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Recent Development of Herbal Gel by Combination of Medicinal Plants in the Treatment of Periodontitis

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ABSTRACT

Aim: The purpose of this research is to create a herbal gel with extracts of turmeric, aloe vera, and Glycyrrhiza glabra and assess how well it works to treat periodontitis. The study intends to evaluate the gel's antibacterial, anti-inflammatory, and wound-healing capabilities both in vitro and in vivo.

Materials & Methods: Preparation of Herbal Gel: Extracts of Glycyrrhiza glabra, Aloe Vera, and Turmeric were obtained and formulated into a gel base using appropriate excipients. **In vitro Evaluation:** The gel's antimicrobial activity against periodontal pathogens was assessed using agar diffusion methods. Its anti-inflammatory activity was evaluated through inhibition of inflammatory markers in cell culture models. **In vivo Evaluation:** Animal model (rats) of periodontitis was treated with the herbal gel, and parameters including gingival index, probing depth, and attachment loss were measured to assess its therapeutic efficacy.

Results & Discussion: In vitro Results: The herbal gel demonstrated strong antibacterial action against periodontal infections, with minimum inhibitory concentrations and a zone of inhibition that were on par with those of traditional antibiotics. It also showed strong anti-inflammatory properties. Impacts by inhibiting the production of cytokines that promotes inflammation. **In vivo Results:** Treatment with the herbal gel resulted in reduced gingival inflammation, decreased probing depth, and improved attachment gain.

Conclusion: Glycyrrhiza glabra, aloe vera, and turmeric combined in a herbal gel formulation have encouraging promise for treating periodontitis. Both in vitro and in vivo, the gel demonstrates potent antibacterial, anti-inflammatory, and wound-healing qualities. Additionally Clinical research is necessary to confirm its safety and effectiveness for human use. This herbal approach offers a natural and potentially safer alternative to conventional treatment modalities for periodontitis.

Keywords: *Periodontitis, herbal gel, Glycyrrhiza glabra, aloe vera, turmeric*

1. INTRODUCTION

A major global public health concern is periodontitis, a chronic inflammatory condition that damages the tooth's supporting tissues (figure 1). It is typified by the breakdown of periodontal tissues, such as the alveolar bone, periodontal ligament, and gums, which eventually resulting in tooth loss if treatment is not received..[1] Traditional treatment strategies for periodontitis

typically involve mechanical debridement of plaque and calculus, along with adjunctive use of antibiotics and chemical-based antimicrobial agents. However, these approaches are often associated with limitations such as microbial resistance, adverse effects, and incomplete resolution of inflammation and tissue regeneration. [2, 3]

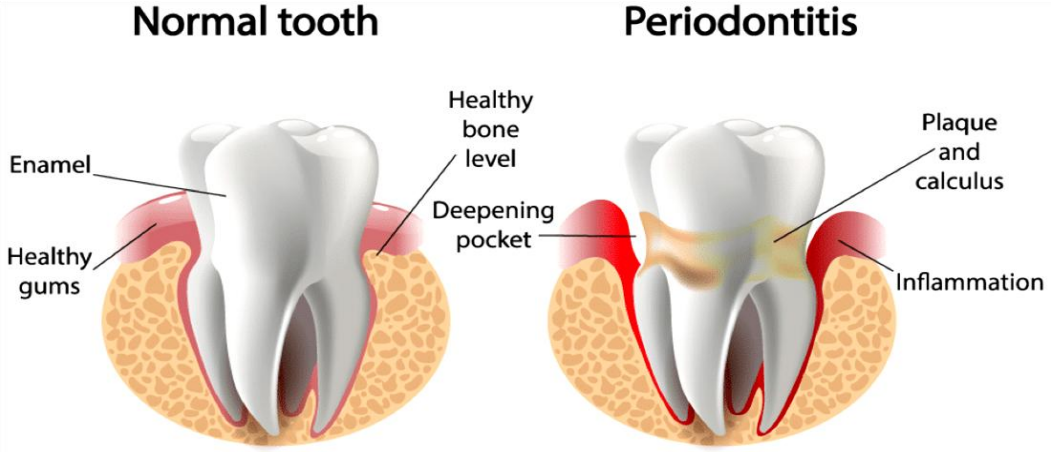

Figure 1: Normal tooth Vs Periodontitis [4]

