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ORIGINAL STUDY

Renoprotective Potential of Ciprofloxacin, Prednisolone, and Infliximab in Acetic Acid-Induced Ulcerative Colitis Rats

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ABSTRACT

Ulcerative colitis (UC) is a chronic inflammatory bowel disease with systemic manifestations, including renal impairment mediated by oxidative stress, inflammation, and electrolyte imbalance. This study investigated the renoprotective potential of ciprofloxacin, prednisolone, and infliximab in rats with acetic acid–induced UC. Fifty male Sprague–Dawley rats (180–200 g) were divided into five groups (n = 10): control, UC control, UC + ciprofloxacin (50 mg/kg, p.o.), UC + prednisolone (4 mg/kg, p.o.), and UC + infliximab (5 mg/kg, i.p.). UC was induced by rectal instillation of 4% acetic acid, and treatments were administered for 42 days. Serum urea, creatinine, electrolytes, and malondialdehyde (MDA) were analyzed, and renal histopathology was assessed using hematoxylin–eosin staining. UC induction caused marked renal dysfunction, reflected by increased urea (+144%), creatinine (+192%), and MDA (+667%) levels, along with significant electrolyte derangements ($p < 0.05$ vs. control). All treatments significantly reduced oxidative stress, improved renal function, and restored electrolyte balance ($p < 0.05$ vs. UC control). Infliximab produced the most pronounced effect, reducing MDA by 78% and preserving normal renal histoarchitecture. Ciprofloxacin, prednisolone, and infliximab confer renoprotective effects in UC by attenuating oxidative and inflammatory injury and restoring renal homeostasis. Infliximab exhibited superior efficacy, highlighting the central role of TNF-α–mediated inflammation in UC-associated renal damage. These findings provide preclinical evidence supporting biologic therapy for extraintestinal complications of UC.

Keywords: Ulcerative colitis, Kidney injury, Ciprofloxacin, Prednisolone, Infliximab, Oxidative stress, Electrolytes

1. Introduction

Ulcerative colitis (UC) is a chronic, relapsing form of inflammatory bowel disease (IBD) characterized by continuous mucosal inflammation of the colon, often beginning in the rectum and extending proximally in a continuous manner [1]. The incidence of UC has been rising globally, with a growing burden in developing nations, posing significant challenges to public health systems [2]. The pathogenesis of UC involves complex interactions among genetic predisposition, intestinal microbiota dysbiosis, environmental triggers, immune dysregulation, and oxidative stress [3]. Although UC primarily affects the gastrointestinal tract, it is increasingly recognized as a systemic disorder with extraintestinal manifestations involving the hepatobiliary, dermatologic, musculoskel et al, and renal systems [4].

Renal involvement in UC, while less frequently studied, contributes significantly to morbidity. Mechanisms implicated in UC-associated nephropathy include chronic systemic inflammation, immune complex deposition, oxidative stress, and electrolyte imbalance [5]. Studies have reported elevated serum urea and creatinine, lipid peroxidation, and histopathological evidence of tubular injury in UC

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patients and experimental models [6]. These findings highlight that kidney injury may be a direct consequence of inflammatory and oxidative processes associated with UC rather than an unrelated comorbidity. Dincer et al. [7] demonstrated that renal manifestations occur in approximately 4–5% of patients with IBD, even during the biologic therapy era, underscoring the need for effective renoprotective interventions in UC.

Current therapeutic approaches for UC include antibiotics, corticosteroids, immunosuppressants, and biologic agents that target key inflammatory mediators [8]. Ciprofloxacin, a fluoroquinolone antibiotic, has been reported to exert beneficial effects in UC not only through its antimicrobial activity but also by modulating the gut microbiota, reducing bacterial translocation, and suppressing pro-inflammatory cytokine release [9, 10]. Lahat et al. [11] further demonstrated that ciprofloxacin reduces interleukin-1β and tumor necrosis factor-alpha (TNF-α) expression in experimental colitis models, suggesting an additional immunomodulatory role.

Prednisolone, a corticosteroid, remains a cornerstone of UC management due to its potent anti-inflammatory and immunosuppressive properties. It acts mainly by inhibiting the nuclear factor kappa B (NF-κB) signaling pathway, thereby downregulating the transcription of cytokines such as TNF-α and interleukin-6 [12]. However, the therapeutic use of corticosteroids is limited by systemic adverse effects, including metabolic disturbances, immune suppression, and renal impairment during prolonged therapy [13].

