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Hypouricemic activities of *C. flammula* leaf extracts in an animal model

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Clematis flammula is a plant widely used in traditional medicine in Algeria to treat gout and various inflammatory disorders. Hyperuricemia and gout are classically treated by drugs such as febuxostat and allopurinol that favour the elimination or degradation of uric acid (UA) through the inhibition of xanthine oxidase (XO). However, these synthetic drugs could cause adverse side effects which instigated researchers to seek alternative plant-derived molecules. In this perspective, hypouricemic activities of ethanol and aqueous phase of ethyl acetate leaf extracts of *C. flammula* were examined in oxonate-treated mice. Male mice were randomized into 10 groups (n=6), 5 were administered extract only and 5 rendered hyperuricemic with an intraperitoneal injection of oxonate (oxo) (250 mg/kg). The latter inhibits uricase, an enzyme that catalyses the conversion of uric acid to allantoine. The hyperuricemic groups were administered orally carboxymethyl cellulose (CMC) at (0.8%), extracts (100, 200 and 400 mg/kg) and allopurinol, respectively, one hour after they received oxo. CMC (0.8%) is considered to be the vehicle in which extracts and allopurinol (10 mg/kg) were dissolved. The duration of the treatment was three days at the end of which the mice were scarified. Blood was collected for serum analysis of uric acid content and livers were excised to determine XO/XDH activity. A significant reduction of uric acid in mice treated with *C. flammula* extracts was observed, from 4.50±0.19 mg/dl in hyperuricemic non-treated mice to 0.69±0.06, 0.69±0.06 and 1.39±0.18 mg/dl in the hyperuricemic groups pre-treated respectively with 100, 200 and 400 mg/kg of ethanolic extract. The hypouricemic effect of the aqueous phase of ethyl acetate was more prominent leading to a higher reduction of uric acid leading to 1.29±0.22, 1.29±0.16, 1.76±0.3 mg/dl in hyperuricemic mice treated with 100, 200 and 400 mg/kg of the extract, respectively. Allopurinol, on the other hand, reduced uric acid level to 0.33±0.02 mg/dl. Regarding XO/XDH activity in the liver of oxonate-treated mice, no inhibition of that activity was noticed for those groups fed with the ethanolic extract. However, a strong inhibition on hepatic XO was exerted by aqueous of ethyl acetate by 68.84%. 74.46%, 71.95% and 73.16% at 100, 200 and 400 mg/kg, respectively, while its percentage inhibitions on XDH were of 61.15, 70.31 and 62.07% suggesting that the extract's hypouricemic effect might be related to enzyme inhibition. Allopurinol, on the other hand showed a higher inhibition of xanthine oxidase than the extract (80.54 and 77.61% on XO and XDH, respectively).

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