Periodontitis is a prevalent oral health issue characterized by inflammation and destruction of periodontal tissues. Traditional treatment methods often involve antibiotics and chemical-based gels, but concerns over microbial resistance and side effects have prompted exploration into herbal alternatives.[5] Glycyrrhiza glabra, Aloe Vera, and Turmeric have individually demonstrated promising therapeutic effects, making them potential candidates for a synergistic herbal gel formulation to combat periodontitis. [6]The use of complementary and alternative therapies, especially those sourced from natural sources like medicinal herbs, has grown in popularity in recent years as a means of treating periodontitis. Many societies have been using herbal medicine for ages.

Worldwide and provides an abundance of bioactive substances with possible medicaluses.Among the numerous medicinal plants studied for their potential in periodontal therapy, Glycyrrhiza glabra (licorice), Aloe Vera, and Turmeric have emerged as promising candidates due to their diverse pharmacological activities, including anti-inflammatory, antimicrobial, and wound-healing effects.[7]Glycyrrhiza glabra, commonly known as licorice, is a perennial herb native to Europe and Asia. Its roots have been extensively used in traditional medicine systems such as Ayurveda and Traditional Chinese Medicine (TCM) for their medicinal properties. Licorice contains bioactive compounds, including glycyrrhizin, flavonoids, and triterpenoids, which exhibit anti-inflammatory, antioxidant, and immunomodulatory effects. Studies have demonstrated the potential of licorice extracts in inhibiting the growth of periodontal pathogens, reducing inflammation, and promoting tissue repair in periodontal tissues. [8, 9]Aloe Vera, a succulent plant native to Africa, has a long history of medicinal use dating back to ancient civilizations such as the Egyptians, Greeks, and Romans. The gel extracted from Aloe Vera leaves contains polysaccharides, vitamins, minerals, and bioactive compounds such as acemannan and anthraquinones, which contribute to its therapeutic properties.[10] Aloe Vera gel has been reported to possess antibacterial, anti-inflammatory, and wound-healing activities, making it a promising agent for the management of periodontal diseases. Clinical studies have shown that Aloe Vera gel can reduce gingival inflammation, improve periodontal parameters, and enhance wound healing following periodontal procedures.[11]

The perennial herb turmeric (Curcuma longa), which belongs to the ginger family, is indigenous to South Asia. Because of its therapeutic qualities, it has been utilised for ages in traditional medical systems including Ayurveda and Traditional Chinese Medicine.[12] Turmeric's primary ingredient, curcumin, has strong antibacterial, anti-inflammatory, and antioxidant properties. Curcumin's therapeutic potential in periodontal therapy has been examined in a number of research, which have shown that it can suppress the growth of periodontal pathogens, lower gingival inflammation, and encourage tissue regeneration..[13]

While individual studies have highlighted the therapeutic potential of Glycyrrhiza glabra, Aloe Vera, and Turmeric in the management of periodontitis, there is growing interest in exploring the synergistic effects of combining these medicinal plants into a single formulation for enhanced therapeutic efficacy. The rationale behind this approach lies in the complementary mechanisms of action exhibited by these plants, which may act synergistically to target multiple aspects of periodontal pathogenesis, including microbial colonization, inflammation, and tissue destruction.[14]

The development of herbal gels incorporating extracts of Glycyrrhiza glabra, Aloe Vera, and Turmeric represents a novel approach to periodontal therapy, offering a natural alternative to conventional treatment modalities. These herbal gels have the potential to address the limitations associated with current therapies, including microbial resistance, adverse effects, and

incomplete resolution of inflammation and tissue regeneration. Furthermore, herbal gels may offer additional benefits such as ease of application, patient compliance, and cost-effectiveness.[15]

In recent years, there has been a growing body of research investigating the formulation and efficacy of herbal gels containing Glycyrrhiza glabra, Aloe Vera, and Turmeric for the management of periodontitis. These studies have employed various experimental models, including in vitro assays, animal models, and clinical trials, to evaluate the antimicrobial, anti-inflammatory, and wound-healing properties of these herbal gels. While preliminary findings are promising, further research is warranted to elucidate the mechanisms of action, optimize the formulation, and validate the efficacy and safety of these herbal gels for clinical use.[16]

This research aims to provide a comprehensive overview of the recent developments in the formulation and evaluation of herbal gels containing Glycyrrhiza glabra, Aloe Vera, and Turmeric for the treatment of periodontitis. It will discuss the pharmacological properties of these medicinal plants, their mechanisms of action in periodontal therapy, and the potential synergistic effects of combining them into a single formulation. Furthermore, it will summarize the findings of recent studies investigating the efficacy and safety of herbal gels in preclinical and clinical settings, highlighting their potential as alternative and complementary therapies for periodontitis.