Infliximab, a chimeric monoclonal antibody against TNF-α, has revolutionized the management of moderate-to-severe UC. It induces clinical remission, promotes mucosal healing, and reduces hospitalization and colectomy rates [14]. Beyond its colonic benefits, infliximab has demonstrated protective effects in experimental models of renal injury, suggesting potential renoprotective properties [15].

Despite these findings, there remains a paucity of data comparing the renoprotective efficacy of ciprofloxacin, prednisolone, and infliximab in UC. Most available studies have focused on colonic inflammation, with limited exploration of secondary organ (renal) injury. This gap underscores the need for comparative experimental studies to elucidate their differential impacts on UC-associated renal dysfunction.

The acetic acid–induced UC model in rats replicates key clinical and histopathological features of human UC, including mucosal ulceration, inflammatory infiltration, oxidative stress, and systemic organ involvement [16]. Therefore, it serves as a suitable platform for evaluating therapeutic interventions beyond the colon.

This study aimed to comparatively evaluate the renoprotective potential of ciprofloxacin, prednisolone, and infliximab in acetic acid–induced ulcerative colitis in rats. The findings are expected to enhance understanding of the extraintestinal effects of UC therapies and contribute to the development of integrated management strategies for UC-associated renal injury.

2. Materials and methods

2.1. Animals and experimental design

Fifty adult male Sprague–Dawley rats (180–200 g) were obtained from the animal facility of Olabisi Onabanjo University. Animals were housed under standard laboratory conditions (12 hours light/dark cycle) with free access to standard chow and water. After 14 days of acclimatization, rats were randomly assigned into five groups (n = 10 each):

- Group A (Control): Distilled water, no UC induction
- Group B (UC control): Acetic acid–induced UC, untreated
- Group C (Ciprofloxacin): UC + ciprofloxacin (15 mg/kg, orally)
- Group D (Prednisolone): UC + prednisolone (4 mg/kg, orally)
- Group E (Infliximab): UC + infliximab (5 mg/kg, intraperitoneally)

All procedures were approved by the Olabisi Onabanjo University Teaching Hospital Animal Ethics Committee (OOUTH-HREC/021/2023AP) and conducted in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals.

2.2. Induction of ulcerative colitis

Ulcerative colitis (UC) was induced by intrarectal instillation of 4% acetic acid (2 mL) under light anesthesia achieved using ketamine (50 mg/kg) and xylazine (5 mg/kg) administered intraperitoneally to ensure minimal discomfort and immobility without deep sedation, as described previously [17]. Animals were maintained in a head-down position for 30 seconds to prevent leakage. Disease induction was confirmed by diarrhea and bloody stools within 24 h.

2.3. Treatment regimens

50 mg of ciprofloxacin (Ratnamani Healthcare PVT. LTD., India) was dissolved in 2 ml of distilled water to give a solution of 50 mg/ml, 15 mg/kg of ciprofloxacin was administered every 72 hours for forty-two days orally [18]. 10 mg of prednisolone (Jiangsu Penyao Pharmaceutical Co. Ltd.,China) was dissolved in 2.5 ml of distilled water to give a solution of 4 mg/ml, 4 mg/kg of prednisolone was administered every 72 hours for forty-two days orally [19]. 5 mg/kg of infliximab (Remsima, Janssen Biotech, USA)was administered bi-weekly for forty two days intra-peritoneal [20].

2.4. Biochemical analysis

At the end of the experimental period, rats were anesthetized with light ether, and blood samples were collected via cardiac puncture using sterile syringes [21]. The samples were allowed to clot at room temperature and then centrifuged at 3000 rpm for 10 minutes to obtain serum, which was aliquoted and stored at − 20 °C until analysis.

Serum urea and creatinine concentrations were determined using commercial colorimetric assay kits (Randox Laboratories Ltd., Crumlin, UK) based on the Berthelot enzymatic method for urea and the Jaffe alkaline picrate method (for creatinine) according to the manufacturer's protocols [22, 23].

Serum electrolyte concentrations—sodium (Na^+), potassium (K^+), and chloride (Cl^-)—were quantified using an automated ion-selective electrode (ISE) electrolyte analyzer (Medica EasyLyte, Bedford, MA, USA), with daily calibration using manufacturer-provided standard solutions.

