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Original Article

Therapeutic Potential of *Allium cepa* in Ulcerative Colitis: Mechanistic Insights, Preclinical Evidence and Future Perspectives

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ABSTRACT

Ulcerative colitis (UC), a major subtype of inflammatory bowel disease, is a chronic inflammatory disorder characterized by continuous mucosal inflammation extending from the rectum through the colon. Its pathogenesis involves complex interactions among genetic susceptibility, environmental triggers, epithelial barrier dysfunction, immune dysregulation, and gut microbiota imbalance. Activation of NF-κB and MAPK signaling pathways promotes excessive production of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, leading to sustained mucosal injury. Although conventional therapies, including 5-aminosalicylic acid derivatives and corticosteroids, effectively control inflammation, their long-term use is limited by adverse effects. *Allium cepa* (onion), particularly its major flavonoid quercetin, has emerged as a promising natural therapeutic candidate in ulcerative colitis management. Preclinical studies using DSS-induced colitis model, TNBS-induced colitis model, and acetic acid–induced colitis models demonstrate that quercetin-rich onion extracts attenuate disease severity by inhibiting NF-κB and MAPK activation, reducing pro-inflammatory cytokine production, suppresing oxidative stress, modulating apoptosis, enhancing short-chain fatty acid production, promoting beneficial gut microbiota such as Bifidobacterium and Lactobacillus species, and supporting epithelial barrier integrity. Collectively, these findings highlight the therapeutic potential of quercetin-rich Allium cepa in ulcerative colitis management

Keywords: Ulcerative colitis, *Allium cepa*, Quercetin, NF-κB, MAPK, Gut microbiota, Preclinical models

INTRODUCTION

Ulcerative colitis is a chronic, idiopathic condition defined by uninterrupted mucosal inflammation that originates in the rectum and moves proximally through the colon. Alongside Crohn's disease, it is classified as one of the two primary types of inflammatory bowel disease (IBD). [1] Clinically, ulcerative colitis is characterized by periodic flare-ups of bloody diarrhea, rectal urgency, tenesmus, and abdominal discomfort, all of which can profoundly diminish a patient's overall quality of life. [2] Fig. 1. show diagrammatic comparison between normal colon and colon affected by ulcerative Colitis. [3] In recent years, the worldwide frequency and prevalence of ulcerative coltis have risen significantly, with a notable surge in emerging industrial nations. This trend underscores the impact of modern lifestyle and environmental shifts on the disease. [4] While the exact cause is still being determined, ulcerative colitis is recognized as a multifactorial condition. It arises from a dynamic interplay between a patient's genetic profile, environmental stressors, compromised intestinal barrier function, immune system errors, and shifts in the gut microbiome. [5] The breakdown of the intestinal epithelial barrier, coupled with an imbalance in gut microbiota (dysbiosis), triggers a disproportionate immune reaction within the mucosa. This activation of the immune system leads to an elevated release of pro-inflammatory cytokines—notably TNF-α, IL-6, and IL-1β—which are responsible for driving chronic inflammation and subsequent damage to the tissues. [6] Central to this inflammatory cycle is the activation of specific intracellular signaling cascades. In particular, the NF-κB pathway acts as a primary regulator, controlling the expression of genes associated with inflammation and ensuring the continued destruction of the mucosal lining. [7]

