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Alternative Medication for the Treatment and the Management of Ulcerative Colitis Disease: A Review

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Abstract:

Ulcerative Colitis UC is a nuisance in United States and other industrial countries. According to the American Gastrological Society UC is defined as acute or chronic idiopathic. Medicines such as sulfasalazine, Balsalazide, Mesalamine and Methotrexate play a key and an important role as pharmacological aspects. In addition, they are strongly threatened with headaches, nausea, vomiting, hypersensitivity reactions, bone marrow depression leads to thrombocytopenia, agranulocytosis, aplastic anemia , intestinal mucosal membrane overflow, oligospermia, spermia impression, absence of menstrual and hyperuricemia. Therefore, we have narrowed down to medicine used in treatment and to reduce these negative effects. In the present review, we focused on the role of medications and therapy in the treatment of ulcerative colitis may be important for future work.

Key Words: Ulcerative Colitis UC, Amino acids , Histopathological , Olsalazine, 5-aminosalicylic acid.

Introduction:

Ulcerative colitis can be weakly impaired and can sometimes lead to life-threatening complications. Although there is no known medicine till now.The treatment can significantly reduce the symptoms of the disease and lead to long-term remissions. Ulcerative Colitis (UC) is an inflammatory bowel disease (IBD) that affects the mucosal membranes of the colon and rectum membrane. Men and women between the ages of 30 and 40 are regarded to be of the highest age [1]. Concerns about the membrane or the most inner lining of the large intestine and rectum generally involve a continuous indication of ulceration and inflammation without tissue segmentation. It can be distinguished clinically as a repeated-occurrence inflammation of the duodenum secreted with several symptoms that cause erratic behavior on various times [2]. Ulcerative prostatic inflammation occurs when inflammation occurs in the colon and rectum, whereas distal colitis occurs when inflammation occurs in the colon and sygmoid intestine.

