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Original article

Efficacy of Combination of Silver-Nano Particles with Curcumin in Treatment of Inflammatory Bowel Disease (Ulcerative colitis) Through Rectal Route

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Abstract:

Background: Inflammatory bowel diseases (IBDs) are groups of chronic inflammatory disorders that had continuous recurrent swelling and irritation of the inner lining of the intestines. **Nano Particles** increase solubility and bioavailability of drugs. Curcumin is known for its wound-healing, antimicrobial, antioxidant, and anti-inflammatory properties. **Aim of the work**: our study aimed to evaluate efficacy of combination of silver nanoparticles with curcumin in the management of inflammatory bowel disease" through rectal route". **Patients and Methods**: the study was done from October 2023 to June 2024, included 90 participates with ulcerative colitis. Treatment Group: forty-five patients received a combination of silver-nanoparticles and curcumin via enema, and injection into the rectal ulcer and mucosa, along with oral mesalazine. Control Group: forty-five patients received a placebo saline enema with oral mesalazine. Disease severity was evaluated by clinical activity and endoscopic indices, at the start, every 2 months, and at the end of the 6-month trial. **Results:** The curcumin-treated group showed improvements in bowel frequency, defecation urgency, blood in stool, and overall well-being.". Extracolonic features of inflammatory bowel disease has been controlled. There was improvement in both clinical response and clinical remission when they were compared to patients treated with ordinary drugs. Evaluation by colonoscope for vascular pattern and erosions/ulcers showed wonderful healing rate in curcumin group and showed stoppage of bleeding due to healing of mucosa. **Conclusion:** Using Curcumin combined with Silver-Nano particles through rectal route can be effective as a treatment option of (IBDs) and improve patients' quality of life.

Key words: Inflammatory Bowel Disease; Silver-Nano particles; Curcumin; rectal route.

Introduction

Inflammatory Bowel Diseases (IBDs) are persistent idiopathic, disorders affecting the intestinal tract in different areas characterized by recurrent and relapsing episodes. They can reduce quality of life and affect millions of people worldwide. Ulcerative colitis (UC) and Crohn's disease (CD) are the most main forms of IBDs. IBDs are noticeable pathologically by intestinal and extra intestinal inflammation and damage both intestinal and epithelial tissues [(1-3)] . IBDs can result in numerous gastrointestinal symptoms, like diarrhea, abdominal distension, bloating, abdominal pain or cramping, bleeding, and weight loss with micronutrient mal absorption. They show extra-intestinal manifestations affecting various organs such as the joints (arthritis or joint pain), eyes (uveitis or episcleritis), skin (erythema nodosum), bones (osteoporosis and bone fractures), liver (primary sclerosing cholangitis) and kidneys [(4)]. IBDs reasons remain unidentified, but there are predisposing factors which influence the development and progression of IBD symptoms include genetic susceptibility, smoking, gut dysbiosis, nutritional habits, psychological stress, and environmental pollution [(5 and 6)]. Gut dysbiosis, gut microbiota imbalance, is clearly accompanied by intestinal inflammatory disorders. This imbalance can intensify inflammation through many mechanisms, such as T-helper cells imbalances, alterations in balance of immune system function, and changes in fermentation products [(7, 8, 9, 10 and 11)]. Psychological stress can aggravate IBDs symptoms by reducing intestinal pain thresholds. This increases the sensitivity of pain and impairs mucosal barrier function [(12)]. The crucial role in maintaining the integrity and function of the intestinal mucosal barrier is the protein complexes (tight junction) of the intestinal mucosa which function as a physical layer against Leaky Gut. Increased Intestinal Permeability allows more luminal antigens to penetrate the intestinal lining and contribute to inflammation [(13)]. Traditional treatment for (IBDs) involves drugs and therapies aimed to make a control of inflammatory flareups and elongate periods of remission. Anti-inflammatory drugs, especially amino salicylates, important drugs as corticosteroids, biological agents, and immunosuppressants are the commonly used [(14 and 15)]. Endoscopy is important for observing the mucosal lining of the intestines, identifying inflammation and ulceration diagnosing of (IBDs). It can display inflammation of mucosa, granularity, edema, altered vascular patterns, pseudo polyp formation, erythema, and superficial ulcers. Severe changes may occur, including deep, serpiginous, and linear ulcerations and cobble stone formation. Histopathological studies are done, to confirm the diagnosis which usually show crypt abnormalities, inflammatory cell infiltration, cellular and glandular metaplasia [(16, 17 and 18)]. Curcumin is a famous yellow powder. It is a natural phenol known as turmeric powder that belongs to the ginger family extracted from the Curcuma longa Linn plant. Turmeric also contains essential oils and many bioactive compounds. [(19)]. Curcumin has immunomodulatory, antioxidant, anticancer, anti-inflammatory, and antimicrobial properties. Also, curcumin has antiplatelet, hypoglycemic,