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

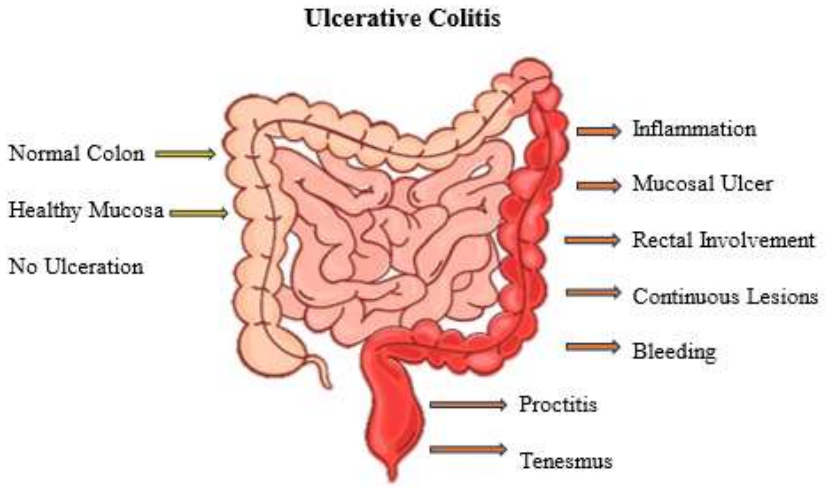


Fig. 1. Diagrammatic comparison between normal colon and colon affected by Ulcerative Colitis [3]

Epidemiology and Risk Factors

Inflammatory bowel disease affects an estimated 1–2 million individuals in the United States, with ulcerative colitis accounting for roughly half of these cases. Although ulcerative colitis may develop at any age, it is most commonly diagnosed before the age of 30. The condition occurs at similar rates in males and females. A familial association has been observed, with nearly 20% of patients reporting a first-degree relative affected by inflammatory bowel disease. [8] Several environmental and lifestyle factors appear to influence disease risk. Breastfeeding during infancy prior appendectomy and cigarette smoking have been associated with a decreased likelihood of developing ulcerative colitis. Conversely, adherence to a Western-style diet, left-handedness and the presence of depression have been suggested as potential risk-enhancing factors. [4]

Conventional Treatment of Ulcerative Colitis

Conventional management of ulcerative colitis includes aminosalicylates and corticosteroids. Aminosalicylates such as Sulfasalazine and 5-ASA formulations including Mesalamine, Balsalazide, and Olsalazine are primarily used to maintain remission. Sulfasalazine is cleaved in the colon to release 5-ASA (active moiety) and sulfapyridine, the latter being responsible for most adverse effects. 5-ASA exerts anti-inflammatory effects by inhibiting pro-inflammatory cytokines (IL-1, IL-2) and NF-κB activity. [9,10] It may also affect butyrate oxidation in colonic epithelial cells, though the clinical relevance remains uncertain. [11] About 30% of patients on sulfasalazine experience adverse effects, including nausea, headache, rash, agranulocytosis, hepatitis, and reversible male infertility; folic acid supplementation is recommended. Sulfa-free 5-ASA agents are generally better tolerated. [12] Corticosteroids such as Prednisone are used for moderate to severe flares. They suppress inflammatory cytokines and inhibit the arachidonic acid pathway. Doses above 40 mg/day usually offer no added benefit. [12] Long-term use is associated with osteoporosis, cataracts, adrenal suppression, and infection risk. The adverse effects and limitations of conventional treatment for ulcerative colitis have shifted research focus toward natural drugs and plant-based therapeutic approaches.

Natural Plant-Based Therapeutic Agent: *Allium Cepa* Extract

Allium cepa, commonly known as onion, is a bulb-forming perennial herb cultivated worldwide as a vegetable crop. Taxonomically, it is traditionally classified within the family Alliaceae, although some earlier literature placed it in Liliaceae. The plant develops an underground bulb that serves as the edible portion and produces one or two hollow, leafless flowering stalks that may reach 75–180 cm in height. Historical records suggest that onions originated in regions corresponding to present-day Afghanistan, Iran, and parts of Central Asia, and they are now cultivated in more than 175 countries globally. [13] Onions are consumed fresh, cooked, or preserved (e.g., pickled), and are valued for both their flavor and

nutritional properties. Red onion varieties are particularly notable for their high quercetin content.