Lipid peroxidation was assessed by determining malondialdehyde (MDA) levels using the thiobarbituric acid reactive substances (TBARS) assay as described by Stocks & Dormandy [24]. 0.5 mL of serum was mixed with trichloroacetic acid (10%) and thiobarbituric acid (0.67%), boiled for 15 min, cooled, and centrifuged. The absorbance of the supernatant was read at 532 nm using a Shimadzu UV–vis spectrophotometer (Japan). MDA concentration was expressed as nmol/mL serum using an extinction coefficient of 1.56×10^5; M^{-1} cm^{-1}.

2.5. Histopathology

Kidney tissues were excised, rinsed in cold saline and fixed in 10% neutral buffered formalin (NBF) for 24-48 hours, followed by dehydration in a series of ethanol solutions (70%, 80%, 90%, and 100%) and clearing in xylene. The tissues were then embedded in paraffin wax, sectioned into 5-μm thick slices using a microtome, and deparaffinized in xylene. The sections were rehydrated in a series of ethanol solutions, stained with Harris' hematoxylin solution for 5-10 minutes, and then stained with eosin Y solution for 1-2 minutes. After dehydration and clearing, the sections were mounted on glass slides using a mounting medium (DPX) and examined under a light microscope to observe tissue morphology and architecture.

2.6. Statistical analysis

All data were expressed as mean ± standard error of the mean (SEM). Statistical analysis was performed using GraphPad Prism 8.0 (GraphPad Software, USA). Group comparisons were made using one-way analysis of variance (ANOVA) followed by Tukey's post hoc test. A value of $p < 0.05$ was considered statistically. significant.

3. Results

The effects of ciprofloxacin, prednisolone, and infliximab on renal function in acetic acid-induced ulcerative colitis (UC) rats

UC rats exhibited significant elevations in serum urea and creatinine compared with controls ($p < 0.05$). Urea increased by ~144% and creatinine by ~192% in the UC group. Treatment with ciprofloxacin, prednisolone, and infliximab significantly reduced both parameters ($p < 0.05$ vs. UC). Among the treatments, infliximab achieved the greatest improvement, restoring urea and creatinine levels close to control values Table 1.

Table 1. The effects of ciprofloxacin, prednisolone, and infliximab on renal function in acetic acid-induced ulcerative colitis (UC) rats.

Group	Urea (mg/dL)	Creatinine (mg/dL)
A – Control	16.67 ± 0.88	0.25 ± 0.20
B – UC control	40.67 ± 1.56[a]	0.73 ± 0.33[a]
C – Ciprofloxacin-treated	26.67 ± 1.41[b]	0.34 ± 0.73[b]
D – Prednisolone-treated	20.67 ± 0.34[b]	0.32 ± 0.33[b]
E – Infliximab-treated	18.33 ± 1.18[bc]	0.28 ± 0.59[b]

Values are expressed as mean ± SEM.Superscripts indicate significant differences ($p \leq 0.05$):

a = significantly different from Group A;

b = significantly different from Group B;

c = significantly different from Group C.

The effects of ciprofloxacin, prednisolone, and infliximab on malondialdehyde (MDA), urea, and creatinine levels in acetic acid-induced ulcerative colitis (UC) rats

Malondialdehyde (MDA) levels were markedly elevated in the UC group, reflecting increased lipid peroxidation ($p < 0.05$ vs. control). All treatment

groups showed significant reductions in MDA ($p < 0.05$ vs. UC), with infliximab producing the largest decrease (~78% reduction compared with UC) Table 2.

Table 2. The effects of ciprofloxacin, prednisolone, and infliximab on malondialdehyde (MDA), urea, and creatinine levels in acetic acid-induced ulcerative colitis (UC) rats.

Group	MDA (μmol/ml)
A – Control	0.03 ± 0.14
B – UC control	0.23 ± 0.43^{a}
C – Ciprofloxacin-treated	0.07 ± 0.23^{b}
D – Prednisolone-treated	0.08 ± 0.26^{b}
E – Infliximab-treated	0.05 ± 0.22^{b}

Values are expressed as mean ± SEM. Superscripts indicate significant differences ($p \leq 0.05$):
a = significantly different from Group A;
b = significantly different from Group B.