antibacterial, and antifungal effects, cholesterol-lowering, cardioprotective, as evidenced by both preclinical and clinical studies [20 and 21]. Curcumin inhibits the activity of IKK, preventing the phosphorylation and subsequent degradation of IκB. This keeps NF-κB in its inactive form in the cytoplasm, thus reducing the expression of pro-inflammatory genes and mediating its anti-inflammatory effects [21].

Curcumin exerts its anti-inflammatory effects through multiple mechanisms, Curcumin activates PPAR-γ, which plays a crucial role in regulating glucose and lipid metabolism and has anti-inflammatory effects. Curcumin inhibits the activation of STATs, particularly STAT3, which participates in promoting inflammation and cell proliferation. Curcumin can inhibit AP-1 activation, leading to decreased expression of pro-inflammatory genes. It can decrease the presence of cyclooxygenase-2 (COX-2) and 5-lipoxygenase (5-LOX), all of which has key role in inflammation [٢٢]. When curcumin taken orally, it shows poor bioavailability because it has poor absorption, rapid metabolism, and rapid systemic elimination, so therapeutic efficacy is limited. To increase the bioavailability of curcumin in humans many particles are used as nanoparticles, liposomes, phospholipid complexes, and structural analogues ([23] . Nanoparticles (NPs) have a lot of advantages, like targeted tissue delivery lead to reduced side effects, decrease toxicity, improve pharmacological activity, potentiate stability, resist chemical and physical degradation. These benefits make NPs a promising method in future for drug delivery in IBD treatment. NPs not only improve the efficacy and power of current medications "but also assist in the advancement of novel treatment techniques" [24].

Subjects and methods

This double-blind, prospective, randomized controlled study was done from October 2023 to June 2024, over 8-12 weeks at the Internal Medicine Department of Benha University Hospital, to assess efficacy of curcumin combined with silver nanoparticles in the management of inflammatory bowel disease" through rectal route" with a focus on improvements in clinical outcomes. Informational consents were obtained from all participants. The study included two groups: **Treatment Group (45 patients**): Received a combination of silver nanoparticles and curcumin by enemas and injection into the ulcer bed and rectal mucosa, along with oral mesalazine. **Control Group (45 patients):** Received a placebo saline enema and oral mesalazine. The extent and progression of symptoms was evaluated after the 12th week of the trial, which lasted for a total of 6 months. The criteria for participants in this study with ulcerative colitis (UC) were as follows: Age Range: 20–65 years, Diagnosis: (UC) was confirmed through a combination of clinical records, colonoscopy findings, and pathological analysis, ensuring an accurate diagnosis. Disease Activity: frequent flare-ups and inflammation, to mild UC, where symptoms were less severe and more manageable.

This structured approach ensured a focused assessment of the intervention's impact on UC severity within a defined timeframe and population.

Ethical approval: This study was approved by the Research Ethical Committee, Faculty of Medicine, Benha University {No. RC 1-10-2023}.

Statistical analysis: The collected data were statistically presented and analyzed using the Statistical Package for Social Science (SPSS) version 20 (IBM. Crop. Armonk). Categorical data were expressed as number and percentage, continuous data were expressed as mean and standard deviation. Student t test was used for comparing continuous variables in 2 independent groups, Chi squared test was used to assess differences and associations between categorical variables. The accepted level of significance in this work was 0.05.