Nutritional Profile and General Health Benefits

Onions consist of approximately 90% water and are a source of dietary fiber and natural sugars. Diets rich in vegetables, including onions, have been associated with reduced risk of several chronic diseases and overall health promotion. [14] They contain essential micronutrients such as vitamins B1 (thiamine), B2 (riboflavin), vitamin C, selenium, and potassium. Epidemiological and experimental studies suggest that onion consumption may contribute to reduced risk of metabolic disorders, cardiovascular diseases, and certain cancers. [15,16] Regular dietary intake of onions has been linked with a lower incidence of colorectal, lung, liver, brain, gastric, ovarian, prostate, and breast cancers, likely due to their high content of flavonoids and organosulfur compounds. [16]

Red Onion and Its By-Products

Red onion (*Allium cepa* L.) is among the most widely cultivated horticultural crops worldwide because of its characteristic flavor and nutritional value.[12] Notably, onion peel has been reported to contain up to 20-fold higher concentrations of quercetin compared with the edible bulb, along with elevated levels of total phenolics, flavonoids, and flavanols.[17] Quercetin has various pharmacological activity such as antiplatelet, antihypertensive, antioxidant, anti-inflammatory, anti-diabetic, anti-ulcer, neuroprotective.[18]

Common Name [19]

Language	Name
English	Onion, bulb onion
Marathi	Kanda
Hindi	Pyaaz
Ayurvedic	Palandu

Hierarchical Classification of *Allium Cepa*[20]

Kingdom	Plantae
Division	Magnoliophyta
Class	Liliopsida
Order	Asparagales
Family	Alliaceae
Genus	Allium
Species	Allium cepa

Chemical Constituents

The peel of *Allium cepa* is a concentrated source of phenolic compounds, with quercetin recognized as the principal flavonoid. Beyond free quercetin, numerous glycosylated derivatives and related polyphenols have been isolated and characterized from onion skin extracts.[21] These identified compounds include quercetin 3,4′-diglycoside, quercetin-7,4′-diglycoside, quercetin-3-glycoside, quercetin-4′-glycoside, isorhamnetin and its glycosides (including isorhamnetin-3,4′-diglycoside and isorhamnetin-4′-glycoside), kaempferol, protocatechuic acid, protocatecoyl quercetin, and 2-(3,4-dihydroxybenzoyl)-2,4,6-trihydroxy-3(2H)-benzofuranone. In addition, oligomeric forms such as quercetin dimers (including 4′-glycoside and hexoside derivatives) and quercetin trimers have also been reported. [21]

Physiopathology of Ulcerative Colitis

Ulcerative colitis is marked by disruption of the intestinal epithelial barrier, dysbiosis of gut microbiota, and immune activation. Damage to tight junctions and the mucus layer increases permeability, allowing commensal bacteria to invade deeper tissues. Macrophages and dendritic cells recognize bacterial antigens via Toll-like receptors (TLRs), triggering pro-inflammatory pathways and secretion of

cytokines such as TNF-α, IL-1β, IL-6, IL-12, and IL-23. [1,22] Bioactive flavonoids, particularly quercetin, present in *Allium cepa* peel, exert potent anti-inflammatory and antioxidant effects. These compounds inhibit NF-κB signaling, suppress pro-inflammatory cytokines (TNF-α, IL-6, IL-1β), reduce neutrophil infiltration, and help preserve intestinal epithelial barrier integrity, thereby mitigating the key pathological mechanisms of ulcerative colitis. [23,24]

NF-κB Inhibition in Ulcerative Colitis

Nuclear factor-kappa B (NF-κB) is a key transcription factor controlling pro-inflammatory genes involved in inflammatory bowel disease (IBD). In murine models of DSS- and TNBS-induced colitis, NF-κB is aberrantly activated in epithelial cells, macrophages, and immune infiltrates. Normally, NF-κB is held inactive in the cytoplasm by IκB proteins, but inflammatory stimuli such as TNF-α, IL-1β, ROS, and bacterial products activate the IκB kinase (IKK) complex. This leads to IκB degradation, allowing the NF-κB p65/p50 heterodimer to enter the nucleus and drive expression of cytokines (TNF-α, IL-6, IL-1β), COX-2, iNOS, and chemokines. Sustained NF-κB activation contributes to epithelial barrier disruption, oxidative stress, leukocyte infiltration, and mucosal injury. Inhibition of NF-κB in experimental colitis reduces cytokine production, myeloperoxidase activity, histopathological damage, and restores epithelial integrity, highlighting NF-κB as a promising therapeutic target. [25,26] Onion (*Allium cepa*) peel is rich in quercetin and flavonoids with strong anti-inflammatory and antioxidant effects. Quercetin inhibits NF-κB by blocking IKK activity, preventing IκB degradation, and reducing nuclear translocation of p65. In preclinical colitis models, onion peel extract decreases NF-κB activation, lowers TNF-α, IL-6, and IL-1β levels, mitigates oxidative stress, and protects colonic mucosa from inflammation and damage. [27,24]

