Abstract

Inflammatory Bowel Disease (IBD) is a set of chronic inflammatory conditions resulting from inappropriate and persistent activation of the mucosal immune system, driven by presence of normal intraluminal flora. The two disorders known as IBD are Crohn’s disease and ulcerative colitis. Conventional therapies used in inflammatory bowel disease are not totally successful in achieving remission or preventing relapse, and may cause serious side effects; therefore patients seek alternative options. The most commonly used alternative remedies are herbal remedies.

Present study aimed to discover newer herbal drugs effective in Inflammatory Bowel Disease (especially ulcerative colitis), the prevalence of which is now increasing in urban and rural population in India. Study attempted to evaluate protective effect of *Aconitum heterophyllum*, *Oroxylum indicum* and *Aagle marmelos* against experimentally induced colitis in rats. Efforts were also made to establish mechanism of action of isolated active fractions from these plants.

Roots, root bark and fruits of *A. heterophyllum*, *O. indicum* and *A. marmelos* respectively, were extracted and evaluated for their preliminary potential against dinitrobenzene sulfonic acid (DNBS) induced colitis in rats. Aqueous extract of *A. heterophyllum* showed prevention of some of symptoms of colitis, but the results were non significant. Whereas aqueous extract of *O. indicum* was found to be protective against DNBS induced colitis by inhibiting macroscopic and microscopic damage to colon, weight loss, diarrhoea, Myeloperoxidase (MPO), Malondialdehyde (MDA) and Nitric oxide (NO) levels with increase in natural antioxidant Glutathione (GSH) levels in rats. The effect was dose dependant and maximum inhibition was found in dose 400 mg/kg p.o. It also prevented castor oil and magnesium induced diarrhoea in rats and mice.

The potently active fractions obtained from *O. indicum* (OI-F) and *A. marmelos* (AM-E) were evaluated against experimentally induced colitis associated colon cancer in rats. OI-F treatment increased survival of rats, decreased incidence of tumour and number of tumours in colon. In dose 100 mg/kg p.o., OI-F improved
Abstract

Phytopharmacological evaluation of some plants useful in treatment of Inflammatory Bowel Disease symptoms of Azoxymethane (AOM) and Dextran sulphate sodium (DSS) treated rats. Body weight, stool consistency and colonic lesion area were found to be improved significantly. But Nuclear Factor-κB (NF-κB) and Interlukin-6 (IL-6) levels in homogenised rat colon were altered slightly. Moreover, in another set of experiment OI-F was found to inhibit Ca^{2+} release-activated Ca^{2+} (CRAC) channels, \textit{in vitro}.

On the other hand, AM-E was also found to inhibit progression of AOM and DSS induced colon cancer significantly. It decreased symptoms of inflammation as well as colon cancer at both doses (i.e. 50 and 100 mg/kg p.o.). AM-E inhibited NF-κB and IL-6 levels significantly as compared with model control. Furthermore, in \textit{in vitro} study, AM-E fraction was found to inhibit response of histamine on H1 receptors dose dependently.

In conclusion, aqueous extract of \textit{O. indicum} was found to be protective against DNBS induced colitis, while aqueous extract of \textit{A. heterophyllum} was only moderately active. The potent active fractions of \textit{O. indicum} (OI-F) and \textit{A. marmelos} (AM-E) showed significant inhibition of symptoms of colitis and also inhibit progression of colitis associated colon cancer. OI-F inhibited Ca^{2+} release-activated Ca^{2+} (CRAC) channels, thereby, might be inhibiting T cell activation and experimentally induced colitis. Alternatively AM-E was found to inhibit response of histamine on H1 receptors dose dependently, thereby, might be inhibiting the progression of UC.