Results

The studied groups showed different variations across several key characteristics, including:

Gender, Age, Duration of UC Disease before the start of treatment (in years), Recurrences during the past 6 months, Clinical Course, Clinical Activity Index (CAI), Endoscopic Index (EI). **(Table 1)**

Extracolonic features of inflammatory bowel disease (IBD) include Musculoskeletal: Include arthritis. Ocular: Inflammatory eye manifestations including uveitis and episcleritis.

Dermatological: Skin manifestations especially erythema nodosum (tender red nodules) and pyoderma gangrenosum (painful ulcers with purulent discharge) Oral: Oral lesions include aphthous stomatitis. Manifestations of gastrointestinal tract and extracolonic manifestations which affect various organs compromise overall patient health and quality of life.**(Table 2)**

Patients were assessed using the Clinical Activity Index (CAI) as defined by Rachmilewitz, The CAI comprises seven items: Stool Frequency varies from (0–3 points)

Blood in Stool ranges between (0–4 points)

General Well-being differ according to patient`s general conditions (0–3 points)

Abdominal Discomfort gives score from (0–3 points), Fever measured by (0–3 points)

Extra-intestinal Manifestations according to how many systems affected (0–9 points)

Laboratory results (erythrocyte sedimentation rate and hemoglobin) vary from (0–4 points)

The total CAI score ranges from 0 to 29. **(Table 2)**

Clinical Remission: demonstrates few or no symptoms, suggesting effective management of the condition. as a CAI score of ≤4.

Clinical Response: if there is a decrease of ≥4 points in the CAI score relative to baseline.

Relapse: if there is an increase in the CAI score by >4 points after gaining clinical remission.

All cases were assessed by Ulcerative Colitis Endoscopic Index of Severity (UCEIS). which is formed of three components, with each component has contributing to the total score through a simple sum:

a) Vascular Pattern distribution of blood vessels (scored 0–2)

b) Bleeding loss of blood) (scored 0–3)
c) Erosions and Ulcers areas of tissue damage in the mucosal lining (scored 0–3)

The evaluation of vascular patterns and erosions/ulcers was assessed by colonoscopic images, while bleeding was assessed according to the reports, which depends on the description of colonoscopy performers about the bleeding during the procedure. **(Table 3)**

The UCEIS total score ranges from 0 to 8 and is classified into four grades:

a) Remission:0–1
b) Mild: 2–4
b) Moderate:5–6
d) Severe: 7–8 **(Table 4).**

There are nodules in the colon and rectum **(fig 1 a,b,c,d)**

Disappearance of nodules in both colon and rectum after treatment with curcumin and silver nanoparticles **(fig 2a, b, c, d)**

Table 1: Socio-demographic features of participants:

Variables	Curcumin treated group (n= 45)	Non-Curcumin treated group (n= 45)	P Value
Age (years)	45.1 ± 13.2	46.6 ± 12.4	0.579
Gender (M/F)n	20/25	16/29	0.11
BMI (kg/m2)	31.9 ± 3.9	29.1 ± 5.7	0.7
Drug, n(%)	45(100%)	44(97.78%)	0.314
Salicylates (5 amino salicylic acid) + immunomodulators + corticosteroids	0(0%)	1(2.22%)	
Disease duration before start of treatment (years)	9.1 ± 4.9	8.4 ± 5.1	0.509
Severity and extent of the disease			0.697
Proctitis	15(33.3%)	18(40.0%)	
Left colon	23(51.1%)	19(42.2%)	
Pancolitis	7(15.5%)	8(17.7%)	

Table 2: Simple Clinical Colitis Activity Index (SCCAI).