Mechanisms of MAPK Regulation in Ulcerative Colitis:

Suppression of Inflammatory Response

The MAPK signaling pathway plays a central role in cellular stress and inflammatory responses, and its dysregulation is closely linked to chronic inflammation and tissue damage in ulcerative colitis ulcerative colitis.[23] Elevated levels of phosphorylated p38MAPK in the intestinal mucosa of ulcerative colitis models are associated with increased proinflammatory cytokines, such as IL-1β and TNF-α, correlating with disease severity.[28] Targeting MAPK has shown therapeutic potential in UC by not only reducing inflammation but also promoting mucosal repair. Inhibition of MAPK decreases proinflammatory cytokine expression, enhances EGFR phosphorylation, and stimulates epithelial cell proliferation and migration. [29,30] Additionally, MAPK inhibition can indirectly reduce inflammation by modulating gut microbiota, increasing beneficial bacteria like Bifidobacterium and Lactobacillus, and lowering proinflammatory factor production, creating a feedback loop that supports intestinal health.[31] Bioactive flavonoids in *Allium cepa* peel, particularly quercetin, suppress MAPK activation (p38, ERK, JNK), lower TNF-α and IL-1β level, and aid in epithelial barrier restoration, highlighting MAPK modulation as a key mechanism in ulcerative colitis amelioration.[24,32]

Alleviating Oxidative Stress

Oxidative stress (OS), caused by an imbalance between reactive oxygen species (ROS) and antioxidant defenses, contributes to mucosal damage, inflammation, and barrier dysfunction in ulcerative colitis.[33] MAPK signaling helps counteract OS by activating p38MAPK, which promotes antioxidant enzyme synthesis (e.g., SOD, GPx) and interacts with the Nrf2/ARE pathway to enhance cellular defense.[34] MAPK also reduces ROS accumulation and mitigates apoptosis by supporting mitochondrial function and autophagy.[32] Bioactive flavonoids in *Allium cepa* peel, particularly quercetin, directly scavenge ROS, activate Nrf2/ARE, increase SOD and GPx expression, inhibit excessive p38MAPK activation, and reduce lipid peroxidation, thereby protecting epithelial cells from oxidative damage.[24] Targeting MAPK-mediated oxidative stress offers a promising therapeutic approach for ulcerative colitis.

Inhibition of Apoptosis

Apoptosis is a regulated form of cell death critical for maintaining intestinal homeostasis, but excessive apoptosis of epithelial cells contributes to mucosal

damage and inflammation in ulcerative colitis. [35] Dysregulated MAPK signaling in UC promotes apoptosis by upregulating pro-apoptotic proteins such as Caspase-3 and Caspase-8, exacerbating intestinal injury. [36] Bioactive flavonoids in *Allium cepa* peel, particularly quercetin, inhibit p38/JNK MAPK activation, suppress pro-apoptotic proteins (Caspase-3, Bax), and increase anti-apoptotic Bcl-2 expression. Combined with antioxidant effects and Nrf2 activation, quercetin protects epithelial cells from oxidative stress–induced apoptosis, highlighting MAPK modulation as a promising therapeutic strategy for ulcerative colitis. [24,32]

