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A REVIEW ON THE HERBAL TREATMENT FOR ULCERATIVE COLITIS

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ABSTRACT

Ulcerative colitis (UC) is a type of idiopathic inflammatory bowel disease (IBD) in which ulcers form on the surface of the bowl lining, causing bleeding. Inflammation begins in the rectum and spreads throughout the colon, making it a recurrent and remitting illness. Because of its comparatively low side effects and simple availability, traditional therapeutic therapies based on the use of plants and plant extracts for the treatment of medical diseases are becoming more popular. Herbal plants contain various phytochemical constituents which have certain therapeutic or pharmacological activity which can be helpful in the treatment of diseases. Ulcerative colitis is treated using common medical plants such as Aloe, Neem, Turmeric, Isabgol, Boswellia, Amla, Pineapple, Green Chiretta or Kalmegh and Ginger. The purpose of this review is to look into and summarise the various types of herbal medicinal plants that can be utilised as an alternative therapy for ulcerative colitis patients.

KEYWORDS:- IBD, Ulcerative colitis, herbal medicine, anti-inflamatory, phytochemical constituents.

INTRODUCTION

Ulcerative colitis (UC) is one of two major kinds of idiopathic inflammatory bowel disease (IBD) that causes ulcers and inflammation in the inner lining of the colon and rectum. Ulcers form on the surface of the intestinal lining in this illness, which can cause bleeding and create mucus.[1] It is an illness that is both acute and chronic.

Continuous mucosal inflammation characterises UC, which begins in the rectum and progresses proximally in a continuous way along the entire colon with varied extent.[2] Rectal bleeding, diarrhoea, abdominal pain and cramps, hematochezia, exhaustion, weight loss, and fever are all signs of this recurrent and remitting condition.[3] UC is defined according to whether the disease is ongoing or in remission, the extent of the disease (proctitis, distal colitis, left side colitis, and pancolitis), and the severity (mild, moderate, and severe).[4]

A mix of clinical, laboratory, imaging, and endoscopic characteristics, including histology, are used to diagnose UC. Continuous colonic inflammation is characterised by erythema, loss of normal vascular pattern, granularity, erosions, friability, bleeding, and ulcerations, according to endoscopic findings.[5] In both men and women, the peak age of disease start is between the ages of 30 and 40 years.[6] Sulfasalazine, corticosteroids, immunosuppressants, antibiotics, and biologic medicines (anti-tumor necrosis factor (TNF-α) are all used in the treatment of ulcerative colitis.[7] However, there are a variety of negative effects associated with the use of these medications, some of which are rather severe.[8] As a result, the use of natural medicines (derived from plants and herbs) in the treatment of ulcerative colitis patients is on the rise.[7] The purpose of this review is to summarise few herbs that can be used to treat Ulcerative Colitis.

Herbal medicinal plants:- Traditional therapeutic therapies based on the use of plants and plant extracts for the treatment of medical disorders are known as herbal medicine. In ulcerative colitis patients, herbal medicine is commonly used.

***Aloe barbadensis* (Aloe vera):-** Aloe vera, also known as *Aloe barbadensis*, is a hardy, perennial, tropical, and drought-resistant succulent plant from the Liliaceae family that is widely used as a medical plant due to its therapeutic properties.[9] Aloe vera succulent leaves contain a mucilagenous extract with a greater water content (approximately 96%), aleosin, aloin, vitamins (vitamin A, B1, B2, B3, B6, B12, C, E), minerals, and enzymes, folic acid, polysaccharides, phenolic compounds, and amino acids. For health purposes, these bioactive chemicals have emollient, purgative, antibacterial, anti-inflammatory, anti-oxidant, anti-helmenthic, antifungal, antiseptic, and cosmetic properties.[10] The anti-inflammatory properties of aloe vera gel support the idea that it could be used to treat ulcerative colitis.[11] The findings imply that particular plant sterols may also play a role in gel's anti-inflammatory properties.[10] Aloe vera gel has been shown to decrease prostaglandin E2 and IL-8 release in human colonic mucosa in vitro, indicating a function in antibacterial and anti-inflammatory

responses.[8] In addition to lowering inflammation, aloe vera treated UC through improving colon mucus barrier functioning.