Variables	Curcumin treated group (n= 45)	Non Curcumin treated group (n= 45)	P Value
Bowel frequency (day)			.002**
0-3 time/day (0)	34 (75.56%)	16 (35.56%)	
4-6 time/day (1)	9 (20%)	24 (53.33%)	
7-9 time/day (2)	1 (2.2%)	3 (6.67%)	
>9 time/day (3)	1 (2.2%)	2 (4.44%)	
Bowel frequency (night)			.0001**
0 no frequency (0)	37 (82.22%)	18 (40%)	
1-3 time/ night (1)	8 (17.78%)	24 (53.33%)	
4-6 time/ night (2)	0	3 (6.67%)	
Urgency of defecation			0.011*
No urgency of defecation (0)	39 (86.67%)	25 (55.56%)	
Hurry up to bathroom (1)			
Immediately (2)	4 (8.89%)	12 (26.67%)	
Incontinence (3)	1(2.2%)	6 (13.33%)	
	1(2.2%)	2(4.44%)	
Blood in stool			.006**
No blood in stool (0)	35 (77.78%)	19 (42.22%)	
Trace amount (1)	7 (15.56)	21 (46.67%)	
Occasionally frank blood (2)	2(4.44%)	3 (6.67%)	
Usually frank blood (3)	1(2.22%)	2(4.44%)	
General well being			<.0001**
Very well feeling healthy. (0)	37 (82.22%)	14 (31.11%)	
Slightly below normal Minor discomfort (1)	7 (15.56%)	19 (42.22%)	
	1(2.22%)	7 (15.56%)	
Poor Significant discomfort (2)	0	3(6.67%)	
Very poor Severe discomfort (3)	0	2(4.44%)	
Terrible Extremely unwell (4)			
Extracolonic features			0.554
No features (0)	40(88.89%)	34 (75.56%)	
1 Extracolonic feature (1)	3(6.67%)	4 (8.89%)	
2 Extracolonic features (2)	1(2.22%)	3(6.67%)	
3 Extracolonic features (3)	1(2.22%)	2 (4.44%)	
4 Extracolonic features (4)	0	1(2.22%)	
5 Extracolonic features (5)	0	1(2.22%)	

Table 3: Explains (Ulcerative Colitis Endoscopic Index of Severity)

Description	A Likert scale typically has anchor points	Explanation of each item
distribution of blood vessels (Vascular pattern)	Normal, no abnormality (0)	A typical vascular pattern reveals clear capillary branching. while blurred or patchy margins indicate potential irregularities.
	Patchy damage and obliteration (1)	Scattered areas of vascular pattern loss indicate patchy obliteration.
	completely destroyed or removed (Obliterated). (2)	Total loss (destroyed or removed) of the vascular pattern indicates complete obliteration.
Bleeding(loss of blood)	No Bleeding (0)	Absence of visible blood indicates complete hemostasis or a lack of bleeding.
	Bleeding confined to Mucosa (1)	superficial mucosal hemorrhages, often seen during procedures like endoscopy. These small spots, dots, or streaks of coagulated blood can indicate minor bleeding, possibly from irritation or trauma to the mucosal surface. They are typically not serious and can be easily removed with rinsing.
	mild Luminal Bleeding (2)	free liquid blood in the lumen indicates significant bleeding within an organ, but the exact volume cannot be determined. This finding can suggest a more serious condition, potentially requiring further investigation.
	Massive significant blood loss in the lumen (3)	significant intraluminal bleeding, likely from a severe source such as a lesion, ulcer, or vascular abnormality. The presence of large amounts of frank blood and oozing from the mucosa indicates active bleeding from hemorrhagic tissue even after washing .
areas of tissue damage in the mucosal lining (Erosions and ulcers)	No tissue breaks (0)	a healthy mucosal surface, indicates the absence of obvious inflammation or damage or cracks, The mucosa appears normal, with no visible erosions, or ulcers present.
	superficial lesions on the mucosal surface (Erosions)(1)	Tiny defects in the mucosa that appear white or yellow with flat edges are often indicative of erosions or small ulcers. (≤5 mm)
	a localized lesion on the mucosal surface deeper than an erosion (Superficial ulcer) (2)	These ulcers extend deeper than erosions but remain relatively superficial. (>5 mm), The fibrin cover indicates a healing process or ongoing inflammation, often with surrounding erythema. .
	Deep ulcer (3)	ulcers penetrate deeper into the tissue compared to superficial ulcers, affecting the submucosal layers with raised edges which indicate granulation tissue or reactive changes around the ulcer.

