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Review

Unlocking the Therapeutic Potential of Phytochemicals Against Colitis: A Review on Pharmacological Activity and Related Molecular Mechanisms

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Abstract

Inflammatory bowel diseases (IBD) are chronic conditions that pose serious health risks and significantly impact global economic development. IBD includes Crohn's disease and ulcerative colitis (UC). UC affects the rectum and may involve part of the colon or the entire colon in a continuous pattern. The purpose of this article is to provide scientific insights into the biological roles, pharmacological activities, and related molecular mechanisms of phytochemicals with anti-colitis potential. To highlight the health benefits of phytochemicals in treating colitis, the present work summarizes scientific findings on various classes of phytochemicals with significant therapeutic effects. Scientific data on the anti-colitis potential of phytochemicals were collected from multiple literature databases. Furthermore, the pharmacological activities of these phytochemicals are discussed to understand their biological potential in colitis treatment. Analysis of the scientific data underscores the medical importance of phytochemicals with anti-colitis properties. Phytochemicals have shown significant effects on colitis. Their molecular mechanisms are also described in this study. The paper presents the anti-colitis potential of compounds such as atractylodin, karanjin, liriodendrin, norisoboldine, okanin, trifolirhizin, phillygenin, sauchinone, oxyberberine, obacunone, ginsenoside Rb1, berberine, arjunolic acid, and curculigoside. The molecular mechanisms of these phytochemicals are also discussed. The presented information will benefit researchers from various disciplines investigating the anti-colitis properties of these compounds. The scientific data in this paper highlight the biological significance of phytochemicals in the treatment of colitis.

Keywords: Colitis, herbal products, medicinal, molecular mechanism, pharmacological, phytochemicals.

INTRODUCTION

Chronic inflammatory gastrointestinal disorders that are extremely morbid and challenging to treat are known as inflammatory bowel diseases (IBD). Their etiology has been linked to immunological dysregulation, environmental factors, genetic predisposition, and changes in the gut microbiota. Their prevalence has increased dramatically worldwide in recent years.[1] IBD, which includes Crohn's disease and ulcerative colitis (UC), is becoming more widespread globally. It is widely believed that immune system dysfunction and genetics play major roles in the pathophysiology of IBD. However, stress and nutrition also contribute. The precise etiology of IBD is still uncertain.[2] Patients with a 30-year history of ulcerative colitis may have up to an 18% risk of developing colon cancer. Nevertheless, current diagnostic techniques for UC are limited and primarily rely on biopsy pathology, colonoscopy, clinical symptoms, and the exclusion of other related conditions. For an accurate diagnosis, mucosal biopsies must be examined histopathologically. Numerous advanced endoscopic imaging methods, including confocal laser endomicroscopy (CLE), endocytoscopy, and chromoendoscopy, have been developed to improve UC diagnosis.[3] Approximately 5 million individuals worldwide suffer from UC, a form of IBD that is increasingly common and significantly reduces quality of life. With remission rates of only 30–60% in patients, achieving a cure remains difficult, even with advanced therapeutic options such as biologics and small-molecule drugs. In addition to genetic predisposition, environmental exposures, and intestinal defense abnormalities, dysbiosis of the gut microbiota and immunological imbalances also contribute to the development and exacerbation of ulcerative colitis. Probiotics have been shown to effectively relieve ulcerative colitis by altering the resident microbiota, improving epithelial barrier functions, modulating local and systemic immune responses, affecting metabolic processes, and participating in systemic signaling via the nervous system.[4] Natural plant-based polyphenolic flavonoids offer various biological benefits and have long been regarded as therapeutic agents for IBD due to their wide range of bioactivities and relatively mild side effects.[5]

When treating IBD, Traditional Chinese Medicine (TCM) offers the advantages of precise efficacy, a low recurrence rate, and few side effects. Numerous studies have shown that TCM can treat IBD by targeting and regulating the composition of the gut microbiota and by mitigating gut barrier dysfunction through multi-component mediation. Wuji Wan, a well-known TCM formula listed in the Chinese Pharmacopeia, has attracted attention from researchers due to its potential benefits in treating various gastrointestinal disorders.[6] At doses of 2 and 4 g/kg, the traditional

MAIN POINTS

- Phytochemicals exhibit significant anti-colitis activity: A diverse range of plant-derived phytochemicals—including atractylodin, karanjin, liriodendrin, and others—demonstrated anti-inflammatory and mucosal protective effects in various experimental colitis models.
- Multiple molecular pathways are involved: The pharmacological actions of these phytochemicals are mediated through modulation of key signaling pathways such as NF-κB, MAPK, TLR4, NLRP3 inflammasome, and Nrf2, contributing to reduced inflammation and restored intestinal barrier function.
- Gut microbiota regulation is a shared mechanism: Many phytochemicals, including okanin, sauchinone, and oxyberberine, were shown to improve colitis by rebalancing gut microbial composition, emphasizing the microbiota's role in disease modulation.
- Potential for clinical application: The findings underscore the therapeutic promise of phytochemicals as complementary or alternative agents for managing ulcerative colitis, warranting further investigation through clinical trials and pharmacokinetic studies.

