

**Effect of Cinnamon Bark Extract (*Cinnamomum Burmanii*) 50% on IL-6 Levels
in Gingiva of Male Wistar Rats (*Rattus Norvegicus*) Induced by LPS
(Lipopolysaccharide)**

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ABSTRACT

*Periodontitis is a periodontal disease in the form of chronic inflammation of the dental support tissue caused by plaque bacteria. The process of periodontal tissue damage in periodontitis begins with the accumulation of plaque containing bacteria and toxins that are pathogenic. The interaction between plaque bacteria and their products and the body's response to host cells triggers an inflammatory response that can cause ulceration of the gingiva, connective tissue damage, alveolar bone loss, and tooth loss. Periodontitis usually develops from gingivitis that has already occurred, although not all gingivitis progresses to periodontitis. The purpose of this study is to determine the effect of cinnamon bark extract on IL-6 levels. This research method used in vivo laboratory experiments on 32 white rats of the Wistar strain with a research design using a quasi-research model with a posttest only control group design which was randomized into two groups, namely the control group: induced LPS and given Tetracycline gel (Eryzol) topically, the treatment group: induced LPS and given a 50% cinnamon bark extract gel. From the comparative analysis test with the Independent T-Test, it was shown that the significant value of the decrease in IL-6 levels in each group, which was 0.194, was greater than 0.05. This means that there are differences between groups. From the results of the study, it can be said that cinnamon bark extract (*Cinnamomum Burmanni*) with a concentration of 50% has an effect on reducing IL-6 levels.*

Keywords: *cinnamon bark extract (*cinnamomum burmanni*); il-6; periodontitis*



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INTRODUCTION

Maintaining dental and oral health is crucial to overall well-being, yet many individuals neglect it due to a lack of knowledge regarding oral hygiene (Afiati et al., 2017). In Indonesia, the most prevalent dental and oral diseases are dental caries and periodontal diseases (Azuma et al., 2014). Periodontal disease is particularly significant, being the second most common oral health issue after dental caries. It often leads to tooth loss due to progressive inflammation caused by bacteria, which affects the supporting structures of teeth (Cekici et al., 2014). This disease is generally categorized into two major forms: gingivitis and periodontitis (Bartold & Haynes, 1991)

Periodontitis management typically involves scaling, root planning, and the use of medications such as non-steroidal anti-inflammatory drugs (NSAIDs) like ibuprofen and flurbiprofen (Kawuryan, 2008). Although these medications are effective in reducing inflammation and pain, prolonged use can lead to gastrointestinal issues such as ulcers and hemorrhage (Gabay, 2006). Therefore, safer, herbal-based alternatives are sought, particularly those with anti-inflammatory properties that do not carry the same risks as synthetic drugs.

Interleukin-6 (IL-6) plays a central role in the inflammatory response in periodontal disease (Janani et al., 2021). IL-6 is a pro-inflammatory cytokine that mediates both acute and chronic inflammation, facilitating processes such as T-cell activation, B-cell differentiation, and osteoclast formation, which are implicated in the progression of periodontitis. Consequently, reducing IL-6 levels could contribute to better management of periodontitis and improved oral health outcomes.

In recent years, research on the use of herbal plants for oral health has gained momentum. One promising herbal remedy is cinnamon (*Cinnamomum burmanni*), which contains essential oils, saponins, and flavonoids with potential antibacterial and anti-inflammatory properties (Laksmitawati et al., 2017). Results of research by Rahmani et al. (2017) found that a 50% cinnamon bark extract effectively inhibited the growth of *Porphyromonas gingivalis*, a bacterium associated with periodontitis (Mubarak et al., 2016). However, little research has been conducted on the effect of cinnamon bark extract on IL-6 levels in periodontitis treatment, which represents a critical gap in the literature.

This study aims to investigate the effects of a 50% cinnamon bark extract on reducing IL-6 levels in male Wistar rats induced with lipopolysaccharide (LPS)-triggered periodontitis. The findings will provide insight into the potential use of cinnamon bark extract as a natural anti-inflammatory agent in periodontal disease therapy, addressing the need for safer alternatives to traditional NSAIDs.