N.B The Ulcerative Colitis Endoscopic Index of Severity (UCEIS): Travis et al (2011).

Table 4: Distribution of the participants according to Vascular pattern, Bleeding, Erosions and ulcers:

Variables	Curcumin treated group (n= 45)	Non-Curcumin treated group (n= 45)	P Value
Vascular pattern			0.086
	(0)4(8.89%)	(0) 6(13.33%)	
	(1)39(86.67%)	(1) 31(68.89%)	
	(2)2(4.44%)	(2) 8(17.78%)	
Bleeding			<.0001**
	(0) 38(84.44%)	(0) 7(15.56%)	
	(1) 6(13.33%)	(1) 23(51.11%)	
	(2) 1(2.22%)	(2) 13(28.89%)	
	0	(3) 2(4.44%)	
Erosions and ulcers			<.0001**
	(0) 35(77.78%)	(0) 9(20%)	
	(1) 6(13.33%)	(1) 26(57.78%)	
	(2) 4(8.89%)	(2) 6(13.33%)	
	0	(3) 4(8.89%)	

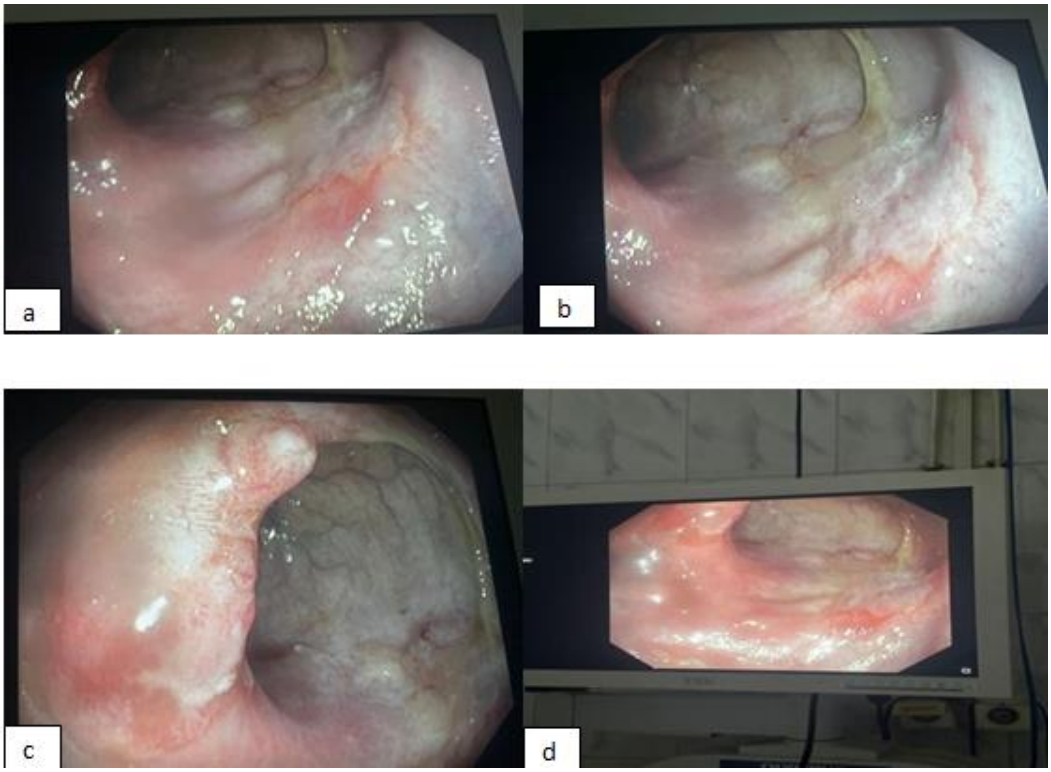

Figure 1: Before treatment with curcumin.combined with silver-nanoparticles

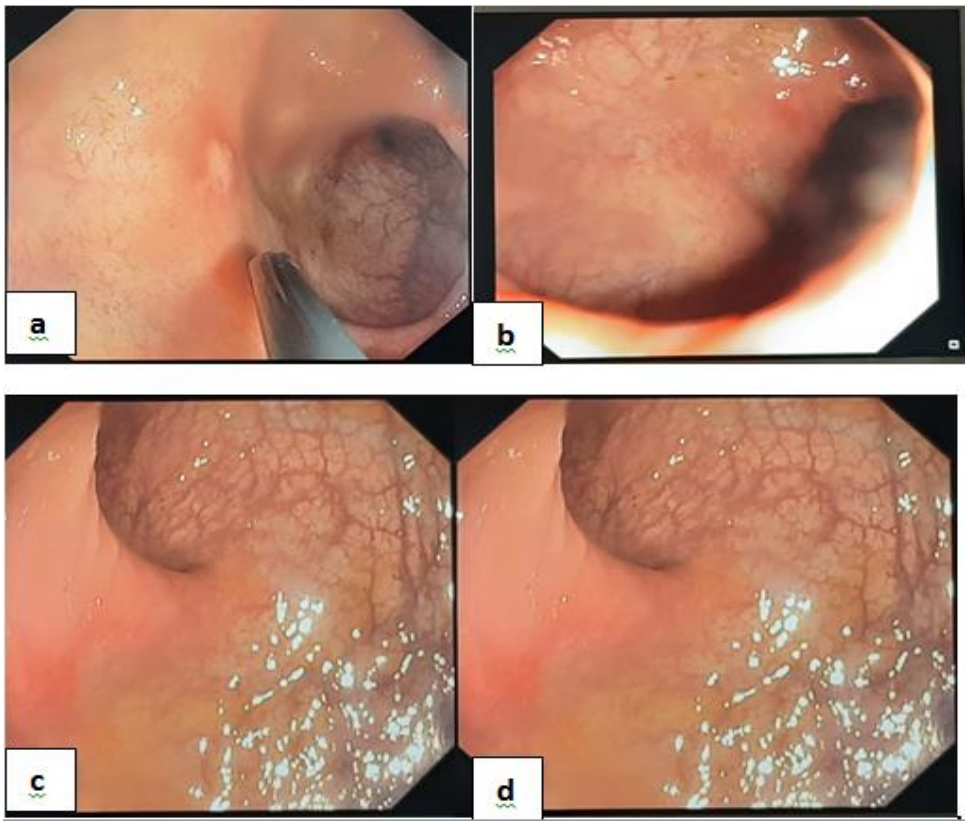

Figure 2: After treatment with curcumin combined with silver-nanoparticles

Discussion

Demographic data between Curcumin group and non-Curcumin group showed no difference in relation to age, sex, BMI, drugs, extent of the disease and duration of treatment before start of the trial.

The BMI improved in curcumin group and the weight slightly increased due to decrease in diarrhea, edema and inflammation of tissues.

The number of bowel frequencies per day improved more in the curcumin group compared to the non-curcumin group. Specifically: The p-value of 0.002 indicated a statistically significant difference, suggesting that curcumin had a special effect on reducing bowel frequency per daytime compared to the non-curcumin group. So, curcumin has enhanced the effectiveness of treatment in decreasing daily bowel frequency.

The number of bowel frequencies per night improved more in curcumin group in comparison to non-curcumin group. Specifically:

With a p-value of 0.0001, the difference was highly significant, indicating that curcumin reduced nighttime bowel frequency compared to the non-curcumin group.

The urgency of defecation improved more in curcumin group compared to the non-curcumin group. Specifically:

With a p-value of 0.011, the difference was statistically significant, indicating that

curcumin had a notable effect on reducing the urgency of defecation.

The presence of blood in stools has improved more in the curcumin group compared to the non-curcumin group. Specifically:

With a p-value of 0.006, the difference was statistically significant, indicating that curcumin reduced the presence of blood in stool compared to the non-curcumin group.

General well-being improved significantly in curcumin groups compared to non-curcumin group. Specifically:

With a p-value of less than 0.0001, the difference was highly significant, indicating that curcumin improved general well-being compared to the non-curcumin treatment.

