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Original Research Article

Effect of Probiotics from *Bifidobacterium infantis* and *Lactobacillus acidophilus* on Tumour Growth Factor-Beta, Interleukin-17, and Interleukin-10 Expression in Dextran Sodium Sulfate-Induced Ulcerative Colitis Rats

Pujiati Pujiati[1*], Mohamad Hifni Aziz Andriansyah[2], Septian Arief Nur Rahman[2], Naufal Adi Pamungkas[2], Susilorini Susilorini[3], Suparmi Suparmi[4*]

[1]*Department of Paediatrics, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia*
[2]*Study Program of Medical Education, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia*
[3]*Department of Anatomical Pathology, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia*
[4]*Department of Biology, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia*

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ABSTRACT

Ulcerative colitis (UC), a subtype of inflammatory bowel disease (IBD), is characterised by chronic inflammation of the colonic mucosa. Probiotics, *Bifidobacterium infantis* and *Lactobacillus acidophilus* have gained attention as a potential therapeutic strategy for UC. This study aims to evaluate the effects of probiotics containing *B. infantis* and *L. acidophilus* (PROBILA) on the expression of tumour growth factor beta (TGF-*β*), interleukin (IL)-17, and IL-10 in dextran sodium sulphate (DSS)-induced ulcerative colitis (UC). Twenty-four healthy adult male rats were randomly assigned to four groups: control, UC, UC+5-aminosalicylic acid (5-ASA), and UC+PROBILA. UC was induced by administering 5% DSS for 5 days, followed by oral treatment of 5-ASA or PROBILA for 8 days. TGF-*β*, IL-17, and IL-10 expression levels were assessed using the hotspot method, enzyme-linked immunosorbent assay, and the Allred scoring system, respectively. PROBILA treatment significantly reduced TGF-*β* expression compared with the UC group. The Mann–Whitney test revealed no significant difference ($p > 0.05$) between TGF-*β* TGF-expression in the DSS+PROBILA and DSS+5-ASA groups. Post-treatment IL-10 levels were higher in the UC+PROBILA group (4.67 ± 1.033 mmol/L) than in the UC group (5 ± 1.265 mmol/L), suggesting the potential efficacy of PROBILA in enhancing IL-10 expression. These findings highlight the immunomodulatory effects of *B. infantis* and *L. acidophilus* (PROBILA) in DSS-induced UC, supporting their potential therapeutic role in managing inflammation.

Keywords: ulcerative colitis, probiotics, *Bifidobacterium infantis*, *Lactobacillus acidophilus*, tumour growth factor beta (TGF-*β*), interleukin (IL)-17, IL-10

Introduction

Ulcerative colitis (UC), a subtype of inflammatory bowel disease (IBD), is characterised by chronic inflammation of the colonic mucosa. Although its exact etiology remains unclear, UC is a multifactorial disease influenced by genetic predisposition, immune dysregulation, environmental factors, and alterations in the gut microbiota.[1] Recent studies have reported the crucial role of the gut microbiome in maintaining intestinal homeostasis and regulating immune responses.[2] Dysbiosis, or an imbalance in the gut microbiota, has been implicated in UC pathogenesis by disrupting mucosal barrier integrity and triggering aberrant immune activation.[3] Probiotics, defined as live microorganisms that provide health benefits to the host when administered adequately,[4] have gained attention as a potential therapeutic strategy for UC.[5] Among the various probiotic strains, *Bifidobacterium infantis* and *Lactobacillus acidophilus* have demonstrated immunomodulatory effects in both preclinical and clinical studies.