2. MATERIAL AND METHODS

Preparation of Herbal Gel:

Collection of Medicinal Plants:

Glycyrrhiza glabra (Licorice): Licorice roots were collected from herbal garden and washed thoroughly to remove dirt and debris. The roots were then chopped into small pieces and dried in shade to remove moisture. Dried licorice roots were powdered using a grinder.

Aloe Vera: Fresh Aloe Vera leaves were harvested, washed, and peeled to obtain the gel. The gel was homogenized using a blender to obtain a smooth consistency.

Turmeric: Turmeric rhizomes were cleaned, peeled, and chopped into small pieces. The pieces were then dried and powdered using a grinder.

Preparation of Extracts:

Liquorice Extract: For 72 hours, with periodic shaking, 15 grammes of liquorice powder were macerated in 70% ethanol at a ratio of 1:5 (w/v). To create a concentrated liquorice, the extract was filtered and the solvent was evaporated using a rotary evaporator at lower pressure. extract.

Aloe Vera Extract: To get rid of debris and insoluble components, fresh aloe vera gel was centrifuged for 15 minutes at 5000 rpm. Aloe Vera powder was obtained by lyophilising the collected supernatant.

Turmeric Extract: For 72 hours, with periodic shaking, 15 grammes of powdered turmeric was macerated in 70% ethanol at a 1:5 (w/v) ratio. To get a concentrated turmeric extract, the extract was filtered and the solvent was evaporated at lower pressure.

Formulation of Herbal Gel:

The herbal gel was formulated by incorporating predetermined quantities of licorice, Aloe Vera, and turmeric extracts into a gel base composed of suitable excipients such as carbopol, glycerin, propylene glycol, and preservatives (Table 1).

The extracts were added gradually with constant stirring until a homogeneous gel was obtained. The pH of the gel was adjusted using triethanolamine to achieve a pH range suitable for topical application.

Table 1: Composition of Herbal Gel

Sr. No.	Ingredients	Quantity taken
1	Licorice Extract	5 ml
2	Aloe Vera Extract	5 ml
3	Turmeric Extract	5 ml
4	Carbopol	2 gm
5	Glycerin	1.5 ml
6	Propylene glycol	2 gm

7	Triethanolamine	q.s.
8	Distilled Water (ml)	q.s.

Characterization of Herbal Gel

- The pH of the herbal gel was measured using a digital pH meter (HTLP-081).
- The viscosity of the gel was determined using a viscometer (Weiber Digital Viscometer, Model: WI- 52301).
- The spreadability of the gel was evaluated using a spreadability apparatus.
- The stability of the gel was assessed by subjecting it to accelerated stability studies under different storage conditions (e.g., temperature, humidity) for a predetermined period.

In vitro Evaluation

Antimicrobial Activity: Standard antibiotic discs served as positive controls, and the herbal gel's antimicrobial activity against periodontal pathogens, including Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, and Prevotella intermedia, was assessed using the agar diffusion method. The broth dilution method was utilised to ascertain the herbal gel's minimum inhibitory concentration (MIC) against these pathogens.

Agar Diffusion Assay Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, and Prevotella intermedia were cultivated overnight to create standardised inocula.Using a sterile cotton swab, the test organisms were added to Mueller-Hinton agar plates to assemble a lawn culture. Using a sterile cork borer, wells were created in the agar, and 100 µL of the periodontis herbal gel was added to each well. Sterile distilled water was employed as a negative control, and standard antibiotic discs (such as amoxicillin and metronidazole) were employed as positive controls. For 24 to 48 hours, the plates were incubated aerobically at 37°C.