The effects of of ciprofloxacin, prednisolone, and infliximab on blood electrolyte levels in acetic acid-induced ulcerative colitis (UC) rats

UC rats showed electrolyte imbalance characterized by hyponatremia, hypochloremia, and hyperkalemia compared with controls ($p < 0.05$). Ciprofloxacin, prednisolone, and infliximab significantly corrected these alterations ($p < 0.05$ vs. UC). Infliximab restored electrolyte concentrations closest to normal ranges Table 3.

The effects of ciprofloxacin, prednisolone, and infliximab on kidney tissue histology in acetic acid-induced ulcerative colitis (UC) rats

Kidneys from control rats displayed normal glomerular and tubular architecture. UC rats exhibited severe tubular degeneration, glomerular shrinkage, inflammatory infiltration, and necrosis. Ciprofloxacin and prednisolone treatments partially ameliorated these histological changes, while infliximab demonstrated the strongest protective effect, preserving glomerular and tubular structures with minimal inflammatory infiltration Fig. 1.

4. Discussion

This study demonstrates that acetic acid–induced ulcerative colitis (UC) is associated with significant renal dysfunction, characterized by elevated serum urea and creatinine, lipid peroxidation, and electrolyte imbalance. These findings corroborate earlier reports that systemic inflammation and oxidative stress play central roles in the extraintestinal manifestations of UC, including nephropathy [5, 7]. Elevated malondialdehyde (MDA) levels reflect enhanced lipid peroxidation and membrane injury, consistent with oxidative stress–driven renal damage previously reported in UC models [1, 4].

The inflammatory cascade in UC is driven by cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β), which contribute to endothelial dysfunction, tubular necrosis, and fibrosis [25, 26]. In this study, the marked improvement in renal biochemical parameters following treatment with ciprofloxacin, prednisolone, and infliximab suggests suppression of these cytokine-mediated pathways. Although cytokine levels were not directly quantified, prior studies provide mechanistic evidence. Ciprofloxacin has been shown to inhibit IL-1β, IL-8, and TNF-α expression in colonic tissue and macrophages, indicating immunomodulatory effects beyond its antibacterial activity [11, 27]. Prednisolone suppresses NF-κB activation, thereby reducing transcription of pro-inflammatory cytokines including TNF-α and IL-6 [28]. Infliximab, by directly neutralizing TNF-α, interrupts the cytokine amplification loop responsible for both colonic and systemic inflammation [29]. These mechanisms likely explain the observed normalization of renal function and histological preservation, particularly in the infliximab-treated group.

Oxidative stress is a well-recognized mediator of tissue injury in UC. Reactive oxygen species (ROS) deplete antioxidants such as superoxide dismutase (SOD) and reduced glutathione (GSH), leading to lipid peroxidation and protein oxidation [30]. Previous work has demonstrated decreased SOD and GSH activities in UC-induced colonic tissues [31]. The reduction of MDA levels following therapy in this study suggests that all three drugs mitigated oxidative damage. According to previous studies, ciprofloxacin may exert antioxidant effects by reducing nitric oxide and inducible nitric oxide synthase (iNOS) expression [10]. [32] prednisolone may restore redox balance through inhibition of phospholipase A_2 and attenuation of ROS generation [33], while infliximab may indirectly enhance antioxidant enzyme activity by suppressing TNF-α–driven oxidative cascades [34]. Therefore, the observed biochemical improvements may reflect restoration of antioxidant defenses and attenuation of oxidative injury.

Renal apoptosis is another mechanism contributing to UC-associated nephropathy. Excess TNF-α and ROS activate caspase-3–mediated apoptotic pathways in tubular epithelial cells [35]. Studies have shown that infliximab and other TNF-α blockers downregulate caspase-3 and Bax while upregulating Bcl-2, thereby preserving cellular integrity [36]. Prednisolone also reduces apoptotic signaling through glucocorticoid receptor–mediated suppression of pro-apoptotic genes [37]. Ciprofloxacin, while less directly anti-apoptotic, protects against apoptosis through modulation of oxidative stress and inhibition of

Table 3. The effects of of ciprofloxacin, prednisolone, and infliximab on blood electrolyte levels in acetic acid-induced ulcerative colitis (UC) rats.