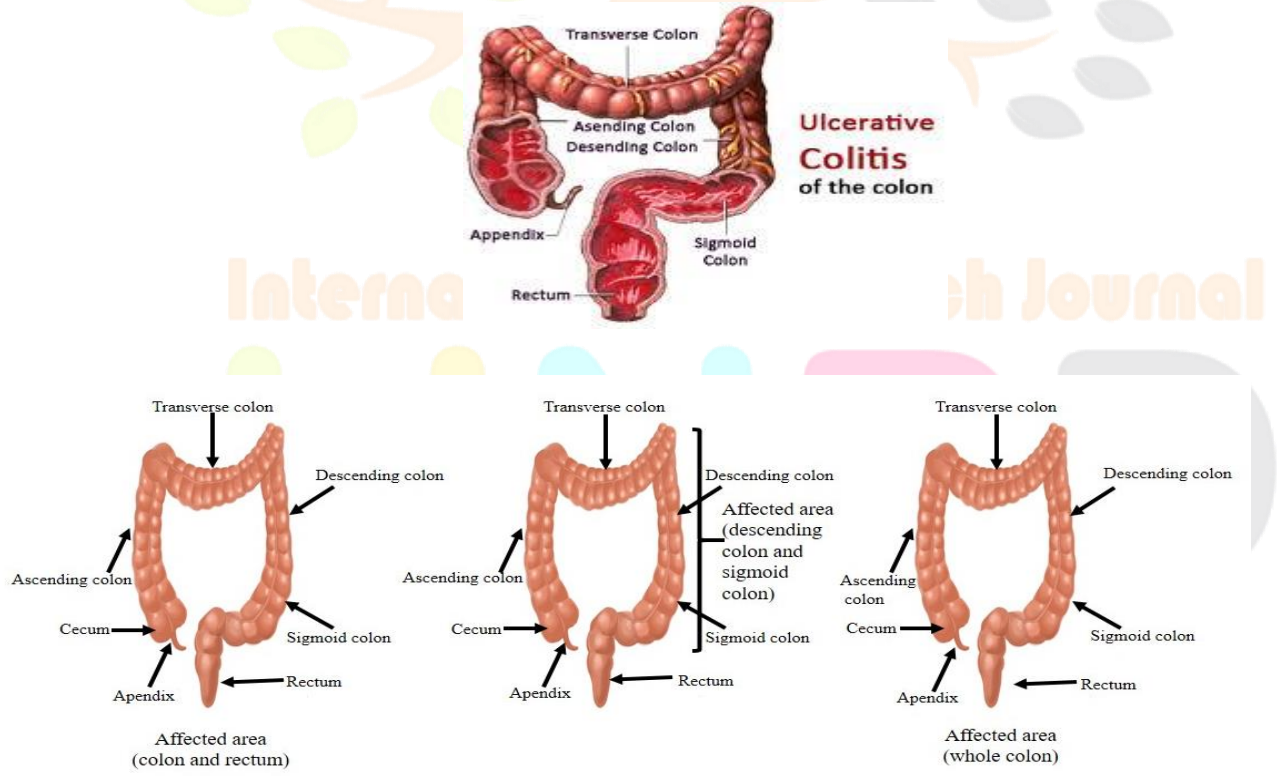
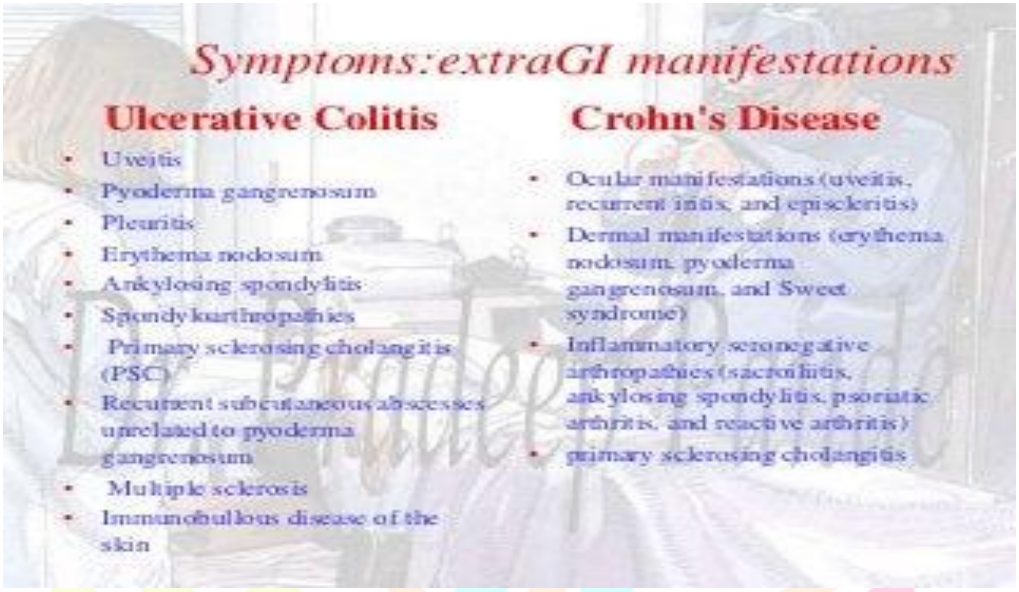


Fig 1. **Ulcerative Proctitis** **Distal Colitis** **Pan Colitis**

UC disease is becoming more of a worldwide burden in terms of healthcare and societal expenditures [3].The cost of UC in the United States was projected to be between USD 8.1 and

14.9 billion [4]. Modified synthesis and release of pro-inflammatory cytokines, gamma interferon (IFN-), growth factor transformation (TGF)-, and increased reactive oxygen species (ROS) are among the agents that cause intestinal inflammation and damage [5].



Amino Acids salicicates, immune suppressants, and steroids, among other synthetic medicines, are being employed in the treatment of UC. Side effects of the anti-ulcer medications absorbed through the circulatory system include vomiting, allergic responses, lymphocytes, diarrhoea, increased liver enzyme release, pancreatic inflammation, and so on. This phrase can refer to both current therapeutic and diagnostic techniques outside of standard medical centers, and it is also known as supplemental medicine or medicine alternative. Natural goods (items derived from natural sources) are becoming more popular in pharmacies nowadays, and according to many studies, natural medicines may be a potential treatment for UC. In temperate Australia and Africa, some 150 genera, including Haphophyllum and 900 species of the Rutaceae family, are found. The Haphillum genus has about 70 species that are found all over the world, from the Mediterranean to Eastern Siberia, from Spain and Morocco to China, and from Romania to Somalia. The Rutaceae family's Haphophyllumtucatturatum has various medicinal uses, including intestinal colic and rheumatoid arthritis. [6]

Some plants are offered as a natural product having anti-ulcerative colitis properties. Anti-ignition agents include colchicine, curcumin, chelerythrine, pinen, phytosterols, xvercetin, saponins, and caviar, many of which are derived from medicinal plants.