Regulation of Intestinal Immunity

In ulcerative colitis MAPK signaling is a key regulator of intestinal immune homeostasis, controlling the activation, differentiation, and cytokine production of mucosal immune cells.[37] Inflammatory macrophages and dendritic cells (DCs) contribute to mucosal damage by releasing cytokines such as TNF-α, IL-1β, and IL-6, driven by p38MAPK and JNK activation and downstream transcription factors like AP-1.[38] p38MAPK also promotes IL-1β maturation via NLRP3 inflammasome activation, amplifying inflammation. Excessive ERK signaling disrupts DC-mediated IL-10 secretion, skewing T cell differentiation toward pro-inflammatory phenotypes. [39] Therapeutically, inhibition of p38MAPK or JNK reduces cytokine levels, immune cell infiltration, and mucosal injury in UC models, while targeting upstream regulators like TLR4 can indirectly modulate MAPK activity.[40] Natural compounds, particularly flavonoid-rich *Allium cepa* peel extract, suppress p38/JNK activation, decrease TNF-α, IL-1β, and IL-6 production, and help restore intestinal immune balance, highlighting MAPK modulation as a promising immunoregulatory strategy in ulcerative colitis.[24]

Repairing the Mucosal Barrier

The intestinal epithelial barrier, composed of tight junctions (TJs), mucus, and immune cells, is essential for preventing pathogen invasion and controlling inflammation in ulcerative colitis. [41] MAPK signaling regulates TJ protein expression and localization, maintaining barrier integrity. In ulcerative colitis, proinflammatory cytokines such as TNF-α and IL-1β activate p38MAPK and JNK, leading to downregulation and degradation of TJ proteins (Occludin, ZO-1, Claudin-1) and increased epithelial permeability, which exacerbates inflammation. [24] Natural compounds, particularly flavonoid-rich *Allium cepa* peel extract, protect barrier function by inhibiting p38/JNK activation, preventing TJ disruption, reducing oxidative stress, and promoting mucosal repair. [42] These effects highlight MAPK modulation as a key strategy for restoring intestinal epithelial integrity in ulcerative colitis.

Modulating Gut Microbiota

Dysbiosis contributes to ulcerative colitis by reducing beneficial bacteria, increasing pathogens, disrupting mucosal integrity, and triggering inflammation. [43] MAPK signaling links host immune responses to microbial metabolism, and its overactivation can worsen dysbiosis and intestinal barrier damage. Targeting MAPK (especially p38) reduces pro-inflammatory cytokines, promotes gut microbiota balance, and supports barrier repair, creating a positive cycle of "MAPK inhibition → microbiota restoration → inflammation alleviation". [44] Natural polyphenol-rich extracts, such as *Allium cepa* peel, enhance beneficial SCFA-producing bacteria (e.g., Lactobacillus, Bifidobacterium), suppress pathogens, improve barrier integrity, and reduce inflammation. Quercetin in the extract inhibits NF-κB and MAPK pathways, further mitigating cytokine-driven inflammation and microbiota-mediated disease progression. [24] These findings suggest MAPK modulation through natural compounds can restore microbial homeostasis and alleviate ulcerative severity.

Preclinical Colitis Models

DSS-Induced Colitis Model

The dextran sodium sulfate (DSS) model is widely used to study ulcerative colitis in rodents. DSS disrupts the colonic epithelial barrier, causing mucosal erosion, inflammatory cell infiltration, and clinical features such as weight loss and diarrhea, mimicking human ulcerative colitis. By varying DSS concentration, duration, or cycles, acute, chronic, or relapsing colitis can be modeled, providing a

reproducible and cost-effective platform for investigating disease mechanisms and testing therapies. [45] Preclinical studies show that *Allium cepa* (onion) extracts protect against DSS-induced colitis. Administration of onion bulb extract (OBE) reduces weight loss, preserves colon length, improves histology, and decreases inflammatory cell infiltration. These effects involve inhibition of MAPK, COX-2, and AKT signaling, suppression of pro-inflammatory cytokines and chemokines, enhancement of neutrophil apoptosis, and reduction of oxidative stress. [46] These findings highlight the potential of *Allium cepa* bioactive compounds as natural therapeutics for ulcerative colitis.

