Beta-1,3/1,6-D-Glucan Extracted from Ganoderma lucidum as Adjunct Therapy in Ulcerative Colitis: A Case Series

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ABSTRACT

The management of ulcerative colitis is primarily focused on the prevention of complications, remission sustenance, and enhancement of overall quality of life. However, long-term use of various pharmacological therapies can be associated with several side effects, including myelosuppression, hepatitis, lupus-like syndrome, and an increased risk of malignancy. These limitations have led to the search for safer therapeutic options, including bioactive compounds such as Beta-1,3/1,6-D-Glucan with immunomodulatory properties. Ganoderma lucidum contains Beta-1,3/1,6-D-Glucan as a principal bioactive compound extracted from its mycelium. Despite the broad therapeutic properties, exploration into its role specifically for ulcerative colitis patients remains scarce. Therefore, this case series aimed to explore the potential role of Beta-1,3/1,6-D-Glucan derived from Mycelium extract of Ganoderma lucidum in managing ulcerative colitis.

Keywords: *Beta-1,3/1,6-D-Glucan, ganoderma lucidum, ulcerative colitis*

ABSTRAK

Tatalaksana kolitis ulseratif hingga saat ini hanya berfokus pada pencegahan komplikasi, pertahanan remisi, dan peningkatan kualitas hidup. Penggunaan berbagai terapi farmakologis jangka panjang berhubungan dengan banyak efek samping, meliputi myelosupresi, hepatitis, sindrom mirip-lupus, dan peningkatan risiko keganasan. Ganoderma lucidum mengandung Beta-1,3/1,6-D-Glucan sebagai senyawa aktif utama dari hasil ekstraksi miselium. Komponen bioaktif ini menunjukkan sifat imunomodulator yang signifikan. Namun, peranannya pada pasien kolitis ulseratif masih belum banyak diteliti. Serial kasus ini memperlihatkan peran potensial Beta-1,3/1,6-D-Glucan yang berasal dari ekstrak Miselium Ganoderma lucidum dalam memperbaiki kolitis ulseratif.

Kata kunci: *Beta-1,3/1,6-D-Glucan, ganoderma lucidum, kolitis ulseratif*

INTRODUCTION

Inflammatory Bowel Disease (IBD) is a challenging immune-mediated condition characterized by chronic gastrointestinal inflammation, primarily manifesting as ulcerative colitis (UC) and Crohn's disease.[1,2] Although historically concentrated in Europe and America with an incidence rate of 24.3 per 100,000 population, recent epidemiological trends have reported a prevalence of UC in Asia and other developing regions.[3] For example, Indonesia has a prevalence rate of 0.55 per 100,000 population, indicating a significant emergence of the disease in previously less affected areas.[4,5] This transformation correlates with factors such as westernization, lifestyle alterations, and urbanization.[6]

The increasing burden of IBD shows the need for effective strategies to control inflammation and maintain long-term disease remission. Current management primarily focuses on symptom alleviation, remission maintenance, and quality of life enhancement, often using anti-inflammatory drugs, immunomodulators, and biological agents. These pharmacological agents function by triggering a Th2-mediated response that can reduce Th1-mediated inflammation.[7] However, long-term use can be associated with substantial side effects. Immunomodulators can cause myelosuppression, hepatitis, and increased risk of malignancy, while Anti-TNF-α therapy is responsible for lupus-like syndrome and malignancy. This shows the need for the exploration of alternative therapies, such as Beta-1,3/1,6-D-Glucan derived from *Ganoderma lucidum*, with good efficacy and lower adverse effects .[8]

Ganoderma lucidum is a traditional Chinese medicinal mushroom belonging to the family of Ganodermataceae, which has been used for the prevention and treatment of various diseases. Among its bioactive compounds, Beta-1,3/1,6-D-Glucan derived from the mycelium extraction has gained significant attention because of its immunomodulatory properties. Beta-1,3/1,6-D-Glucan has shown biological activity in several disease contexts, including arthritis, cancer, and immune-related disorders.[9,10] Furthermore, studies in IBD patients have indicated a reduction in pro-inflammatory cytokines TNF-α, IFN-γ, and IL-17A after *Ganoderma lucidum* administration, suggesting its potential as a therapeutic agent.[8]