Colocasiaesculenta, Aloe Vera from the Xanthroeaceae family, Triticumaestivum from the Poaceae family, rographispaniculata from the Acanthaceae family, and Bosveliaserrata from the Burseraceae family are some medicinal plants that can be used to treat IBD and UC [7].

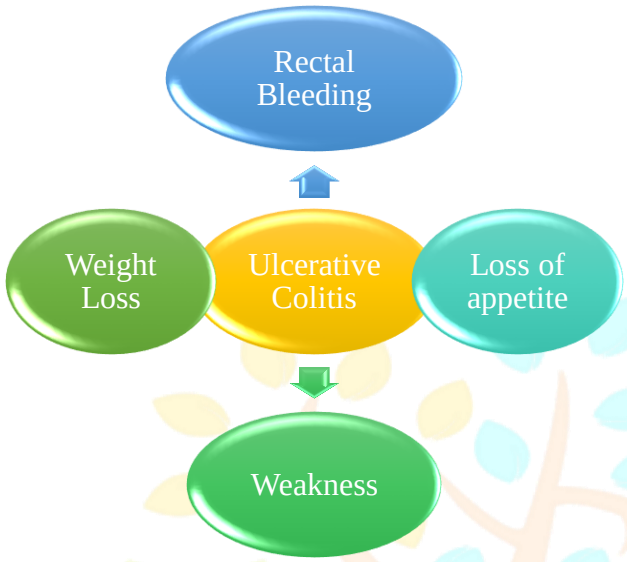


Fig 2. Various clinical Symptoms Associated with UC

Blood or mucus in the stool, diarrhoea, and abrupt bowel suction, as well as stomach pains, are all symptoms of UC. UC may also be linked to severe tenesmus defection.

A Quick Overview of Epidemiology:

Two demographic surveys were conducted in India to assess the burden of UC. The first survey was carried out in Haryana,in northern India, in 1984.The prevalence was identified in 42.8/100000 UC patients in a study of about 21,971 people. The second research was carried out in Punjab (a nearby state of Haryana), India, after 15 years.There were 51,910 persons under supervision, with 2/3 of them in the Punjab rural region and the remainder in the city. In 100,000 people, 44.3 patients were found to be underdiagnosed. After a year, the population density was 6.02 per 100,000. These circumstances demonstrate that UC is not uncommon in India. In comparison to South India, North India is more likely to charge IBD, according to the report. In Asia, the weight of UC is estimated to be about double that of the West [8-10]. In comparison to the West, which is nearly twice as large, Asian nations are more likely to charge IBD.

Asian countries are expected to have about doubled the IBD burden compared to Western ones [11-13].