Chinese herbal formulation Huang Lian Jie Du decoction alleviated DSS-induced chronic colitis in mice by reducing inflammation and impairing macrophage activity in colonic tissues through the Csf1r/Src pathway. Additionally, the gut microbial profile may be altered by the Huang Lian Jie Du formula. Strong correlations were observed among gut microbiota, spleen weight, colon length, and disease activity index (DAI).[7] Rats treated with Shaoyao decoction showed improved general health and reduced intestinal injury. This decoction alleviates TNBS-induced UC symptoms by reducing intestinal damage and inflammation while maintaining the balance between Th17 and Treg cells. It modulates the Th17/Treg ratio by influencing the IL-6/STAT3 axis.[8]

Colitis in mice was significantly reduced by Modified Gegen Qinlian Decoction (MGQD), potentially due to the restoration of goblet cell function, alterations in gut microbiota, and changes in bile acid (BA) metabolism. However, the improvement of UC by MGQD may also be attributed to factors other than gut microbiota.[9] A traditional Chinese herbal remedy combining Portulacae Herba and Granati Pericarpium has demonstrated a generally positive therapeutic effect by reducing diarrhea and irregular stools.[10] *Pueraria lobata* plays a crucial role in cytokine regulation. In a dose-dependent manner, exosome-like nanovesicles (PLDENs) derived from *Pueraria lobata* showed notable protective effects against DSS-induced colitis and colon pathological changes. PLDEN treatment may also effectively reduce pulmonary inflammation.[11]

Through dietary intervention, pomegranate parts and their abundant ellagitannins—particularly the main constituents punicalagin and ellagic acid—can regulate the intestinal barrier and flora, reduce oxidative and inflammatory responses, and serve as an anti-ulcerative colitis resource.[12] Dietary supplementation with *Agaricus blazei* Murrill polysaccharide (ABP) significantly reduced oxidative stress, inflammation, and DSS-induced colitis symptoms. ABP intervention preserved intestinal mechanical barrier integrity by promoting the expression of tight junction proteins ZO-1 and Occludin and increasing mucus secretion. Additionally, non-targeted metabolomics revealed metabolic reorganization, while 16S rRNA sequencing showed that ABP mitigated DSS-induced gut microbiota disturbances.[13]

By inhibiting the NOS2-mediated JAK2/STAT3 pathway, Rauwolfia polysaccharide can slow the progression of ulcerative colitis.[14] To alleviate UC symptoms in mice, the rutin and astragaline components of *Tetrastigma hemsleyanum* root extract activated the B-cell receptor signaling pathway and restored gut microbiota diversity by binding to SYK protein.[15] Extracellular vesicles (EVs) derived from the diminished commensal bacterium F. prausnitzii (Fp-EVs) alleviated DSS-induced colitis by altering intestinal mucosal barrier function and the immune profile. According to our research, Fp-EVs reduce DSS-induced colitis severity through their impact on both mucosal barrier integrity and immune modulation.[16]

Qing-Dai, also known as indigo naturalis, is an herbal remedy used to treat various inflammatory conditions. Since 1960, it has been employed in China for treating ulcerative colitis. Its two main components, indigo and indirubin, act as endogenous ligands for aryl hydrocarbon receptors. Indigo naturalis inhibits ferroptosis and upregulates the expression of antioxidant genes. Furthermore, it increases Helios-positive T regulatory cells in the colons of patients with ulcerative colitis, indicating additional mechanisms through which it may provide therapeutic benefits.[17]

PHARMACOLOGICAL ACTIVITY OF PHYTOCHEMICALS

Atractylodin

The biological potential of atractylodin in exerting anti-colitis effects has been explored through its molecular targets. Luciferase assays, *in vitro* binding studies, and docking simulation research have shown that atractylodin has a preference for peroxisome proliferator-activated receptor alpha (PPARα). In a mouse model of colitis induced by dextran sodium sulfate (DSS), mice treated with 40 mg/kg of atractylodin daily exhibited a higher survival rate, suggesting that atractylodin may be an effective option for treating colitis.[18] The molecular mechanism underlying atractylodin activity against DSS-induced ulcerative colitis in mice has been studied. Atractylodin significantly alleviated DSS-induced symptoms, including weight loss, increased disease activity index scores, shortened colon length, and histological alterations in the colon. Furthermore, atractylodin may increase the population of beneficial bacteria while reducing harmful bacteria in the digestive tract. In the lipopolysaccharide (LPS)-induced macrophage model, atractylodin was shown to suppress the mitogen-activated protein kinase (MAPK) pathway and inhibit the production of inflammatory factors by macrophages. Additionally, atractylodin inhibits lactate formation, GAPDH activity, GAPDH malonylation, and TNF-α translation, highlighting its therapeutic potential for treating ulcerative colitis.[19] Research on the biological activity of herbal components using primary fibroblasts activated with tumor necrosis factor α (TNF-α) demonstrated that atractylodin suppresses the production of interleukin 6 (IL-6). Under TNF-α stimulation, atractylodin induces tri-methylation of histone H3 at lysine residue 9, which hinders the binding of NF-κB to the IL-6 promoter on genomic DNA.[20,21]