In contemporary clinical practice, *Ganoderma lucidum* mycelium polysaccharide extract containing Beta-1,3/1,6-D-glucan is used as a nutraceutical or adjunctive immune-modulating supplement. Although recent preclinical and early clinical data suggest potential benefits in IBD/UC, this extract has not been established as a standard or guideline-based therapy, which remains an investigational adjunct rather than a conventional option. Despite the results, there are still limited investigations on the impact of Beta-1,3/1,6-D-Glucan on UC. Therefore, this case series aims to describe clinical and endoscopic outcomes of UC patients receiving adjunctive commercially available Beta-1,3/1,6-D-Glucan.

CASE ILLUSTRATIONS

This case series describes the first five consecutive patients with mild-to-moderate ulcerative colitis (UC) at the institution who provided informed consent to receive adjunctive Beta-1,3/1,6-D-Glucan alongside standard therapy. The clinical and endoscopic courses of these patients are detailed as follows.

Patient 1

A 55-year-old male patient with a history of multiple sessile polyps was referred for assessment due to chronic diarrhea, hematochezia, and weight loss. Furthermore, the patient had grade 1 internal hemorrhoids. During a previous visit to another healthcare facility, mesalazine 500 mg was administered three times daily for one month. Colonoscopy results showed multiple erosions without active bleeding, edematous mucosa, and an absent vascular pattern in the ascending colon (Mayo endoscopic score 2), with baseline Mayo score of 5. The patient was prescribed mesalazine 500 mg three times daily as standard medication, alongside a regimen of *Ganoderma lucidum* mycelium polysaccharide extract containing Beta-1,3/1,6-D-Glucan, encapsulated in 650 mg capsules, administered three times daily for 90 days. During the subsequent follow-up appointment, partial improvement of symptoms was observed (Mayo score 3). The colonoscopy results indicated mild hyperemia of the ascending colon mucosa, reduced mucosal edema, and normal vascular patterns (Mayo endoscopic score 1), as presented in **Figure 1.**

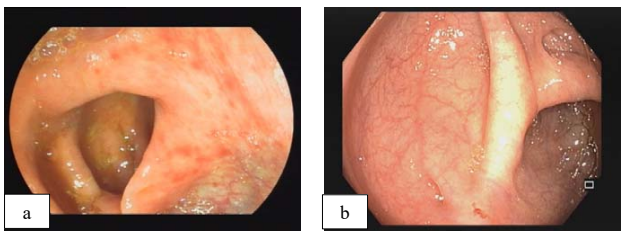

Figure 1. Multiple erosions and absent vascular pattern before therapy (a) and improvement in endoscopic findings after therapy (b)

Patient 2

A 63-year-old female patient presenting with a history of hematochezia and weight loss was referred for advanced therapy following a diagnosis of UC based on a prior colonoscopy conducted at another medical facility. During previous healthcare visits, the patient had been regularly prescribed mesalazine 500 mg three times daily for three months. Colonoscopy results showed multiple erosions without active bleeding, edematous mucosa, and several hyperemic ulcers in the descending colon (Mayo endoscopic score 2). Multiple polyps were also observed in the transverse colon (NICE 1), while baseline Mayo score was 4. The patient was directed to adhere to a standard therapeutic regimen involving the administration of mesalazine 500 mg three times daily. This was complemented by a regimen of *Ganoderma lucidum* mycelium polysaccharide extract containing Beta-1,3/1,6-D-Glucan, encapsulated in 650 mg capsules, to be ingested three times daily for 90 days. During the subsequent follow-up appointment, partial alleviation of symptoms was observed (Mayo score 2). Colonoscopy results showed mild hyperemic area of the descending colon mucosa, reduced edematous mucosa, and improvement in the healing status of multiple ulcers (Mayo endoscopic score 1), as shown in **Figure 2.**

