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In vitro and *in vivo* studies on the hepatic effect of acute administration of *Chelidonium majus* alone and in association with acetaminophen

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Background Several cases of hepatotoxicity after consumption of herbal preparations containing *Chelidonium majus* L. have been reported (Mazzanti G et al. *J Ethnopharmacol* 2009;124:328-32)

Present work was aimed to assess if the co-treatment of *C. majus* and sub-toxic doses of acetaminophen can induce liver damage.

Materials and methods Cytotoxicity of test substances was assessed in Buffalo normal Rat Liver cell line (BRL-3A) by the MTT reduction method, after 24 h of exposure. *In vivo* hepatotoxicity was evaluated male Wistar rats. Four experimental groups (n=8) were treated as follow: 1vehicle (polyethylene glycol and saline solution 1:1) + vehicle, 2vehicle+ acetaminophen (0.5 g/kg); 3 *C. majus* extract (1.5 g/kg) + vehicle; 4 *C. majus* extract (1.5 g/kg) + acetaminophen (0.5 g/kg), according to the treatment schedule of Janbaz and Gilani (*Food Chem Toxicol* 1999; 37: 603-7). Blood and liver samples were obtained from rats after anaesthetization with ethylic ether and were analyzed.

Results *C. majus*, up to 5 mg/ml did not reduce significantly the cell proliferation. Acetaminophen, at the sub-toxic dose of 0.1 mg/ml, did not significantly increase the *C. majus* effect.

The treatment with *C. majus* did not alter liver function parameters. Rats treated with acetaminophen showed a significant increase in total bilirubin, AST, and ALT. The administration of both *C. majus* and acetaminophen did not increase the effect induced by the single substances.

C. majus did not affect hepatic histomorphology while acetaminophen induced focal hepatocellular necrosis and light inflammatory cells infiltration. The co-administration of *C. majus* extract did not increase the alterations induced by acetaminophen. Alpha-SMA expression in hepatic stellate cells was negative for all experimental groups.

Conclusions The co-administration of *C. majus* and acetaminophen does not have any synergistic effect in our experimental model, suggesting that the suspected hepatotoxicity in humans is not caused by association of *C. majus* with potential hepatotoxic drugs.

Key words
Hepatotoxicity, Chelidonium majus, liver function, acetaminophen, interactions