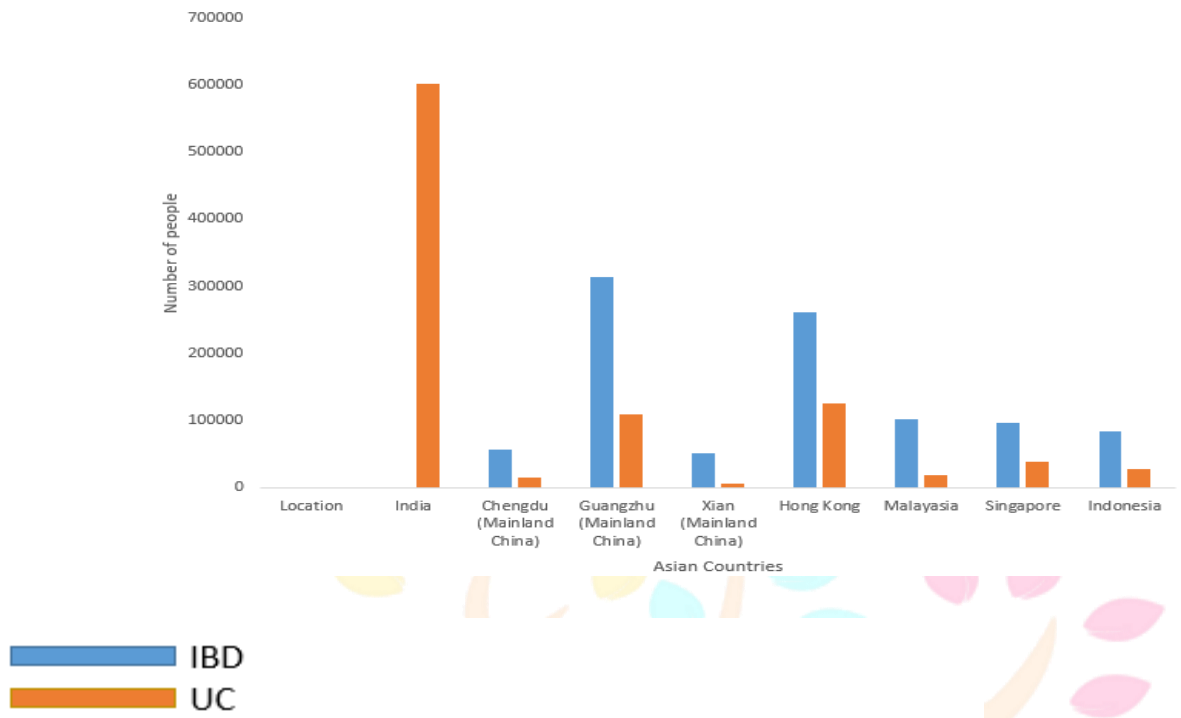


Fig 3. Incidence of IBD & UC in India & Some Asian Countries

The burden of UC has increased in Asian nations compared to CHRON (CD), whereas the situation is radically different in Australia [10].According to research, there has been a rise in the number of UC cases for about 15-20 years before the increase in CD-related accidents [14].The growing CD curve was less than the expanding UC curve and plateaued [15-16],but the difference between UC and CD decreased and changed with time.

The link between UC and CD has also been observed to be limited in Asia [17-18]. As the burden of disease grows, India may see a change in the prevalence of UC and CD. The IBD epidemic in India is unrelated to the North-South divide in the United States and Europe, where the burden of IBD is higher in the north than in the south [19-20]. IBD was found to be present in almost all regions of North and South India in a 2012 study [21]. The development of the IBD curve in Asian nations resembles that of Western ones [22]. When we compared the illness burdens of eastern and western nations, we discovered that India has the greatest total disease burden. India has a population of 1.4 billion people in 2010.

A Lacune Revisited: A Histopathological Study:

IBD, CD, and UC are chronic inflammatory illnesses that affect the gastrointestinal (GI) tract [23].In the pathophysiology of UC, defects in the mucosal barrier, colonocytes,and colonies are particularly loose. Proteins generated from goblet cells as a result of mucosal adhesion to the cell membrane in UC patients. Barrier inadequacy is the primary cause of UC, which is exacerbated by the fact that UC patients have less goblet cells and a penetrating mucus membrane [24]. ILC3 is the key mediator of severe intestinal inflammation, and innate lymphoid cells (IRC) might be at the heart of IBD pathophysiology. ILC3 of UC patients has higher levels of cytokine expression, such as Il17A and IL22, cytokines like IL23R, and transcription factors like RORC and AHR [25]. IBD patients had lower levels of immunoglobulin M and G. However, it was eventually shown that the quantity of IgG1 antibodies in UC patients had grown significantly. Both congenital and adaptive cellular immunity are implicated in illness development in the current study. According to a previous study, UC is a type Th2 disease that has changed, whereas CD is a type Th1 disease [26].

