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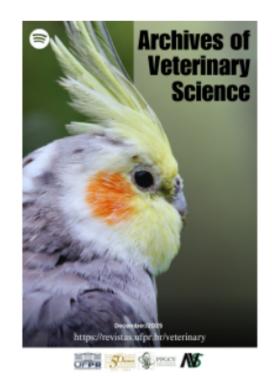
The Effect of Silver Water (Ag)
Administration on NF-kB Expression
and Histopathology of Gastric in Rats
Model of Inflammatory Bowel Disease

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## OF VETERINARY SCIENCE





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The Effect of Silver Water (Ag) Administration on NF-KB Expression and Histopathology of Gastric in Rats Model of Inflammatory Bowel Disease

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Abstract: This study investigated the therapeutic effects of silver water on indomethacin-induced Inflammatory Bowel Disease (IBD) in rats. Male white rats (12 weeks old, ~250g) were divided into five groups; negative control (untreated), positive control (indomethacin-induced), and three treatment groups (T1, T2, T3) receiving 1, 2, and 3 ml of 25 ppm silver water, respectively for 14 days following indomethacin induction (15 mg/kg BW). The study evaluated NF-xB expression via immunohistochemistry and gastric histopathological changes using hematoxylin-eosin staining. Data were analyzed using ANOVA followed by the Tukey test ( $\alpha = 0.05$ ). Results demonstrated that silver water therapy at all tested volumes significantly reduced NF-xB expression, inflammatory cell infiltration, and epithelial erosion in gastric tissues compared to the positive control. The 3 ml dose showed the most pronounced therapeutic effect. These findings suggest that silver water possesses anti-inflammatory properties that suppress the NF-kB inflammatory pathway and promote gastric tissue repair in indomethacin-induced IBD, potentially offering a novel therapeutic approach for IBD management

Keywords: Anti-inflammatory, Antioxidant, IBD, Indomethacin, Silver Water, Pathology.

#### 1. Introduction

Inflammatory Bowel Disease (IBD) is a chronic inflammation of the digestive tract characterized by relapses, with the exact cause still unknown. Generally, IBD is classified into Crohn's disease (CD) and ulcerative colitis (UC) (Ghattamaneni et al, 2019). Crohn's disease (CD) can affect any part of the gastrointestinal tract from the mouth to the anus (Pariente et al, 2018). Ulcerative colitis (UC) is a nonspecific inflammatory disorder of the large intestine, often starting in the rectum and extending proximally with varying degrees of involvement (Taku et al., 2020).

The prevalence of IBD in dogs is 36% presenting with vomiting and 48% being asymptomatic (Craven et al., 2004). Based on research by Wagner et al (2018), there were 21 cases of Inflammatory Bowel Disease reported at the Clinic for Small Animals, Faculty of Veterinary Medicine, Hannover University, Germany. The pathomechanism of IBD involves inflammation triggered by increased pro-inflammatory cytokine expression, followed by NF-xB activation, which leads to tissue damage, including gastric mucosal inflammation and ulceration (Yao et al., 2019). Clinical manifestations of tissue damage include melena, diarrhea, and damage to the digestive organs (Ananthakrishnan and Xavier, 2020).

According to Sairenji and Evans (2017), IBD induction uses a non-steroidal anti-inflammatory drug (NSAID) such as indomethacin. Indomethacin can inhibit cyclooxygenase (COX), thereby preventing the conversion of arachidonic acid into prostanoids (Abdellatif et al., 2021). Prostanoids regulate mucus production and gastric acidity. Reduced mucus in the stomach reduces gastric protective barriers and increases gastric acid production, leading to irritation and damage to the gastric mucosa (Gvires, 2005).

While many studies have investigated the therapeutic effects of natural substances, the use of metal materials for therapeutic purposes remains relatively rare. Metals, such as silver, can be used for various medical purposes due to their physicochemical properties as anti-inflammatory and antimicrobial agents (Park et al., 2011). Silver has the potential to manage inflammation and exert antibacterial and antifungal effects (Burdusel et al., 2018). This potential suggests a tendency to influence inflammatory

However, the molecular mechanisms underlying the therapeutic effects of silver water on IBD, particularly in the stomach, remain unclear. One of the key signaling pathways in IBD pathogenesis is Nuclear Factor-kappa B (NF-kB) (Papoutsopoulou & Campbell, 2021). NF-xB is a transcription factor that plays a central role in regulating inflammatory and immune responses (Bhatt & Ghosh, 2014). Excessive NF-kB activation has been associated with increased production of pro-inflammatory cytokines and tissue damage in patients with IBD (Neurath, 2014). Therefore, modulation of NF-xB expression is a potential therapeutic target for the management of IBD (Szatkowski et al., 2020).

Although several studies have investigated the effects of silver water on various inflammatory conditions, a knowledge gap remains regarding its influence on NF-xB expression and gastric histopathology in IBD. A better understanding of these molecular mechanisms could pave the way for the development of new, effective, and safe treatment strategies for IBD. This study aims to evaluate the effect of silver water (Ag) administration on NF-xB expression and gastric histopathology in a rat model of Inflammatory Bowel Disease.

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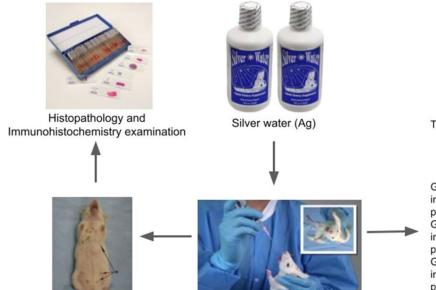
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#### **GRAPHICAL ABSTRACT**

The Effect of Silver Water (Ag) Administration on NF-κB Expression and Histopathology of Gastric in Rats Model of Inflammatory Bowel Disease



**Euthanasia and Tissue Collection** 

Silver water was given orally



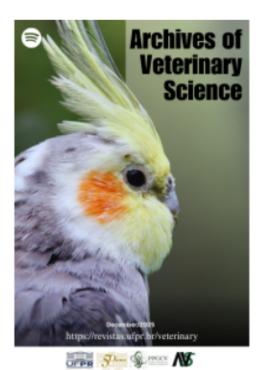
25 male rats induced by indomethacin orally



The rats were divided into five treatment groups:

Group 1 consisted of untreated rats (C-);
 Group 2 consisted of rats induced with IBD using indomethacin 15 mg/kg BW once (C+);

Group 3 consisted of IBD-induced rats using indomethacin 15 mg/kg BW once treated with 25 ppm silver water at a dose of 1 ml (T1); Group 4 consisted of IBD-induced rats using indomethacin 15 mg/kg BW once treated with 25 ppm silver water at a dose of 2 ml (T2); and Group 5 consisted of IBD-induced rats using indomethacin 15 mg/kg BW once treated with 25 ppm silver water at a dose of 3 ml (T3). The experimental interventions were conducted over a period of 14 days.



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