

Anti-inflammatory and antibacterial properties of insulin leaves (*Tithonia diversifolia*) for Periodontitis

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Abstract

Introduction: Periodontal disease or disorders can arise from disruption of homeostasis in the periodontal tissue. Ninety percent of people worldwide suffer from periodontal disease, making it the most common dental disease. Periodontitis may increase the rate of mortality and morbidity significantly. Prevention strategies can be carried out with alternative materials. The use of *Tithonia diversifolia* or insulin leaves has been practiced folklorically by different ethnic groups without scientific evidence, especially for the treatment of conditions related with pain and inflammation.

Methods: The search of literature is conducted through PubMed, Cochrane, the Web of Science, and Google Scholar using keywords for the role of insulin leaf extract (*Tithonia diversifolia*) as anti-inflammatory and antibacterial for periodontitis. Journal published at least five years ago is acquired. The journal covered the topics of various risk factors for Varicella. The criteria for this study are national and international accredited journals by Scopus and non-Scopus.

Results: Of the 15 articles reviewed, it is known that there is a role for insulin leaf extract (*Tithonia diversifolia*) in the treatment and prevention of periodontitis.

Conclusion: From the literature review article obtained, there are several roles of insulin leaf extract (*Tithonia diversifolia*) in the treatment and prevention of periodontitis with anti-inflammatory and antibacterial mechanisms. Using insulin leaves as mouthrinse can also improve oral health and reduce tooth decay.

Keywords: *Tithonia diversifolia*; Periodontitis; Anti-inflammatory; Antibacterial

1. Introduction

A wide variety of bacteria, fungi, and viruses can be found in the oral cavity, and they all play a crucial part in maintaining the health of the mouth and the body. On the other hand, "microbial dysbiosis," or a disruption in the oral microbiota's equilibrium, the pathogen causes a number of systemic diseases by purposefully evading the body's immune response. Overall health and oral health are interdependent and have an impact on one another.^{1,2}

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The composition of tissue surrounding the tooth is one of the major variables that affects dental health. The structural components of the periodontium are gingiva, connective tissue underneath it, the root's surface covered in cementum, alveolar bone, as well as the periodontal ligament that joins it to the cementum.³ Periodontal tissue has three specific purposes for the tooth: to keep the tooth firm in place, to protect the teeth from the bacteria in the mouth, and to adhere the tooth to the bone.^{4,5} Homeostasis disorder in the periodontal tissue may lead to an abnormality or periodontal disease.

Periodontal diseases or abnormalities can arise from homeostasis disorders in the periodontal tissues.⁴ The global burden of periodontal disease increased by 25.8% between 2006 and 2016. Periodontal disease, especially mild to moderate cases, is common in the adult population around the world, with a prevalence rate of approximately 50%.^{3,4} Based on age norms, Indonesia had a higher incidence and prevalence of severe periodontitis in 2010 (17% and 747 per 100,000 people each year) than the world average. There are 74 cases of periodontitis (0.1%) in Indonesia today. According to the Basic Health Research (Riset Kesehatan Dasar/Riskesdas) data in 2018, the Province of Central Java has the highest number of dental and oral health problems, followed by the West Java and East Java.^{6,7}

Periodontal disease is mostly caused by bacterial invasion in the oral cavity. The two main facultative anaerobic Gram-positive bacteria that colonize the oral cavity are *Actinomyces* and *Streptococcus*. Periodontitis is a complex disease with several risk factors, such as diabetes mellitus (DM), smoking, and, most often, inadequate oral hygiene (OH). Ineffective tooth brushing, neglected interdental cleaning, and insufficient dental examinations are the main causes of accumulation in plaque and dental calculus.^{8,9}

Periodontitis may increase a person's mortality and morbidity. Therefore, prevention and treatment must be done immediately. Preventive strategies can be done with medicines and alternative ingredients. The use of *Tithonia diversifolia* or insulin leaves has been practiced folklorically by different ethnic groups without scientific evidence, especially for treating conditions associated with pain and inflammation. In its native region and the majority of its invasive territory, *Tithonia diversifolia* is used as a medicinal source to treat a variety of illnesses. The leaves are also useful as anti-bacterial, anti-inflammatory and anti-oxidant.^{10,11} However, its role in the prevention and treatment of periodontitis has not been well proven. Based on the explanation, In order to treat periodontitis, we are interested in investigating the anti-inflammatory and antibacterial qualities of insulin leaf extract (*Tithonia diversifolia*).

2. Methodology

2.1. Terms and Search Strategy

International online databases (Science Direct, PubMed, Research Gate, Cochrane Library, and Google Scholar) are used to search for articles in this systematic review. The search term is based on adapted PICO questions and MeSH terms such as "*Tithonia diversifolia*" OR "insulin leaves" AND "anti-inflammatory" AND "antibacterial" AND "periodontitis". All articles published between 2018 and 2023 are included in this study.

2.2. Inclusion and Exclusion Criteria

The method in this research uses a library study through several journals obtained. The inclusion criteria are:

- The journals included in this research are research articles, editorial, commentary, library reviews in quantitative, qualitative or mixed method research.
- Research articles on health or related topics released no more than 5 years ago.
- The journal discussed the role of insulin leaf extract (*Tithonia diversifolia*) as an anti-inflammatory and anti-bacterial for periodontitis.
- There are 15 articles that fulfilled the inclusion criteria and mainly discussed oral health and the role of insulin leaf extract (*Tithonia diversifolia*) as anti-inflammatory and anti-bacterial for periodontitis.