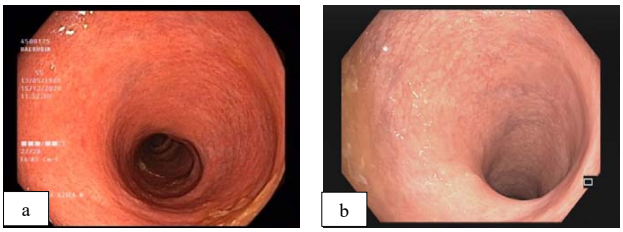

Figure 2. Multiple erosions and ulcers before therapy in descending colon (a) and improvement in endoscopic findings after therapy (b)

Patient 3

A 26-year-old male patient with a history of UC was referred for evaluation due to hematochezia and abdominal pain. During the visit, the patient reported experiencing chronic diarrhea and reduced appetite. The patient had been consistently taking mesalazine 500 mg three times daily during previous visits and continued the same regimen for one year at the current referral medical facility, although hematochezia persisted. Colonoscopy results showed multiple hyperemic ulcers without active bleeding, edematous mucosa, and an absent vascular pattern in the descending colon (Mayo endoscopic score 2), while baseline Mayo score was 5. This was followed by mesalazine 500 mg given three times daily as the standard therapeutic regimen, supplemented with *Ganoderma lucidum* mycelium polysaccharide extract containing Beta-1,3/1,6-D-Glucan in 650 mg capsules, administered three times daily for 90 days. During the subsequent follow-up appointment, partial improvement of symptoms was observed (Mayo score 3). The colonoscopy results indicated healing of multiple ulcers, reduced edematous mucosa, and improved vascular patterns in the descending colon (Mayo endoscopic score 1), as presented in **Figure 3.**

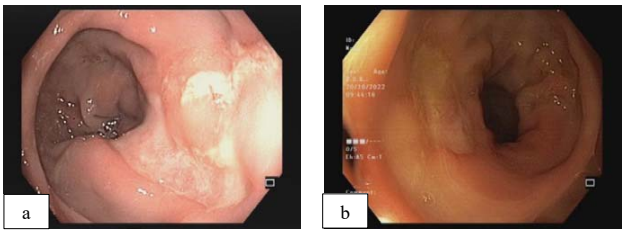

Figure 3. Multiple hyperemic ulcers with edematous mucosa before therapy (a) and improvement in endoscopic findings after therapy (b)

Patient 4

A 68-year-old male patient with a medical history was referred for further diagnostic procedures due to chronic constipation and hematochezia. The patient had consistently maintained a regimen of mesalazine 500 mg three times daily for one month during a previous visit to the healthcare facility. Colonoscopy results showed hyperemic ulcers without active bleeding, edematous mucosa, and a decreased vascular pattern throughout the colon (Mayo endoscopic score 1), while baseline Mayo score was 4. As part of the therapy plan, mesalazine 500 mg was prescribed three times daily. Additionally, a regimen of *Ganoderma lucidum* mycelium polysaccharide extract containing Beta-1,3/1,6-D-Glucan encapsulated in 650 mg capsules was administered three times daily for 90 days. After subsequent follow-up, partial amelioration of symptoms was observed (Mayo score 2), with colonoscopy results indicating ulcer healing, reduced mucosal edema, and improved vascular patterns throughout the colon (Mayo endoscopic score 0), as presented in **Figure 4.**

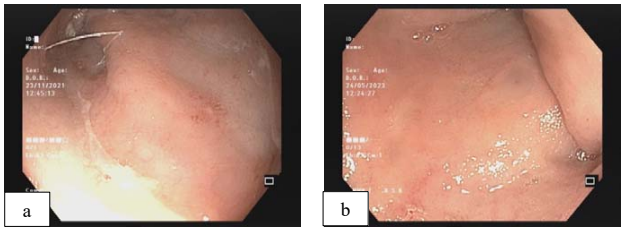

Figure 4. Multiple hyperemic ulcers with decreased vascular pattern before therapy (a) and improvement in endoscopic findings after therapy (b)

