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Solanum xanthocarpum: Nature's Remedy for Healthy Periodontium- Unveiling the Therapeutic Potential against Chronic Periodontal Diseases

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Abstract

Solanum xanthocarpum, commonly known as yellow-fruit nightshade, is a noteworthy herb in the ayurvedic medicine belonging to the Solanaceae family. This perennial herb is widely distributed in tropical and subtropical regions, especially in India and Southeast Asia. The plant is characterized by its thorny stems, small purple flowers, and distinctive yellow berries. Traditionally, Solanum xanthocarpum has been used in the treatment of respiratory disorders, fever, and inflammatory conditions. Phytochemical studies reveal that the plant is rich in bioactive compounds like alkaloids, flavonoids, and steroids, which contribute to its therapeutic properties with notable antioxidant, anti-inflammatory, and antimicrobial activities. Periodontitis is a chronic inflammatory disorder, multifactorial in origin, and destroys the supporting periodontal apparatus by triggering the inflammatory cascade. Inflammation and the disruption of the equilibrium between oxidative stress and antioxidants play a pivotal role in the disease progression. This is mainly treated by mechanical debridement of the biofilm, local drug delivery of antibiotics and anti-inflammatory agents, and surgical management if deemed necessary. The inadvertent use of antibiotics has led to the emergence of resistance to drugs. Advances in research have validated the pharmacological properties of traditional medicine, whose properties outweigh the constraints of antibiotics. Thus, Solanum xanthocarpum could be one such plant whose derivatives could be used in the treatment of periodontitis. This review emphasizes the potential of Solanum xanthocarpum to be formulated and utilized in the prevention and management of periodontal diseases.

Keywords: *Antibacterial, Antioxidant, Anti-Inflammatory, Alkaloids, Flavonoids, Periodontitis, Solanum xanthocarpum.*

Introduction

Periodontitis is an infectious disease characterized by inflammation of the tooth-supportive tissues, which gradually destroys the periodontal ligament, and alveolar bone and eventually causes tooth loss. It is the major cause of tooth loss and the sixth most prevalent

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disease condition globally [1]. The prevalence of periodontitis among adults aged over 30 years is considerably high, and it ranges up to 64% in adults aged >65 years. Periodontitis poses a major threat to public health by causing disability in mastication, leading to a negative impact on general health [2]. In addition, it significantly affects patients' oral health-related quality of life (OHRQoL), adversely impacting their functional and psychological well-being.

The anatomy of the periodontium is varied. It consists of soft tissues, namely, the gingiva and the periodontal ligament, and hard tissues, namely, cementum and the alveolar bone. The hallmark of periodontitis is chronic inflammation and alveolar bone loss due to the stimulation of osteoclastogenesis, which is irreversible and leads to the destruction of periodontium [3]. Periodontitis is multifactorial in origin, primarily of microbial aetiology along with other risk factors like chronic systemic illness or condition, genetic polymorphism, smoking, obesity, and immunosuppression [4].

Periodontal disease is strongly associated with red complex organisms, *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola*. Although they are present in minor constituents, the influence of these organisms on the oral ecosystem is much stronger by altering the quantity and community organization of commensal bacteria at the site and dysregulating innate immunity pathways. One of the principal mechanisms of periodontal destruction is the evasion of the host defence mechanism. The progression of periodontitis is caused by a plethora of factors, including an anaerobic milieu, inflammatory conditions, and an enormous number of substrates originating from tissue destruction, all of which enhance the growth of inflammophilic periodontal pathogens and pathobionts [3]. In addition, periodontitis is stimulated by a reciprocally reinforced association between a dysbiotic microbiome and dysregulated inflammation. Inflammation, via mediating tissue dysfunction and damage, drives further growth of selectively dysbiotic communities of bacteria (inflammophiles), thereby evolving a self-sustained perceptron loop that perpetuates the disease [5]. Thus, this condition is primarily attributed to polymicrobial origin, and its progression is multifactorial.

Characteristics of Chronic Periodontitis

A hallmark of chronic periodontitis is the occurrence of periodontal pockets and gingival recession, gradually leading to tooth mobility and eventual tooth loss if not intervened. However, it has garnered significant attention due to its influence on systemic diseases and conditions. Since the late 1980s, studies have supported the causal association between systemic health and periodontitis. This association could be due to the direct spillover of the microbial burden to the circulation, such as in cardiovascular disease, or indirectly by the chronic inflammatory burden, which initiates systemic diseases such as rheumatoid arthritis and type 2 diabetes Mellitus [6]. Evidence from the literature strongly demonstrates a bidirectional link between periodontitis and diabetes, in which the inflammatory burden in periodontitis exacerbates insulin resistance. On the other hand, advanced glycation end products produced due to the hyperglycemic state of diabetes potentially enhance periodontal destruction [7].

Furthermore, chronic periodontitis is associated with cardiovascular diseases. Inflammatory mediators released in periodontitis, such as cytokines and prostaglandins, contribute to atherogenesis and thromboembolic events. Studies have also demonstrated higher incidences of coronary artery disease and stroke in patients with periodontitis [8]. In addition, chronic periodontitis elicits a negative impact on pregnancy outcomes with the risk of preterm birth and low birth weight [9]. The morbidity and mortality rates of type 2 diabetes Mellitus, cardiovascular disease, and rheumatoid arthritis

are elevated with the prevalence of periodontitis. The association of periodontitis with various systemic diseases and conditions is represented in Figure 1. Hence, periodontitis is a complex disease with a nonlinear character, and its consequence on immune response is rather disproportional. The treatment of periodontitis targets preventing further disease progression, minimizing symptoms, restoring lost tissues, and supporting patients in maintaining a healthy periodontium.

