secretion. In addition to the transport systems involved in hepatic uptake of organic anions, MRP1 and MRP3 are expressed on the basolateral membrane. It has been suggested that these transporters play a pivotal role when transport across the canalicular membrane is blocked. The expression of MRP1 is induced during liver regeneration and under conditions of experimentally induced cholestasis. The MRP3 expression is induced by medications such as rifampin. Additionally, MRP3 expression is enhanced in the cases of MRP2 deficiency due to disease (e.g., Dubin–Johnson syndrome) or genetic disruption (e.g., TR– rats).

5. GASTROINTESTINAL TRANSPORT

5.1. Traditional View of Intestinal Absorption

The most common route for drug delivery is oral administration. The traditional view of oral drug absorption is that it occurs primarily from the small intestine and proceeds via a passive transcellular process. The small intestine represents the primary site of absorption in the GI tract because of the functional specialization of the intestinal cells (creating a large surface area for absorption) combined with the prolonged intestinal transit time.