Patient 5

A 26-year-old male patient presenting with a history of UC was referred for evaluation due to hematochezia and abdominal pain, alongside multiple cholelithiasis and grade 1 internal hemorrhoids. Previously, the patient had consistently adhered to a regimen of mesalazine 500 mg three times daily for two months during visits to the previous healthcare facility. Colonoscopy results showed erythema and edematous mucosa with an absent vascular pattern in the descending colon (Mayo endoscopic score 1), while baseline Mayo score was 4. The therapy plan was to include mesalazine 500 mg three times daily. Furthermore, a regimen of *Ganoderma lucidum* mycelium polysaccharide extract containing Beta-1,3/1,6-D-Glucan encapsulated in 650 mg capsules was administered three times daily for 90 days. After subsequent follow-up, partial improvement of symptoms was observed (Mayo score 2). The colonoscopy results showed reduced mucosal erythema and edema, accompanied by improved vascular patterns in the descending colon (Mayo endoscopic score 0), as presented in **Figure 5.**

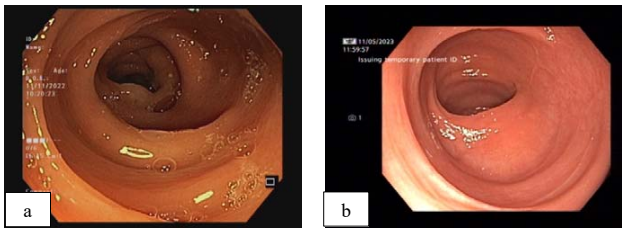

Figure 5. Erythema and edematous mucosa before therapy (a) and improvement in endoscopic findings after therapy (b)

In this case series, no adverse events were observed in the five UC patients who received *Ganoderma lucidum* during the observation period **(Table 1).**

DISCUSSION

Therapeutic targets in UC patients can be observed through improved symptoms and the enhancement of endoscopic results, specifically mucosal healing in colonoscopy.[1,2] Mucosal healing is an important therapeutic target because endoscopic improvement is associated with reduced risks of recurrence and complications.[11] Therefore, assessment of endoscopic activity and inflammatory severity in UC patients receiving colonoscopy is commonly conducted using the Mayo endoscopic score.[11,12] This scoring system ranges from Score 0 to 3, evaluating features such as erythema, vascular pattern, friability, erosion, bleeding, and ulceration within the colon.[13] In this case series, patients 1, 2, and 3 showed improvement from Mayo score of 2, indicated by erythema, absent vascular pattern, friability, and erosions, to 1 (erythema, decreased vascular pattern, mild friability). Improvement in endoscopic outcomes was observed in patients 4 and 5, transitioning from a Mayo score of 1 to 0, showing normal or inactive disease, which indicated mucosal healing.

The management of UC places significant emphasis on inhibiting the cascade of inflammatory processes, thereby influencing the reduction or disappearance of associated symptoms. Primarily, the therapeutic objective is to attain a state of remission in the disease

Table 1. Summary of clinical, endoscopic, and outcome characteristics of the five patients