*Corresponding author. Email: pujiatiabbas@unissula.ac.id; suparmi@unissula.ac.id
Tel: (62) 821-3455-5381

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These probiotics influence intestinal immune responses by modulating the production of pro-inflammatory and anti-inflammatory cytokines.[6] The interplay between cytokines, such as interleukin (IL)-17, IL-10, and transforming growth factor-beta (TGF-*β*), is central to both the pathogenesis and resolution of UC, making them key biomarkers for evaluating probiotic efficacy.[7]

IL-17, a proinflammatory cytokine produced by Th17 cells, is often elevated in UC and contributes to tissue damage by promoting neutrophil recruitment and amplifying inflammatory cascades.[8] By contrast, IL-10, an anti-inflammatory cytokine, is crucial in maintaining intestinal homeostasis by suppressing excessive immune responses.[9] TGF-*β*, another key regulatory cytokine, has a dual role in UC, facilitating epithelial repair and preserving mucosal tolerance, potentially promoting fibrosis if dysregulated.[10] Maintaining a balance among these cytokines is essential for controlling inflammation and promoting mucosal healing in UC.

Experimental studies using dextran sodium sulfate (DSS)-induced UC models in rodents have been instrumental in elucidating UC pathophysiology and assessing therapeutic interventions.[11,12] The DSS model replicates many histological and immunological characteristics of human UC, making it a widely used preclinical tool. Nopwinyoowong et al. (2022) reported that DSS-induced UC mice exhibited suppressed expression of Cyp1a1, Cyp1a2, Cyp2b9/10, Cyp2e1, Cyp2c29, Cyp2d9, Cyp3a11, and Cyp3a13 mRNAs.[13] Previous studies have demonstrated that probiotic supplementation can mitigate DSS-induced colitis by modulating gut microbiota composition and immune responses.[14] A histopathological analysis revealed decreased inflammation and variable lymphocyte presence after administering Lampung Robusta coffee extract and *Lactobacillus*

acidophilus in the colon of mice infected with *Shigella flexneri*.[15] However, the specific effects of *B. infantis* and *L. acidophilus* on IL-17, IL-10, and TGF-*β* expression in UC remain inadequately explored.

This study evaluated the effects of probiotics containing *B. infantis* and *L. acidophilus* on TGF-*β*, IL-17, and IL-10 expression in a DSS-induced ulcerative colitis rat model. By elucidating the immunomodulatory properties of these probiotics, this study contributes to the growing body of evidence supporting probiotic-based therapies as a complementary approach to UC management.

Materials and Methods

Chemicals

All chemicals used were of analytical grade. Wistar rats (*Rattus norvegicus*), mesalazine containing 5-aminosalicylic acid (5-ASA), DSS, and a probiotic tablet containing 10^9 colony-forming units (CFUs) of *B. infantis* and 10^9 CFUs of *L. acidophilus* (PROBILA) were obtained from the Nutrition Laboratory of the Inter-University Center, Universitas Gadjah Mada, Yogyakarta, Indonesia.

Experimental animals

The study was performed from February 2024 to March 2024 at the Nutrition Laboratory of the Inter-University Center, Universitas Gadjah Mada, Yogyakarta, Indonesia. Ethical approval was obtained from the Ethics Committee of the Faculty of Medicine, Universitas Islam Sultan Agung, Indonesia, with the document number 487/XII/2023/Bioethics Committee. Male Wistar albino rats weighing 150–200 g were housed in standard polypropylene cages with a hard bottom and maintained at 23°C ± 2°C under a 12:12 light/dark cycle. Rats were acclimated for 7 days before the start of the experiment and provided free access to laboratory chow and tap water.

DSS was dissolved in distilled water at a concentration of 5% and administered orally at 1 mL/200 g body weight (BW) per day for 5 consecutive days. A probiotic tablet (PROBILA) containing *B. infantis* and *L. acidophilus* was dissolved in 50 mL of distilled water and administered orally at 1 mL/200 g BW per day. Mesalazine containing 5-ASA was dissolved in distilled water and administered orally at 36 mg/kg BW.

A total of 24 healthy adult male rats were randomly assigned to 4 groups (N = 6 per group). The control group received distilled water orally for 13 days. The UC group, a negative control, received DSS for 5 days, followed by distilled water for 8 days. The positive control (UC+5-ASA) group received DSS for 5 days, followed by mesalazine (5-ASA) for 8 days. The treatment group (UC+PROBILA) received DSS for 5 days, followed by PROBILA for 8 days.