Figure 1. Association of Periodontitis with Various Systemic Diseases and Conditions

Modes of Periodontal Therapy

The periodontal treatment utilizes a plethora of therapeutic interventions to achieve these goals, such as individually tailored oral hygiene instructions, smoking-cessation support, subgingival instrumentation to remove plaque and calculus, local and systemic pharmacotherapy, and surgical interventions [1]. The management requires a combination of therapeutic modalities and a lifelong commitment to periodontal self-care.

The primarily advised approach and the cornerstone of periodontal therapy is Nonsurgical Periodontal Therapy (NSPT). The various modes of periodontal therapy are depicted in Figure 2. It includes plaque removal, control, supragingival and subgingival scaling root planing (SRP), and adjunctive use of chemical agents. However, the complete removal of the periodontopathogens is questionable in conventional mechanical debridement, especially in inaccessible areas such as furcation, grooves, concavities, and deep pockets. The literature states that the effects of mechanical therapy might be augmented using antimicrobial agents, which further control the colonization of the remaining pathogens [10]. Other recent advances that have gained popularity as an adjunct to NSPT are the application of lasers, photodynamic therapy (PDT), and hyperbaric oxygen therapy. One emerging solution used as an adjunct to mechanical debridement is herbal medicine. They gained recognition due to the resistance developed by the microbial strains to conventional antibiotics [11].

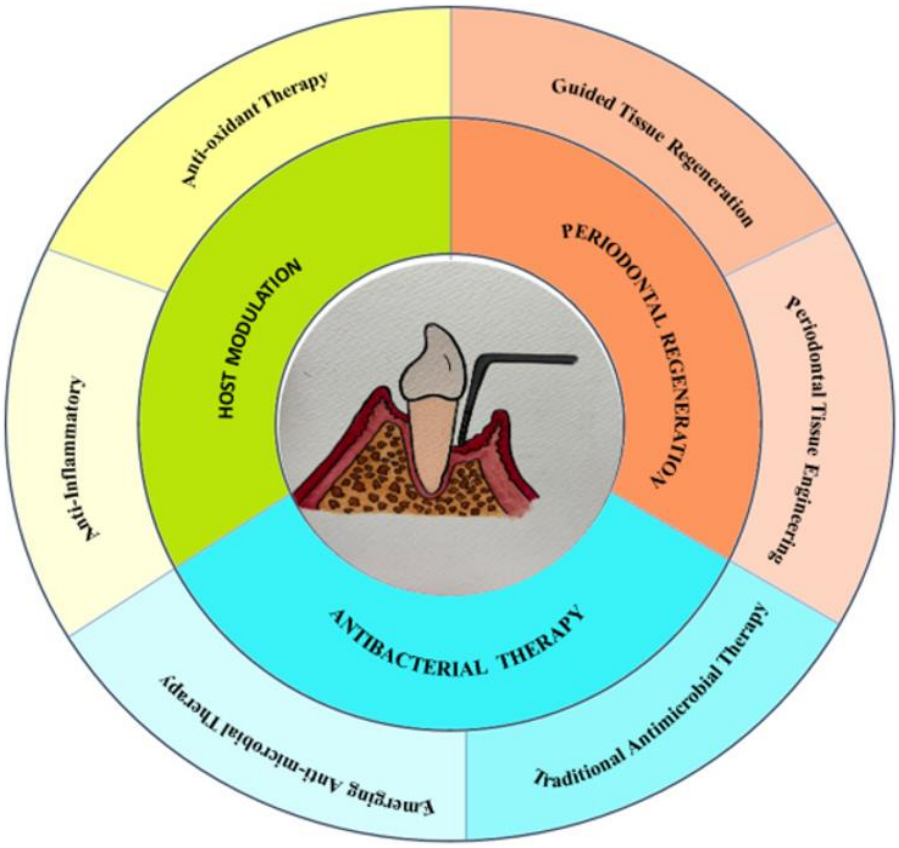

Figure 2. Various Modes of Periodontal Therapy

Possible Role of Phytotherapy in Periodontal Diseases

Phytotherapy is defined as treating a disease or condition using health-promoting plants. Most herbal components possess several beneficial properties, such as antibacterial, anti-inflammatory, analgesic, and antioxidant, making them a potential treatment option for chronic inflammatory diseases. According to Karygianni *et al.*, in their systematic review, *Azadirachta indica*, *Camellia Sinensis, Coffea arabica,* and *Mikania laevigata* possessed antagonist activity against *Streptococcus spp*. *S. persica* and *Solanum xanthocarpum* also showed antibacterial activity [12]. Thus, an ideal and systematic methodology in the selection and biological evaluation of plant-based products could lead to the development of new alternatives.