Pt	Age/ Sex	Baseline Symptoms	Baseline Mayo Score	Baseline Endoscopy (Mayo Endoscopic score/ MES)	Follow-up	Follow-up Mayo Score	Follow-up Endoscopy (Mayo Endoscopic Score/MES)	Clinical Outcome	Adverse Events
1	55/M	Chronic diarrhea, weight loss, hematochezia.	5	Multiple erosions, edematous mucosa, absent vascular pattern - ascending colon (MES 2)	90 days	3	Mild hyperemia, reduced edema, normal vascular pattern (MES 1)	Partial improvement	None
2	63/F	Hematochezia, weight loss	4	Multiple erosions, edematous mucosa, multiple hyperemic ulcers - descending colon (MES 2); polyps in transverse colon (NICE 1)	90 days	2	Mild hyperemic area, reduced edema, improved ulcer healing (MES 1)	Partial improvement	None
3	26/M	Hematochezia, abdominal pain, chronic diarrhea, reduced appetite	5	Multiple hyperemic ulcers, edematous mucosa, absent vascular pattern - descending colon (MES 2)	90 days	3	Ulcer healing, reduced edema, improved vascular pattern (MES 1)	Partial improvement	None
4	68/M	Chronic constipation, hematochezia.	4	Hyperemic ulcers, edematous mucosa, decreased vascular pattern - throughout colon (MES 1)	90 days	2	Ulcer healing, reduced edema, improved vascular pattern (MES 0)	Partial amelioration (mucosal healing)	None
5	26/M	Hematochezia, abdominal pain.	4	Erythema, edematous mucosa, absent vascular pattern - descending colon (MES 1)	90 days	2	Reduced erythema/edema, improved vascular pattern (MES 0)	Partial improvement (mucosal healing)	None

and extend duration, as well as mitigate potential complications.[14,15] However, complications that arise in patients include perforation, fistula, cancerous changes, pseudopolyp formation, toxic megacolon, and stenosis.[16] The management of UC is based on degree of severity and location, including proctitis, left-sided colitis, and extensive colitis, in accordance with current guidelines.[17] For mild-to-moderate UC, initial therapy typically comprises topical mesalazine in conjunction with topical steroids, oral mesalazine, or systemic steroids. Second-line options include systemic steroids or biologics for induction therapy, while mesalazine and immunomodulator biologics are considered for maintenance therapy. The options used for mild-to-moderate disease overlap with the first-line methods used for moderate-to-severe UC, particularly when initial therapy fails to achieve adequate disease control.[18]

Among various therapies, 5-Aminosalicylic acid (5-ASA) plays an integral and first-line role in both inducing and maintaining remission in UC.[17,19] This compound exerts various anti-inflammatory effects, including the inhibition of enzymes such as cyclooxygenase, lipoxygenase, B-cells, and numerous other inflammatory cytokines.[20] A significant constraint of 5-ASA as a maintenance therapy is in the level of therapy adherence, because low compliance correlates with poorer long-term outcomes characterized by recurrent flares and neoplastic complications, which often lead to elevated costs for the healthcare system. Regarding oral mesalazine, the regimen requiring administration two to three times daily, the necessity for multiple pill intake, and concerns regarding potential side effects are the primary factors contributing to suboptimal adherence.[18] Additionally, 5-ASA paradoxically increases symptoms of colitis, resembling those observed in UC, including abdominal pain, diarrhea, and rectal bleeding.[21]

Corticosteroids are the recommended therapeutic methods or inducing remission in patients with moderate-to-severe active UC, as well as mild-to-moderate condition not responding to 5-ASA.[17] Although the precise mechanism of action remains unclear, corticosteroids suppress intestinal inflammation by inhibiting cytokine production through the inactivation of NFKß.[22] Despite their indisputable role in inducing remission and managing disease flares in UC, corticosteroids are not recommended for maintenance therapy. This is because long-term use is associated with adverse effects, which may include severe cardiovascular events and hip fractures.[23,24]

For patients with mild-to-moderate UC who are intolerant or unresponsive to 5-ASA, as well as steroid-dependent patients responding to immunomodulatory therapy, thiopurines may be considered for maintenance.[17] Despite the effectiveness as steroid-sparing agents and proven ability to maintain remission in UC, long-term use of thiopurines is limited by adverse events.[18] Male patients under 30 or over 50 years old with primary Epstein-Barr virus (EBV) infection have a clear risk of lymphoma. Therefore, EBV serological status should be assessed before initiating thiopurine therapy to support appropriate risk stratification[25]

Biological agents commonly used for UC therapy include infliximab, adalimumab, certolizumab, and fontalizumab[18] to neutralize the cytokine tumor necrosis factor (TNF). However, the TNF cascade plays an essential role in promoting wound healing in epithelial tissue. Several experimental studies on mouse models have shown that TNF contributes to the regulation and resolution of intestinal inflammation. Consequently, blocking TNF activity may produce variable therapeutic responses, and some patients may experience therapy failure during anti-TNF therapy.[26]