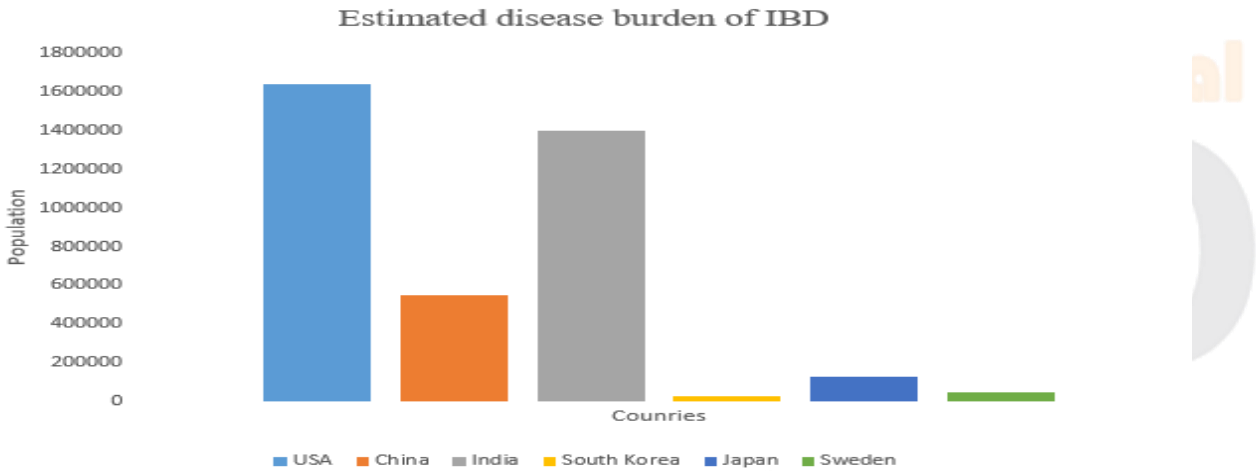


Fig 4. Estimated Disease Burden of IBD

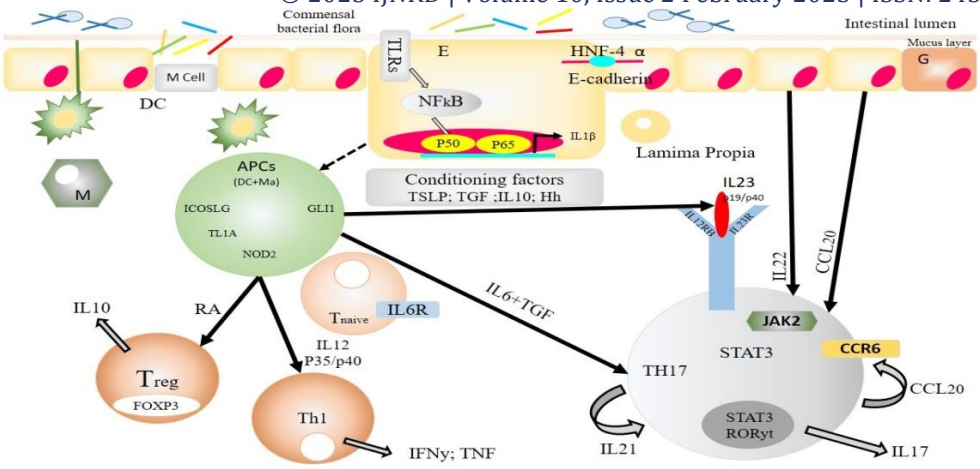


Fig 5. Molecular Pathophysiology of UC

Pathway of IL10: IL-10 Cytokine Family Signaling Pathway:

lL10, cytokine immunity, makes it harder for Th1 cells and macrophages to produce pro-inflammatory cytokines. It also inhibits cells when antigen is present [27]. In young people, IBD is thought to be caused by a monogenic gene deficiency. The IL10 receptor gene has been altered, leading the IL10 signal to be attenuated in babies. Although mutations in the IL10RA and IL10RB proteins result in the failure of these IL10R1 and IL10R2 proteins as a consequence of phosphory STAT3 treatment by IL10 stimulation, they produce abnormalities in single-nuclear peripheral blood cells that inhibit TNF- and prozapoling cytokines. In Asia, 5 of 13 (38.5%) Chinese VEO-IBD patients and 7 of 14 (50%) Korean VEO-IBD patients were successfully tested for IBD caused by an IL10RA or IL10RB mutation [23-27]. Perianal fistula, poor response to medication therapy, and the requirement for early surgery were all reported in children with IL10 mutations, a single gene mutation of over 50 kinds has been identified in children with IBD-like symptoms, including the deletion of ADAM17, XIAP deficiency, and FOXP3 mutation [28-30].