Solanum xanthocarpum- Opening Avenues in Periodontal Therapy

Solanum xanthocarpum (SX) belongs to the *Solanaceae* family, commonly called the Indian nightshade or yellow berried nightshade. It is a wild plant that thrives in dry and tropical areas and is distributed in India, Southern China, Arabia, Sri Lanka, Malaysia, Vietnam, and Thailand. It is considered one of the dashamula (ten roots) in Ayurveda. SX is commonly used for its medicinal properties, such as expectorant, antipyretic, anti-inflammatory, anti-allergic, and antifungal properties in Ayurveda. It has been used for treating ailments such as asthma, chronic cough and catarrhal fever, rheumatic arthritis, toothache, sore throat, carbuncle, furuncle, and other inflammatory diseases [13,14,15]. Figure 3 shows a schematic representation of the possible role of SX in the management of periodontal diseases.

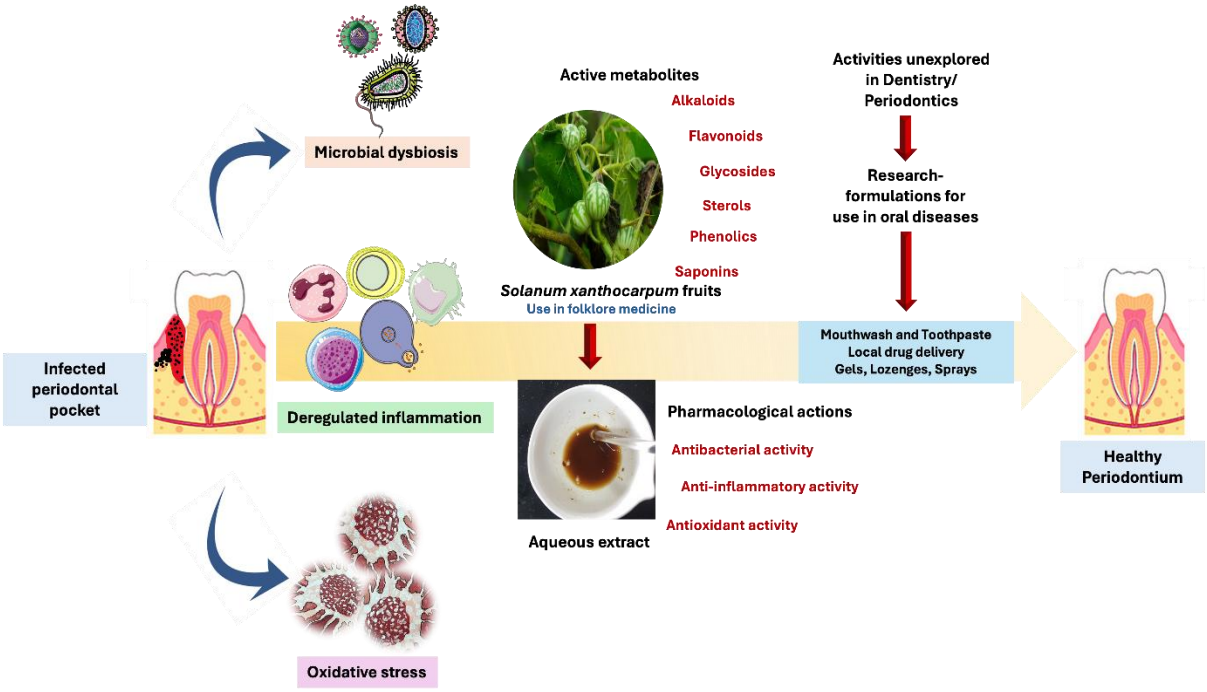

Figure 3. Schematic Representation of The Possible Role of Solanum Xanthocarpum in The Management of Periodontal Diseases

Morphologic and Chemical Characteristics

Solanum xanthocarpum is an herbaceous plant. It generally flourishes from March to April and fruits from May to June. It is a bright green herb, prickly with a woody base, which is perineal and grows to 2-3 m with zig-zag-like arranged branches. The leaves are either ovate or elliptical, 5-10 in number per branch with 2.5-5.7 cm [16]. They are sub-pinnatifid or sinuate. They bear yellow or white coloured fruits encased in an enlarged calyx, which ranges up to 1.3 cm in diameter. The fruit yields sterols such as solanocarpidine and campesterol, and their seeds are used as diuretics. They encompass flavones, phenolics, and coumarins such as apigenin, scopoletin, and esculetin. Components like campesterol, sitosterol, cycloartenol, stigmasterol, and lupeol, categorized as steroids and triterpenoids, are also isolated. Steroidal alkaloids and glycoalkaloids such as solasodine, diosgenin, and solamargine are also present, along with potassium nitrate, fatty acid, histamine, and acetylcholine [16]. Some of its key bioactive components and their pharmacological activities are documented in the literature and are shown in Table 1.