Karanjin

Researchers have examined the potential therapeutic benefits of karanjin, a compound extracted from *Pongamia pinnata* fruits, in treating experimental colitis in Balb/c mice. Experimental colitis was induced by rectal administration of a 2% solution of 2,4,6-trinitrobenzenesulfonic acid (TNBS) in 50% methanol. The effects of karanjin at doses of 100 and 200 mg/kg, administered daily for seven consecutive days, were compared with those of sulfasalazine in colitic mice. Compared to the TNBS control group, karanjin significantly reduced macroscopic dam-

age and histological abnormalities such as cellular infiltration, tissue necrosis, and mucosal and submucosal damage. The findings suggest that karanjin may be an effective treatment for colitis induced by intracolonic TNBS injection.[22,23]

Liriodendrin

The biological effects of liriodendrin on DSS-induced colitis in a mouse model have been investigated to identify potential pathways involved. Liriodendrin (100 mg/kg/day) significantly increased superoxide dismutase (SOD) and glutathione peroxidase (GPx) activities in the colon while markedly decreasing myeloperoxidase (MPO) and malonaldehyde (MDA) activities. Additionally, liriodendrin reduced the levels of pro-inflammatory cytokines such as TNF-α, interleukin-1 beta (IL-1β), and IL-6, while improving DAI), colon length, and histological condition of the colon. Moreover, liriodendrin enhanced the expression of ERβ in the colon and significantly inhibited the activation of the Akt and NF-κB pathways. The *in vivo* conversion of liriodendrin to syringaresinol may contribute to its anti-inflammatory effects. Liriodendrin appears to be a promising preventative therapeutic agent for colitis treatment.[24,25]

Norisoboldine

The protective effects of norisoboldine on DSS-induced UC in mice have been studied. Norisoboldine treatment significantly alleviated colitis symptoms by reducing levels of IL-1β, TNF-α, interferon-gamma (IFN-γ), and IL-17A; inhibiting the expression of extracellular signal-regulated kinase (ERK), p38 MAPK, and nuclear factor kappa B (NF-κB)-p65; and increasing both mRNA and protein levels of IL-10. An *in vitro* study also indicated that norisoboldine promotes Treg cell development.[26]

C57BL/6 mice, along with healthy control mice, have been used as models for DSS-induced colitis to further investigate the toxicological profile of norisoboldine (NOR). In DSS colitis mice, a dose of 90 mg/kg of NOR worsened symptoms and colonic lesions compared to the control group. No notable adverse effects were observed in healthy mice. These findings suggest that norisoboldine toxicity varies depending on the physiological condition of the animal. While a 90 mg/kg dose may be safe in healthy mice, it may be unsuitable for those with DSS-induced colitis.[27]

Although the biological effects of norisoboldine on colitis have been explored, its mechanism involving NLRP3 inflammasome activation has only recently been investigated. In TNBS-induced colitis in mice, norisoboldine reduced disease symptoms and significantly suppressed the expression of cleaved IL-1β, NLRP3, and cleaved Caspase-1 in the colon, but not ASC. Similarly, in THP-1 cells stimulated with ATP and LPS, NOR inhibited NLRP3, cleaved Caspase-1, and cleaved IL-1β expression, but not ASC. Additionally, NOR decreased reactive oxygen species (ROS) levels and increased Nrf2 levels in these cells. By modulating the AhR/Nrf2/ROS signaling pathway and inhibiting NLRP3 inflammasome activation, norisoboldine improved TNBS-induced colitis in mice.[28]

Researchers have also explored the mechanisms behind norisoboldine-induced Treg differentiation under hypoxic conditions and its anti-UC effects via the AhR/miR and AhR/glycolysis axes. Compared to normoxia, norisoboldine had a greater effect on Treg differentiation under hypoxia. In hypoxic conditions, it activated AhR in CD4+ T cells and downregulated the expression of miR-31—rather than miR-219 or miR-490—as well as suppressed glycolysis and reduced Glut1 and HK2 expression. Notably, NOR-induced Treg polarization was significantly disrupted by the HK2 plasmid but not by the miR-31 mimic. These findings indicate that norisoboldine facilitates Treg differentiation and helps prevent colitis by regulating the AhR/glycolysis axis and the downstream NAD+/SIRT1/SUV39H1/H3K9me3 signaling pathway.[29] Further research has confirmed norisoboldine's impact on DSS-induced UC in mice. Doses of 20 and 40 mg/kg significantly reduced colitis symptoms, decreased IL-1β and TNF-α levels, and inhibited activation of ERK, p38 MAPK, and NF-κB-p65. Norisoboldine also significantly increased IL-10 levels at both the mRNA and protein levels in mouse colons while only marginally decreasing IFN-γ and IL-17A levels. Additionally, it may promote the phosphorylation of Smad2/3 in colonic tissue and enhance Treg cell differentiation *in vitro* from naïve T cells. By reducing pro-inflammatory cytokines and selectively inducing Treg cells in the colon, norisoboldine can effectively alleviate DSS-induced ulcerative colitis in mice.[23,30]