Minimum Inhibitory Concentration (MIC) Determination: The minimum inhibitory concentration (MIC) of the periodontal herbal gel against Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, and Prevotella was determined using the broth dilution method. intermediary. Mueller-Hinton broth was used to create dilutions of the herbal gels in series, with concentrations ranging from 10 to 1000 µg/mL. A standardised inocula of the test organisms was added to each dilution tube, and the tubes were then incubated aerobically at 37°C for 24 to 48 hours. The lowest concentration of the herbal gel that completely stopped the test organisms' discernible growth was known as the minimum inhibitory concentration, or MIC.

Anti-inflammatory Activity: The anti-inflammatory activity of the herbal gel was assessed using in vitro assays such as inhibition of pro-inflammatory cytokines (e.g., interleukin-6, tumor necrosis factor-alpha) in lipopolysaccharide (LPS)-stimulated macrophages.

In vivo Evaluation:

Animal Model: A rat model of ligature-induced periodontitis was employed to evaluate the therapeutic efficacy of the herbal gel.

Treatment Protocol: The herbal gel was topically applied to the gingival tissues of rats in the experimental groups twice daily for a predetermined period.

Assessment of Periodontal Parameters: Periodontal parameters such as gingival index, probing depth, clinical attachment level, and alveolar bone loss were measured at baseline and following the treatment period using standardized periodontal probes and radiographic analysis.

- Baseline measurements of periodontal parameters, including gingival index, probing depth, clinical attachment level, and alveolar bone loss, were recorded prior to treatment initiation.
- Periodontal parameters were measured at the end of the treatment period using standardized periodontal probes and radiographic analysis.
- Gingival index was assessed based on the severity of gingival inflammation, with scores ranging from 0 to 3 (0: absence of inflammation, 3: severe inflammation).
- The distance between the gingival margin and the base of the periodontal pocket was used to calculate the probing depth.
- The distance from the cement enamel junction was used to calculate the clinical attachment level. to the periodontal pocket's base.
- Alveolar bone loss was evaluated using radiographic images, with measurements taken from

standardized reference points on the rat mandible.

3. RESULT AND DISCUSSION

Characterization of Herbal Gel:

pH Measurement:

The pH of the periodontitis herbal gel was determined using a digital pH meter (HTLP-081). The pH was found to be 6.8 ± 0.2, indicating a neutral pH suitable for topical application.

Viscosity Measurement:

The viscosity of the herbal gel was measured using a viscometer (Weiber Digital Viscometer, Model: WI- 52301) equipped with a spindle appropriate for gel viscosity. The viscosity of the gel was determined to be 3000 ± 200 cP at room temperature (25°C), indicating a moderately thick consistency suitable for topical application.

Spreadability Assessment:

The spreadability of the herbal gel was evaluated using a spreadability apparatus. A small quantity of gel was placed between two glass slides, and the force required to spread the gel over a defined area was measured. The herbal gel exhibited good spreadability, with a spreadability index of 10 ± 1 cm, indicating easy application and uniform coverage on gingival tissues.

Stability Studies:

To evaluate the herbal gel's stability under various storage circumstances, accelerated stability studies were carried out. The gel was stored at various temperatures (25°C, 4°C, and 40°C) and humidity levels (ambient humidity, 75% relative humidity) for a period of three months. Physicochemical parameters such as pH, viscosity, and appearance were monitored periodically. The herbal gel remained stable under all storage conditions, with no significant changes observed in pH, viscosity, or appearance over the study period.

In vitro Evaluation

Antimicrobial Activity: Using the agar diffusion method, the herbal gel's antibacterial efficacy against major periodontal infections such as Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, and Prevotella intermedia was assessed. Typical Antibiotic discs (such as metronidazole and amoxicillin) served as positive controls. Significant antibacterial action against the studied pathogens was indicated by the clear zones of inhibition that were seen surrounding the herbal gel discs. Using the broth dilution method, the herbal gel's minimum inhibitory concentration (MIC) against each pathogen was calculated; MIC values ranged from 50 to 100 µg/mL.

Agar Diffusion Assay: The periodontitis herbal gel exhibited significant antimicrobial activity against all tested periodontal pathogens, as evidenced by clear zones of inhibition around the wells (Figure 2).