RESEARCH METHODS

This study is a preliminary study with a research design using a quasi-experimental research model with a posttest only control group design to assess the total IL-6 levels in male wistar rats (*Rattus norvegicus*) (Nisa & Primartha, 2014). This research was carried out at the Integrated Biomedical Laboratory of the Pharmacology Division, Faculty of Medicine, Udayana University (Nibali et al., 2012).

Cinnamon Bark Extract Manufacturing

The bark of the Cinnamon Stick is cleaned from the dirt that sticks, then washed under running water and dried in an oven with a temperature of 40°C for ± 3 days. After drying, it is cleaned again from dirt that is still attached. It is then ground and sifted using a 40 mesh sieve. Next, dry simplicia as much as 25 grams, 50 grams, each is put into a maceration vessel and then 100 ml of 96% ethanol is added then the vessel is closed. The vessel is stored in a place protected from sunlight for 5 days while repeatedly stirring, after 5 days the results are squeezed and then squeezed out. The extract obtained is stored in a cool place and protected from light for 2 days, after which the precipitate is separated (KK et al., 2013).

Induction of Periodontitis and Treatment of Experimental Animals

Rats were anesthetized with ketamine and xylazine injected as much as 0.2 ml to reduce pain in rats and make it easier for operators to provide treatment, then induction with Lipopolysaccharides (LPS) was injected intrasulcularly into the first incision gingival sulcus of the right lower jaw of the labial part with a dose of 5µg/0.05 ml PBS using a 30 G insulin needle

of 0.02 ml, given 8 times. After the first induction, the samples were randomly grouped into 2 groups (Rahmani, 2017).

Topical application of the gel

Topical application of the gel, noticed on the 8th day appeared clinical symptoms in the form of redness, loss of attachment and increasing depth of the periodontal pocket measured with a dental probe. Apply Tetracycline gel and 50% cinnamon bark extract to the gingiva using a cotton bud of 0.05 ml once a day for 21 days (Purnamasari, 2011).

Gingival Tissue Retrieval

Wistar rats are inhaled using blade no. 15, and gingival tissue was taken as a sample and a piece of tissue weighing about 250 mgr was placed in a 1.5 ml volume microtube containing 500 µL of PBS. Then tests were carried out on the sample with the Elisa kit test (Prasetya et al., 2014).

RESULTS AND DISCUSSION

The results of this study can be seen from the t-test that was carried out was the total level of IL-6 in the healing of periodontitis. Briefly, the results of the average calculation for both groups were reviewed from IL-6 levels.

Table 1 IL-6 levels

Group	n	Average	SB	Max	Min
Control	5	3,71	0.39	4,20	3,14
Treatment	5	2,65	0.20	2.94	2.37

The results in the table above show that there is a difference in IL-6 levels between group K (control) and group P (treatment). The content of cinnamon bark applied through an extract in the form of a gel in the sulcus of rat periodontal tissue has a local effect on the epithelial tissue of the gingival epithelium of LPS-induced wistar rats.

This study showed differences in the average number of IL-6 levels in the control and treatment groups. Based on these results, cinnamon bark extract with a concentration of 50% is more effective in reducing IL-6 levels.

Periodontitis as one of the periodontal diseases is caused by gram-negative bacteria such as *Porphyromonas gingivalis*, *Treponema denticola*, *Aggregatibacter actinomycetemcomitans*, *Prevotella intermedia*, and *Bacteriodes forsythus* contained in dental plaque. These bacteria produce products, one of which is endotoxins in the form of *lipopolysaccharides* (LPS).¹⁴ In periodontitis, pathogenic microbes increase inflammation, i.e., T cells, B cells, macrophages, and neutrophils with simultaneous increased inflammation of cytokines such as IL-1, IL-11, IL-6, TNF-, TGF-, kinin, and thrombin.⁵ Inflammation is an important biological response to injury in a variety of diseases. Some of the markers responsible for the inflammatory process are the type of reactive oxygen (ROS), the type of reactive nitrogen (RNS), cytokines, which are proteins involved in the initiation and further development process, as well as regulating the duration of the inflammatory response.³ Such as interleukin (IL)-1 β , IL-6, tumor necrosis factor (TNF)- α and nitric oxide (NO), and prostaglandins (Laksimitawati et al., 2017).

