**Purpose:** Drug-induced liver injury (DILI) has led to the withdrawal of drugs from the market. One postulated mechanism of DILI is cholestasis, improved by inhibition of the bile salt efflux pump (BSEP). BSEP inhibition can be measured in vitro with BSEP expressing vesicles. However, not all drugs identified as BSEP inhibitors cause DILI as there are many pathways involved in cholestatic toxicity. An in vitro system which models human hepatocyte in vivo transport sparing and functionality more completely may better predict the potential of drugs to cause cholestasis or DILI. We evaluated the hepatobiliary disposition of taurocholic acid (TCA) in the presence of cholestasis agents using B-CLEAR® human sandwich-cultured hepatocytes.

**Methods:** Compounds were screened for effect on uptake, efflux, and intracellular concentration (ICC) of TCA using B-CLEAR® human sandwich-cultured hepatocytes. The presence of 4% FBS, BSA, and LpH-nat. were pre-incubated with inhibitor for 10 min and then co-incubated with inhibitor and TCA for 30 min. Follow up work may indicate inhibition of uptake, conversion buffer was then removed and replaced with 300 μL Plus (+) buffer containing 2.5 μM taurocholic acid (TCA) and the inhibitors previously isolated and incubated in the presence of 4% FBS for an additional 30 min. At the end of the incubation, cells were washed three times in Plus (+) buffer. TCA accumulation and Kp ratio for TCA may provide information on the integrated effects of inhibition of uptake and efflux by a xenobiotic. Overall, the use of a drug which more closely models in vivo conditions can lead to better predictions of hepatic transporter inhibition and toxicity.

**Results:** Table 1 shows the results of screening assays are described in the table. The biliary excretion index (BEI), intracellular concentration (ICC), and Kp ratio for TCA may provide information on the integrated effects of inhibition of uptake and efflux by a xenobiotic. Several factors may be more responsible for the ICC and Kp ratio for TCA which more closely models in vivo conditions can lead to better predictions of hepatic transporter inhibition and toxicity.

**Conclusions:** Drug-induced liver injury (DILI) is characterized as liver injury due to intake of medications or xenobiotics, which leads to liver abnormalities or dysfunction. There are many xenobiotics which inhibit cholestasis or DILI. The presence of clinically relevant cholestatic agents may indicate inhibition of uptake into hepatocytes may lead to a risk of systemic toxicity. Therefore, the use of an in vitro system which more accurately models in vivo conditions can lead to better predictions of cholestasis and DILI.

**Materials & Methods:**

**Materials:** Human hepatocytes were isolated and purified at XenTech Inc., and characterized for use at Qualyst Transporter Solutions, LLC. Brain cell culture and media, and Fluorometric substrate assay buffer, and Fluorometric substrate assay buffer were obtained from Qualyst Transporter Solutions, LLC. Taurocholic acid (TCA) was obtained from Panreac Immuno & Analytical Sciences (Waltham, MA, USA). Bovine serum albumin, carboxymethyl cellulose, mannosylamine, and glycosaminoglycan were obtained from Cambrex Chemicals (Arbor, MI, USA).

**Results:** Table 1 shows the results of screening assays are described in the table. The biliary excretion index (BEI), intracellular concentration (ICC), and Kp ratio for TCA may provide information on the integrated effects of inhibition of uptake and efflux by a xenobiotic. Several factors may be more responsible for the ICC and Kp ratio for TCA which more closely models in vivo conditions can lead to better predictions of hepatic transporter inhibition and toxicity.

**Conclusions:** The B-CLEAR® human sandwich-cultured hepatocyte assay demonstrates the ability to utilize the accumulation of a probe substrate to assess both inhibition of uptake as well as efflux. Many xenobiotics which inhibit cholestasis or DILI. The presence of clinically relevant cholestatic agents may indicate inhibition of uptake into hepatocytes may lead to a risk of systemic toxicity. Therefore, the use of an in vitro system which more accurately models in vivo conditions can lead to better predictions of cholestasis and DILI.