In this context, adjunctive therapies such as *Ganoderma lucidum* have gained significant attention because of their broad immunomodulatory properties. These include augmentation of antigen-presenting cell (APC) function, enhancement of the mononuclear phagocyte system, bolstering of humoral immunity, and fortification of cellular immunity.[27] Multiple studies have substantiated the immunomodulatory properties of *Ganoderma lucidum* polysaccharides, both in vivo and in vitro. Among bioactive compounds, Beta-1,3/1,6-D-Glucan derived from the extraction of *Ganoderma lucidum* mycelium has a significant effect on immune-cell activity. This compound promotes activation and proliferation of B cells, thereby inducing the release of T cells from TNF-α and interferon-γ (IFN-γ), enhancing the activation and maturation of immature dendritic cells. Furthermore, Beta-1,3/1,6-D-Glucan promotes the differentiation and maturation of macrophages. These effects are mediated through various cascades, as presented in **Figure 6.**[28]

A study conducted by Jin et al.[9] investigated the impact of *Ganoderma lucidum* polysaccharides on the integrity of the intestinal mucosal barrier, including mechanical, immunological, and biological aspects in mice. The results showed that *Ganoderma lucidum* polysaccharide extract significantly modulated the expression of occludin, nuclear factor-κB p65 (NF-κB

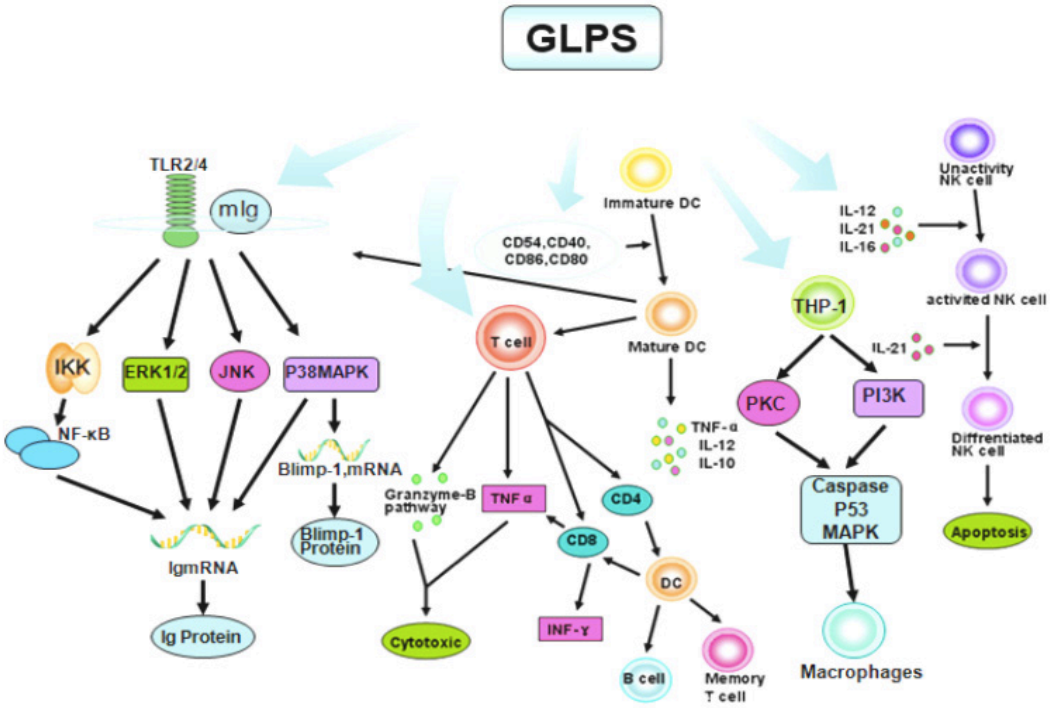

Figure 6. *Ganoderma lucidum* polysaccharides and their immunomodulatory effects on immune cells[28]

