# SUMMARY

Irritable bowel diseases including ulcerative colitis (UC) is disorder with recurrent inflammatory involvement of large intestine. In UC, the colon becomes inflamed, often causing recurring abdominal pain including diarrhoea, blood in the stool and weight loss. Though exact etiology and pathophysiology is not known with certainty but genetic, immunological, reactive oxygen species (ROS) and environmental factors play a crucial role in the development of UC.

*Azadirachta indica* (AI) leaves indicated the presence of active principles with proven antioxidants, anti-inflammatory, immunomodulatory, free radical scavenging and healing properties. *Aegle marmelos* (AM) fruit is traditionally used to treat jaundice, constipation, chronic diarrhoea, dysentery, stomach-ache, fever, asthma, inflammations, abdominal discomfort, acidity, indigestion, ulcers, swelling. *Terminalia chebula* (TC) is called Haritaki in Hindi and fruit has been advocated in treatment of parasitic infections, digestive diseases, irregular fevers, urinary diseases, flatulence, constipation, ulcers, vomiting and colic pain and is also reported to have antimicrobial, anti-inflammatory, antioxidant, immunomodulatory and adaptogenic properties.

Acetic Acid (AA)-induced colitis is an easily inducible model of IBD and the inflammatory phase bears some resemblance to acute human intestinal inflammation. AA led to increase necrosis, hydropsia, erosion and ulceration while, trinitrobenzene sulfonic acid (TNBS) (a hapten) induces a delayed-type hypersensitivity which proceeds to develop colitis by chronic immunological inflammation followed by liberation of inflammatory markers like cytokines and arachidonic acid metabolites leading to oxidative stress, tissue damage and delayed healing. Considering their traditional uses and the role of oxidative stress in the pathogenesis of UC and the presence of a number of compounds with antioxidant and anti-inflammatory properties in them prompted us to investigate the healing effect of 50% ethanol extract of dried leaves of AI (AIE), dried fruit pulp of AM (AME) and TC (TCE) on AA/TNBS-induced colitis in rats.

AIE (500 mg/kg), AME (200 mg/kg) and TCE (600 mg/kg) were administered orally, once daily for 14 days after TNBS-induced colitis. Rats were given intracolonic normal saline (negative control) or AA/TNBS (control) alone or AA/TNBS plus oral AIE/AME/TCE (Test extracts) and sulfasalazine (SS, 100 mg/kg, Positive control). Test extracts were studied for their *in vitro* antibacterial activity against Gram-negative intestinal bacteria and on AA/TNBS-induced changes in colonic damage, weight and adhesions (macroscopic and microscopic), diarrhea, body weight, food and water intake and colonic levels of free radicals (nitric oxide and lipid peroxidation), antioxidants (superoxide dismutase, catalase and reduced glutathione) and acute inflammatory marker (myeloperoxidase (MPO) in colonic tissue of rats. Intracolonic AA/TNBS increased colonic mucosal damage and inflammation, diarrhea, but decreased body weight which was reversed by AIE, AME and TCE and SS treatments. Test extracts showed antibacterial activity and presence of flavonoids (Rutin and quercetin), reported to have wound healing activity. Extracts enhanced the antioxidants but decreased free radicals and myeloperoxidase activities affected in AA/TNBS-induced colitis. The above effects of test extracts were similar to that of SS treatment.

AIE, AME and TCE thus, healed colitis by promoting antioxidant status and decreasing intestinal bacterial load, free radicals and myeloperoxidase responsible for tissue damage and delayed healing.