Assessment of TGF-β expression

Following the manufacturer's protocol, IL-17 levels were measured in serum samples using an enzyme-linked immunosorbent assay (ELISA). Serum samples were collected, centrifuged to remove debris, and stored at -80°C until analysis. A commercially available IL-17 ELISA kit, which included precoated 96-well plates, standards, and detection reagents, was used. Standards and samples were added in duplicate and incubated with the detection antibody and substrate solution. The reaction was terminated using a stop solution, and absorbance was measured at 450 nm by using a microplate reader (ZENIX-320, Taoyuan, Taiwan). A standard curve was generated to determine IL-17 levels in the samples.[16]

IL-17 level measurement

Following the manufacturer's protocol, IL-17 levels were measured in serum samples using an enzyme-linked immunosorbent assay (ELISA). Serum samples were collected, centrifuged to remove debris, and stored at -80°C until analysis. A commercially available IL-17 ELISA kit, which included precoated 96-well plates, standards, and detection reagents, was used. Standards and samples were added in duplicate and incubated with the detection antibody and substrate solution. The reaction was terminated using a stop solution, and absorbance was measured at 450 nm by using a microplate reader. A standard curve was generated to determine IL-17 levels in the samples.[17]

Assessment of IL-10 expression

IL-10 expression was assessed using the Allred scoring system, which combines the proportion of positively stained cells with staining intensity. Tissue samples were fixed in formalin, embedded in paraffin, sectioned, and stained with an anti-IL-10 antibody using an immunohistochemical approach. The proportion score ranged from 0 (no staining) to 5 (>75% positive cells), whereas the intensity score ranged from 0 (negative) to 3 (strong). The total Allred score, obtained by summing the proportion and intensity scores, ranged from 0 to 8.[18]

Statistical Analyses

All graphs, calculations, and statistical analyses were performed using GraphPad Prism software (version 10.1.0, GraphPad Software, San Diego, CA, USA) for Mac. Data are presented as mean ± standard deviation. Group means for numerical variables were compared using a one-way analysis of variance (ANOVA), followed by the least significant difference (LSD) test as a post hoc analysis. A *p*-value of <0.05 was considered statistically significant.

Results and Discussion

Effect of probiotics from B. infantis and L. acidophilus (PROBILA) on TGF-β expression

Figure 1 presents a comparative analysis of TGF-*β* expression across different treatment groups in rat colon mucosa, illustrating the extent of inflammatory responses and potential therapeutic effects. DSS-induced colitis led to inflammatory cell infiltration in the lamina propria and increased TGF-*β* expression. Brown staining in inflammatory cells (Figure 1b) indicated an increased inflammatory response compared with the control group (Figure 1a). Treatment with 5-ASA reduced TGF-*β* expression, suggesting its potential anti-inflammatory effects (Figure 1c). Administration of *B. infantis* and *L. acidophilus* (PROBILA) resulted in a noticeable reduction in brown-stained cytoplasm, indicative of the healing process in DSS-induced ulcerative colitis (Figure 1d). 5-ASA and PROBILA treatments significantly reduced TGF-*β* expression compared with the DSS-induced UC group. However, the Mann–Whitney test revealed no statistically significant difference ($p > 0.05$) between TGF-*β* expression levels in PROBILA-treated and 5-ASA-treated DSS-induced UC rats (Figure 2).

Effect of probiotics from B. infantis and L. acidophilus (PROBILA) on IL-17 and IL-10 expression