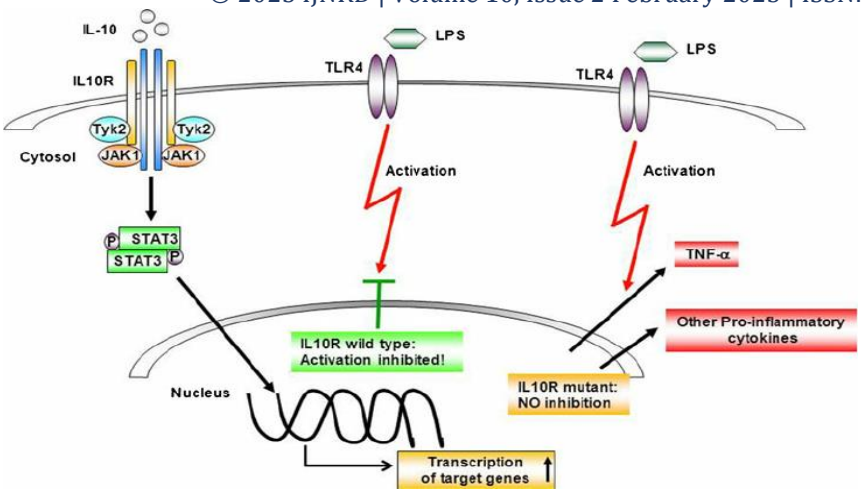


Fig 6: IL-10 Cytokine Family Signaling Pathway

Pathway of IL23R Gene:

The IL23 pathway has certain components that are IBD-sensitive genes, which are well-known for being linked to the occurrence of UC and CD. IL12B, IL23r, STAT3, and tyrosine kinase 2 (TYK2), as well as Janus 2 are among these components (JAK2). In the Th1 and Th17 pathways, IL23R and IL12B aid in the development of T-helpera cells, the end products of which are IFN- and IL17 [31-32].

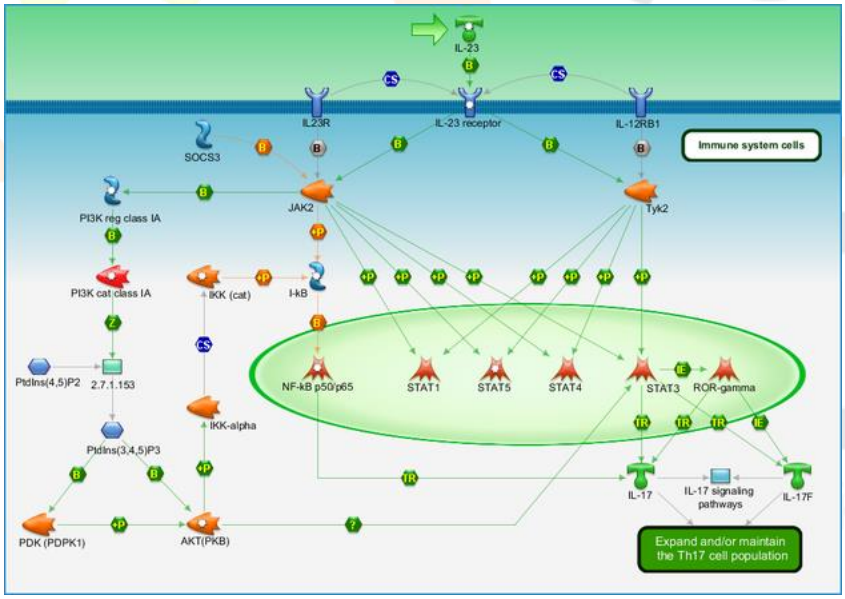


Fig 7 : IL23R Gene pathway

TNF superfamily member 15 (TNFSF15):

TNFSF15 is one of the most promising IBD genes for encoding a novel factor like TNF-like. CD4+ T cells, CD8+ monocytes/macrophages, and umbilical cord endothelial cells all express

TNFSF15 [33-35]. A pathogen-related TLR activation stimulates its expression. It links to certain T-cell receptors and, in combination with IL12 and IL18, stimulates CD4+ T cells. TNFSF15 can create IFN- through cell membrane cells and T-homing CCR9+ cells, resulting in an enhanced Th1 response and mucosal inflammation [35]. In active monocytes, NKT cells, B cells, CD8+, NK cells, and CD4+ T-helper cells, the two major receptors TNFSF15 are unregulated. It enhances the proliferation and effectiveness of CD8+ cytotoxic T cells, Th2 and Th17 cells when attached to the receptor in the presence of TCR activation via NF-Bsignaling [36]. The risk variant of the TNFSF15 IBD gene may increase macrophage expression, thereby increasing MAPK/NF-B/PI3K pattern recognition receptor activity and promoting cytokine production [37].