Table 1. *Solanum xanthocarpum:* Active Components, Known for Their Various Pharmacological Properties

Component Name	**Category**	**Key Properties and Uses**
Solasodine	Alkaloid	Utilized in steroid production, possesses fever-reducing effects and antimicrobial activity.
Solasonine	Glycoalkaloid	Known for anti-inflammatory and cancer-fighting properties
Solamargine	Glycoalkaloid	Demonstrates cytotoxicity against cancer cells
Diosgenin	Steroidal Saponin	Precursor for synthesizing corticosteroids and sex hormones
Solanocarpine	Alkaloid	Shows antimicrobial effects

Tomatidine	Glycoalkaloid	Exhibits anti-inflammatory and anticancer activities
Chlorogenic Acid	Phenolic Acid	Acts as an antioxidant and reduces inflammation
Caffeic Acid	Phenolic Acid	Possesses antioxidant and anti-inflammatory qualities
Kaempferol	Flavonoid	Antioxidant combats inflammation and exhibits anticancer effect
Quercetin	Flavonoid	Has strong antioxidant properties, reduces inflammation, exhibits anticancer activities
Ferulic Acid	Phenolic Acid	Functions as an antioxidant and anti-inflammatory agent
Rutin	Flavonoid	Supports cardiovascular health and acts as an antioxidant
Beta-sitosterol	Phytosterol	Lowers cholesterol, has anti-inflammatory properties
Tropine	Alkaloid	Exhibits anticholinergic effects
Lupeol	Triterpenoid	Exhibits anti-inflammatory, anticancer, and antimicrobial activity

Pharmacological Properties (Table 2)

Anti-Inflammatory Activity

Chronic diseases usually present with chronic inflammation, as seen in auto-immune disorders, cancer, arthritis, and vascular conditions. Various herbaceous compounds possess anti-inflammatory properties; *Solanum xanthocarpum* is one such compound. Solanidine, α-solanine, and α-chaconine are the phytochemicals obtained from them and exhibit potent anti-inflammatory properties. This property is claimed by targeting the phosphatidylinositol-3-kinase (P13)/Akt, Fas, Wnt/βcatenin, kappa B (NFkB), cFLIP, and Kras nuclear factors in a variety of cells [17]. Pungle *et al.*, stated that SX exhibits its anti-inflammatory property by preventing the denaturation of proteins, which was equivalent to the efficiency of diclofenac [18].

Lupeol, another component obtained from the SX, affects and targets the inflammatory pathways. Studies state that when administered at therapeutic dosage, lupeol does not exhibit any toxicity to the normal cell, claiming its role in anti-inflammatory treatment [16]. Our previous study also states that SX aqueous extracts exhibit potent anti-inflammatory potential, which may be attributed to the presence of lupeol.

A crucial mechanism in upregulating the inflammatory process is through the protease. Serine protease plays a pivotal role in triggering the inflammatory process. The protease inhibitors antagonize the inflammatory response, facilitated by mediators released by leukocytes in response to proteases. The extracts from the seeds of SX had an analogous effect with proteinase inhibitors [18].

Another persuasive pro-inflammatory mediator is Nitrous Oxide (NO). They are biphasic, i.e., under physiological conditions, the NO produced by the endothelial cells is anti-inflammatory. In contrast, when the NO production is upregulated in the inflammatory condition, it leads to collateral damage [19]. SX also possesses an anti-inflammatory effect on these pathways. Zhen-Peng Xu *et al.*, stated that extract from the SX fruits showed an anti-inflammatory effect by downregulating the LPS-induced NOS. The molecular docking studies reveal that the phenolic compound from the SX extracts has a high affinity towards the iNOS proteins by targeting the residues of the active cavities of iNOS [20].

The extracts of the fruits of SX possess immunomodulatory activity. Rokeya Sultana *et al.*, in their study, assessed them immunomodulatory action of the extracts of SX fruits in cyclophosphamide immunosuppressed rats and stated that the extract-treated animal

had overcome the side effects of the drugs. The results indicate that the extracts have balancing and adaptogenic potential, and they also provide a non-specific immune response by increasing the margination of the neutrophils [21].

Antioxidant Properties: Free Radical Scavenging Activity

Free radicals such as the reactive oxygen species, nascent oxygen, and hydrogen peroxide are produced due to the prolonged activation of the phagocytes, which again pose a threat to the host tissues along with the antigen either by membrane destruction by lipid peroxidation or by activating the matrix metalloproteinase (MMP) [22]. Thus, any approaches targeting free radicals are favourable antioxidant treatment options. SX shows promising avenues in this aspect. Kumar *et al.,* stated in their study that SX showed superior free radical scavenging properties when using the DPPH assay [23].

Lipid peroxidation also creates oxidative stress initiated by the $Fe_3^{+,}$ which produces peroxyl radicals when reacting with lipid hydroperoxides, which produce malondialdehyde (MDA). This phenomenon is counteracted by the extracts of SX by quenching the Fe_3^{+}, thus preventing oxidative stress [15].

Anti-Asthmatic Properties

Bronchial asthma is an airway inflammatory disorder characterized by bronchial hyperresponsiveness, airway obstruction, and airway eosinophilic inflammation. Globally, 7-10% of the population suffers from the disorder. Various treatment regimens are put forth; most provide only symptomatic and are short-lived with varied side effects. Thus, the focus turns toward phytotherapy, and various studies elicit the anti-asthmatic and anti-allergic properties of the SX. The pathophysiology of asthma is smooth muscle contraction, upregulation of histamine, eosinophils, and mast cell degranulation. Various studies on Solanum species elicited smooth muscle relaxation and antihistaminic properties [24]. This paved the way for conducting research in the phytochemicals of solanum species for therapeutic approach.

Gautham *et al.,* in their study, stated that ethanolic extract of SX promoted antagonistic activity of mast cell degranulation, antihistaminic activity, and smooth cell relaxation of the histamine-induced goat tracheal chain preparation. This property instigates SX extract in treating bronchial asthma [25].

