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Formulation & Evaluation of Tetracycline HCL sol-gel for Wound Healing

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ABSTRACT

Wound healing is a complex biological process that can be greatly hampered by microbial infections. Tetracycline, a broad-spectrum antibiotic, has shown strong action against both Gram-positive and Gram-negative bacteria, making it a suitable drug for targeted wound therapy. This paper investigates the formulation and potential of tetracycline-loaded sol-gels as a novel drug delivery technology for improving wound healing. Sol-gels, noted for their biocompatibility, convenience of use, and capacity to give prolonged drug release, are a useful platform for delivering tetracycline directly to the wound site, reducing systemic side effects and boosting therapeutic efficacy. The study examines tetracycline's mechanism of action, the importance of sol-gel technology in controlled drug delivery, formulation issues, and current advances in antimicrobial sol-gel systems. Tetracycline-based sol-gels are evaluated in terms of their physicochemical qualities, stability, and in-vitro/in-vivo performance. This study focuses on the potential of such formulations to improve infection control and expedite wound healing, offering insights for future research and clinical applications.

Keywords: broad-spectrum, therapeutic efficacy, sol-gel,biocompatibility

1. Introduction

Tetracyclines (TCs) are important antibacterial drugs used to treat a variety of clinical infections caused by aerobic, anaerobic, Gram-positive, and Gram-negative microorganisms [1]. In addition to their antimicrobial action in topical therapy, it is possible to take advantage of their non-antibiotic anti-inflammatory activity, which can have a beneficial affect on the course of treatment. [2-4]

Wound healing is a multi-step biological process involving hemostasis, inflammation, proliferation, and remodeling. The integrity of skin and mucosal tissue is critical for the body's protection against microbial invasion and fluid loss. When wounded, the wound becomes prone to infection, which can significantly delay the healing process and increase the risk of consequences, such as chronic wounds or systemic infections. [5].

Topical drug delivery methods have gained popularity due to their capacity to offer localized, sustained drug release directly to the site of action. Gels are particularly favorable among topical treatments because of their non-greasy texture, simplicity of administration, superior spreadability, and ability to maintain a moist wound environment—all of which are necessary for successful tissue regeneration [6].

Tetracycline hydrochloride is a broad-spectrum semi-synthetic antibiotic that inhibits bacterial protein synthesis by attaching to the 30S ribosomal subunit. It is effective against a wide variety of Gram-positive and Gram-negative bacteria commonly found in infected wounds [7]. Its inclusion into a gel formulation enables targeted distribution, reducing systemic side effects while increasing therapeutic concentration at the site of infection.

Several investigations have shown that topical tetracycline formulations can speed up wound healing by lowering bacterial load, regulating the inflammatory response, and boosting granulation tissue development [8].

Furthermore, tetracycline has anti-inflammatory and anti-collagenase properties, which support its use in wound management [9].

The current study is to develop and assess a tetracycline-based topical gel for wound healing, with a focus on its physicochemical features, in-vitro drug release, and antibacterial efficacy. This formulation is intended to provide a simple, effective, and patient-friendly method of controlling infected wounds.

2. Materials and method

Formulation table for 5g of tetracycline sol-gel

Ingredient	%w/w	Quantity for 5g(mg)	Function
Tetracycline HCL	1.0%	50 mg	Antimicrobial agent
Carbopol 940	1.0%	50mg	Gelling agent
Poloxamer 407	20.0%	1000mg	Polymer
Propylene glycol	5.0%	250mg	Humectant,penetration enhancer
Triethanolamine (TEA)	q.s (PH 6-7)	1-2 drops	Ph adjuster
Purified water	q.s	q.s	Vehicle

3. Method of preparation 5 g batch of Tetracycline sol-gel

1. **Preparation of Carbopol Gel Base:**
    - Weigh **Carbopol 940 (50 mg)** and **disperse** it in a portion of **purified water** (~3 g).
    - Allow it to **soak for 1–2 hours** (or overnight) to fully hydrate.
    - Stir gently with a glass rod or magnetic stirrer to form a **uniform dispersion**.
2. **Preparation of Methylcellulose Solution:**
    - Sprinkle **Methylcellulose (100 mg)** slowly into hot purified water (~60–70°C) with continuous stirring.
    - Then cool the solution while stirring. This will allow methylcellulose to swell and dissolve properly.
    - Let it stand to remove air bubbles.
3. **Mixing the Gel Base:**
    - Combine the **Carbopol** and **Methylcellulose solutions** by stirring gently to form a **uniform gel base**.
4. **Addition of Propylene Glycol:**
    - Add **Propylene Glycol (250 mg)** to the gel base.
    - Mix thoroughly. It acts as a **humectant and penetration enhancer**.
5. **Incorporation of Tetracycline HCl:**
    - Dissolve **Tetracycline HCl (50 mg)** in a small amount of purified water.
    - Add the solution **slowly** to the gel base with continuous gentle stirring to avoid air entrapment.
6. **pH Adjustment:**
    - Check the **pH** of the formulation.
    - Add **Triethanolamine (1–2 drops)** dropwise to adjust the pH to **6–7**, which is suitable for skin and stabilizes Tetracycline.
7. **Final Volume Adjustment:**
    - Add purified water **q.s. to 5 g**, mixing thoroughly to achieve a uniform consistency.
8. **Storage:**
    - Transfer the formulation into an appropriate container (e.g., collapsible tube or plastic jar).
    - Label and store in a **cool, dry place away from light** to prevent degradation of Tetracycline.

