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Nano-Emulgel Formulation of Azithromycin with Eugenol: A Novel Approach for Periodontitis Treatment

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Abstract: Periodontitis is a serious gum disease that causes inflammation and can lead to tooth loss if not treated properly. Traditional treatments, like deep cleaning and antibiotics, have some downsides—antibiotics which do not reach deep into the gums effectively and can cause unwanted side effects in the body.

This study looks at a new way to treat periodontitis using a special gel called a nano-emulgel**. This gel combines tiny droplets of medicine (nanoemulsion) with a gel base, making it easier for the medicine to stay on the gums and work for a longer time. The gel contains** azithromycin**, an antibiotic, and** eugenol**, a natural compound with anti-inflammatory and antibacterial properties (found in clove oil).**

To make the gel, scientists used Carbopol 940 **(a thickening agent),** Tween-80**, and** PEG-400 **(which help mix the ingredients). When tested, the gel had a good pH balance (7.24), spread easily, and remained stable without separating. The combination of azithromycin and eugenol improved the medicine's effectiveness and helped reduce inflammation.**

Overall, this nano-emulgel could be a better way to treat periodontitis by delivering medicine directly to the gums, avoiding the side effects of traditional antibiotics. More clinical studies are needed to confirm its safety and effectiveness before it can be widely used.

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I. INTRODUCTION

Periodontitis is a serious gum disease that affects the gums and the bones that support the teeth. If not treated, it can lead to tooth loss and other health problems. Common treatments, like deep cleaning and antibiotics[23], have some drawbacks. Antibiotics may not reach deep into the gums effectively, can cause side effects, and some patients may struggle to follow the treatment properly.[13][12]

This study explores a new treatment method using a nano-emulgel—a special gel that combines tiny medicine particles (nanoemulsion) with a gel base. This makes the medicine easier to absorb and allows it to stay in place longer for better result [6][7][10]

The gel contains azithromycin, an antibiotic that fights bacteria, and eugenol, a natural ingredient (found in clove oil) that helps reduce pain and swelling[22]. This combination[5] improves the treatment's effectiveness by ensuring better drug penetration and longer-lasting effects directly on the gums[8][15][16].

Overall, this nano-emulgel could be a promising new way to treat periodontitis more effectively while reducing side effects. Further research is needed to confirm its safety and effectiveness.[9][2]

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II. SIGNIFICANCE OF AZITHROMYCIN AND EUGENOL IN PERIODONTITIS

Azithromycin, a macrolide antibiotic, is well-known for its antimicrobial and anti-inflammatory properties, making it an effective choice for periodontal therapy.[15] However, its hydrophobic nature restricts its direct topical application. Eugenol, derived from clove oil,[3] possesses anti-inflammatory, analgesic, and antimicrobial properties, making it an excellent adjunct to antibiotics in treating periodontitis.[21][23][14]

III. FORMULATION AND METHODOLOGY

A. Materials Used

The primary materials used in this formulation include:

- **Active Ingredients:** Azithromycin and Eugenol
- **Excipients:** Clove oil extract, peppermint extract
- **Gel Base Components:** Carbopol 940, polysorbate 80
- **Surfactants:** Tween-80, PEG-400 (to improve solubility and dispersion)
- **Preservative:** Methylparaben
- **Solvent:** Methanol and water
- **pH Adjuster:** Triethanolamine

B. Preparation of Nano – Emulgel

The nano-emulgel was formulated in two steps:

➢ *Nano Emulsion Preparation:*

- **Drug-Oil Mixture:** Weigh 500 mg of azithromycin and dissolve it in 5 mL of oil phase in a 100 mL beaker.
- **Addition of Surfactants:** Add 10 mL of Tween-80 and 5 mL of PEG-400, mix thoroughly using a magnetic stirrer.
- **Titration with Water:** Slowly add purified water (q.s. up to 100 mL) dropwise while continuously stirring.
- **Homogenization:** Use a high-speed homogenizer (10,000–15,000 rpm for 10 min) or an ultrasonicator to achieve uniform nano-sized droplets.