Extracolonic features improve more in curcumin group compared to the non-curcumin group. Specifically:

Overall, the curcumin group showed a higher percentage of patients with no extracolonic features and fewer with multiple features compared to the non-curcumin group.

Clinical Remission: If all symptoms are significantly controlled and the Clinical Activity Index (CAI) score of ≤4 that occurs in the curcumin group.

Clinical Response: means improvement following a treatment or intervention and occurs if there is a decrease of ≥4 points in the CAI in relation to the baseline score.

The definitions of clinical remission differ from one to another: (absence of active inflammation and improvement of symptoms means Remission of the disease, and cessation ulcerative colitis when Simple Clinical Colitis Activity Index (SCCAI) score ≤2 points, This threshold provides a sensitivity of 0.79 and a specificity of 0.82 for accurately identifying patients in remission [25,26].

In the study by, clinical remission was assessed when SCCAI scored 2 points. The results showed that 83.9% of patients treated with curcumin achieved clinical remission, in contrast to only 43.8% of patients treated with placebo [27].

The Clinical Improvement Definition according to Clinical improvement was defined as a reduction of ≥3 points in the SCCAI score. In this study, 93.5% of patients treated by curcumin and 59.4% of patients treated by placebo achieved this level of improvement [27].

According to the assessment of Ulcerative Colitis Endoscopic Index of Severity, vascular pattern distribution shows the following:

Pattern (0):

Curcumin Group: 8.89% and Non-Curcumin Group: 13.33%

Pattern (1):

Curcumin Group: 86.67% and Non-Curcumin Group: 68.89%

Pattern (2):

Curcumin Group: 4.44% and Non-Curcumin Group: 17.78%

With a p-value of 0.086, there is a slight improvement in the vascular pattern distribution in the group which is treated by curcumin in comparison to the group which did not receive curcumin, particularly with a higher percentage of

Pattern (1) and lower percentages of Patterns (0) and (2).

Bleeding patterns differ significantly between the curcumin and non-curcumin groups,

With a p-value appears to be less than 0.0001, the difference shows highly significant. This indicates that curcumin is associated with a substantial reduction in bleeding patterns, suggesting that it aids in decreasing blood loss, improving blood pictures, and potentially reducing anemia in patients of ulcerative colitis.

In this trial, treatment with curcumin showed greater improvement in the healing of erosions and ulcers compared to those who did not receive curcumin (Fig1& 2).

With a p-value of less than 0.0001, the difference was highly significant, indicating that curcumin significantly aids wound healing, reduces inflammation and ulcer formation, promotes mucosal healing and coverage, and consequently decreases bleeding while improving disease symptoms.

In the curcumin group, most patients experienced significant symptom improvement, with many achieving remissions and only few showed mild symptoms. In contrast, the non-curcumin group included a range of outcomes, with some patients in remission and others experiencing exacerbations, including both mild and moderate symptoms.

Holt's study (2005) began with 5 patients receiving 5-ASA before the study began. Participants in the treatment group received 550 mg of curcumin two times per day for the first month, then increased to three times daily for the second month. Curcumin might have potential as a complementary therapy due to its anti-inflammatory properties, enhancing the healing process when combined with conventional treatments like 5-ASA. All five patients improved, with two discontinuing 5-ASA and two reducing their dosage. Additionally, five patients with Crohn's disease took curcumin at 360 mg three times per day for one month, then increase to 360 mg four times per day for the next month. This regimen showed a 55% decrease in the activity index of the disease. [٢٨]

Banerjee & co-workers (2021) investigated the efficacy of curcumin paired with mesalamine as a treatment for mild and moderate ulcerative colitis. This combination leads to greater success in achieving clinical and endoscopic remission compared to placebo or mesalamine alone. [٢٩]

Grammatikopoulou & colleagues (2018) reviewed randomized clinical trials evaluating curcumin as an adjunctive and added therapy for ulcerative colitis. Their work approved that curcumin has a positive effect on remission rates [٣٠].