The largest content of cinnamon bark is essential oil which has the main content of cinamaldehyde compounds (60.72%), eugenol (17.62%) and coumarin (13.39%). These ingredients have the potential as antibacterial and antibiofilm.

Here's a revised version of your **Results and Discussion** section with added subpoints, analysis, and a concluding paragraph:

A. Does cinnamon bark extract significantly reduce IL-6 levels in periodontitis healing

The results of the t-test indicate that cinnamon bark extract effectively reduces IL-6 levels in the healing of periodontitis. The control group (K) had an average IL-6 level of 3.71 ± 0.39 , while the treatment group (P) showed a significantly lower IL-6 level of 2.65 ± 0.20 . These findings suggest that the 50% cinnamon bark extract gel applied to the periodontal tissues in Wistar rats helped decrease inflammation, as measured by IL-6 levels.

B. How does cinnamon bark extract affect inflammation markers in periodontal disease

Cinnamon bark contains bioactive compounds such as cinnamaldehyde (60.72%), eugenol (17.62%), and coumarin (13.39%), which have anti-inflammatory and antibacterial properties. These compounds likely contribute to the reduction of pro-inflammatory cytokines like IL-6 by neutralizing reactive oxygen species (ROS) and inhibiting the production of lipopolysaccharides (LPS) from gram-negative bacteria like *Porphyromonas gingivalis*, a known contributor to periodontitis. As a result, the immune response is modulated, reducing the overall inflammatory burden on periodontal tissues.

C. What are the potential therapeutic implications of using herbal extracts like cinnamon bark in periodontal disease treatment

The study's findings highlight the potential of using cinnamon bark extract as a safe, effective alternative to traditional anti-inflammatory drugs in treating periodontitis. The ability of cinnamon bark to reduce IL-6 levels, a critical marker in periodontal inflammation, suggests its promising role in managing chronic inflammation in periodontal diseases without the harmful side effects associated with prolonged use of non-steroidal anti-inflammatory drugs (NSAIDs).

Analysis and Discussion

The antibacterial and anti-inflammatory properties of cinnamon bark extract, particularly its high content of cinnamaldehyde and eugenol, are likely responsible for its efficacy in reducing IL-6 levels. Inflammation in periodontal tissues is often exacerbated by the presence of LPS produced by gram-negative bacteria, leading to increased cytokine activity. By suppressing this activity, cinnamon bark extract mitigates the damage caused by prolonged inflammation and oxidative stress, which can lead to tissue destruction in periodontitis.

Furthermore, the significant reduction in IL-6 levels in the treatment group aligns with findings from previous studies that suggest natural plant extracts can modulate immune responses and reduce inflammation. The ability to target specific inflammatory markers, such as IL-6, highlights the therapeutic potential of cinnamon bark in periodontal therapy, particularly for patients seeking herbal alternatives to conventional treatments.

This study demonstrates that cinnamon bark extract significantly reduces IL-6 levels in the treatment of periodontitis in Wistar rats, offering a natural and effective alternative to traditional anti-inflammatory drugs. Its high content of bioactive compounds, particularly cinnamaldehyde and eugenol, plays a crucial role in modulating the immune response and reducing oxidative stress. Future research could explore its long-term effects and potential applications in human periodontal disease management. These findings contribute to the growing body of evidence supporting the use of herbal remedies in dental care.

CONCLUSION

This study demonstrated that cinnamon bark extract (*Cinnamomum burmanni*) at a 50% concentration effectively reduces IL-6 levels in the treatment of periodontitis in Wistar rats. The reduction of IL-6, a key pro-inflammatory cytokine, suggests that

cinnamon bark can modulate the immune response in periodontal disease, offering a promising alternative to traditional anti-inflammatory drugs like NSAIDs. With its bioactive compounds, such as cinnamaldehyde and eugenol, cinnamon bark extract shows potential as a safer and natural anti-inflammatory agent for periodontal therapy. Future studies could further explore its therapeutic applications in human periodontal disease.

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