

SOLVO MOUSE BSEP VESICULAR TRANSPORT ASSAY

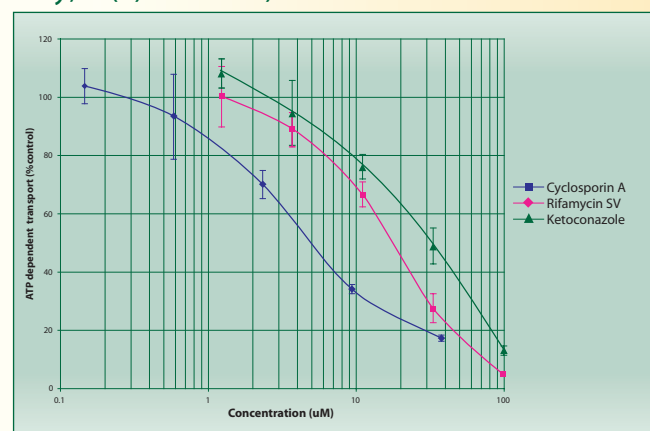
Bile is formed in the vertebrate liver by the active secretion of the bile salts, organic anions and lipids across the canalicular membrane of the hepatocytes. The canalicular secretion of bile salts is predominantly mediated by **Bsep** transporter (**bile salt export pump**). Bsep, also called sister of P-glycoprotein (sPgP), is a member of the ABC transporter family and is closely related to the Pgp (MDR1, ABCB1). Mutations in the gene of human BSEP were indentified as the cause of progressive familial intrahepatic cholestasis type 2 (**PFIC-2**). It has been shown that inhibition of BSEP may impair bile acid transport into the bile, and thus may contribute to extensive **cholestasis**, leading to **drug-induced hepatotoxicity**.

ABC transporter proteins mediate transport of substrates against a concentration gradient, and the energy for this transporter is derived from vanadate-sensitive ATP-hydrolysis, which is coupled to substrate translocation. One of the simplest methods invented to detect the substrate translocation is the vesicular transport assay.

The standard Vesicular Transport assay is an indirect inhibitory-type assay, and is performed with cold test compounds. It provides information on any interaction between the ABC transporter and the test drug that would affect the transport of the reporter substrate (radioactive compound). In this assay the transport of a known substrate - the reporter substrate - is measured in the presence of the test drug. Values are presented on a relative scale with 100% defined as transport in the absence of the test compound (no inhibition),

and 0% defined as transport measured in the absence of ATP (no transporter activity). IC₅₀ is defined as the concentration required to inhibit the transport of the reporter substrate by 50%.

Taurocholate, the reporter substrate used in SOLVO's Bsep VT assay, is the major endogenous substrate of Bsep. In SOLVO's indirect mouse Bsep vesicular transport assay the interaction of compounds with mouse Bsep is detected as the inhibition of the transport of **³H-Taurocholate**, therefore the assay shows the effect of the test drug on the physiological function of the transporter. The assay utilizes **Sf9 cell** membranes containing **mouse Bsep** protein. Expression of the protein is achieved by baculoviral transfection that was first described by Noe J, et al. (Hepatology. 2001 May;33(5):1223-31.)



ATP dependent mouse Bsep mediated transport of **³H-Taurocholate** at different concentrations of various test compounds.

The mouse Bsep Vesicular Transport Assay is either available as a product (SB-mouseBsep-Sf9-VT membrane preparation) for in house screening or as the Fee-For-Service Screening performed in the SOLVO Screening Laboratory.