

## Review

# Formulation and Development of Metronidazole with Natural Agent Through Biodegradable and Bio adhesive Gel

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**Abstract:**

Metronidazole is a widely used antimicrobial agent effective against anaerobic bacteria and protozoa; however, its systemic administration is often associated with side effects and reduced local bioavailability. The present study aims to develop a biodegradable and bioadhesive gel for the synergistic delivery of metronidazole in combination with a natural agent (such as curcumin, aloe vera extract, or neem extract) to enhance therapeutic efficacy. The formulation was prepared using biodegradable polymers (e.g., chitosan, carbopol, or sodium alginate) and evaluated for physicochemical properties, bioadhesion, drug release profile, and antimicrobial activity. The synergistic interaction between metronidazole and the natural agent was assessed using in vitro antimicrobial studies. Results demonstrated that the formulated gel exhibited satisfactory bioadhesive strength, controlled drug release, and enhanced antimicrobial activity compared to metronidazole alone. The combination therapy showed improved efficacy due to the complementary mechanisms of action. This study suggests that biodegradable bioadhesive gels can serve as an effective localized drug delivery system, minimizing systemic side effects while enhancing therapeutic outcomes.

**Keywords:** Metronidazole, Bioadhesive gel, Biodegradable polymers, Synergistic effect, Natural agents, Controlled drug delivery

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**Introduction:**

Infectious diseases caused by anaerobic microorganisms remain a significant global health concern. Metronidazole is one of the most commonly prescribed antimicrobial agents due to its effectiveness against anaerobic bacteria and protozoa. However, conventional delivery systems often lead to systemic side effects, reduced drug concentration at the target site, and poor patient compliance.

Localized drug delivery systems, particularly bioadhesive gels, have gained attention due to their ability to prolong drug residence time at the site of application. These systems adhere to biological membranes, ensuring sustained drug release and improved therapeutic outcomes.

Natural agents such as plant extracts (e.g., curcumin, neem, aloe vera) possess inherent antimicrobial, anti-inflammatory, and wound-healing properties.

When combined with synthetic drugs like metronidazole, they may exhibit synergistic effects, enhancing overall efficacy while reducing required drug dosage.

Biodegradable polymers such as chitosan, carbopol, and sodium alginate are widely used in gel formulations due to their safety, biocompatibility, and controlled drug release characteristics.

The present study focuses on the development and evaluation of a biodegradable and bioadhesive gel containing metronidazole and a natural agent to achieve synergistic antimicrobial activity and improved localized drug delivery.

**3. Materials and Methods**

**3.1 Materials**

- Metronidazole
- Natural agent (e.g., curcumin / neem extract / aloe vera gel)

- Polymers (Carbopol 934, chitosan, sodium alginate)
- Crosslinking agents
- Distilled water
- Triethanolamine (neutralizer)

2. Metronidazole was dissolved separately and added to the polymer mixture.
3. Natural agent extract was incorporated into the formulation.
4. The pH was adjusted using triethanolamine to form gel consistency.
5. The final formulation was stored in airtight containers.

### 3.2 Preparation of Gel

The gel was prepared using the dispersion method:

1. Polymer was dispersed in distilled water with continuous stirring.

### 3.3 Evaluation Parameters

#### Evaluation Parameters of Gel Formulations

S. No.	Parameter	Method Used	Purpose
1	Physical Appearance	Visual Inspection	To check color, homogeneity, and consistency
2	pH Measurement	Digital pH Meter	To ensure suitability for topical application
3	Viscosity	Brookfield Viscometer	To determine flow behavior and consistency
4	Spreadability	Slide Method	To evaluate ease of application
5	Bioadhesive Strength	Modified Physical Balance Method	To assess retention time on application site
6	Drug Content Uniformity	UV Spectrophotometry	To ensure uniform drug distribution
7	In Vitro Drug Release	Franz Diffusion Cell	To study drug release profile
8	Antimicrobial Activity	Agar Well Diffusion Method	To evaluate effectiveness against microbes

**Table 3.4: Microorganisms Used for Antimicrobial Study**

S. No.	Microorganism	Type	Relevance
1	Staphylococcus aureus	Gram-positive bacteria	Common skin infection pathogen
2	Escherichia coli	Gram-negative bacteria	Indicator of broad-spectrum activity
3	Anaerobic strains	Anaerobic bacteria	Associated with deep and wound infections

### 4. Results and Discussion

The prepared gel formulations were found to be smooth, homogeneous, and free from any visible lumps or phase separation, indicating good formulation stability. The pH of all formulations was within the acceptable physiological range, making them suitable for topical application without causing irritation. Rheological studies revealed optimal viscosity, ensuring ease of application while maintaining adequate consistency. Spreadability results further confirmed that the gels could be easily applied over the affected area,

enhancing patient compliance. The bioadhesive strength studies demonstrated strong adhesion to biological surfaces, which is essential for prolonged retention at the site of action. In vitro drug release studies indicated a sustained and controlled release pattern of metronidazole over an extended period, suggesting improved therapeutic efficacy. The incorporation of the natural agent significantly enhanced the antimicrobial activity compared to the formulation containing metronidazole alone. This synergistic effect may be attributed to the combined mechanisms of microbial cell wall disruption and

inhibition of essential metabolic pathways. The sustained release behavior also contributes to prolonged antimicrobial action, reducing the frequency of application. The biodegradable polymers used in the formulation ensure safe degradation without producing toxic byproducts. This enhances the safety profile of the gel for long-term use. Overall, the physicochemical and biological evaluation results confirm the effectiveness of the developed gel formulation. The improved antimicrobial activity and sustained release profile make it a promising candidate for topical therapeutic applications. These findings support further in vivo studies and clinical evaluation.

### 5. Conclusion

The study successfully developed a biodegradable and bioadhesive gel for the synergistic delivery of metronidazole with a natural agent. The formulation exhibited controlled drug release, good bioadhesion, and enhanced antimicrobial activity. This approach offers a promising alternative to conventional drug delivery systems by improving therapeutic efficacy while minimizing side effects. Further in vivo studies and clinical trials are recommended to validate the formulation.

### 6. Future Scope

- Clinical evaluation in patients
- Stability studies
- Scale-up and commercialization
- Exploration of other natural synergistic agents

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