I Rodeiro et al., Med Chem 2014, 4:12
http://dx.doi.org/10.4172/2161-0444.S1.013

OMICS Group Conferences
Accelerating Scientific Discovery

3rd International Conference on
Medicinal Chemistry & Computer Aided Drug Designing
December 08-10, 2014 DoubleTree by Hilton Hotel San Francisco Airport, USA

New experimental evidences about of modulation of hepatic P450 enzymes by one marine plant *Thalassia testudinum* extract, potential herb-drugs interactions

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The aqueous-ethanol extract from marine plant *Thalassia testudinum* leaves with cytoprotective and anti-tumour properties is currently being developed in Cuba as a nutritional supplement. Its phytochemical composition demonstrates it is a rich source of natural antioxidants with potential applications in pharmaceutical and food industries. We disclose here the *in vivo* effects of this product over several P450 isoforms. Male Wistar rats were administered orally with 20, 200 and 400 mg/kg of the extract for 10 days. The activities of 7-ethoxy, 7-methoxy, 7-penthoxy and 7-benzoxyl resorufin-O-deethylases, 4-nitrophenol hydroxylation and erythromycin N-demethylation were used to asses the function of CYP1A1, CYP1A2, CYP2B1, CYP1B2, 2E1 and 3A in liver microsomes. Protein expressions of cythocromes were determined by western blot and mRNA levels by RT-PCRq. Microsoms were used as metabolic fraction for the Ames test. Other animals, after receive the same doses of the extract, were administered orally with theophylline (10 mg/kg), blood samples were taken in order to determine the theophylline concentration in plasma. *Thalassia testudinum* extract (200 mg/kg) was able to induce CYP1A1 (1.5-fold). Meanwhile, after 400 mg/kg the activity did increase, but no significant differences were found. The lowest dose (20 mg/kg) induced increments of CYP1A2 and 2B1 activities, but no significant differences were seen. A reduction (near to 20%) of CYP2B2, 2E1 and 3A activities was also found. The increase of the CYP1A1 activity was in agreement with the elevation of the protein, but mRNA levels were no modified. The extract increased the mutagenicity of the benzo(a)pyrene at the highest doses (1.8 and 2.3-fold), confirming its influence on the CYP1A1 activity. Pharmacokinetic profile of theophylline changed in treated rats: Cmax and clearance of theophylline were significantly increased. The elimination rate constant increased twice and the half-life time was 2-fold reduced. *Thalassia testudinum* acts as inducer of the CYP1A1/2 enzymes under these experimental conditions, suggesting potential herb-drug interaction when patients use the extract concomitantly or in advance of drugs which are substrates of P450s, especially CYP1A1/2.

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