Okanin

Researchers have investigated the biological potential of okanin, a compound derived from *Coreopsis tinctoria* Nutt, in DSS-induced colitis and its effects on behavioral and clinical symptoms in mice. Okanin regulated the hematoxylin and eosin (HE) staining score and goblet cell expression in colon tissue. It also modulated pro-inflammatory cytokines, including TNF-α, IL-1β, and IL-6, at the molecular level. Additionally, okanin demonstrated regulatory effects on tight junction proteins and the NF-κB signaling pathway at the protein level. According to 16S rRNA sequencing, okanin played a critical role in maintaining gut flora balance. These findings underscore the importance of okanin in managing DSS-induced colitis.[31,32]

Poncirin

The anti-colitic effects of poncirin were studied in a TNBS-induced colitis mouse model. Poncirin was found to attenuate TNBS-induced colitis by preventing colon shortening, reducing myeloperoxidase activity, inhibiting NF-κB activation, and suppressing Th17 cell differentiation. *In vitro*, poncirin inhibited the expression of Foxp3 and IL-17 and suppressed the differentiation of splenocytes into Th17 cells. These findings indicate that orally administered poncirin alleviates colitis by inhibiting LPS binding to macrophages and thereby reducing NF-κB activation.[33,34]

Sinensetin

Researchers have explored the biological effects of sinensetin, a flavonoid extracted from citrus and tangerine peels, on intestinal barrier dysfunction in colitis. Sinensetin significantly enhanced epithelial cell autophagy, reduced epithelial cell apoptosis, and decreased mucosal claudin-2 expression. It also reversed the increased intestinal permeability associated with colitis. In both rats and mice, sinensetin reduced colitis symptoms.[35] Additionally, sinensetin was studied for its role in suppressing sarcopenia in satellite cells derived from thigh and calf muscle tissues of both young and aged rats. Compared to untreated groups, satellite cell numbers were noticeably higher in aged rat cells treated with sinensetin.[36,37]

Dehydrocrebanine

This study aimed to explore the potential therapeutic effects of dried bark from *Ailanthus altissima* (Mill.) Swingle on ulcerative colitis using virtual screening, molecular docking, and activity evaluation technologies. Using AutoDock Vina, 22 compounds from secondary screening were docked with ulcerative colitis-related target proteins (IL-1R, TLR, EGFR, TGFR, and Wnt). The top-scoring compounds showed binding

energies of –8.5, –8.0, –9.2, –7.5, and –8.5 kcal/mol, respectively, with the active cavities of the human IL-1R, TLR, EGFR, TGFR, and Wnt proteins. Based on scoring function and docking mode analysis, the promising compounds identified were kaempferol, ailanthone, and dehydrocrebanine.[38,39]

Trifolirhizin

The therapeutic potential of trifolirhizin for UC was evaluated using a DSS-induced mouse model of colitis. Trifolirhizin was found to alleviate symptoms in mice with DSS-induced colitis. It contributed to inflammation reduction and modulation of the T helper 17 (Th17) to regulatory T (Treg) cell ratio. In addition, trifolirhizin inhibited NLRP3 inflammasome activation in colitic mice. It was also shown to regulate the thioredoxin-interacting protein (TXNIP)–AMP-activated protein kinase (AMPK) signaling pathway. Notably, suppression of AMPK blocked the anti-inflammatory effects mediated by trifolirhizin in DSS-induced UC mice.[40]

Phillygenin

The biological potential of phillygenin in DSS-induced colitis has been investigated, with results showing that it enhances the intestinal mucosal barrier. Furthermore, phillygenin restored the levels of inflammatory cytokines (TNF-α, IL-1β, IL-6, and IL-10) and regulated oxidative stress markers including MPO, SOD, and malondialdehyde (MDA) in colitic mice.[41,42]

Sauchinone

The biological effects of sauchinone have been studied in a mouse model of UC induced by DSS, along with its underlying molecular mechanisms. Sauchinone prevented mucosal barrier damage, reduced inflammation, and alleviated pathological symptoms. Additionally, sauchinone modulated the composition and diversity of the gut microbiota in mice.43 Moreover, it improved experimental colitis by inhibiting Th17 cell development and pathogenicity.[44,45]

Oxyberberine

Oxyberberine has been shown to effectively alleviate experimental colitis induced by dextran sulfate sodium in rats by reducing inflammation, altering gut microbiota, and strongly inhibiting the TLR4-MyD88-NF-κB signaling pathway. Oxyberberine also demonstrates a superior safety profile compared to berberine, with an LD_{50} value exceeding 5000 mg/kg in mice. Additionally, following oral administration of berberine, a significant amount of protein-bound oxyberberine was detected in hydrolyzed blood samples from rats.[46] The biological potential and mechanism of action of oxyberberine in DSS-induced colitis in Balb/c mice have also been studied. In colitic mice, oxyberberine significantly reduced clinical symptoms, colon shortening, and histological damage. It also improved intestinal epithelial barrier function and reduced the colonic inflammatory response. Furthermore, oxyberberine corrected DSS-induced gut dysbiosis, restoring microbial balance. Through preservation of colonic integrity, suppression of inflammation, and modulation of gut microbiota, oxyberberine effectively mitigated DSS-induced experimental colitis.[47]