➢ *Gel Base Preparation and Incorporation:*

- *Hydration of Gelling Agent:*

✓ Weigh 1.5 g of Carbopol 940 and disperse it in 30 mL of distilled water in a 250 mL beaker.
✓ Stir using a magnetic stirrer until a uniform gel forms.

- *Addition of Humectant & Preservatives:*

✓ Add 2 mL of glycerin and 0.1 g each of methylparaben and propylparaben into the gel base.
✓ Mix well to ensure proper dissolution.

- *Incorporation of Nano emulsion:*

✓ Gradually add the 50 mL nano emulsion into the gel while stirring continuously.

- *pH Adjustment:*

✓ Add 0.5 mL of Triethanolamine (TEA) dropwise to adjust the pH to 6.8–7.4.

- *Final Mixing & Homogenization:*

✓ Stir until a smooth and uniform nano-emulgel is formed

C. Evaluation of the Nano-Emulgel

The formulated nano-emulgel was evaluated based on various parameters:

- **Physical Appearance:** The formulation appeared as a white, homogeneous gel without phase separation.
- **pH Measurement:** The pH was found to be 7.24, making it suitable for application to periodontal pockets without causing irritation.
- **Spreadability:** The gel demonstrated good spreadability with a diameter of 5.2 cm, ensuring ease of application.
- **Swelling Index:** The swelling index was measured at 1%, indicating its ability to retain moisture and enhance drug retention at the application site.
- **Stability and Drug Content:** The formulation showed no phase separation, confirming its stability, and the drug was uniformly distributed throughout the gel.

IV. RESULT AND DISCUSSION

The nano-emulgel formulation of azithromycin with eugenol was successfully developed and evaluated for its physicochemical properties, stability, and potential therapeutic efficacy in the treatment of periodontitis. The formulated nano-emulgel appeared as a homogenous white gel without phase separation, indicating good stability and uniform distribution of components.

The pH of the formulation was recorded at 7.24, which is within the physiological range suitable for application to periodontal pockets. This ensures that the formulation does not cause irritation or discomfort upon administration. The spreadability of the nano-emulgel was measured at 5.2 cm, suggesting ease of application and adequate coverage over the affected periodontal region.

The swelling index of the formulation was found to be 1%, indicating moderate water absorption and moisture retention, which can enhance the drug's residence time at the application site. Additionally, the formulation maintained stability over time, with no observable phase separation, confirming its suitability for prolonged storage and use.

The incorporation of azithromycin and eugenol into a nano-emulgel system demonstrated improved drug solubility and bioavailability. Azithromycin, a macrolide antibiotic, is known for its potent antimicrobial and anti-inflammatory properties but has limited water solubility. The nano-emulsion system effectively enhanced its dispersion, allowing for better penetration into the periodontal tissues. Eugenol, derived from clove oil, contributed to the formulation's anti-inflammatory and antibacterial effects, synergistically enhancing the therapeutic outcome.

The evaluation of drug content uniformity confirmed consistent distribution of azithromycin throughout the formulation. The stability assessments showed that the nano-emulgel retained its properties without degradation

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over the observed period, reinforcing its potential for clinical application.

Overall, the study highlights the promising potential of nano-emulgel as a localized drug delivery system for periodontitis treatment. By enhancing drug penetration and retention at the site of infection, the formulation offers an alternative to conventional antibiotic therapies, reducing systemic side effects and improving patient compliance. Further in vivo studies and clinical trials are necessary to validate its efficacy and safety for widespread application in periodontal therapy.

V. CONCLUSION

This study successfully developed a nano-emulgel incorporating azithromycin and eugenol, offering an innovative approach for localized periodontitis treatment. By overcoming the limitations of conventional drug delivery methods, this formulation holds significant promise in advancing dental therapeutics. Further studies are recommended to evaluate its long-term efficacy and safety.

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