Govindan *et al.,* compared extracts of SX with conventional bronchodilators such as theophylline and salbutamol by assessing respiratory function. The results claimed that SX extracts alleviate asthma symptoms but are less efficient than theophylline and salbutamol [26].

Apigenin is another flavonoid found in the SX extracts. It exhibits anti-inflammatory action. Choi *et al.* created an ova-albumin-induced asthma model in mice. The test animals presented with an increase in eosinophil count and bronchoconstriction. Administration of apigenin to mice decreased the burden of the allergens [27].

Antibacterial Activity

The resistance to antimicrobial therapy has paved way for research to elucidate natural alternatives. Along with other health benefits, SX also possesses antibacterial activity. Gavimath *et al.,* stated that SX extracts exhibited a zone of inhibition to Gram-positive organisms such as *Corynebacterium diphtheriae* and Gram-negative organisms such as *E coli* and *Pseudomonas spp* [28].

Our previous studies evaluated the antibacterial properties of SX extracts against bacteria isolated from the dental plaque biofilm of patients with gingivitis. Different extracts of SX were prepared with solvents, namely, ethanolic, aqueous, ethyl acetate, chloroform,

and hexane, and tested at various concentrations. The findings revealed notable antibacterial activity, with the ethanolic extract demonstrating the highest efficacy [29].

Antifungal Activity

The extracts of the *Solanum xanthocarpum's* fruit and roots were tested on four fungal pathogens, namely, *Rhizoctonia solani, Rhizoctonia bataticola, Fusarium solani, and Alternaria alternata* by poison food technique and bavistin (a broad-spectrum systemic fungicide) was used as a standard fungicide. A profound antifungal activity of SX was noted against the above species [30].

Notable zones of inhibition were observed when the *Aspergillus niger* was treated with the methanol extracts of the SX [31]. Thus, SX could be considered a potential source of natural antifungal agents with good economic and significant medicinal importance.

Anti-HIV Activity

Various studies have demonstrated that the phytochemicals are anti-replicative and anti-infective agents to viruses such as herpes simplex, adenovirus, para-influenza, and respiratory syncytial [32]. According to Kumar S *et al.,* the extracts of the SX fruits exhibit low inhibitory levels of HIV RT. Since the crude extracts contain various chemical constituents, isolation of the specific moiety can enhance the inhibitory activity [15].

Hepato-Protective Activity

Jigrine is an herbal formulation containing 14 medicinal plant aqueous extracts, including SX, used for liver disease. The study by Najmi *et al.,* stated that Jigrine, a component of SX, has hepatoprotective potency and scavenges DPPH free radicals against galactosamine-induced hepatotoxicity in rats [33].

Ramesh *et al.,* in their study, demonstrated that the administration of SX extract to experimental animals subjected to liver injury induced by CCl4 administration showed a dose-dependent decrease in the serum hepatic enzymes. Moreover, it lowered the lipid peroxidation level in the liver and reestablished the activity of enzymes, namely, glutathione, superoxide dismutase, and catalase [34].

Anti-Helminthic Effect

The ethanolic extracts of SX revealed the anti-helminthic activity by paralyzing and killing the worms compared to piperazine citrate. The efficiency was higher when administered at higher concentrations [35].

Table 2. Studies Demonstrating Pharmacological Effects of Phytocomponents in *Solanum xanthocarpum*

S No	Phytocomponent of Solanum xanthocarpum	Inference	References
Anti-Inflammatory Properties			
1	Solanidine, α-solanine, α-chaconine	Anti-inflammatory property is achieved by targeting the phosphatidylinositol-3-kinase (P13)/Akt, Fas, Wnt/βcatenin, kappa B (NFkB), cFLIP, and Kras nuclear factors in a variety of cells.	17
2	Lupeol	Lupeol elicits anti-inflammatory properties by inhibiting the inflammatory pathways.	16
3	Ethanolic extract of seeds and leaves of SX	The SX extract showed an inhibition of albumin denaturation.	18
4	Extracts of SX fruit	Extracts from the SX fruit down-regulate LPS induced inflammation.	20
Antioxidant Properties			

1	Extracts of SX roots	SX root extracts exhibit superior free radical scavenging properties.	23
2	Extracts of SX fruits	The antioxidant potential of the SX extract is obtained by quenching the Fe_3^+, thus preventing the oxidative stress by downregulation.	15
Anti-Asthmatic Properties			
1	Extracts of SX flowers	Ethanolic extract of the SX promoted antagonistic activity of mast cell degranulation, antihistaminic activity, and smooth cell relaxation of the histamine-induced goat tracheal chain preparation.	25
2	Extracts of SX	Extracts of SX, in comparison with theophylline and salbutamol, alleviate the symptoms of asthma.	26
3	Apigenin	Administration of apigenin to mice decreased the eosinophilic count and bronchoconstriction.	27
Chemotherapeutic Activity			
1	Extracts of SX	SX extracts revealed a zone of inhibition to Gram-positive organisms and Gram-negative organisms.	28

Discussion

According to WHO, 80% of the world population relies on traditional medicines as primary health care [36]. The plant kingdom contributes to a varied structural biodiversity. Compared with synthetic substances, natural products offer the forecasts of discovering more compounds with sterically more complex structures and new pharmacophores. In the investigation of the bioactive compounds, only 5-15% of the plant kingdom has been studied, thus stating that, nature's biodiversity largely remains unexplored, paving the way for a new evolution in phytochemistry [37]; one such species is *Solanum xanthocarpum*.