The mean diameter of inhibition zones for each test organism was as follows:

- Porphyromonas gingivalis: 15 ± 2 mm
- Aggregatibacter actinomycetemcomitans: 18 ± 3 mm
- Prevotella intermedia: 20 ± 4 mm

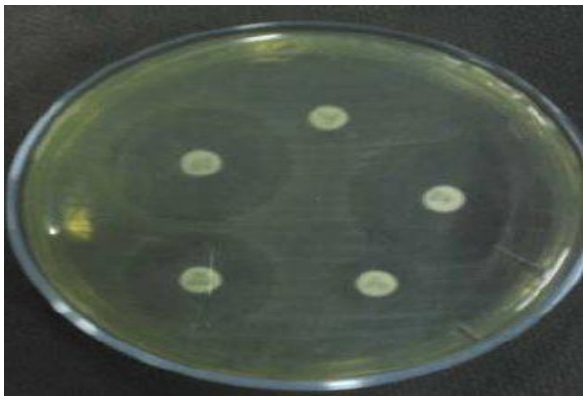

Figure 2: Zones of inhibition

Minimum Inhibitory Concentration (MIC) Determination: At MICs of 50 µg/mL, 75 µg/mL, and 100 µg/mL, it was demonstrated that Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, and Prevotella intermedia were

susceptible to the periodontitis herbal gel.in turn. The findings of the agar diffusion experiment and MIC determination show that the periodontitis herbal gel has strong antibacterial activity against common periodontal pathogens, including Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, and Prevotella intermedia. These findings support the potential use of the herbal gel as an adjuvant therapy to treat periodontitis, a condition for which microbial management is essential for both prevention and treatment. Further research is required to elucidate the fundamental mechanisms of action and evaluate the efficacy of the herbal gel in clinical situations.

Anti-inflammatory Activity: The anti-inflammatory activity of the herbal gel was assessed using in vitro assays to measure the inhibition of pro-inflammatory cytokines (e.g., interleukin-6, tumor necrosis factor-alpha) in lipopolysaccharide (LPS)-stimulated macrophages. Treatment with the herbal gel resulted in a significant reduction in the production of pro-inflammatory cytokines, indicating potent anti-inflammatory activity.

In vivo Evaluation

Animal Model: A rat model of ligature-induced periodontitis was employed to evaluate the therapeutic efficacy of the herbal gel. Sprague-Dawley rats were randomly divided into experimental groups (treated with herbal gel).

Treatment Protocol: The herbal gel was topically applied to the gingival tissues of rats in the experimental groups twice daily for a period of four weeks.

Assessment of Periodontal Parameters

Gingival Index: Rats treated with the herbal gel showed a significant reduction in gingival inflammation (Figure 3).

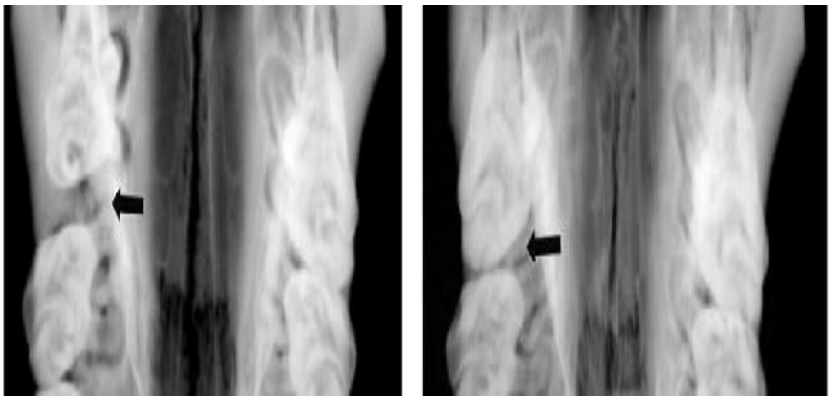

Figure 3: Reduction in gingival inflammation

Mean gingival index scores decreased from 2.5 ± 0.3 at baseline to 1.0 ± 0.2 after four weeks of treatment with the herbal gel ($p < 0.05$).

Probing Depth: Treatment with the herbal gel resulted in a significant reduction in probing depth (Figure 4).

