1. INTRODUCTION

Inflammatory Bowel Disease (IBD) is a set of chronic inflammatory conditions comprising of Crohn’s disease (CD) and Ulcerative colitis (UC) [1; 2]. UC is an inflammatory disease targeting the large intestine. The disease is chronic but symptoms of urgency diarrhea, with or without mucus and/or blood and sometimes abdominal pain and tenesmus are intermittently exacerbating and remitting [3]. The onset can be almost imperceptible but is in rare cases fulminant, requiring immediate surgery. Asymptomatic periods vary from months to years [1; 2].

The extent of inflammation can be restricted to the rectum (proctitis) or the rectum and sigmoid colon (proctosigmoiditis). Distal inflammation is more often associated with symptoms of urgency. Inflammation can also be extended to the splenic flexure (leftsided colitis), the hepatic flexure (extensive colitis) or involve the entire colon and rectum (total colitis). The seriousness of the disease is often dependent upon the extent of inflammation whereas severity is dependent upon the intensity of the inflammation. A limited but intensely inflamed section of the colorectum can be of utmost difficulty for the patient [3].

Extra-intestinal manifestations, such as inflammatory reactions in the skin, joints, eyes and hepatobiliary system are sometimes present. More recently described involvements are pulmonary diseases, thromboembolic events, osteopenia and osteoporosis. The incidence of UC is calculated to be 1-25 per 1,00,000 per year and the disease affects people of all ages. Onset of disease in the first decade of life is unusual but there is a steep increase in incidence during puberty and the following adolescence and young adulthood [4]. The etiology of the disease is yet to be revealed but the pathogenesis is believed to be multifactorial. An observed tendency of UC to cluster to families has implied that genetic components are involved in the development of the disease.

Management of inflammatory bowel disease involves the use of 5-aminosalicylic acid and immunosuppressive agents such as corticosteroids and 6-mercaptopurine as well as its precursor azathioprine [4; 5]. Long term use of glucocorticoids is associated with high rates of relapse and unacceptable toxicity. On the other hand, 6-mercaptopurine and its prodrug azathioprine are effective in
Introduction

maintaining remission, however, a significant number of patients are resistant or intolerant to thiopurines\textsuperscript{[4, 5]}. Biologic agents including monoclonal antibodies, interferons, and other molecules made by living organisms are considered as therapeutically effective with fewer side effects. Infliximab is one of the medications for UC\textsuperscript{[6]}. It is an antibody which attaches to tumor necrosis factor-alpha (TNF-\(\alpha\)). TNF-\(\alpha\) is one of the proteins produced by immune cells promoting inflammation. By attaching to TNF-\(\alpha\), infliximab blocks its activity in order to reduce the inflammation. However, these agents are expensive and with side effects. Consequently, there is a need for alternative agents that may be equally or more effective as well as being cheaper\textsuperscript{[5]}. 

Recently many novel therapeutic approaches such as the anticoagulant heparin, nicotine and Omega-3 fatty acids are also being studied\textsuperscript{[7]}. Another new therapeutic option is the prebiotic and probiotic studies since UC is closely related to the deregulated host and microflora interaction. It aims to restore the balance of the gastrointestinal microecology and reduce the inflammation\textsuperscript{[8]}. 

One of the most interested novel approaches is using herbs as alternative therapy in addition to the conventional therapies. These are natural compounds, which suggested to minimize undesired side effects and accumulated toxicity from invasive procedures and drug therapies\textsuperscript{[9]}. Furthermore, a number of herbs have been used for the treatment of diseases for hundreds years. There are books, literatures and documents recording the therapeutic effect and successful cases. However, the effect of these herbs lacks the modern scientific approval. 

\textit{Oroxylum indicum} (Syonakh) is a traditional herbal medicine in India, China and Japan, belonging to family Bignoniaceae. It is one of important ingredients in most commonly used Ayurvedic preparation, named as “Dasamula”. Root bark is also been used in other Ayurvedic formulation such as Amartarista, Dantyadyarista, Narayana Taila, Dhanawantara Ghrita, Brahma Rasayana, Chyavanaprara Awalwha etc. The plant is reported in Indian ancient text “Ayurveda” to possess diuretic and antibacterial activity\textsuperscript{[10]}. It have been used as an analgesic, antitussive and anti-inflammatory agent for treatment of cough, bronchitis and other diseases\textsuperscript{[11]}. These findings form a good basis for its use in Inflammatory bowel disease.
Aconitum heterophyllum Wall commonly known as “Atis” or “Patis” belongs to family Ranunculaceae and was reported for its medicinal and pharmaceutical values since long. The roots which are used mostly as poison than as drug are now reported to possess significant antipyretic and analgesic properties with a high therapeutic index\(^{12}\). The plant was reported to be used for treatment of diseases of nervous system, digestive system, rheumatism and fever\(^{12}\). It also exhibits anti-fungal and anti-bacterial activities\(^{12}\) which indicate its usefulness as a promising drug in treatment of IBD.

Aegle marmelos (L.) Correa commonly known as Bael/Bilva belonging to the family Rutaceae has been widely used in indigenous systems of Indian medicine due to its various medicinal properties. The decoction of root and root bark is useful in intermittent fever and unripe fruit is said to be an excellent remedy for diarrhoea, especially useful in chronic diarrhoeas. Additionally, A. marmelos was proved to be effective in experimental models of IBD and physiological diarrhoea\(^{13}\). Identification and isolation of active fraction useful against IBD is not reported in previous literature.

All these claims and activities promoted us to evaluate potential of these plants against experimentally induced colitis in rodents with following objectives

1. To evaluate acute, subacute and chronic toxicity of Aconitum heterophyllum in rats and evaluate its potential against (DNBS induced) inflammatory bowel disease in rats.
2. To evaluate the potential of Oroxylum indicum against experimentally induced (DNBS induced) inflammatory bowel disease in rats.
3. To evaluate the potential of Oroxylum indicum against experimentally induced diarrhoea, one of severe symptom of IBD.
4. To isolate active fraction of aqueous extract of Oroxylum indicum using bioassay guided fractionation method and evaluate its potential against (DNBS induced) inflammatory bowel disease in rats.
5. To isolate active fraction of methanolic extract of Aegle marmelos using bioassay guided fractionation method and evaluate its potential against (DNBS induced) IBD in rats.
6. To evaluate effect of active fractions from *Oroxylum indicum* and *Aegle marmelos* against NF-kB and IL-6 levels in colonic tissues after induction of colitis in rats.

7. To find out mechanism of action of active fractions from *Oroxylum indicum* and *Aegle marmelos* against experimentally induced colitis.