Kuraridin

This study investigated for the first time the pharmacodynamic effects of *Sophora flavescens* ethyl acetate (EtOAc) extract (SFE) in a rat model of UC induced by dextran sodium sulfate. The pharmacodynamic findings indicated that SFE repaired colon tissue damage, reduced colon bleeding, and significantly decreased body weight loss and colon shortening in UC rats. A total of 28 prototype compounds and 41 metabolites were identified in rat plasma and urine, either definitively or inferentially. Of these, 28 prototypes and 3 phase I metabolites shared 40 UC-related targets, which were involved in 51 metabolic pathways across 5 functional modules. Based on a comprehensive analysis of network pharmacology data, *in vivo* metabolic profiling, and prior research, kuraridin and other phytochemicals were proposed as potential active constituents of SFE for UC treatment.[48]

Obacunone

Obacunone is a naturally occurring limonoid compound widely found in citrus fruits, with reported antiviral, antioxidant, and antitumor properties. Although recent studies have demonstrated its anti-inflammatory activity *in vitro*, its efficacy against intestinal inflammation required further evaluation. In this study, a DSS-induced UC mouse model was used to assess the effects and mechanisms of obacunone. The results showed that obacunone effectively reduced colitis severity by modulating the gut microbiota composition and suppressing the overactivation of the toll-like receptor 4 (TLR4)/NF-κB signaling pathway. In DSS colitis mice, activation of inflammatory cascades was associated with intestinal epithelial barrier disruption; obacunone reversed this effect by inhibiting inflammatory signaling and promoting the expression of tight junction proteins such as occludin and TJP1.[49] Furthermore, the physicochemical properties and biological activities of phytochemicals in Coptidis Rhizoma (CR) were analyzed through bioinformatics. The study evaluated the binding activities, target pathways, and functions of CR compounds, including obacunone. Findings demonstrated that major phytochemicals in CR exhibit favorable drug-likeness and bioactivity. The previously mentioned signaling pathways may represent the mechanisms by which these compounds exert therapeutic effects against UC.[50]

Ginsenoside Rb1

Ginsenoside Rb1 (GRb1), a key component of ginseng, plays a regulatory role in metabolism and autoimmunity. In UC mice, GRb1 treatment corrected intestinal barrier dysfunction and reduced inflammation. Specifically, GRb1 increased levels of the anti-inflammatory cytokine IL-10 while decreasing levels of pro-inflammatory cytokines such as TNF-α and IL-6. Additionally, GRb1 therapy elevated the expression of tight junction proteins like ZO-1, occludin, and E-cadherin, which are crucial for maintaining intestinal barrier integrity. By regulating intestinal inflammation and preserving barrier function via the VDR, PPARγ, and NF-κB signaling pathways, GRb1 effectively alleviated UC.[51]

Ginsenoside Rg1 also significantly reduced symptoms associated with UC, including weight loss, high DAI scores, and shortened colon length. Rg1 reduced DSS-induced oxidative damage by decreasing TNF-α, IL-1β, and IL-6 levels in serum and cell supernatants, and it lowered MPO content in the colon. Additionally, Rg1 treatment increased SOD levels and reduced MDA levels in the serum, colon, and cell supernatants. In both RAW 264.7 cells and UC mice, Rg1 restored the Nrf2/HO-1/NF-κB signaling pathway, while Nrf2 siRNA blocked these effects.[52]

Berberine

The therapeutic effects of berberine on UC have been investigated using network pharmacology, molecular docking, and dynamic simulations, supported by *in vitro* and *in vivo* validations. Molecular docking predicted that berberine has strong binding affinity to key targets such as TLR4, NF-κB, HIF-1α, and the HIF inhibitor KC7F2. *In vivo* experiments demonstrated that berberine reduced clinical symptoms in DSS-induced UC mice, including decreased weight loss, intestinal inflammation, and DAI scores. Berberine downregulated the mRNA

and protein expression of TLR4, NF-κB, and HIF-1α, and suppressed pro-inflammatory cytokines IL-6 and TNF-α. *In vitro* results further confirmed that berberine inhibits the TLR4/NF-κB/HIF-1α pathway and effectively reduces inflammatory cell injury, showing efficacy comparable to KC7F2.[53]

Arjunolic Acid

Arjunolic acid improved intestinal barrier function and alleviated colitis in Il-10-deficient mice. It reduced levels of Bax and cleaved caspase-3 and inhibited intestinal epithelial cell apoptosis in Il-10-/- mice and LPS-induced colon organoids. Arjunolic acid also suppressed LPS-induced TLR4 signaling activation in both models. By preventing apoptosis, it protected the intestinal barrier in colitis that resembles Crohn's disease. Furthermore, arjunolic acid altered gut microbiota composition and inhibited TLR4 signaling, providing potential new therapeutic strategies for treating Crohn's disease.[54]

Curculigoside

Curculigoside (CUR), the primary active compound in *Curculigo orchioides* Gaertn, reduced inflammation in mice with chronic colitis.

