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DEVELOPMENT AND CHARACTERIZATION OF STIMULI-RESPONSIVE *IN-SITU* HONEY GEL FOR IMPROVED WOUND HEALING APPROACH

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AIM & INTRODUCTION

Aim: To develop and characterize the stimuli-responsive *in-situ* honey gel for improved wound healing

Introduction: Honey has been used as a wound-healing agent for hundreds of years. This issue has recently gained popularity, most likely because of the emergence of antibiotic resistance in microbial pathogens[1]. The composition of honey impacts its bioactivity and, as a result, its wound-healing capacity[2].

Hydrogel is aqueous, viscous, semisolid preparation consisting of a gel matrix that can deliver drugs entrapped into its matrix. Hydrogel is ideal for local administration because it persistently releases drugs at a specific site[3].

Thermo-responsive hydrogel has an exceptional sol-gel transformation property, phase transition occurs in hydrogel when it reaches body temperature. Thermo-responsive hydrogel can be used as a therapeutic carrier for local administration where the sustained release of the therapeutic agent from the gel matrix promotes wound healing capability[3].

RESULTS

- Gelation temperature: The hydrogel maintains no-flow condition at 33°C, i.e., the temperature at topical wound environment. The sol-to-gel conversion takes place within 30 seconds of exposure, indicating quick conversion of the formulation into a gel for better retention at the site of application.

- Spraybility test: The ovality of the spraying patterns showed a diameter of approximately 6.2 ± 0.754 cm in the blank formulation, where the loading of honey in the formulation altered to 5.6 ± 0.532 cm. The alteration in the spray diameter is statistically not significant. The finding indicated better coverage while spraying over the wound area.

- Mucoadhesive strength: Mucoadhesive properties of the formulation assist in longer retention of topical formulation. Increase in mucoadhesive strength from 6.35 ± 0.861 g at 25ºC to 13.45 ± 0.973 g at 33ºC indicating longer retention of the formulation at the application site.
- pH: The pH of the formulation was found to be 6.5 ± 0.240, which would be favorable to be applied to the topical.
- Viscosity: Viscosity reflects the flowability of the formulation. The viscosity of the formulation was found to be 330 ± 11.56 cP, which indicated that the formulation can be easily sprayed while at the storage temperature of 25°C.
- Anti-microbial activity: Based on the findings, it can be concluded that the hydrogel formulation with honey performed well in antimicrobial efficacy. Thus, this formulation was further explored in the *in-vivo* experiments.

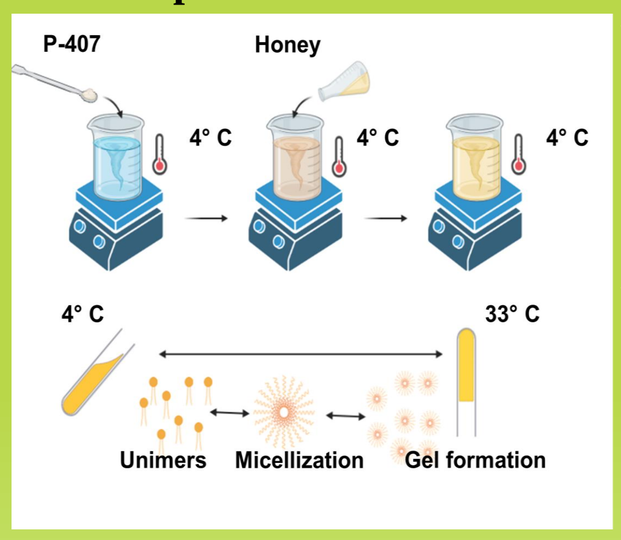
S. Aureus

E. Coli

- *In-vivo* effect: Comparing the wound contraction capability of the test formulation with that of the standard, it can be said that Group III showed better diabetic wound contraction capability compared to Group I & II. After day 14, the "percentage wound contraction" of the test group (Group III) was 98.50± 0.89 whereas Group I & II contracted 58.33 ± 0.61 & 88.50 ± 0.43 respectively.

METHODOLOGY

A. Preparation:



- ✓ Determination of pH: pH of the formulation was measured using a pH meter (Mettler Toledo pH meter)8.
- ✓ Anti-microbial activity: The honey hydrogel formulations were screened for their in vitro antibacterial activity against standard organisms, Gram-positive bacteria [Staphylococcus aureus MTCC 96 (*S. aureus*)] and Gram-negative bacteria [Escherichia coli MTCC 443 (*E. coli*)]. The agar disc diffusion technique was used to conduct the antibacterial activity[9].

B. Characterization:

- ✓ Test tube inversion method: This method was performed in a water bath where the temperature of the sample was increased slowly to record the change in the property[4,5].
- ✓ Spraybility test: The influence of Poloxamer 407 on the aerosol performance of the hydrogel formulation was also investigated in terms of the spray pattern. The spray of the formulation was done from a distance of 7 cm on graph paper maintained at 33° C. The obtained spray patterns were then analyzed[6].
- ✓ Texturometric analysis: Mucoadhesive property of the formulation was performed using a TA-XT Plus Texture Analyser[7].
- ✓ Rheological study: The viscosity of the formulation was measured using a cup and bob viscometer (Bohlin Visco 88 viscometer)[8].
- ✓ *In-vivo* antidiabetic screening: The study was conducted in healthy Sprague–Dawley rats (n = 9). Nine rats were divided into three groups fed a high-fat diet for a period of 3 weeks. After dietary manipulation, the experimental rats were fasted overnight. They were intraperitoneally injected with a freshly prepared solution of streptozotocin (STZ) (40 mg/kg) in 50 mM citrate buffer (pH 4.5) to induce type 2 diabetic model.
  - ❖ (**A**) Group I (control) untreated diabetic animals (**B**) Group II (standard) diabetic animals treated with Soframycin skin cream (framycetin sulphate 1% w/w), topically for 14 days. (**C**) Group III (test) diabetic animals treated with honey hydrogel formulation.
  - ❖ An excision wound of 500 mm² circular area was made on the back of each animal.
  - ❖ The areas of wounds were measured on days 4, 8, 12, and 14 post-wounding days and the mean percentage of wound closure was calculated.

CONCLUSION

The present study demonstrated the potential of the stimuli-responsive *in-situ* hydrogel formulation containing honey as a viable alternative to the conventional use of honey for the treatment of topical wounds.

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