Fig. 1: Aloe vera.

***Azadirachta indica* (Neem): -** The Neem tree, *Azadirachta indica*, is an evergreen tropical tree of the Meliaceae family.[12] Due to its vast spectrum of therapeutic characteristics, it is a very important medicinal plant that has been traditionally used to cure a variety of disorders. The leaves, flowers, seeds, fruits, roots, and bark of the evergreen Neem tree have all been traditionally used to cure a variety of ailments, including inflammation, infections, fever, skin problems, and dental disorders.[13] Nimbolinin, nimbin, nimbidin, nimbidol, sodium nimbinate, gedunin, salannin, and quercetin are the bioactive chemicals found in neem.[14]

Due to the restoration of epithelial functioning, neem extract reduced mucous and bloody diarrhoea, as well as stool frequency, while increasing body weight.[15] According to Deshmukh CD et al., *Azadirachta indica* extract treatment resulted in regenerating mucosa with slight crypt distortion and mild lymphoplasmacytic infiltration in the lamina propria, with an impact comparable to sulfasalazine treatment. These effects may be attributable to *Azadirachta indica*'s anti-inflammatory, immunomodulatory, and antiulcer characteristics.[16]

Neem extract is helpful in lowering IL-6 and TNF- levels in rats with colon cancer, according to a study by Patel et al.[17] In rats with oral squamous cell carcinoma, neem leaf extract has been shown to lower circulating pro-inflammatory cytokines.[18] Because of its anti-inflammatory properties, neem is expected to be an alternative or adjuvant therapy for colitis sufferers.[19]

Fig. 2: ***Azadirachta indica.***

Curcuma longa **(Turmeric):-** Turmeric, also known as *Curcuma longa*, is a Zingiberaceae (ginger) family perennial herb. The plant's rhizome, which is a yellow powder, is used as a flavouring in various cuisines and as a medication to treat a variety of ailments, including flatulence, jaundice, menstruation troubles, hematuria, haemorrhage, and colic. It can also be used as an ointment to treat a variety of skin conditions. The flavonoid curcumin (diferuloylmethane) and numerous volatile oils, such as tumerone, atlantone, and zingiberone, as well as carbohydrates, proteins, and resins, are the active ingredients in turmeric.[20]

Turmeric compounds may reduce oxidative stress, neutrophil influx, and ROS-related cellular damage, as well as prevent neutrophil and iNOS migration in the colon and liver, lowering oxidative damage in IBD patients with colitis.[21] In patients with UC, daily intake of 1,500 mg curcumin for 8 weeks could induce clinical remission, enhance clinical response, improve quality of life, and lower hs-CRP and ESR levels, according to Narges Sadeghi.[21]

Curcumin has the potential to be a remarkable therapeutic agent for a range of inflammatory and cancer disorders. Curcumin's anti-inflammatory and anti-oxidative activities have been proven in human lymphocytes and gut epithelial cell lines in vitro, and curcumin has also been found to alleviate mice experimental colitis.[22]

Fig. 3: ***Curcuma longa.***

***Plantago ovata* (Isabgol):-** P. Ovata is a short-stemmed annual herb that grows to a height of 10–45 cm and belongs to the Plantaginaceae family. This plant's seed husk is known as Psyllium or Isabgol (in Hindi), and it's a very powerful laxative.[23] This plant can also be used to cure ulcers in the intestines, as well as to stop diarrhoea and bleeding. It contains tannins, coumarins, flavonoids, polyphenols, and gluten, which are responsible for pharmaceutical properties like mucilage, superdisintegrant, gelling agent, and suspending agent, as well as pharmacological activity like anti-diarrheal, anti-constipation, wound healer, anti-ulcerative, anti-fever hypocholestrolemic, and hypoglycemic.[24,25] P. Ovata major seeds may be explored for the supplemental management of UC, according to Atiyeh Baghizadeh et al., because they can successfully alleviate abdominal soreness, gastroesophageal reflux, and gastric pain in UC when compared to placebo.[25]