Table 1. Molecular mechanism of different phytochemicals for their anti-colitis potential

Phytochemical	Molecular mechanism	Reference
Atractylodin	Atractylodin significantly inhibited tumor necrosis factor-α-induced phosphorylation of nuclear factor-κ-light-chain-enhancer of activated B in HCT116 cells. Atractylodin could inhibit the activation of colonic macrophages by inhibiting the MAPK pathway and alleviate intestinal inflammation. Atractylodin protect the intestinal barrier by inhibiting the decrease of the tight junction proteins, ZO-1, occludin, and MUC2. Atractylodin attenuated colitis induction which showed the inhibition of KDM4A activity as a strategy to suppress IL-6 production and attenuate colitis induction.	18–20
Karanjin	Karanjin reduces the activity of myeloperoxidase (MPO), depressed malondialdehyde (MDA), and nitric oxide (NO) level. Restoring the level of catalase (CAT), superoxide dismutase (SOD), and reduced glutathione (GSH) level to normal when compared to the TNBS colitis group.	22
Liriodendrin	Liriodendrin down-regulated production of pro-inflammatory cytokines and suppressed NF-κB signalling pathways in LPS-induced RAW 264.7 macrophages.	24
Norisoboldine	Norisoboldine prominently relieved colonic mucosal damage and inflammatory response via suppressing NLRP3 inflammasome activation and regulating the AhR/Nrf2/ROS signaling pathway. Norisoboldine could activate aryl hydrocarbon receptor (AhR) in THP-1 cells, inducing CYP1A1 mRNA expression, and promoting dissociation of AhR/HSP90 complexes, association of AhR and ARNT, AhR nuclear translocation, XRE reporter activity and binding activity of AhR/ARNT/XRE.	26–28
Sinensetin	Sinensetin significantly alleviated intestinal barrier dysfunction in colitis by promoting epithelial cell autophagy, and inhibiting apoptosis and promoting claudin-2 degradation. Sinensetin can alleviate age-related sarcopenia by increasing differentiation rate and protein levels of myoD and myogenin.	35,36
Trifolirhizin	Trifolirhizin significantly improved the symptoms and the pathological damage in DSS-induced UC mice. Trifolirhizin regulated the balance of Th17/Treg cells and inflammation in the UC mice through inhibiting the TXNIP-mediated activation of NLRP3 inflammasome.	40
Phillygenin	Phillygenin inhibited the activation of tyrosine kinase Src and reduced the phosphorylation of downstream proteins p38, JNK, and NF-κB in colitis mice.	41
Sauchinone	Sauchinone significantly inhibited LPS-induced Dendritic cells (DC) activation. Sauchinone suppressed the ability of LPS-primed DC to induce Th1/Th17 cell differentiation.	44
Oxyberberine	Oxyberberine appreciably inhibited TLR4-MyD88-NF-κB signaling pathway through down-regulating the protein expressions of TLR4 and MyD88. Inhibiting the phosphorylation of IκBα, and the translocation of NF-κB p65 from cytoplasm to nucleus.	47
Obacunone	Obacunone attenuated the symptoms of experimental UC in mice through modulation of the gut microbiota, attenuation of TLR4/NF-κB signaling cascades, and restoration of intestinal epithelial barrier integrity.	49
Ginsenoside Rb1	Ginsenoside Rb1 ameliorated inflammation and oxidative stress in colitis via Nrf-2/HO-1/NF-kappaB pathway	52
Berberine	Berberine enhances UC treatment outcomes by inhibiting the TLR4/NF-κB/HIF-1α axis.	53
Arjunolic acid	Arjunolic acid increased the abundance of short-chain fatty acid-producing bacteria in the stool of Il-10-/- mice, and transplantation of feces from AA-treated mice improved CD-like colitis.	54
Curculigoside	Nrf2 served a pivotal role in inhibition of UC by curculigoside via interaction with Kelch-like ECH-associated protein 1 (Keap1).	55

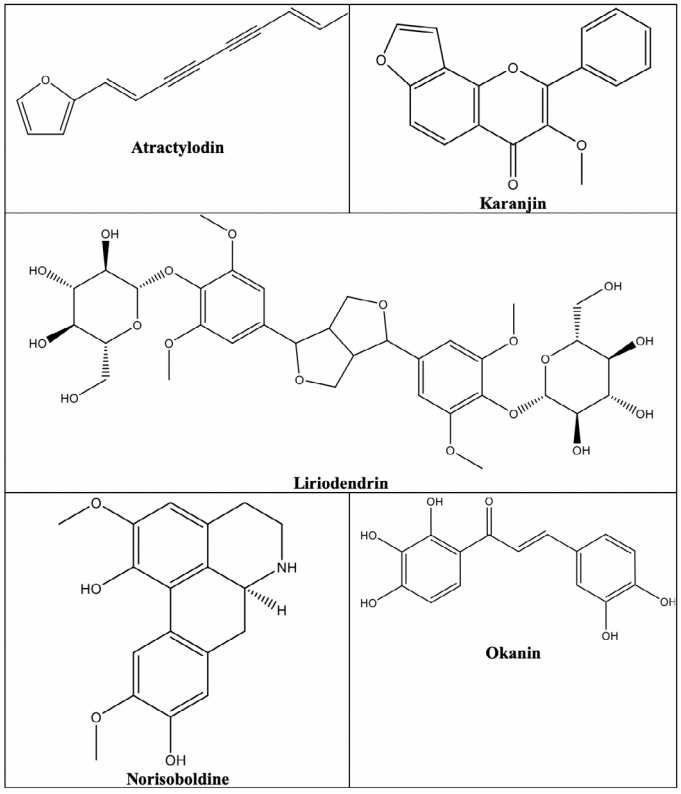

Figure 1. Chemical structure of phytochemical having anti-colitis potential.