Group	Na^+ (mmol/l)	K^+ (mmol/l)	Cl^- (mmol/l)
A – Control	137.67 ± 0.33	3.36 ± 1.63	100.33 ± 0.37
B – UC control	103.61 ± 0.24[a]	7.87 ± 0.22[a]	71.00 ± 0.47[a]
C – Ciprofloxacin-treated	141.00 ± 0.58[b]	4.93 ± 0.67[b]	99.67 ± 0.33[b]
D – Prednisolone-treated	139.33 ± 1.33[b]	4.97 ± 0.34[b]	102.00 ± 0.31[b]
E – Infliximab-treated	140.35 ± 0.49[b]	3.73 ± 0.28[b]	100.01 ± 0.47[b]

Values are expressed as mean ± SEM. Superscripts indicate significant differences ($p \leq 0.05$):

a = significantly different from Group A;

b = significantly different from Group B.

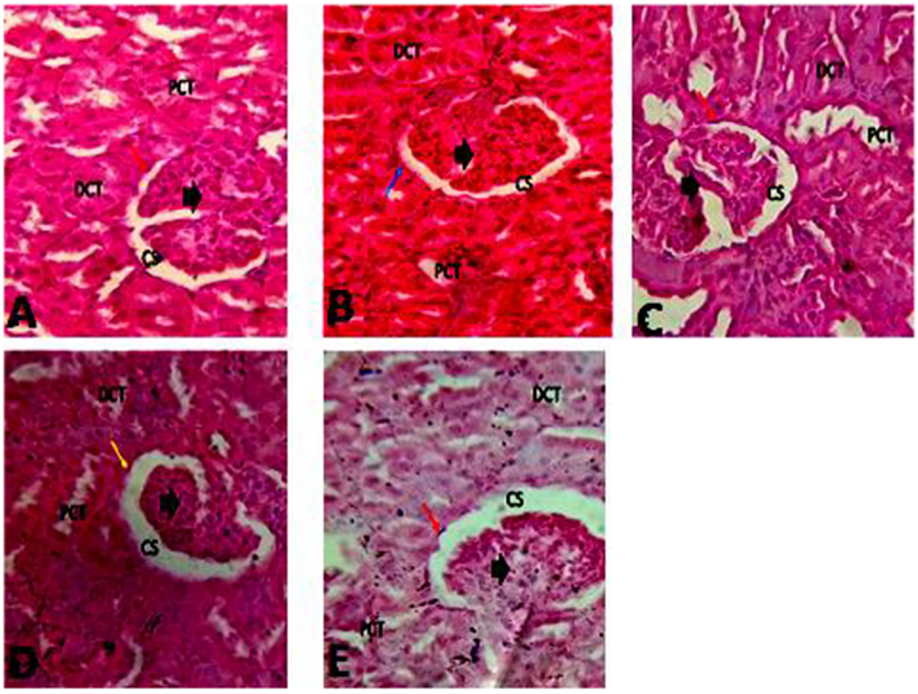

Fig. 1. The effects of ciprofloxacin, prednisolone, and infliximab on kidney tissue histology in acetic acid-induced ulcerative colitis (UC) rats. A. Control group: Normal kidney histology showing well-differentiated glomerulus (black arrow) with podocytes, distinct capsular space (CS), and proximal (PCT) and distal convoluted tubules (DCT) lined with simple squamous epithelial cells (red arrow). B. UC group: Kidney section showing thickened and constricted PCT and DCT, glomerulus (black arrow) with slight epithelial cell loss (blue arrow), and capsular space (CS). C. Ciprofloxacin treated group: Kidney histology revealing thickened walls of PCT and DCT, normal glomerulus (black arrow), distinct capsular space (CS), and intact epithelial cells (red arrow). D. Prednisolone treated group: Kidney section displaying constricted PCT and DCT, slightly distorted glomerulus (black arrow), dilated capsular space (CS) with reduced epithelial cells (yellow arrow). E. Infliximab treated group: Kidney histology showing constricted PCT and DCT, dilated capsular space (CS), normal glomerulus (black arrow), and simple squamous epithelial cells. H/E staining, magnification (x400), all micrographs were captured under light microscopy.

bacterial endotoxin-induced signaling [10]. The improved renal histoarchitecture in the treated groups is consistent with these anti-apoptotic and cytoprotective effects.