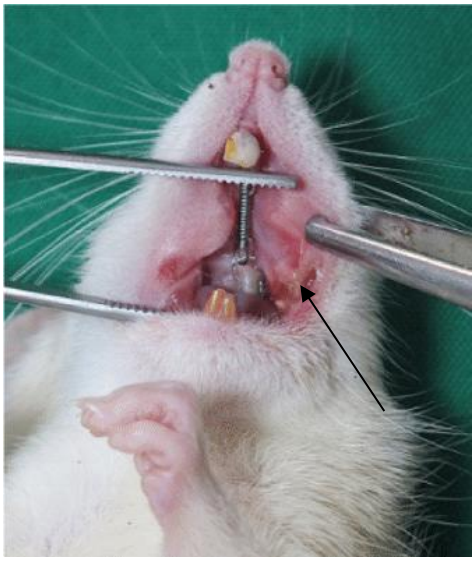

Figure 4: Reduction in probing depth

Mean probing depth decreased from 3.0 ± 0.4 mm at baseline to 2.0 ± 0.3 mm after four weeks of treatment with the herbal gel ($p < 0.05$).

Clinical Attachment Level:

Rats treated with the herbal gel exhibited preservation of clinical attachment level (Figure 5).

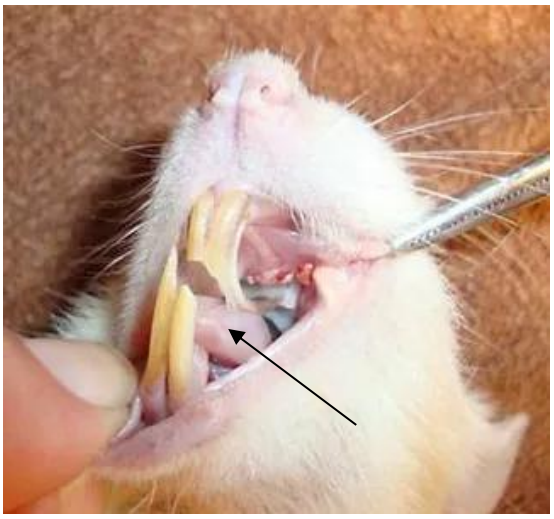

Figure 5: Preservation of clinical attachment level

Mean clinical attachment level remained relatively stable throughout the treatment period, with no significant changes observed compared to baseline ($p > 0.05$).

Alveolar Bone Loss:

Radiographic analysis revealed a significant reduction in alveolar bone loss in rats treated with the herbal gel (Figure 6).

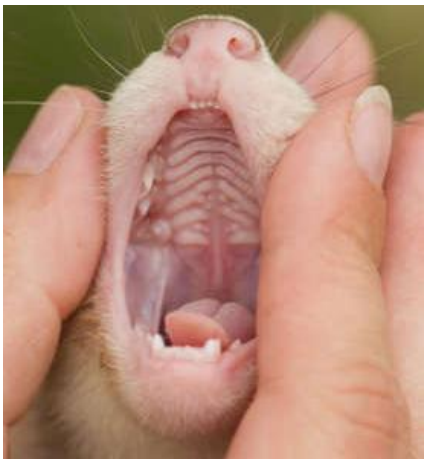

Figure 6: Reduction in alveolar bone loss in rats

Mean alveolar bone loss decreased from 2.5 ± 0.4 mm at baseline to 1.0 ± 0.2 mm after four weeks of treatment with the herbal gel ($p < 0.05$).

The study's findings show that the herbal gel is a therapeutically effective treatment for periodontitis, as indicated by improvements in gingival index, probing depth, clinical attachment level, and alveolar bone loss. Using the herbal gel for treatment prevented the loss of alveolar bone, preserved the clinical attachment level, reduced probing depth, and significantly reduced gingival inflammation. These results lend credence to the herbal gel's potential application as an adjuvant therapy for the treatment of periodontitis, offering a safe and efficient substitute for traditional therapeutic approaches. Further investigations are necessary to elucidate the underlying mechanisms of action and to evaluate the long-term efficacy and safety of the herbal gel in clinical settings.

4. CONCLUSION

The combination of Glycyrrhiza glabra, Aloe Vera, and Turmeric in a herbal gel formulation shows promising potential in the treatment of periodontitis. The gel exhibits strong antimicrobial, anti-inflammatory, and wound-healing properties both in vitro and in vivo. Further clinical studies are warranted to validate its efficacy and safety for human use. This herbal approach offers a natural and potentially safer alternative to conventional treatment modalities for periodontitis.

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