Figure 3a shows that posttreatment IL-10 levels in the UC+PROBILA group (4.67 ± 1.033 mmol/L) were significantly higher than those in the UC group (5.00 ± 1.265 mmol/L), suggesting that PROBILA enhances IL-10 expression. The Allred Score further indicated that IL-10 expression intensity was greater in UC rats treated with PROBILA than in those receiving standard therapy with 5-ASA (UC+5-ASA), which had a level of 3.67 ± 1.366 mmol/L. These findings indicate the immunomodulatory potential of *B. infantis* and *L. acidophilus* (PROBILA) in modulating IL-10 expression. Figure 3b demonstrates that IL-17 expression remained unchanged between pretreatment and posttreatment assessments across all experimental groups, suggesting that none significantly modulated IL-17 levels. These findings provide valuable insights into the immunomodulatory effects of PROBILA on cytokine expression in experimental colitis models. The figure presents the paired *t*-test results for IL-17 expression in rat colon mucosa before (pretest) and after (posttest) treatment across the four groups: control, UC, UC+ASA, and UC+PROBILA. Although a slight reduction in IL-17 expression was observed in the UC+ASA group post-treatment, the change was not statistically significant ($p>0.05$). Similarly, PROBILA treatment led to a minor downward trend in IL-17 levels; however, the difference between pretest and posttest values remained statistically nonsignificant ($p > 0.05$). IBD is a chronic autoimmune disorder characterised by persistent gastrointestinal inflammation, with immune cell abnormalities playing a central role in colitis development. In DSS-induced colitis (UC), TGF-*β* expression increased, whereas IL-10 and IL-17 expression decreased. These findings are consistent with those of previous studies.[19–22] The increased TGF-*β* levels in DSS-induced UC likely reflect its dual role in mediating inflammation and promoting tissue repair in response to injury.

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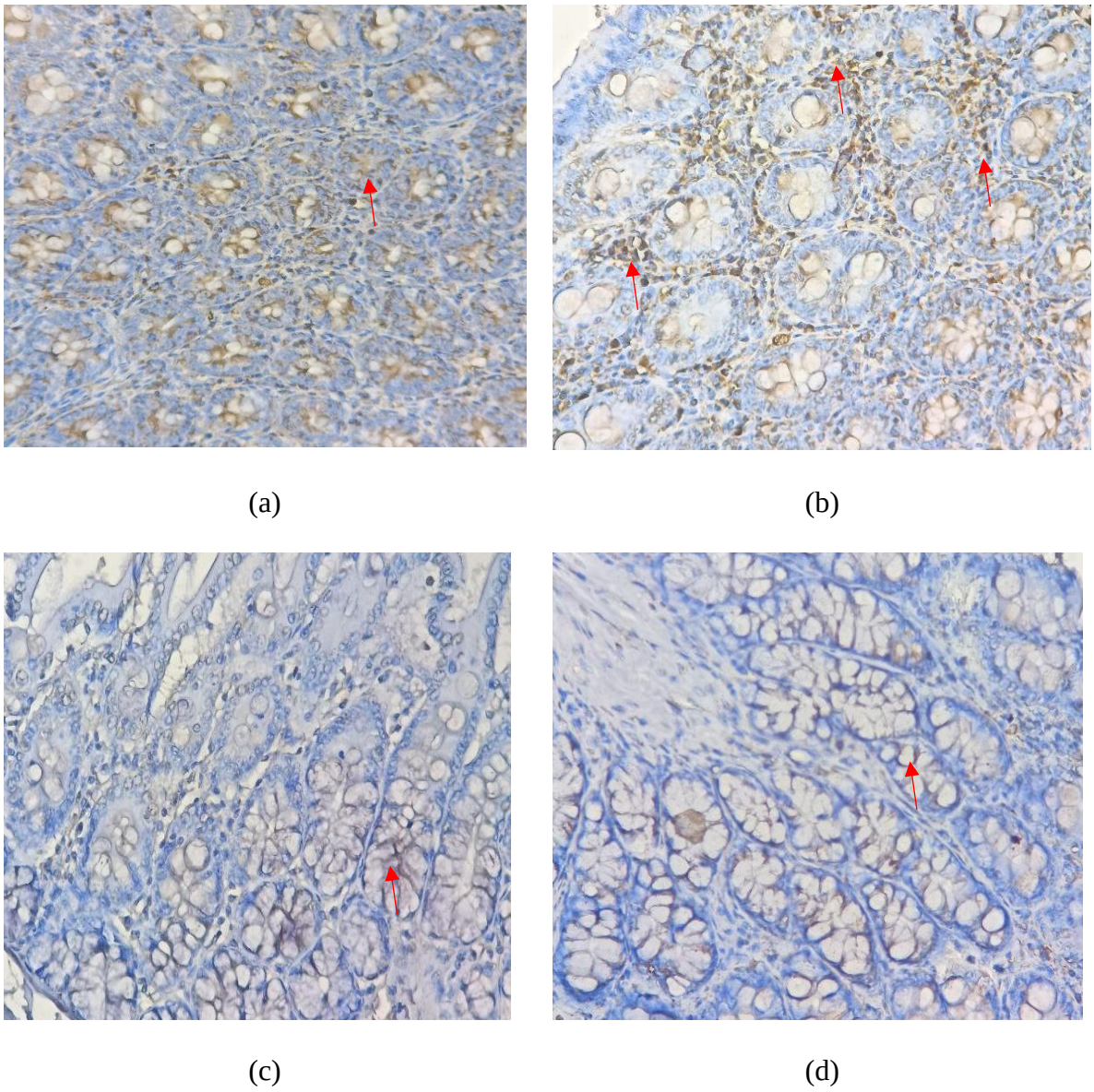