When tested in a transgenic rat model, psyllium was found to be an intestine anti-inflammatory agent, lowering inflammatory mediators involved in the inflammatory process such as NO, leukotriene B4, and TNF.[24]

Fig. 4: *Plantago ovate.*

***Boswellia serrata* (Indian frankincense):-** Boswellia, also known as Salai guggul or Indian frankincense, is an oleo-gum resin derived from the *Boswellia serrata* tree, which is a moderate to large branching tree of the Burseraceae family.[26,27] This tree can be found growing wild in India's dry hilly regions, and it has been used to treat cancer, inflammation, arthritis, asthma, psoriasis, colitis, Crohn's disease, and hyperlipidemia.[26] Essential oil, gum, and resin are all found in Boswellia. Monoterpenes, diterpenes, and sesquiterpenes, as well as phenolic chemicals and a diterpene alcohol, are found in its essential oil (serratol). Gum is made up of carbohydrates such pentose and hexose, as well as oxidising and digesting enzymes. Resin is mostly composed of pentacyclic triterpene acids, the active component of

which is boswellic acid.[26] According to Inder Gupta et al., boswellic acid is a non-redox, non-competitive selective inhibitor of the enzyme 5-lipoxygenase, which is a major enzyme involved in the inflammatory response.[28]

Fig. 5: ***Boswellia serrata.***

Fig. 6: ***Boswellia resins.***

Emblica officinalis **(Amla):-** Phyllanthus emblica, Indian gooseberry, or Amla are all names for *Emblica officinalis*, which belongs to the Euphorbeaceae family.[29] It is commonly utilised in many indigenous medicine remedies to treat a wide range of ailments.[30] Tannins, mucic acid, amino acids, alkaloids, flavone glycosides, phenolic glycosides, flavanol glycosides, phenolic acids, sesquiterpenoids, nor-sesquiterpenoids, and carbohydrates are among the phytochemical elements of E. officinalis.[31] Gallic acid, chlorogenic acid, ellagic acid, and quercetin are among the phytoconstituents found in amla juice.[31] Amla is a fruit that is high in vitamin C. Vitamin C levels are higher in this fruit than in oranges, tangerines, lemons, or other fruits.[32]

Hepatoprotective, cardioprotective, diuretic, laxative, refrigerant, stomachic, restorative, alterative, antipyretic, and anti-inflammatory effects are all claimed for E. officinalis. E. officinalis is a hair tonic that also reduces peptic ulcer dyspepsia and acts as a digestive medication.[32] Memory enhancement, cholesterol reduction, ocular diseases, snake venom defusing, and antibacterial agent were all found to be useful properties of Indian gooseberry.[33] In order to determine the antiulcerogenic activity of E. officinalis, Goel and Bhattacharya accounted for the effects of methanolic extract of E. officinalis on offensive factors like acid-pepsin secretion and defensive factors like cellular mucus, mucin secretion, cell proliferation, and cell shedding.[34] Ulcers are primarily produced by a misalignment of defensive and attacking forces. The methanolic extract of Emblica officinalis displayed antiulcerative efficacy by reducing offensive factors and boosting defensive mucosal factors, according to a group of researchers.[35] Methanolic fruit extract of E. officinalis, according to

Deshmukh et al., can protect against acetic acid-induced ulcerative colitis and may be useful in individuals with inflammatory bowel disease.[30]

Fig. 7: *Emblica officinalis* (Amla).

***Ananas comosus* (Pineapple):-** The pineapple is one of the most widely consumed tropical fruits in the world. The chemical constituents present in plant are anthocyanin, catechin, and iso-catechin.[37] Bromelain, a chemical found in the fruit's juice and stem, has become a popular nutritional supplement. Bromelain is made up of enzymes that have a variety of powerful actions. Its capacity to reduce inflammation is one of its most potent features. Bromelain is also an anti-inflammatory, diuretic, and digestive aid that has been claimed to benefit the digestive, respiratory, and circulatory systems, as well as the immunological system. They also drank it to help with sore throats, seasickness, and labour induction.