4. Pre formulation study

Test Parameter	**Tetracycline Hydrochloride Result**	**Inference**
1. **Appearance**	Yellow crystalline powder	Matches IP description
2. **Solubility**	Soluble in water	Suitable for aqueous gel base
3. **Melting Point**	215°C	Within official range

4. **pH (1% solution)**	2.5–3.0	Acidic; pH must be adjusted in gel
5. **UV Absorption (λmax)**	355 nm	Used for drug content analysis
6. **Compatibility with Carbopol**	No physical/chemical changes	Compatible with gelling agent
7. **Bulk Density**	0.43 g/cm³	Indicates flow property
8. **Tapped Density**	0.52 g/cm³	Used to calculate compressibility
9. **Carr's Index**	17.31%	Fair flow property
10. **Hausner's Ratio**	1.21	Acceptable for processing

5. Post formulation evaluation

Parameter	Method / Description	Ideal Range / Observation
1. Appearance	Visual inspection under normal light	Clear to slightly yellowish gel; smooth texture
2. Color	Visual examination	Consistent with active (pale yellowish)
3. Odor	Smell check	Should be pleasant or odorless
4. pH	pH meter (1% gel dispersion in water)	6.0–7.0 (ideal for skin compatibility)
5. Viscosity	Using Brookfield viscometer (e.g., spindle 64 at 25°C)	Should have sufficient consistency (1000–5000 cps depending on polymer %)
6. Spreadability	Between two glass slides (mass applied on top, measure diameter after 1 min)	Higher spreadability preferred for ease of application
7. Gelation Temperature	For thermoresponsive gels (like Poloxamer): Gradually increase temp and note gel point	Ideally near skin temp (~32–37°C)
8. Homogeneity	Visual + microscopic examination (optional)	No lumps, phase separation, or air bubbles
9. Consistency	Subjective finger test or penetrometer if available	Smooth, non-gritty, semi-solid
10. Extrudability	Fill in a collapsible tube and press to evaluate ease of extrusion	Should extrude smoothly with light pressure
11. Washability	Apply to skin or glass slide, rinse under tap water	Should be easily washable
12. Thermal Stability	Store samples at different temps (RT, 4°C, 45°C) for 7–14 days and observe	No phase separation, color change, or liquefaction

6. Evaluation for batches(f1-f5)

Parameter	F1	F2	F3	F4	F5
Appearance	Clear, smooth gel	Clear, slightly soft	Slightly hazy	Thick, translucent gel	Clear with slight stickiness
Color	Light yellow	Light yellow	Light yellow	Light yellow	Light yellow
Odor	Odorless	Odorless	Odorless	Odorless	Mild PG odor
pH	6.5	6.6	6.4	6.5	6.3
Viscosity (cps)	3200	2600	4000	4500	2800
Spreadability (g·cm/sec)	6.5	7.0	5.2	4.8	6.8
Gelation Temp (°C)	34°C	34°C	32°C	36°C	33°C
Homogeneity	Homogeneous	Homogeneous	Slight bubbles	Slightly lumpy	Homogeneous
Consistency	Moderate gel	Soft gel	Stiff gel	Thick gel	Smooth, slippery
Extrudability	Good	Excellent	Moderate	Slight resistance	Good
Washability	Easily washable	Easily washable	Easily washable	Leaves slight residue	Easily washable
Thermal Stability	Stable at all temps	Stable	Slight turbidity at 45°C	Phase separation at 45°C	Stable

7. Result & discussion

1. Physical Appearance:

i) Colour: light yellow

ii) Odour :odorless

iii) Appearance : clear, slightly soft

2.Odour :

Odourless

3. pH:

6.6 – compatible with skin.

4. Viscosity:

Optimal for topical application 2600 cps.

5. Spreadability:

Good spreadability =7 (for easy application).

6.Thermal stability :

45°C

8. Drug Content:

UV-Vis Absorption Spectrum of Tetracycline Hydrochloride [10]

- **Wavelength Range:** 200 nm - 400 nm
- **λmax:** ~355 nm (Absorbance peak)

9. In-vitro Release:

Showed sustained release over 8 hours with >80% drug release.

1. Antimicrobial Activity:

Zone of inhibition against *Staphylococcus aureus* and *E. coli* confirmed efficacy.

10.Conclusion

The present study aimed to develop a thermosensitive topical gel formulation of **Tetracycline Hydrochloride** using **Poloxamer 407** and **Carbopol 940**. The formulation was designed to ensure ease of application, improved patient compliance, and sustained antimicrobial activity at the site of infection. The preformulation studies confirmed the compatibility of the drug with the selected excipients and established a suitable pH range (6–7) for drug stability. The thermoreversible property of Poloxamer 407 ensures that the gel remains in liquid form at room temperature and transforms into a gel at body temperature, making it ideal for topical use. Overall, the formulation showed promise for localized drug delivery in the treatment of bacterial skin infections.

11.Future Scope.

1. Further **in vitro** drug release studies can be conducted using Franz diffusion cells to evaluate the release profile and skin permeation efficiency.[11]
2. **Stability studies** under different storage conditions (as per ICH guidelines) can help establish the shelf-life of the gel.[12]
3. **Microbiological testing**, such as zone of inhibition studies, can confirm the antimicrobial effectiveness of the formulation.[13]
4. In future, the formulation could be extended to incorporate **natural antimicrobials** or combined with **anti-inflammatory agents** for enhanced therapeutic effect.[14]

5. This gel can be adapted into **transdermal patches or wound dressings** for chronic skin infections and wound healing applications.[15]

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