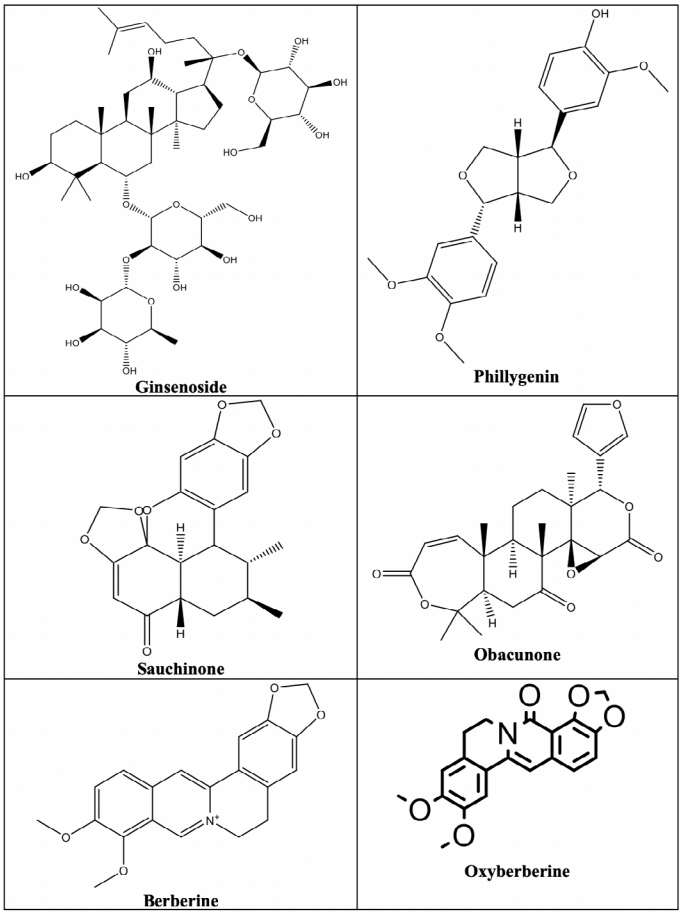

Figure 2. Chemical structure of phytochemical having anti-colitis potential.

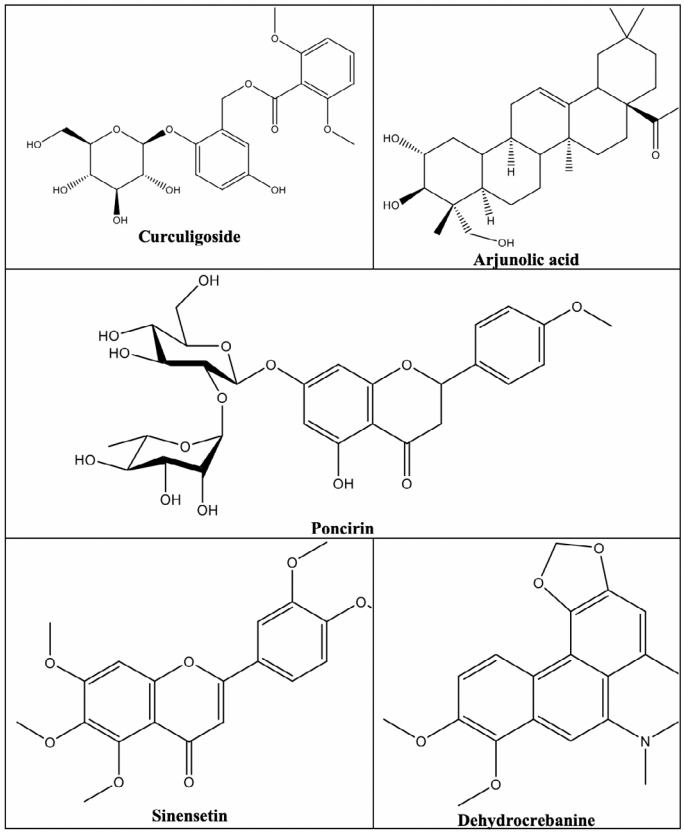

Figure 3. Chemical structure of phytochemical having anti-colitis potential.

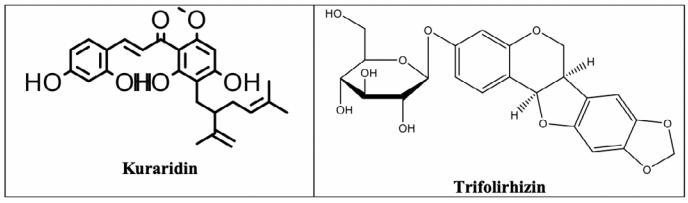

Figure 4. Chemical structure of phytochemical having anti-colitis potential.