Being an annual herbaceous plant, *Solanum xanthocarpum* is widely distributed throughout South Asian countries and is known for its varied medicinal properties, which are channelized by its phyto-components such as alkaloids, sterols, saponins, flavonoids, and their glycosides. Traditionally, they are used for their anti-inflammatory, antimicrobial, antioxidant, anti-asthmatic, and hepato-protective activity [38]. Yet, enormous properties are still unexplored, which opens the gateway for research in SX phytochemistry.

In our previous study, the pharmacological properties of the aqueous extract of *S. xanthocarpum* were investigated, revealing significant antioxidant, anti-inflammatory, and antimicrobial effects. Active phytochemical components were identified through gas chromatography-mass spectrometry (GC-MS) analysis. Molecular docking and simulation studies highlighted the interaction between the phytochemicals, Solasodine, Lupeol, and Quercetin and the RgpB protein of *Porphyromonas gingivalis*, further indicating that Lupeol exhibited the highest binding energy [39]. These findings suggested that *S. xanthocarpum* formulations hold promise as adjuvants to mechanical therapy in managing periodontal diseases.

According to Pungle R *et al.,* SX ethanolic extracts of seeds and leaves demonstrate anti-inflammatory and antioxidant activity due to the presence of alkaloids in the extracts [18]. The anti-inflammatory activities are achieved by membrane stabilization, protease inhibitor activity, targeting the inflammatory pathway, or scavenging the free radicals [17, 18]. During inflammation, the neutrophils are primed and release the lysosomal enzymes by the

degranulation of the cells. This mechanism is known to be controlled by the alkaloids of SX by stabilizing the membrane.

According to Xu *et al.*, the SX extracts down-regulate the LPS and the NOS by targeting their inflammatory pathway. It was also noted that the SX extracts have a higher affinity towards the iNOS and exhibit their antioxidant activity [20]. Gavimath *et al.*, stated that the SX extracts inhibit the gram-positive and gram-negative bacterial colonies [28].

Periodontitis is a multifactorial disease in origin, which is primarily initiated by the microbial biofilm and supplemented further by the host-microbial interaction, leading to chronic inflammation and destruction of the tooth-supportive structures. The inflammatory processes are initiated by bacterial endotoxins, such as LPS [40]. To counteract the microbial emergence, there is an increase in the inflammatory infiltrates, priming of the neutrophils, and upregulation of the pro-inflammatory cytokines. Thus, SX has proven potential pharmacological activities in various medical attributes, and its role in periodontal pathogenesis has recently been emphasized and explored. Thus, it can be concluded that optimum concentrations of SX in various formulations could be used in therapeutic strategies to prevent and manage periodontal diseases.

Potential Formulations and Applications of *Solanum xanthocarpum* Extract in Periodontal Disease Prevention and Management

Several formulations based out of herbal extracts have been investigated for managing periodontal diseases [41-43]. The properties discussed above demonstrate the potential use of SX extract in various formulations for preventing and managing the periodontal disease process. Mouthwashes containing this extract can effectively deliver its antibacterial, antioxidant, and anti-inflammatory properties to all parts of the oral cavity, reducing the pathogenic bacteria and regulating oxidative stress and inflammation. Integrating the extract into toothpaste can prove a viable option for delivering its daily dosage effortlessly, which in turn can aid in preventing gingival inflammation. In case of gingiva showing clinical signs of inflammation, topical gels can be applied, which may offer targeted delivery of anti-inflammatory effect and promote healing. The extract can also be incorporated into local drug delivery devices like films and fibres, providing sustained release of active substances for managing the disease process. SX extract can also be infused into periodontal dressings for its use post-surgically which can help prevent infection and enhance healing. In addition, bioactive phytochemicals can be separately isolated from the crude extract and can be incorporated into various drug delivery substrates to obtain a targeted effect. Moreover, other drug delivery aids, such as oral sprays, lozenges, and chewing gums can be formulated to prevent and manage different forms of periodontal diseases. Each of the above-mentioned formulations can be effectively customized to meet specific requirements, thus facilitating oral/periodontal health and combating disease progression.

Future Directions and Conclusion

Further, *in-vitro* studies should be conducted to investigate the molecular and cellular processes through which SX may exercise its action in counteracting the progression of periodontal disease. Understanding these intricate processes may guide in refinement of formulations to meet the specific needs of patients. In addition, the long-drawn-out effects of these SX-based formulations should be validated through clinical studies. Moreover, safety and cytotoxicity studies should be conducted to ensure that formulations are free from causing adverse effects. Informing several sectors of healthcare professionals, especially dental professionals and patients, about the usefulness of such formulations may play a

pivotal role in incorporating them into routine use. To conclude, the current review emphasizes that these nature-based formulations render a potent substitute to conventional antibiotic-based therapies and intend to support the growing body of evidence for a patient-centred and holistic approach in preventing and treating periodontal diseases.

References

[1]. Graziani F., Karapetsa D., Alonso B., Herrera D., 2017, Nonsurgical and surgical treatment of periodontitis: how many options for one disease? Periodontology 2000,75(1),152-88.

[2]. Durham J., Fraser H. M., McCracken G. I., Stone K. M., John M. T., Preshaw P. M., 2013, Impact of periodontitis on oral health-related quality of life. *J Dent*, 41(4),370-6.