3. Results

Through the review and selection process, 15 journals that meet the inclusion and exclusion criteria and are pertinent to the study were found by the researchers. Every article that is used is written in English. Based on the results of the articles reviewed, there are several roles of insulin leaf extract (*Tithonia diversifolia*) in the treatment and prevention of periodontitis with anti-inflammatory and anti-bacterial mechanisms. Using insulin leaves as mouthrinse can also improve oral health and reduce tooth decay.

4. Discussion

4.1. Periodontitis

The disease known as periodontitis first affects the gingival tissue. If untreated, this inflammation can spread to deeper tissues, upsetting bone homeostasis and leading to tooth loss. One of the most prevalent conditions that harms teeth is periodontitis, which results in the loss of the surrounding and supporting tissues.¹² Globally, periodontal disease affects between 20-50% of people.¹³ The main organisms associated with deep destructive periodontal lesions are *Porphyromonas gingivalis*, *Prevotella intermedia*, *Bacteroides forsythus*, *Actinobacillus actinomycetumcomitans*, and *Treponema denticola*.^{14,8} The primary goals of periodontal therapy are to halt additional tissue damage and lessen the spread of infection and inflammation. The degradation of periodontal tissue can be stopped by eliminating pathogenic biofilms and reducing inflammation, but the amount of tissue that can be recovered is limited and varies based on age, systemic health, and the type of tissue damage. In advanced cases, additional systemic antimicrobials to lower the pathogen load or surgery to remove residual pockets in order to improve the ecology of the periodontal site are sometimes combined with the active anti-infective treatment phase.^{3,12}

4.2. *Tithonia diversifolia*

The use of *Tithonia diversifolia* has been practiced folklorically by different ethnic groups without scientific evidence, especially for the treatment of pain and inflammation related conditions. *Tubaeformis Tithonia (Jacq.) Cass.* is a member of the *Tithonia* genus (family: *Compositae*) of medicinal plants native to Mexico, commonly known as Mirasol (Acahualí). *T. Tubaeformis* is a three-meter-tall shrub with highly pubescent, non-lobed leaves and solitary, compound, yellow ligule flowers with 120 florets. Its phylum is distinguished by its linear pubescence. The 13 taxa that make up the genus *Tithonia* are divided into 11 species, the most studied of which is *T. diversifolia*, which has potent anti-inflammatory, analgesic, antimalarial, antiviral, antidiabetic, antidiarrheal, antimicrobial, chemotherapeutic, antiemetic, bioinsecticide, and repellent qualities. This plant has been traditionally used to treat chronic painful and debilitating joint conditions, and it is of great interest for phytomedicine research and health care. Extracted plant extracts and compounds have been shown in experiments to have potential anti-inflammatory and antinociceptive effects, in addition to other significant medicinal qualities. Animal nociception models with varying degrees of noxious stimuli (thermal stimuli and chemically induced tissue damage) have been used to study *T. diversifolia*'s analgesic properties.^{15,10} According to Guinoiseau et al., the properties of essential oils weaken bacterial cell walls, which can enhance the potential antimicrobial activity of *T. diversifolia* species. As a result, using essential oils as an antimicrobial agent may be more effective.¹⁶

4.3. Anti-inflammatory and Antibacterial Properties of Insulin Leaves (*Tithonia diversifolia*) for Periodontitis

Tithonia diversifolia extract showed antinociceptive effects, in mouse models. Likewise, several phytochemical compounds have been identified such as saponins, tannins, phenols, and flavonoids in the methanol extract, which have anti-inflammatory activity. Previous research showed that there is a difference in the number of lymphocytes in Wistar rats with periodontitis after being given insulin leaf extract gel versus those not given. Insulin leaf extract gel and a concentration of 75% was the most effective dose for reducing the number of lymphocytes in Wistar rats with periodontitis. Similar to nonsteroidal anti-inflammatory drugs, the extract inhibits edema but does not inhibit cell recruitment. Stronger antimicrobial activity of the extract was observed against cariogenic microorganisms. When both extracts were added to human gingival fibroblasts at non-toxic concentrations, *Streptococcus mutans* was significantly less likely to produce acid.^{17,18,19}

Another study from Broering et al. (2019) showed oral administration of *T. diversifolia* resulted in decreased neutrophil migration, total protein, TNF, IL-1 β , and CXCL1 levels in inflammatory exudates. *T. diversifolia* treatment in vitro may release β 2 integrin expression while leaving CD62L expression unchanged. The complicated process of attracting neutrophils to inflammatory sites involves both molecular and cellular mechanisms. Neutrophils exhibit the expression of β 2-integrin during this phase, which plays a crucial role in facilitating the strong attachment of neutrophils to the endothelium and their eventual transmigration to the extracellular matrix. Following transmigration, chemotactic mediators released by activated resident cells cause neutrophils to migrate straight to the site of injury. Then, by releasing intracellular granules and nuclear contents and engaging in vigorous phagocytosis, neutrophils eliminate harmful agents from the inflammatory tissue, producing reactive oxygen species (ROS) and nitrogen (RNS). Later on in the phase of inflammation resolution, neutrophils die so that they can be phagocytosed by M2 macrophages that are anti-inflammatory. In order to successfully resolve inflammation and initiate tissue repair in the oral region and prevent additional periodontal tissue infection, it is imperative that this process be followed.²⁰ Additionally, it was demonstrated that these leaves prevented the formation of acid at concentrations lower than the bactericidal concentrations found

for *S. mutans*. This suggests that the inhibition may have resulted from a direct impact on the bacterial glycolytic pathway rather than from antibacterial activity.²¹

5. Conclusion

There are several roles of insulin leaf extract (*Tithonia diversifolia*) in the treatment and prevention of periodontitis with anti-inflammatory and antibacterial mechanisms. Using insulin leaves as mouthrinse can also improve oral health and reduce tooth decay.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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