TNBS-Induced Colitis Model

The 2,4,6-trinitrobenzene sulfonic acid (TNBS) model induces colitis in rodents by haptenizing colonic proteins after ethanol-mediated barrier disruption, triggering a Th1-mediated immune response and transmural inflammation. It produces weight loss, diarrhea, colon shortening, immune cell infiltration, and elevated pro-inflammatory cytokines (TNF-α, IFN-γ, IL-6), modeling deeper, immune-driven intestinal injury compared with the DSS model. [47] Bioactive compounds from *Allium cepa*, especially quercetin, protect against TNBS-induced colitis. Quercetin reduces macroscopic and histological colon damage, edema, and inflammatory infiltration, suppresses TNF-α and IL-1β, inhibits NF-κB and p38 MAPK signaling, and enhances antioxidant defenses, thereby limiting oxidative stress and mucosal injury. [48] These findings highlight the anti-inflammatory and immunomodulatory potential of *Allium cepa* flavonoids in immune-mediated colitis models.

Acetic Acid-Induced Colitis Model

The acetic acid model induces colitis in rodents via direct chemical injury to the colonic mucosa, causing epithelial necrosis, ulceration, edema, hemorrhage, and inflammatory cell infiltration. It is characterized by increased oxidative stress, elevated TNF-α and IL-1β, and enhanced MPO activity, making it useful for studying acute mucosal injury and screening anti-inflammatory agents. [49] *Allium cepa* extract, particularly quercetin, protects against acetic acid–induced colitis by reducing macroscopic and histological damage, suppressing pro-inflammatory cytokines, inhibiting NF-κB signaling, lowering oxidative stress markers (e.g., MDA), and enhancing antioxidant enzymes such as SOD and CAT. It also attenuates neutrophil infiltration and preserves mucosal architecture, highlighting its anti-inflammatory and antioxidant therapeutic potential in ulcerative colitis. [50]

Outcome Measures in Experimental Colitis Models

In chemically induced colitis models (DSS, TNBS, acetic acid), standardized outcome measures are used to assess disease severity and therapeutic effects. The Disease Activity Index (DAI), combining body weight loss, stool consistency, and rectal bleeding, evaluates clinical severity. Colon shortening serves as a macroscopic indicator of inflammation, while myeloperoxidase (MPO) activity reflects neutrophil infiltration and acute inflammatory responses. Histological scoring of mucosal damage, epithelial erosion, crypt architecture, and inflammatory cell infiltration remains the gold standard for assessing tissue injury. Together, these parameters provide a comprehensive assessment of disease progression and treatment efficacy in experimental ulcerative colitis. [49,50]

Advantages of *Allium Cepa* Compared with 5-ASA and Corticosteroids

Compared to conventional therapies like 5-aminosalicylic acid (5-ASA) and corticosteroids, *Allium cepa* offers potential benefits, including lower systemic toxicity and fewer side effects. Its bioactive compounds, particularly quercetin, provide combined antioxidant and immunomodulatory effects by inhibiting NF-κB signaling, suppressing pro-inflammatory cytokines, and reducing oxidative stress. Additionally, as a dietary phytochemical, *Allium cepa* has nutraceutical value, making it a promising option for long-term adjunctive management of inflammatory bowel disease. [32,51]

DISCUSSION

The intestinal microbiota is essential for maintaining immune balance and epithelial barrier integrity. In ulcerative colitis reduced microbial diversity and