Among the tested agents, infliximab exhibited the most pronounced renoprotective effect, normalizing renal biomarkers and preserving tubular morphology. This superiority can be attributed to its targeted inhibition of TNF-α, a master regulator of inflammatory and oxidative pathways. These findings are in agreement with previous reports that infliximab reduces renal injury markers and restores antioxidant capacity in models of colitis and nephrotoxicity [34, 36]. Prednisolone conferred partial protection, consistent with its broad but non-specific anti-inflammatory profile and potential metabolic side effects [33]. Ciprofloxacin produced moderate improvement, aligning with earlier studies where its benefits were attributed to microbial modulation and secondary reduction of systemic inflammation rather than direct immunosuppression [10, 32].

These findings support prior evidence that controlling systemic inflammation ameliorates extraintestinal organ injury in UC. Dincer et al. [7] documented

renal manifestations in ~5% of UC patients, suggesting that systemic cytokine overproduction and oxidative stress underlie UC-associated nephropathy. The observed restoration of renal function and reduction of oxidative damage in treated rats thus mirror clinical improvements reported in patients receiving TNF-α blockade or corticosteroid therapy. However, our study extends these observations by demonstrating comparative renoprotective effects across three mechanistically distinct therapies.

5. Conclusion

Ciprofloxacin, prednisolone, and infliximab each significantly ameliorated renal dysfunction in acetic acid-induced ulcerative colitis, as reflected by marked reductions in serum creatinine (by approximately 53%, 56%, 61%, respectively), urea levels (by 35%, 50%, 55% respectively) and malondialdehyde (MDA; by 69%, 65%, 78%, respectively) level compared with untreated UC rats, alongside restoration of electrolyte balance and histological improvement in renal architecture. Among the treatment groups, infliximab demonstrated the most pronounced renoprotective effect, underscoring the pivotal role of TNF-α–mediated signaling in UC-associated renal injury. However, this study is limited by the absence of direct measurements of inflammatory cytokines (TNF-α, IL-6), antioxidant enzymes (SOD, GSH), and apoptotic markers (caspase-3), which would have provided stronger mechanistic confirmation of the proposed pathways. Furthermore, longer study durations and dose-response analyses are needed to evaluate chronic renal adaptations and potential toxicity. Future studies should incorporate these molecular assays and explore signaling pathways such as NF-κB and Nrf2 to clarify the interplay between inflammation and oxidative stress. Collectively, these findings emphasize that UC exerts systemic effects beyond the intestine and suggest that targeting TNF-α pathways—particularly through infliximab—may offer superior therapeutic benefit for preventing or managing renal complications associated with UC.

Acknowledgment

None.

Conflict of interest

The authors declared no conflict of interest.

Ethical approval

All procedures were approved by the Olabisi Onabanjo University Teaching Hospital Animal Ethics Committee (OOUTH-HREC/021/2023AP) and conducted in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals.

Data availability

The authors confirm that the data supporting the findings of this study are available within the article.

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Author contribution

Conceptualization and Methodology: **Oyesola O.A., Kukoyi B.I.;** Supervision: **Oyesola O.A.;** Formal analysis, Investigation, Data curation: **Olayemi O.E., Oyesola O.A. Kukoyi B.I;** Writing—Original draft: **Olayemi O.E., Kukoyi B.I.;** Writing—Reviewing and Editing: All author's read and approved the final writing.

References

1. Tian T, Wang Z, Zhang J. Pathomechanisms of oxidative stress in inflammatory bowel disease and potential antioxidant therapies. *Oxidative medicine and cellular longevity*. 2017;2017:4535194. https://doi.org/10.1155/2017/4535194.
2. Ng SC, Shi HY, Hamidi N, Underwood FE, Tang W, Benchimol EI *et al.* Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. *Lancet (London, England)*. 2017;390(10114):2769–2778. https://doi.org/10.1016/S0140-6736(17)32448-0.
3. Khor B, Gardet A, Xavier RJ. Genetics and pathogenesis of inflammatory bowel disease. *Nature*. 2011;16;474(7351):307–17.
4. Yandian F, Caravaca-Fontán F, Herrera Hernandez LP, Soler MJ, Sethi S, Fervenza FC. Kidney diseases associated with inflammatory bowel disease: Impact of chronic histologic damage, treatments, and outcomes. *Kidney international reports*. 2023;9(2):383–394. https://doi.org/10.1016/j.ekir.2023.11.011.
5. Corica D, Romano C. Renal involvement in inflammatory bowel diseases. *Journal of Crohn's and Colitis*. 2016;10(2):226–35.
6. Muro P, Zhang L, Li S, Zhao Z, Jin T, Mao F *et al.* The emerging role of oxidative stress in inflammatory bowel disease. *Frontiers in endocrinology*. 2024;15:1390351. https://doi.org/10.3389/fendo.2024.1390351.