The extract of pineapple fruit, according to Mallik D et al., has ulcer-protective properties. It indicates that the action is attributable to the plant's antioxidant property, which could be ascribed to the plant's polyphenolic components (flavonoids and tannins).[37] According to Fatma A. Khalil et al., therapy with fresh pineapple juice or bromelain reduced acetic acid-induced colonic mucus content while also preventing oxidative and inflammatory responses. Fresh pineapple juice consumption helps to reduce the severity of colitis by reducing oxidative stress due to its high antioxidant content, as well as bromelain, which acts as an immunomodulator by eliminating bromelain-sensitive molecules and therefore lowering proinflammatory cytokines like TNF.[38]

Fig 8: *Ananas comosus* (Pineapple).

***Andrographis paniculate* (Green chiretta or kalmegh):-** A. paniculata is an annual, branching, upright, and herbaceous plant of the Acanthaceae family, and is one of the most widely used medicinal plants for the treatment of a variety of diseases.[41,42] The aerial parts, roots, and entire plant of A. paniculata have been used as traditional medicine in Asia for generations to cure a variety of ailments.[41] Andrographolide (diterpenoids), diterpene glycosides, 14-deoxyandrographolide, 14-deoxy-11,12-dehydroandrographolide, neoandrographolide, polysaccharides, lactones, flavonoids, and flavonoid glycosides are all found in *Andrographis paniculata* extract.[42] A. paniculata has been shown to have anticancer, antidiarrheal, antihepatitis, anti-HIV, antihyperglycemic, anti-inflammatory, antimicrobial, antimalarial, antioxidant, cardiovascular, cytotoxic, hepatoprotective, immunostimulatory, and sexual dysfunctions pharmacological effects.[42]

The active ingredient in *Andrographis paniculata* is andrographolide. Andrographolide's anti-inflammatory properties suggested that it could be used to treat UC.[39] Andrographolide, according to Peifen Zheng et al., inhibits the activity of the IL-23/IL-17 axis as well as downstream pro-inflammatory factors TNF-, IL-1, IL-6, and IL-17A in the serum and colon tissues, suppressing inflammation response and alleviating UC.[39] Patients with mild to moderately active ulcerative colitis treated with A. paniculata extract (HMPL-004) at a dose of 1,800 mg daily were more likely to achieve clinical response than those treated with placebo, according to Sandborn et al.[40] Changhong Wang et colleagues found that 80 mg/kg andrographolide had a stronger therapeutic effect than SASP (sulfasalazine, positive control group, 500 mg/kg) in alleviating OXZ-induced UC. Andrographolide inhibited signal transduction by lowering IL-4/IL-13 specific binding to the IL-4 receptor (IL-4R) and suppressing phosphorylation of the signal transducer and activator of transcription 6

(STAT6), according to the findings of the anti-inflammatory mechanism (p-STAT6). In conclusion, androghrapholide, in addition to natural botanicals, may be a candidate element for UC therapy.[43]

Fig. 9: *Andrographis paniculate*
(Green chiretta or Kalmegh)

Zingiber officinale **(Ginger):-** Ginger (Zingiber officinale) is a perennial tuberous or rhizomatous root with an upright annual stem and green leaves that belongs to the Zingiberaceae family. Traditional herbal treatment has also employed the rhizome of ginger.[47] Zingiberene, zingiberol, zingerone, shogaols, bisabolene, -sesquiphellandrene,and other active compounds in ginger are listed below.[48]

Loss of appetite, nausea, asthmatic diseases, bloated stomach, inflammatory arthritis, weariness, stomachache, allergies, throat-related problems, cough, common cold, fever owing to infections, and so on are all popular uses for ginger.[47] Antiviral, radioprotective, anti-inflammatory, anticancer, and antioxidant characteristics are among Ginger's pharmacological effects. Ginger has anti-inflammatory characteristics, lowering serum C-reactive protein levels, as well as antioxidant properties, lowering lipid peroxidase marker, malondialdehyde levels, and enhancing renal superoxide dismutase activity. Because it includes protein kinase B (Akt) and the nuclear factor kappa light chain enhancer of activated B cells (NF-B), Z. officinale is particularly helpful in inflammatory bowel illness. As a result, there was an increase in anti-inflammatory cytokines and a decrease in pro-inflammatory cytokines. M. Nikkhah-Bodaghi et al. found that ginger active compounds inhibit lipid peroxidation, p38 protein expression, and myeloperoxidase activity, as well as decrease