[3]. Könönen E., Gursoy M., Gursoy U. K.,2019, Periodontitis: a multifaceted disease of tooth-supporting tissues, *Journal of Clinical Medicine*, 31;8(8),1135.

[4]. Darby I., 2022, Risk factors for periodontitis & peri-implantitis, Periodontology 2000, 90(1),9-12.

[5]. Hajishengallis G., Chavakis T., Lambris J. D., 2020, Current understanding of periodontal disease pathogenesis and targets for host-modulation therapy, *Periodontology* 2000, 84(1),14-34.

[6]. Pisano M., Giordano F., Sangiovanni G., Capuano N., Acerra A., D'Ambrosio F.,2023, The Interaction between the Oral Microbiome and Systemic Diseases: A Narrative Review, Microbiology Research, 14(4):1862-78.

[7]. Păunică I., Giurgiu M., Dumitriu A. S., Păunică S., Pantea Stoian A. M., Martu M. A., Serafinceanu C., 2023, The bidirectional relationship between periodontal disease and diabetes mellitus—A review, Diagnostics,11;13(4):681.

[8]. Sanz M., Marco del Castillo A., Jepsen S., Gonzalez-Juanatey J. R., D'Aiuto F., Bouchard P., Chapple I., Dietrich T., Gotsman I., Graziani F., Herrera D., 2020, Periodontitis and cardiovascular diseases: Consensus report, *Journal of clinical periodontology*, 47(3):268-88.

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Conflict of Interest

The authors declare no conflict of interest

[9]. Butera A., Maiorani C., Morandini A., Trombini J., Simonini M., Ogliari C., Scribante A., 2023, Periodontitis in Pregnant Women: A Possible Link to Adverse Pregnancy Outcomes, InHealthcare 11(10),1372.

[10]. Dragoo M.,1992, A clinical evaluation of hand and ultrasonic instruments on subgingival debridement I. With unmodified and modified ultrasonic inserts, *Int J Periodont Restor Dent*,12,311.

[11]. Munasur S. L., Turawa E. B., Chikte U. M., Musekiwa A.,2020, Mechanical debridement with antibiotics in the treatment of chronic periodontitis: effect on systemic biomarkers—a systematic review. *International Journal of Environmental Research And Public Health*, 17(15),5601.

[12]. Karygianni L., Al-Ahmad A., Argyropoulou A., Hellwig E., Anderson A. C., Skaltsounis AL.,2016, Natural antimicrobials and oral microorganisms: a systematic review on herbal interventions for the eradication of multispecies oral biofilms. Frontiers in Microbiology,14(6),1529.

[13]. Parmar S., Gangwal A., Sheth N.,2010, *Solanum xanthocarpum* (yellow berried nightshade): a review. Der Pharm Lett, 2(4),373-83.

[14]. Xu Z. P., Liu Y., Wang S. Y., Li Z. W., Lu D. X., Jiang P et al.,2022, Phenolic compounds of *Solanum xanthocarpum* play an important role in anti-inflammatory effects, *Arabian Journal of Chemistry*, 2022,15(7):103877.

[15]. Kumar S., Pandey A, K., 2014, Medicinal attributes of *Solanum xanthocarpum* fruit consumed by several tribal communities as food: an in vitro antioxidant, anticancer and anti-HIV perspective. BMC Complementary and Alternative Medicine,14,1-8.

[16]. Singh O. M., Singh T. P.,2010, Phytochemistry of *Solanum xanthocarpum*: an amazing traditional healer,69(10), 732-740.

[17]. Fathima T., Joghee S., Akaash M.,2019, *Solanum xanthocarpum*: A review. *International Journal of Pharmacognosy and Chinese Medicine*, 3(3),1-7.

[18]. Pungle R., Tambe A., More A., Kharat A.,2018, Anti-inflammatory and antioxidant potentiality of *Solanum xanthocarpum*. *African Journal of Biotechnology*,17(37),188-95.

[19]. Hu, Y. S., Han, X., Yu., P. J., Jiao., M. M., Liu, X. H., Shi, J. B., 2020, Novel phenol derivatives: Design, synthesis and anti-inflammatory activity in vitro and in vivo, Bioorg. Chem. 98, 103735.

[20]. Xu Z. P., Liu Y., Wang S. Y., Li Z. W., Lu D. X., Jiang P et al., 2022, Phenolic compounds of *Solanum xanthocarpum* play an important role in anti-inflammatory effects. *Arabian Journal of Chemistry,* 2022,15(7),103877.

[21]. Sultana R., Khanam S., Devi K., 2011, Immunomodulatory effect of methanol extract of *Solanum xanthocarpum* fruits. *Int J Pharm Sci Res*, 2(2), 93-7.

[22]. Santa K., 2023, Macrophages: Phagocytosis, Antigen Presentation, and Activation of Immunity. In Phagocytosis-Main Key of Immune System, IntechOpen.

[23]. Kumar S., SharmaU. K., Sharma A. K., Pandey A. K., 2012, Protective efficiency of *Solanum xanthocarpum* root extracts against free radical damage: phytochemical analysis and antioxidant effect. Cellular and Molecular Biology, 58(1),174-181.

[24]. Janssen L. J., Killian K.,2006, Airway smooth muscle as a target of asthma therapy: history and new directions. Respiratory research,7:1-2.