depletion of beneficial bacteria are commonly observed, accompanied by an increase in pro-inflammatory species. [52,53] This imbalance promotes exaggerated immune activation, enhanced cytokine release, and persistent mucosal inflammation. Restoration of microbial homeostasis is therefore considered a key therapeutic target in ulcerative colitis management. [55] Dietary fibers obtained from *Allium cepa* contain inulin-type fructans that act as prebiotics. These compounds resist digestion in the upper gut and are fermented in the colon, selectively stimulating beneficial bacteria such as Bifidobacterium and Lactobacillus species. [56,57] Improved growth of commensal bacteria supports mucosal immunity and may reduce inflammatory activity in ulcerative colitis. Fermentation of onion fiber results in the production of short-chain fatty acids (SCFAs), particularly butyrate. Butyrate serves as an energy source for colonocytes and contributes to epithelial repair and anti-inflammatory signaling. [58] Decreased SCFA production has been reported in UC patients, suggesting that enhancing SCFA levels may help attenuate intestinal inflammation. [59] Prebiotic supplementation can help rebalance gut microbial composition by promoting beneficial microbes and limiting opportunistic pathogens. This microbial correction improves tight junction function, reduces intestinal permeability, and mitigates inflammatory responses in experimental colitis models. [60] Bioactive constituents of onion, including flavonoids, exhibit antimicrobial and anti-inflammatory activities. These compounds may suppress pathogenic bacterial growth and downregulate inflammatory mediators involved in ulcerative colitis progression. [60] The intestinal microbiota is essential for maintaining immune balance and epithelial barrier integrity. In ulcerative colitis reduced microbial diversity and depletion of beneficial bacteria are commonly observed, accompanied by an increase in pro-inflammatory species. [52,53] This imbalance promotes exaggerated immune activation, enhanced cytokine release, and persistent mucosal inflammation. Restoration of microbial homeostasis is therefore considered a key therapeutic target in ulcerative colitis management. [54] Dietary fibers obtained from Allium cepa contain inulin-type fructans that act as prebiotics. These compounds resist digestion in the upper gut and are fermented in the colon, selectively stimulating beneficial bacteria such as Bifidobacterium and Lactobacillus species. [55,56] Improved growth of commensal bacteria supports mucosal immunity and may reduce inflammatory activity in ulcerative colitis. Fermentation of onion fiber results in the production of short-chain fatty acids (SCFAs), particularly butyrate. Butyrate serves as an energy source for colonocytes and contributes to epithelial repair and anti-inflammatory signaling. [57] Decreased SCFA production has been reported in ulcerative colitis patients, suggesting that enhancing SCFA levels may help attenuate intestinal inflammation. [58] Prebiotic supplementation can help rebalance gut microbial composition by promoting beneficial microbes and limiting opportunistic pathogens. This microbial correction improves tight junction function, reduces intestinal permeability, and mitigates inflammatory responses in experimental colitis models. [59,60] Bioactive constituents of onion, including flavonoids, exhibit antimicrobial and anti-inflammatory activities. These compounds may suppress pathogenic bacterial growth and downregulate inflammatory mediators involved in ulcerative colitis progression. [60] Such properties suggest a supportive role for onion-derived components in controlling mucosal inflammation.

FUTURE PERSPECTIVE

Future research should prioritize standardized extract development, mechanistic validation in established colitis models, and advanced formulation strategies to enhance bioavailability. Studies exploring gut microbiota modulation, safety profiling, and herb–drug interactions are essential. Well-designed human clinical trials are needed to establish therapeutic efficacy and define the role of *Allium cepa* as an adjunct or alternative treatment for UC.

CONCLUSION

The present review. highlights the therapeutic potential of Allium cepa in the management of ulcerative colitis, highlighting its anti-inflammatory, antioxidant, and immunomodulatory activities. Bioactive constituents, particularly quercetin, appear to play a pivotal role in regulating key inflammatory signaling pathways, mitigating oxidative stress, and modulating immune dysfunction associated with disease progression. Evidence from preclinical studies suggests that *Allium cepa* may attenuate

intestinal inflammation, restore epithelial barrier integrity, and promote mucosal healing. However, despite these promising findings, clinical translation remains constrained by challenges related to extract standardization, limited bioavailability of active compounds, and the scarcity of well-controlled human trials. Further investigations focusing on molecular mechanisms, long-term safety profiling, optimized formulations, and robust clinical validation are essential. Collectively, current evidence supports the potential of Allium cepa as a promising natural adjunct within the evolving therapeutic landscape of ulcerative colitis.

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