Figure 1: Histological image of the rat colon mucosa in (a) control, (b) UC, (c) UC+5-ASA, and (d) UC+PROBILA groups. The red arrows indicate TGF-β expression, shown as brown staining in the cytoplasm of inflammatory cells within the lamina propria. Immunohistochemistry staining at 400× magnification

By contrast, reducing IL-10, a key anti-inflammatory cytokine, may worsen inflammation.[19,20] Although IL-17 is primarily a proinflammatory cytokine, its levels are often reduced in DSS-induced colitis. This decrease may compromise mucosal barrier integrity and exacerbate symptoms because IL-17 also has protective functions. IL-17 neutralisation can aggravate colitis, indicating its complex role in disease progression.[21,22]

This study demonstrated that probiotics containing *B. infantis* and *L. acidophilus* (PROBILA) alleviated intestinal inflammation in DSS-induced colitis by reducing TGF-β, IL-17, and IL-10 expression, suggesting their potential therapeutic role in IBD and colorectal cancer prevention. The comparable efficacy of PROBILA and 5-ASA in lowering TGF-β expression and PROBILA's superior effect on IL-10 upregulation highlights the potential of probiotics as a promising treatment strategy for UC. The ability of PROBILA to enhance anti-inflammatory cytokine profiles without significantly affecting IL-17 levels suggests a targeted modulation of immune responses, which may help minimise the risks associated with broad-spectrum immunosuppression. Previous studies have identified *B. infantis* as a promising dietary supplement or functional food for UC management.[23–25] In addition, *L. acidophilus* contributes to UC treatment by downregulating TGF-β and IL-17 to mitigate inflammation while upregulating IL-10 to enhance anti-inflammatory responses.[26–28] The combination of *B. infantis* and *L. acidophilus* (PROBILA) exerts additional immunomodulatory effects beyond those of conventional treatments such as 5-ASA. Findings from this study suggest that PROBILA mitigates inflammation in UC by modulating gut microbiota and strengthening intestinal barrier integrity. However, some studies indicate that probiotics may not provide significant clinical benefits in maintaining remission. Ihara et al. (2017) reported that TGF-β plays a crucial role in preserving intestinal homeostasis by regulating immune function, epithelial integrity, and gut microbiota, all of which are central to the pathogenesis of IBD.[29] The observed increase in IL-10 levels following PROBILA treatment supports the hypothesis that these probiotics enhance the anti-inflammatory environment, promoting mucosal healing in DSS-induced colitis.