NOD2/CARD15: Nucleotide-binding oligomerization domain-containing protein 2 (NOD2) known as caspase recruitment domain-containing protein 15 (CARD15):

SNP5 and JW1 in NOD2 have been linked to a variety of illnesses in individuals with CD in India, Malaysia, and China [40]. Susceptibility genes are defined by functional problems of the intestinal epidermis, the immune system of the mycotic membrane, and the micro-fauna present, as indicated by IBD histopathology.

Due to mutations in the NO2/CARD15, TLR4 and CD14 genes in IBD-related individuals, which may cause anomalies in the treatment of intestinal bacteria, the fundamental mechanism in CD and UC etiology is decreased genetic control of the immune response.

Pattern recognition receptors, immune system cells, Toll-like receptors (TLR), monocytes, and macrophages, as well as nose-like receptors scattered across or inside epithelial cells, can all be employed to identify intestinal microbes.

Enteric bacteria and non-nor TLR RECEPTORS cross-link the host. Inflammation occurs when receptors with a genetic defect fail to recognize microbiological antigens [38].

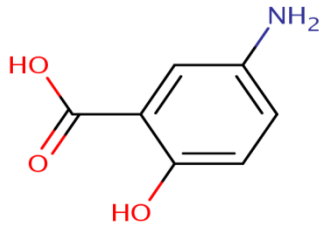
When the NOD2/CARD15, Arg702Trp, Gly908AR, and Leu1007fsinsC mutations occur, these are seconded operational experts associated with an inadequate antimicrobial defense system corresponding to the danger of CD development in both East Asian and European nations [39].

Patients with CD in India, Malaysia, and China [40] had t, SNP5, and JW1 mutations in NO2, which resulted in a variety of other disorders.

Modern Treatment Challenges: A Quick Overview and Risks:

Sulfasalazine, Osalazine, Methotrexate, mesalazine, Balsalazid, mesalamine, Azathiopine, Mercapropurin, Cyclodonryna, and Tofacitinib are currently labelled synthetic drugs used to treat UC. They have a variety of acute and severe side effects.

5-aminosalicyclic acid:



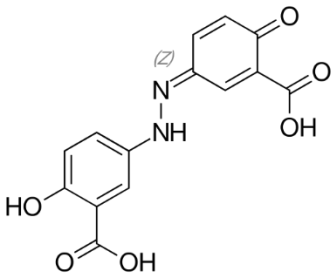
5-aminosalicylic acid

Compounds containing 5-aminosalicylic acid, such as mesalazine and Balsalazid, are used to treat tissue inflammation and can be taken orally or injected into the rectum via edoema.

However, there are some drawbacks to these compounds' administration methods, such as when inflammation occurs in the upper colon, the edoema solution is unable to achieve this high concentration, and when given orally, the majority of the medicine is absorbed in the stomach and upper part of the small intestine [41].

Sulfasalazine reduces intestinal inflammation and symptoms linked with UC such as diarrhoea, stomach discomfort, and rectal circulation. Oral administration is used to administer it. Nausea, headache, skin rash, extinction, anaemia, and, in rare cases, renal inflammation and hepatitis are all side effects of sulfasalazine. When given to humans, sulfasalazine may induce an unfavorable drop in sperm count [42].

Olsalazine is made up of two 5-ASA molecules linked together.



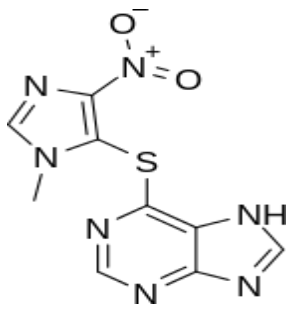
Olsalazine

The drug helps to reduce intestinal inflammation and can help with UC symptoms like diarrhea, abdominal pain, and rectal circulation. Oral administration is used to administer it. This is sometimes linked to a specific type of diarrhoea [43]. Although corticosteroids such as prednisolone, hydrocortisone, and others are thought to have a powerful anti-inflammatory impact, they do not need to come into direct contact with inflamed intestinal tissue to have an effect. They can be taken orally or intravenously. Some people may become reliant on corticosteroids and experience UC symptoms on a regular basis if corticosteroids are used below a particular threshold in UC therapy. Acne, diabetes, sleeplessness, increased body hair, mood swings, moon face, increased susceptibility to infection, glaucoma, high blood pressure, depression, weight gain, irritability, cataract, personality change, muscular weakness, and osteoporosis are among of the most prevalent adverse effects. When administered to youngsters, growth might be disrupted [44].