mucosal MDA, hydrogen peroxide (H_2O_2), and protein carbonyl (PCO) levels in a dose-dependent manner. In individuals with active mild to moderate UC, a randomised, placebo-controlled trial indicated that taking 2000 mg of ginger per day can reduce disease severity index and oxidative stress.[44] In mice, ginger relieved colitis-related pathogenic alterations and reduced interleukin-6 and inducible nitric oxide synthase mRNA expression levels.[45] Guo et al. found that ginger reduces the severity of DSS-induced colitis in mice, and that ginger treatment changed the intestinal microbiomes of colitis mice, relieved weight loss, and reduced DAI in colitis animals, as well as equivalent effects on colon length and spleen index.[45]

Fig. 10: *Zingiber officinale* (Ginger).

Table 1: Summary of Herbal Medicinal plants for the treatment of Ulcerative colitis.

S. No.	Plant	Part used	Major constituents	Experimental Studies/ Models	Reference
1.	*Aloe barbadensis* (Aloe vera)	Whole plant	Water (approx. 96%), vitamins, folic acid, aleosin, aloin, polysaccharides etc.	-	-
2.	*Azadirachta indica* (Neem)	Leaves, Stem	Nimbolinin, gedunin, salannin, quercetin etc.	Acetic acid induced colitis in rat	[15], [16]
3.	*Curcuma longa* (Turmeric)	Rhizome	Curcumin (diferuloylmethane)	Patients with ulcerative colitis Randomized Controlled Trial	[21], [22]
4.	*Plantago ovata* (Isabgol)	Seed husk	Polysaccharides	Randomized clinical trial	[25]
5.	*Boswellia serrata* (Indian Frankincense)	Resins	Boswellic acid	Patients with chronic colitis	[28]
6.	*Emblica*	Fruit	Vitamin C, Tannins,	Acetic acid	[30],

	officinalis (Amla)		mucic acid, amino acids etc.	induced colitis in rat. Ethanol, Aspirin, Cold restraint stress, Pylorus-ligation and acetic acid induced ulcer models.	[35]
7.	*Ananas comosus* (Pineapple)	Fruits, Stem	Bromelain, anthocyanin, catechin, and iso-catechin	Ethanol induced antiulcer model in albino rat Acetic acid-induced ulcerative colitis in rat	[37], [38]
8.	*Andrographis paniculate* (Green chiretta or Kalmegh)	Whole plant	Andrographolide & its derivatives, polysaccharides, lactones, flavonoids, and flavonoid glycosides	TNBS-induced colitis in mice. A randomized, double-blind, placebo-controlled trial (224 adults) Oxazolone (OXZ)-induced UC rat model	[39] [40] [43]
9.	Zingiber officinale (Ginger)	Rhizome	Zingiberene, zingiberol, zingerone, shogaols, bisabolene, β-sesquiphellandrene,	Randomized, placebo-controlled, clinical trial DSS induced colitis in Male BALB/c mice	[44] [45]

CONCLUSION

Ulcerative colitis is both acute and chronic idiopathic inflammatory bowel disease (IBD) and commonly occurs in patients aged 30-40 years. Herbs can treat a wide range of acute and chronic GI conditions, including UC. Herbs are readily and abundantly available throughout India. Therefore, medicinal plants can provide cheaper treatment with fewer side effects for the treatment of UC. This review summarizes several medicinal plants that may be useful in the treatment of UC due to their anti-inflammatory and antioxidant properties.

Abbreviations

UC – Ulcerative colitis

TNF - Tumour Necrosis Factor

IBD - Inflammatory bowel disease

IL – Interleukin

iNOS – Inducible nitric oxide synthase

hs-CRP – High sensitivity C-reactive protein

ESR – Erythrocyte sedimentation rate

NO – Nitric oxide

TNBS - 2,4,6-trinitrobenzene sulfonic acid

OXZ – Oxazolone

p-STAT6 – phospho-Signal transducer and activator of transcription 6

DSS - dextran sulfate sodium

MDA – Malondialdehyde

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