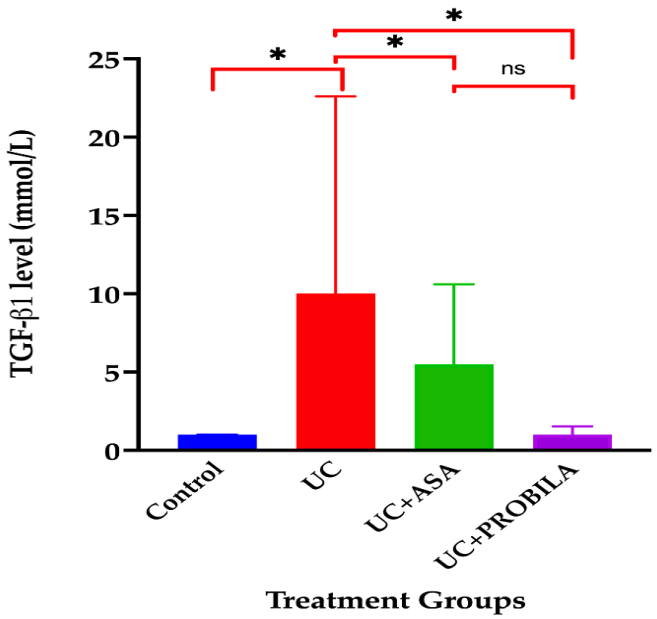

Figure 2: Effect of PROBILA on TGF-*β* expression in the rat colon mucosa in 4 treatment groups: control, UC, UC+ASA, and UC+PROBILA. *indicates a significant difference ($p < 0.05$), ns = not significant ($p > 0.05$) based on Mann–Whitney Test

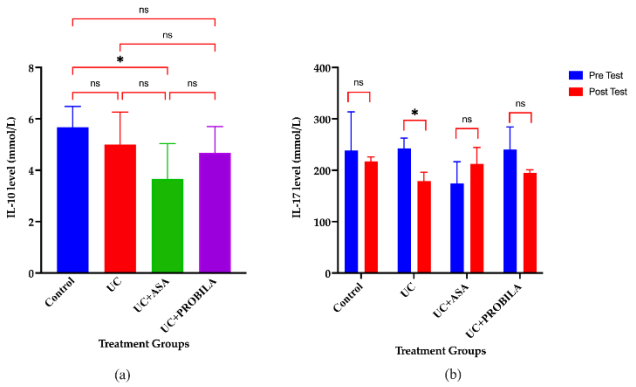

Figure 3: Effect of PROBILA on (a) IL-10 expression and (b) IL-17 expression before (pretest) and after treatment (posttest) in the rat colon mucosa in 4 treatment groups: control, UC, UC+ASA, and UC+PROBILA. *indicates a significant difference ($p < 0.05$); ns = not significant ($p > 0.05$) based on the LSD test and paired *t* test for IL-10 and IL-17, respectively.

A detailed molecular analysis of probiotic interactions with immune signalling pathways is necessary to identify strains inhibiting the IL-23/Th17 axis without increasing TNF or reducing IL-10. Such targeted modulation could offer a promising therapeutic approach for UC while avoiding adverse effects noted in Crohn's disease. This distinction is particularly relevant given that *Lactobacillus* and *Bifidobacterium* strains have been shown to counteract *Adherent-Invasive Escherichia coli* virulence.[30]

These findings suggest that PROBILA's therapeutic effects primarily enhance anti-inflammatory pathways rather than directly suppress IL-17-mediated inflammation. Although the slight reduction in IL-17 levels observed in the UC+ASA group was not statistically significant, it highlights the need for further investigation into distinct mechanisms through which probiotics and standard anti-inflammatory drugs exert their effects. Pujiati et al. (2022) reported that administration of *Lactobacillus brevis* and *Leuconostoc mesenteroides* probiotics did not affect TGF-*β* or IL-12 expression in ovalbumin-induced asthma rats.[31] Although the current findings support the potential of PROBILA in modulating immune responses, several limitations should be acknowledged. First, the relatively small sample size may limit the generalizability of the results. Second, the molecular mechanisms underlying PROBILA's effects were not examined in detail.

Conclusion

Probiotics containing *B. infantis* and *B. acidophilus* (PROBILA) alleviated intestinal inflammation in DSS-induced colitis by reducing TGF-*β*, IL-17, and IL-10 expression, suggesting their potential therapeutic strategy for IBD and colorectal cancer prevention. Future studies should focus on elucidating the specific pathways through which PROBILA modulates cytokine expression and assessing its long-term impact on disease progression. Moreover, clinical trials are necessary to validate its therapeutic potential in patients with UC.

Conflict of Interest

Authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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