[25]. Vadnere G. P., Gaud R. S., Singhai A. K., 2008, Evaluation of anti-asthmatic property of *Solanum xanthocarpum* flower extracts, Pharmacologyonline, 1:513-22.

[26]. Govindan S., Viswanathan S., Vijayasekaran V., Alagappan R., 1999, A pilot study on the clinical efficacy of *Solanum xanthocarpum* and *Solanum trilobatum* in bronchial asthma, *Journal of Ethnopharmacology*, 66(2):205-10.

[27]. Choi J. R., Lee C. M., Jung I. D., Lee J. S., Jeong Y. I., Chang J. H et al., 2009, Apigenin protects ovalbumin-induced asthma through the regulation of the GATA-3 gene, *International Immunopharmacology*. 9(7-8), 918-24.

[28]. Gavimath C. C., Kulkarni S. M., Raorane C. J., Kalsekar D. P., Gavade B. G., Ravishankar B. E et al., 2012, Antibacterial potentials of *Solanum indicum, Solanum xanthocarpum,* and *Physalis minima*, *Int J Pharma Appl*, 3:414-8.

[29]. Deepavalli A., Gopinath S., Arun K. V., Balaji S. K., 2023, An *In Vitro* Evaluation of the Antibacterial Efficacy of *Solanum xanthocarpum* Extracts on Bacteria from Dental Plaque Biofilm, Cureus, 15(9).

[30]. Sharma B., Verma N., Tomar M. S., 2020, Evaluation of antifungal potential of *Solanum xanthocarpum* Schrad. and Wendl., an important medicinal plant of arid region, *International Journal of Advanced Research in Biological Sciences*, 7,163-8.

[31]. Mamta P. R., Dalei J., 2016, Qualitative evaluation of phytochemicals and antifungal activity of *Solanum xanthocarpum* (Schrad. & Wendl.), *IOSR J Pharm Biol Sci,* 11(3), 99-104.

[32]. Wang H. K., Xia Y., Yang Z. Y., Nitschke S. L., Lee K. H,1998, Recent advances in the discovery and development of flavonoids and their analogues as antitumor and anti-HIV agents. Adv Exp Med Biol, 439,191–225.

[33]. Najmi A. K., Pillai K. K., Pal S. N., Aqil M.,2005, Free radical scavenging and hepatoprotective activity of jigrine against galactosamine induced hepatopathy in rats, *Journal of Ethnopharmacology*, 97(3), 521-5.

[34]. Gupta R. K., Hussain T., Panigrahi G., Das A., Singh G. N., Sweety K et al., 2011, Hepatoprotective effect of *Solanum xanthocarpum* fruit extract against CCl4 induced acute liver toxicity in experimental animals. *Asian Pacific Journal of Tropical Medicine*,4(12), 964-8.

[35]. Gunaselvi G., Kulasekaren V., Gopal V., 2010, Anthelmintic activity of the extracts of *Solanum xanthocarpum* Schrad and Wendl fruits (Solanaceae), 1772-4.

[36]. World Health Organization., 2009, The use of herbal medicines in primary health care. WHO Regional Office for Southeast Asia.

[37]. Vlietinck A. J., Van Hoof L., Totte J., Lasure A., Berghe D. V., Rwangabo PC et al., 1995, Screening of hundred Rwandese medicinal plants for antimicrobial and antiviral properties. *Journal of Ethnopharmacology*, 46(1), 31-47.

[38]. Subharani K., 2016, Chemical constituents and medicinal properties of *Solanum xanthocarpum*. A review, *Int J Sci Res*, 5(10), 824-6.

[39]. Arumuganainar D., Subramanian G., Basavarajappa S., Hashem M. I., Arun K. V., Balaji S. K et al., 2023, Bioactive Efficacy of Identified Phytochemicals Solasodine, Lupeol and Quercetin from *Solanum xanthocarpum* against the RgpB Protein of Porphyromonas gingivalis- A Molecular Docking and Simulation Analysis, Processes, 11, 1887.

[40]. Nascimento G. G., Leite F. R., Scheutz F., López R., 2017, Periodontitis: from infection to inflammation. *Current Oral Health Reports*, 4:301-8.

[41]. Minervini G, Marrapodi MM, Tirupathi S, Afnan L, Di Blasio M, Cervino G, Isola G, Cicciù M., 2024, Comparative anti-plaque and anti-gingivitis efficiency of Triphala versus chlorhexidine mouthwashes in children: a systematic review and meta-analysis. *J Clin Pediatr Dent.,* Sep;48(5):51-59.

[42]. A. Sakthivel, K. Sankaran, G. Rengasamy, V. Vishnu Priya, P. Sathishkumar, 2024, Formulation of Mouthwash Using Combined Herbal Extracts to Control the Predominant Oral Pathogens and Biofilm. *Journal of Herbal Medicine*, 46,100905.

[43]. Deolikar, S., Jawdekar, A., Saraf, T., Thribhuvanan, L., Tirupathi, S., 2024, Comparative Evaluation of the Antimicrobial Efficacy of *Elettaria cardamomum* (0.5%) Mouthwash, *Camellia sinensis* (0.5%) Mouthwash, and 0.12% Chlorhexidine Gluconate Mouthwash against *Streptococcus mutans:* An *In Vitro* Study. *Int J Clin Pediatr Dent*., Apr;17(4):461-466.