Research Article

PASS-Predicted Hepatoprotective Activity of Caesalpinia sappan in Thioacetamide-Induced Liver Fibrosis in Rats

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The antifibrotic effects of traditional medicinal herb Caesalpinia sappan (CS) extract on liver fibrosis induced by thioacetamide (TAA) and the expression of transforming growth factor β1 (TGF-β1), α-smooth muscle actin (αSMA), and proliferating cell nuclear antigen (PCNA) in rats were studied. A computer-aided prediction of antioxidant and hepatoprotective activities was primarily performed with the Prediction Activity Spectra of the Substance (PASS) Program. Liver fibrosis was induced in male Sprague Dawley rats by TAA administration (0.03% w/v) in drinking water for a period of 12 weeks. Rats were divided into seven groups: control, TAA, Silymarin (SY), and CS 300 mg/kg body weight and 100 mg/kg groups. The effect of CS on liver fibrogenesis was determined by Masson’s trichrome staining, immunohistochemical analysis, and western blotting. In vivo determination of hepatic antioxidant activities, cytochrome P450 2E1 (CYP2E1), and matrix metalloproteinases (MMPs) was employed. CS treatment had significantly increased hepatic antioxidant enzymes activity in the TAA-treated rats. Liver fibrosis was greatly alleviated in rats when treated with CS extract. CS treatment was noted to normalize the expression of TGF-β1, αSMA, PCNA, MMPs, and TIMPI proteins. PASS-predicted plant activity could efficiently guide in selecting a promising pharmaceutical lead with high accuracy and required antioxidant and hepatoprotective properties.

1. Introduction

Liver fibrosis is known to result in distortion of normal tissue architecture of the liver. This alteration resulted from chronic liver damage as seen in chronic alcoholic abuse, viral hepatitis, or inherited metabolic disease [1]. Several biological and biochemical disturbances may also lead to hepatic cirrhosis [2]. A fibrotic liver may contain a substantial increase in most of the matrix proteins, in particular, the interstitial collagen types I and III which are under the influences of cytokines like transforming growth factor beta 1 (TGF-β1) and α-smooth muscle actin (αSMA) [3, 4]. These cytokines not only are present in greater amounts but also are deposited in abnormal sites within the liver microanatomy [5]. In case of thioacetamide- (TAA-) induced liver cirrhosis, other parameters such as oxidative stress have been postulated to be major molecular mechanisms basic to tissue alteration [6].

Caesalpinia sappan (CS), commonly named as Brazil or Sappan, belongs to the family of Caesalpiniaceae, a native plant in Southeast Asia [7]. Several studies have shown that CS has antimicrobial and bactericidal activity [8] and anti-allergic [9], neuroprotective [10], and hypoglycaemic effects [11]. Others found that extract from CS can be used for treating ascites, tumor, leukemia [12], and arteriosclerosis [13]. This could be due to its antioxidant activity