Lang and others (2015) divided patients into curcumin group and a control group, with both groups receiving oral 5-ASA. The treatment group took curcumin capsules (3 g/day), while the other group received a placebo at the same dosage. After four weeks, more than half (53.8%) of the patients receiving curcumin showed beneficial results and became relieved, in contrast, none of the patients in the control group experienced any improvement in their symptoms." [٣١]

Masoodi and researchers (2018) conducted a study involving participants

with mild to moderate UC, who were divided and assigned to either a treatment group or a control group. (80 mg of curcumin three times daily) with mesalazine (3 g/day) are given to treatment group, "Conversely, the control group was administered the same dosage of placebo in conjunction with mesalazine. Disease severity was measured at the conclusion of the fourth week. The treatment group exhibited a significantly lower average score on the Simple Clinical Colitis Activity Index (SCCAI) compared to the control group (1.71 ± 1.84 vs. 2.68 ± 2.09, p = 0.05)." [٣٢]

Singla & colleagues (2014) run out a study involving patients with mild cases to severe cases of UC that affect the colon specially the distal part, all participants received mesalazine for a minimum of 8 weeks before the study began."[٣٣]

The patients were randomized and classified into 2 groups: the treatment group, which received a curcumin enema in addition to oral mesalazine, and the control group, which received a placebo enema along with oral mesalazine.

Results indicated that the treatment group exhibited greater rates of remission and clinical response, with remission rates of 43.4% versus 22.7% and response rates of 56.5% compared to 36.4%. "The results showed that the treatment group noted improved remission and clinical response rates, with remission to the level of 43.4% compared to 22.7% and improvement of response to 56.5% compared to 36.4% (34). (Fig1 and 2)

Hanai et al. (2006) found that the intervention group, (treatment group) experienced less relapses compared to the control group. Additionally, Other studies found that the intervention group experienced a higher rate of remission. [٣٤].

In this study, patients received weekly rectal enemas for 8-12 weeks. Forty-five patients were treated with a combination of silver-nanoparticles and curcumin enemas, along with injections of silver-nanoparticles into the rectal mucosa, while also taking mesalazine orally.

These findings agree with Singla et al. (2014) who stated that absorption of curcumin might be more effective when administered via enema rather than orally. This is due to its direct delivery to the area of action in inflammatory bowel disease [٣٣].

Six randomized controlled trials have compared the use of curcumin as an adjunctive and added therapy with 5-ASA in patients with UC. "All evaluations showed enhancement in clinical response and a reduction in symptoms.". This disagrees with the study by Kedia et al. (2017) who commented no significant difference in clinical or endoscopic remission rates between the curcumin and placebo groups (٣٥).

Curcumin is classified by the Food and Drug Administration as “safe” with no toxic effects. An acceptable daily intake of curcumin ranging from 0 to 3 mg/kg/day as registered and recommended by both the FAO/WHO Joint Expert Committee on Food Additives also with the European Food Safety Authority (٣٦, ٣٧).

The potency of curcumin micellar formulation is 185 times greater than that of the curcumin alone. (٣٨)

Rectal therapies of UC is promising as they escape the hepatic metabolism also due to high rectal vasculature and

relatively low enzymatic activity, so it enhances the high concentration and therapeutic efficacy of Curcumin.

N.B Green synthesis of silver nanoparticles (Ag NPs) was achieved using an aqueous extract of curcumin rhizome and thyme leaves. A total of 0.2 g of plant material was stirred in 100 mL of DI water at 80°C for 40 minutes. The extract was filtered (Whatman paper, then 0.22 µm syringe filter) and stored at 4°C in a dark place. To synthesize Ag NPs, 1 mL of the extract was added to 20 mL of 2 mM AgNO3 solution. The reaction mixture changed from light yellow to dark brown, confirming the formation of Ag NPs. The UV–visible spectra related to the synthesis of Ag NPs is in the range of 400–460 nm related to the surface plasmon resonance (SPR) of the formed Ag NPs (39)

Conclusion

Curcumin can be of value in therapy for ulcerative colitis (UC). Several systematic reviews highlight its anti-inflammatory effects and its role to stop the progression of UC. Clinical trials and meta-analysis propose that curcumin can improve disease activity and raise remission rates

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