p65), and secretory immunoglobulin A (SIgA) in the ileum. Additionally, the extract elevated the levels of interferon-γ (IFN-γ), interleukin-2 (IL-2), and IL-4, while reducing serum diamine oxidase (DAO) levels. This suggests that *Ganoderma lucidum* polysaccharide extract possesses the potential as an agent for regulating intestinal barrier function[9] and suppressing the Th17 cell response in mice induced with artificial colitis. Additionally, it significantly inhibits the secretion of TNF-α, IL-1β, IL-6, IL-17A, IL-4, B cells, NK cells, and NKT cells in the lamina propria lymphocytes.

Another study reported that *Ganoderma lucidum* polysaccharide extract significantly improved the survival rate and mitigated bowel length shortening, weight loss, histopathological scores, and Disease Activity Index (DAI) in mice with induced colitis.[29] In addition to the immunomodulatory properties, *Ganoderma lucidum* significantly reduced animal DAI scores by promoting the production of short-chain fatty acids (SCFAs), thereby increasing SCFA-producing bacteria such as *Ruminococcus_1* and diminishing pathogens such as *Escherichia-Shigella* in both the small intestine and cecum of mice.[30,31] Furthermore, *Ganoderma lucidum* regulated 11 genes, comprising six upregulated (Ccl5, Cd3e, Cd8a, Il21r, Lck, and Trbv) and five downregulated (Ccl3, Gro, Il11, Mhc2, and Ptgs) genes enriched in six inflammation-related Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways. This regulation caused an enhancement of immunity and reduction of inflammatory responses.[31]

In this case series, all five patients received *Ganoderma lucidum* mycelium polysaccharide extract in 650 mg capsules containing Beta-1,3/1,6-D-Glucan, administered three times daily for 90 days. After the therapy period, improvements were observed across endoscopic evaluation compared to baseline, as indicated by a decrease in Mayo endoscopic scores. *Ganoderma lucidum* has been reported to cause mild adverse effects, including dizziness, dry mouth, nausea, and gastrointestinal discomfort, posing potential risks in certain populations or interacting with concomitant medications. However, no adverse events were observed in the patients included in this case series.

Despite the significant contribution of the results, this case series has several limitations. First, the outcomes were derived from a small case series evaluating the use of *Ganoderma lucidum* in UC patients, which limited the generalizability of the results. Disease activity was also assessed solely using the Mayo endoscopic score, without incorporation of objective inflammatory biomarkers such as C-reactive protein (CRP) or fecal calprotectin. The observed endoscopic improvements cannot be definitively attributed to the intervention alone. All patients in this case series continued to receive mesalazine throughout the period of *Ganoderma lucidum* administration. Consequently, the observed endoscopic improvement reflects the effect of background maintenance therapy,

a delayed response to previous optimization of standard therapy, or the natural fluctuating course of UC, rather than a specific effect of the intervention. The lack of a control group receiving mesalazine alone prevents determination of whether *Ganoderma lucidum* provides any incremental benefit over standard therapy. Consequently, larger and well-designed controlled studies are recommended to confirm efficacy and establish causality. In resource-limited settings where biologic therapies are often inaccessible, *Ganoderma lucidum* may represent a low-cost adjunctive option worth exploring. However, this potential role should only be established through well-designed controlled trials, not extrapolated from the current preliminary results.

CONCLUSION

In conclusion, this preliminary result suggests the potential role for *Ganoderma lucidum* as an adjunct to standard therapy in UC. However, due to the small sample size, absence of a control group, and concurrent use of mesalazine, controlled studies are recommended to establish causality before any therapeutic recommendation.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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AUTHOR CONTRIBUTIONS

S.A.N and M.S. conceived the presented idea. S.A.N and M.S supervised the results of this case series. All authors discussed the results and contributed to the final manuscript.

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Ganoderma lucidum mycelium polysaccharide extract containing Beta-1,3/1,6-D-Glucan (PSP□) was used as the preferred therapy in this case series.

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