This was evidenced by decreased neutrophil infiltration, reduced myeloperoxidase activity, and downregulated pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β. CUR's antioxidative capacity was demonstrated in organoids stimulated with TNF-α and in Caco-2 cells exposed to H_2O_2. Both *in vitro* and *in vivo*, CUR activated Nrf2 and enhanced autophagy. Experimental findings showed that CUR increased Nrf2 expression via the Keap1/Nrf2 axis, reducing oxidative stress and promoting autophagy. These results suggest that CUR may have clinical utility in UC treatment and can effectively alleviate colitis.[55]

CONCLUSION

This review outlined the pharmacological activities and molecular mechanisms of various classes of phytochemicals to explore their biological potential in treating colitis. It summarized scientific information on the biological potential, pharmacological activity, and molecular mechanisms of atractylodin, karanjin, liriodendrin, norisoboldine, okanin, trifolirhizin, phillygenin, sauchinone, oxyberberine, obacunone, ginsenoside Rb1, berberine, arjunolic acid, and curculigoside in relation to their anti-colitis properties. Furthermore, while chemical structures of these phytochemicals are shown in Figures 1-5, their molecular mechanisms are presented in Table 1 and Figure 6.

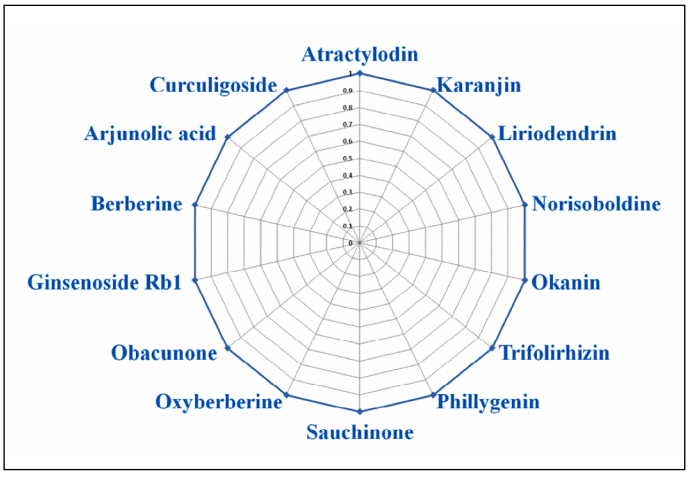

Figure 5. Phytochemicals having anti-colitis potential.

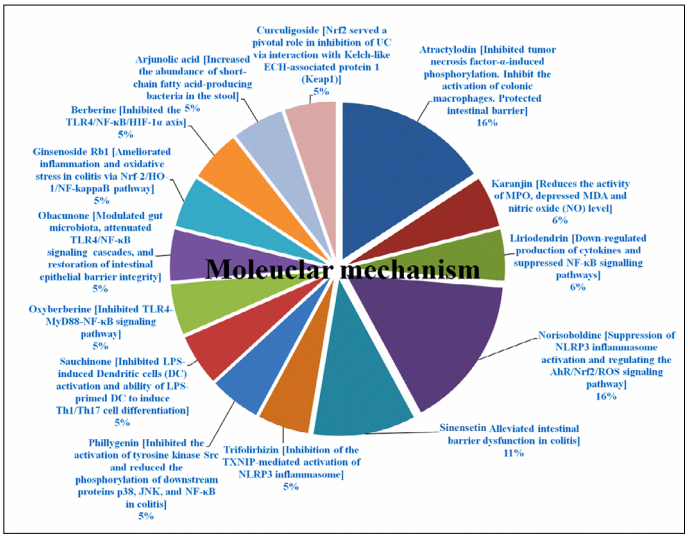

Figure 6. Molecular mechanisms of phytochemicals having anti-colitis potential.

The scientific data presented in this paper highlight the anti-colitis potential of these phytochemicals in medicinal applications. This information may be valuable to researchers across various scientific disciplines for further investigation into the health benefits of plant-based phytochemicals in the treatment of colitis.

FUTURE RESEARCH DIRECTIONS

To explore their potential roles in treating IBD and UC, the biological potential and pharmacological activities of various plant-derived phytochemicals have been reviewed for their efficacy against colitis. Although the pharmacological properties and medicinal relevance of many phytochemical classes discussed in this review have been supported by scientific data, further research is needed to examine their natural occurrence and application in medicine.

Despite the broad range of biological activities exhibited by plant phytochemicals, future studies should also evaluate their effectiveness in addressing other secondary human complications. The plasma profiles of these phytochemicals must be determined using a variety of analytical methods and clinical studies to better assess their safety profiles in clinical medicine.

Building on the documented biological actions of plant phytochemicals, future research should focus on developing novel pharmacological compounds aimed at improving human health outcomes related to colitis. Incorporating more specific references to clinical trials or case studies in future research will further enhance scientific understanding. Additionally, identifying promising areas for further investigation and addressing current gaps in clinical application knowledge will help guide the direction of future studies.

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