World Academy of Science, Engineering and Technology
International Journal of Pharmacological and Pharmaceutical Sciences
Vol:8, No:10, 2014

Chemopreventive Efficacy of Andrographolide in Rat Colon Carcinogenesis Model Using Aberrant Crypt Foci (ACF) as Endpoint Marker

Authors : Maryam Hajrezaie, Mahmood Ameen Abdulla, Nazia Abdul Majid, Hapipa Mohd Ali, Pouya Hassandarvish, Maryam Zahedi Fard

Abstract : Background: Colon cancer is one of the most prevalent cancers in the world and is the third leading cause of death among cancers in both males and females. The incidence of colon cancer is ranked fourth among all cancers but varies in different parts of the world. Cancer chemoprevention is defined as the use of natural or synthetic compounds capable of inducing biological mechanisms necessary to preserve genomic fidelity. Andrographolide is the major labdane diterpenoidal constituent of the plant Andrographis paniculata (family Acanthaceae), used extensively in the traditional medicine. Extracts of the plant and their constituents are reported to exhibit a wide spectrum of biological activities of therapeutic importance. Laboratory animal model studies have provided evidence that Andrographolide play a role in inhibiting the risk of certain cancers. Objective: Our aim was to evaluate the chemopreventive efficacy of the Andrographolide in the AOM induced rat model. Methods: To evaluate inhibitory properties of andrographolide on colonic aberrant crypt foci (ACF), five groups of 7-week-old male rats were used. Group 1 (control group) were fed with 10% Tween 20 once a day, Group 2 (cancer control) rats were intra-peritoneally injected with 15 mg/kg Azoxymethan, Gropu 3 (drug control) rats were injected with 15 mg/kg azoxymethan and 5-Flourouracil, Group 4 and 5 (experimental groups) were fed with 10 and 20 mg/kg andrographolide each once a day. After 1 week, the treatment group rats received subcutaneous injections of azoxymethane, 15 mg/kg body weight, once weekly for 2 weeks. Control rats were continued on Tween 20 feeding once a day and experimental groups 10 and 20 mg/kg andrographolide feeding once a day for 8 weeks. All rats were sacrificed 8 weeks after the azoxymethane treatment. Colons were evaluated grossly and histopathologically for ACF. Results: Administration of 10 mg/kg and 20 mg/kg andrographolide were found to be effectively chemoprotective, as evidenced microscopily and biochemically. Andrographolide suppressed total colonic ACF formation up to 40% to 60%, respectively, when compared with control group. Pre-treatment with andrographolide, significantly reduced the impact of AOM toxicity on plasma protein and urea levels as well as on plasma aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH) and gamma-glutamyl transpeptidase (GGT) activities. Grossly, colorectal specimens revealed that andrographolide treatments decreased the mean score of number of crypts in AOM-treated rats. Importantly, rats fed andrographolide showed 75% inhibition of foci containing four or more aberrant crypts. The results also showed a significant increase in glutathione (GSH), superoxide dismutase (SOD), nitric oxide (NO), and Prostaglandin E2 (PGE2) activities and a decrease in malondialdehyde (MDA) level. Histologically all treatment groups showed a significant decrease of dysplasia as compared to control group. Immunohistochemical staining showed up-regulation of Hsp70 and down-regulation of Bax proteins. Conclusion: The current study demonstrated that Andrographolide reduce the number of ACF. According to these data, Andrographolide might be a promising chemoprotective activity, in a model of AOM-induced in ACF.

Keywords : chemopreventive, andrographolide, colon cancer, aberrant crypt foci (ACF)
Conference Title : ICPPS 2014 : International Conference on Pharmacy and Pharmacological Sciences
Conference Location : Osaka, Japan
Conference Dates : October 12-13, 2014