Immuno-modulators lower tissue inflammation by lowering the number of immune cells or disrupting their protein synthesis, both of which enhance immune system activation and inflammation. Patients become more vulnerable to infection as resistance is reduced [45].

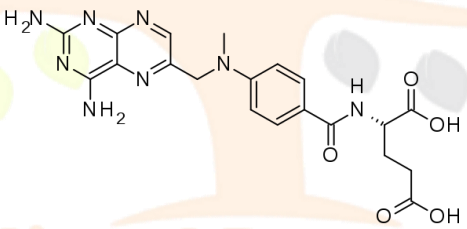
Azathioprine and 6-Mercaptomine (6-MP) are used for patients with serious illness from UC and CD who have not responded to corticosteroids, as well as patients who have experienced unexpected side effects from corticosteroids or who are at risk for serious diseases such as pancreatitis, hepatitis, or bone marrow toxicity. The usage of 6-MP by men may result in a reduction in sperm count. If a male patient takes 6-MP, his girlfriend is at risk for several miscarriages and vaginal koxel. Azathioprine and 6-mercaptomomacomputic analogueues are purine analogueues that interfere with the metabolism of nucleic acid by acting as competitive opponents of substrates, leading to immunosuppressive and reduced cell proliferation and used

to maintenance of remission in ulcerative colitis. Breathing difficulties in neonates have been reported [46].

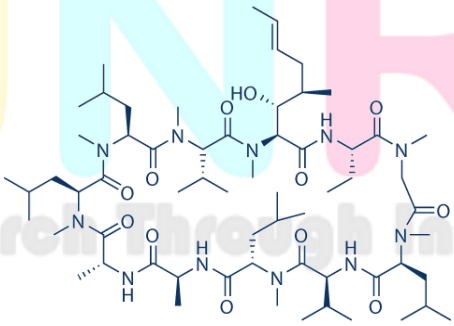


6-Mercaptomine (6-MP)

Methotrexate is a drug prescribed for people who have a moderate or severe CD, don't get a credit with Azatiopirin or 6-Mercaptomine 6-MP, or can tolerate these medicines. Orally or intramuscularly, the value is given (IM). The patient may develop liver cirrhosis in the long run. Pneumonia may happen at any time. Furthermore, there is the potential to diminish the amount of WBCs. During pregnancy, it is inconsistent [47-48].



Methotrexate



Cyclosporine

Table 1: Adverse effects of various UC medications:

Medications	Adverse effects
Sulfasalazine	Headache, nausea, vomiting, loss of appetite, rash, decreased WBC, pancreatitis.
Mesalamine	Headache, nausea, gas, diarrhoea, dizziness, hair loss, kidney problem, pancreatitis.
Olsalazine	Headache, nausea, fatigue, hair loss, rash pancreatic
Balsalazide	Headache, nausea, vomiting, diarrhoea, abdominal pain.
Corticosteroid methyl prednisone	Insomnia, high blood sugar level, osteoporosis,(prednisone, cataracts, weight gain, high BP, acne).

Conclusion:

Ulcerative colitis UC is a serious problem in developed and non-developing countries. Symptoms usually develop over time [49]. Ulcerative colitis is a long-term condition in which colon and rectum become inflammation. Small ulcers may develop on the lining of the colon and may cure. Sulfasalazine, Balsalazide, mesalamine drugs are plays an important role in the management of UC, but they are associated with various types of adverse reactions such as nausea, vomiting, headache, hypersensitivity reactions. Treatment of ulcerative colitis UC is intended to reduce symptoms during the flash and prevent the return of symptoms. Therefore, we have focused on the treatment of UC disease accessible of drugs used to remedies and to reduce these negative effects.

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Declaration of competing interests:

The author declared that there are no conflicts of interest.

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