7. Dincer MT, Dincer ZT, Bakkaloglu OK, Yalin SF, Trabulus S, Celik AF *et al.* Renal manifestations in inflammatory bowel disease: A cohort study during the biologic era. *Medical science monitor: international medical journal of experimental and clinical research*. 2022;16(28):e936497–1.
8. Sales-Campos H, Basso PJ, Alves VB, Fonseca MT, Bonfá G, Nardini V *et al.* Classical and recent advances in the treatment of inflammatory bowel diseases. *Brazilian journal of medical and biological research = Revistabrasileira de pesquisasmedicas e biologica*. 2015;48(2):96–107. https://doi.org/10.1590/1414-431X20143774.
9. Jha DK, Mishra S, Dutta U, Sharma V. Antibiotics for inflammatory bowel disease: Current status. *Indian journal of gastroenterology: Official journal of the Indian Society of Gastroenterology*. 2024;43(1):145–159. https://doi.org/10.1007/s12664-024-01537-x.
10. Thai T, Salisbury BH, Zito PM. Ciprofloxacin. In StatPearls. *StatPearls Publishing*. 2023.
11. Lahat G, Halperin D, Barazovsky E, Shalit I, Rabau M, Klausner J *et al.* Immunomodulatory effects of ciprofloxacin in TNBS-induced colitis in mice. *Inflammatory bowel diseases*. 2007;13(5):557–565. https://doi.org/10.1002/ibd.20077.
12. Ungaro R, Mehandru S, Allen PB, Peyrin-Biroulet L, Colombel JF. Ulcerative colitis. *Lancet*. 2017;389(10080):1756–1770. doi:10.1016/S0140-6736(16)32126-2.
13. Rella V, Rotondo C, Barile R, Erroi F, Cantatore FP, Corrado A. Glucocorticoids treatment and adverse infectious events in rheumatic diseases. *Hospital Practice*. 2024;19;52(4–5):130–42.
14. Orfanoudaki E, Foteinogiannopoulou K, Theodoraki E, Koutroubakis IE. Recent advances in the optimization of anti-TNF treatment in patients with inflammatory bowel disease. *Journal of clinical medicine*. 2023;12(7):2452. https://doi.org/10.3390/jcm12072452.
15. Kavak P, Kirbas A, Yilmaz S *et al.* Effect of infliximab on renal injury due to methotrexate in rats. *J Toxicol Environ Health A*. 2015;78(9):604–610.
16. Yadav V, Varum F, Bravo R, Furrer E, Bojic D, Basit AW. Inflammatory bowel disease: Exploring gut pathophysiology for novel therapeutic targets. *Translational research: The journal of laboratory and clinical medicine*. 2016;176:38–68. https://doi.org/10.1016/j.trsl.2016.04.009.
17. Al-Rejaie SS, Abuohashish HM, Al-Enazi MM, Al-Assaf AH, Parmar MY, Ahmed MM. Protective effect of naringenin on acetic acid-induced ulcerative colitis in rats. *World journal of gastroenterology*. 2013;19(34):5633–5644. https://doi.org/10.3748/wjg.v19.i34.5633.
18. Parashuram S, Krishna P, Lahkar M. Comparative evaluation of different doses of ciprofloxacin alone and in combination with sulfasalazine in experimentally induced inflammatory bowel disease in rats. *International Journal of Basic & Clinical Pharmacology*. 2017;5(4):1629–1635. https://doi.org/10.18203/2319-2003.ijbcp20162484.
19. Abuohashish NA, Sarah I, Enass YO. Comparing the efficacy of carvedilol and celecoxib to prednisolone in acetic acid-induced ulcerative colitis in male albino rats. *Journal of Advances in Medicine and Medical Research*. 2023;35(16):55–68. https://doi.org/10.9734/jammr/2023/v35i165089.
20. Infliximab (Remsima SC): Therapeutic Area: Crohn Disease and Ulcerative Colitis. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; Aug 2024.
21. Parasuraman S, Raveendran R, Kesavan R. Blood sample collection in small laboratory animals. *Journal of pharmacology & pharmacotherapeutics*. 2010;1(2):87–93. https://doi.org/10.4103/0976-500X.72350.
22. Fawcett JK, Scott JE. A rapid and precise method for the determination of urea. *Journal of clinical pathology*. 1960;13(2):156–159. https://doi.org/10.1136/jcp.13.2.156.
23. Jaffé M. Ueber den Niederschlag, welchenPikrinsäure in normalem Harn erzeugt und übereineneue Reaction des Kreatinins. 1886.
24. Stocks J, Dormandy TL. The autoxidation of human red cell lipids induced by hydrogen peroxide. *British journal of haematology*. 1971;20(1):95–111. https://doi.org/10.1111/j.1365-2141.1971.tb00790.x.
25. Leppkes M, Neurath MF. Cytokines in inflammatory bowel diseases - update 2020. *Pharmacological research*. 2020;158:104835. https://doi.org/10.1016/j.phrs.2020.104835.
26. Neurath MF. Cytokines in inflammatory bowel disease. Nature reviews. *Immunology*. 2014;14(5):329–342. https://doi.org/10.1038/nri3661.
27. Kolios G, Manousou P, Bourikas L, Notas G, Tsagarakis N, Mouzas I, Kouroumalis E. Ciprofloxacin inhibits cytokine-induced nitric oxide production in human colonic epithelium. *European Journal of Clinical Investigation*. 2006;36(10):720–9.
28. Ingawale DK, Mandlik SK. New insights into the novel anti-inflammatory mode of action of glucocorticoids. *Immunopharmacology and immunotoxicology*. 20203;42(2):59–73.
29. Jiang XL, Cui HF, Gao J, Fan H. Low-dose infliximab for induction and maintenance treatment in Chinese patients with moderate to severe active ulcerative colitis. *Journal of clinical gastroenterology*. 2015;49(7):582–8.
30. Alemany-Cosme E, Sáez-González E, Moret I, Mateos B, Iborra M, Nos P, Sandoval J, Beltrán B. Oxidative stress in the pathogenesis of Crohn's disease and the interconnection with immunological response, microbiota, external environmental factors, and epigenetics. *Antioxidants*. 2021;10(1):64.
31. Nakutis FS, Nishitokukado I, Dos Santos FM, Ortiz-Agostinho CL, de Alencar DT, Achtschin CG, Nunes VS, Leite AZA, Sipahi AM. Evaluation of oxidative stress in an experimental model of Crohn's disease treated with hyperbaric oxygen therapy. *Clinics (Sao Paulo, Brazil)*. 2023;78:100305. https://doi.org/10.1016/j.clinsp.2023.100305.
32. Kolios G, Manousou P, Bourikas L, Notas G, Tsagarakis N, Mouzas I, Kouroumalis E. Ciprofloxacin inhibits cytokine-induced nitric oxide production in human colonic epithelium. *European journal of clinical investigation*. 2006;36(10):720–729. https://doi.org/10.1111/j.1365-2362.2006.01710.x.
33. Vandewalle J, Luypaert A, De Bosscher K, Libert C. Therapeutic mechanisms of glucocorticoids. *Trends in Endocrinology & Metabolism*. 2018;29(1):42–54.
34. Kirbas A, Cure MC, Kalkan Y, Cure E, Tumkaya L, Sahin OZ, Yuce S, Kizilkaya B, Pergel A. Effect of infliximab on renal injury due to methotrexate in rat. *Iranian journal of kidney diseases*. 2015;9(3):221–229.
35. Kasuya Y, Kim JD, Hatano M, Tatsumi K, Matsuda S. Pathophysiological roles of stress-activated protein kinases in pulmonary fibrosis. *International Journal of Molecular Sciences*. 2021;22(11):6041.
36. Nageeb MM, Talaat A, Reda SM, Elsammak GA. Infliximab abrogates adenine-induced chronic kidney disease via modulation of the MAPK/JNK/ASK signaling pathway in rats. *Naunyn-Schmiedeberg's archives of pharmacology*. 2024;397(1):207–219. https://doi.org/10.1007/s00210-023-02585-4.
37. Ma R, Wang Y, Xu Y, Wang R, Wang X, Yu N, Li M, Zhou Y. Tacrolimus protects podocytes from apoptosis via downregulation of TRPC6 in diabetic nephropathy. *Journal of Diabetes Research*. 2021;2021(1):8832114.