Original Article

Formulation and Characterization of Mupirocin Nanomicelles in Insulin-Based Gel for Dermatological Application

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Abstract

Aim: To produce and analyze mupirocin nanomicelle (MP-NM) in insulin-based gel. **Procedures:** MP-NM was prepared using solvent evaporation with Tween 80 as a surfactant. HPMC polymer prepared gel. MP-NM was characterized by globular diameter, polydispersity index (PDI), pH, entrapment efficiency (EE), and transmission electron microscopy (TEM). NM MP release was studied *in vitro*. **Results:** The revolutionary MP-NM in insulin-based gel dissolves MP completely without precipitation due to its unique physical and chemical properties. MP had 8.64 ± 0.2 nm globular diameter, high EE (98.85 ± 0.01%), and normal homogeneous dispersion (PDI, 0.143 ± 0.003) in NM. MP's formula showed rapid first-order kinetics release. **Conclusion:** To our knowledge, this is the first MP-NM nano-drug delivery system employing insulin-based gel. It has promising pre-clinical and clinical uses.

Keywords: *Mupirocin, nano-drug delivery, nanomicelle, Tween 80*

Introduction

Nanomicelles (NM), self-assembling colloidal dispersions of 10–100 nm, have a hydrophobic core and a hydrophilic shell.[1] NM decrease drug breakdown, reduce side effects, and increase tissue penetration with minimum irritation, promoting medication bioavailability.[2]

Originally from pseudomonas fluorescens, mupirocin (MP) is a naturally occurring derivative of crotonic acid used as a topical antibiotic against gram-positive Staphylococcal and Streptococcal bacteria.[3] The antibiotic treats primary and secondary dermatological infections.[4] MP rapidly shuts down RNA and protein production by attaching to and inhibiting bacterial isoleucyl-tRNA synthetase.[5]

MP, a frequent antibiotic for dermatological infections, has a short half-life, strong protein binding, and bacterial resistance.[6] Hence, several de novo MP delivery systems, such as hydrogel dressings, liposomes, microsponges, nanofibres, and nanomicelles,[7] have been developed to improve patient compliance, reduce resistance, boost antibiotic delivery, and overcome classic formulation challenges.

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The current research developed a novel 2% MP-NM in insulin-based gel to preserve and increase MP release and deposition.

Materials and Methods

Materials

Baoji Guokang BioTechnology Co., Ltd. Supplied MP powder and Tween 80. (China). Ethanol came from Scharlab S. L. (Spain), and Wallocell supplied HPMC polymer, grade E10M. (Netherlands). Sigma-Aldrich (USA) supplied the PBS capsule, pH 7.4, while Eli Lilly and Co. supplied the soluble insulin (Indanapolis, USA).

Methods

Characterisation of mupirocin

λ max

Double beam ultra-violet visible (UV-vis) spectrometry (Cecil Instruments, England) within the

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200–400 nm wavelength spectrum was employed to establish the λ max of stock solutions.[8]

Calibration curve

Mixing 5 mg MP and 10 mL 10% aqueous ethanol generated a concentrated stock solution. Little aliquots, 0.5, 1, 2, 3, 4, 5, and 6 mL amounts, were collected from this solution and each built up to 10 mL using 10% aqueous ethanol to give a series of seven MP solution concentrations, 1.5, 2, 2.5, 3, 3.5, and 4 mg/mL. UV-vis spectroscopy determined concentration spectrum.[9,10]

Preparation of mupirocin-loaded nanomicelles

4% MP-NM was prepared by solvent evaporation. A glass screw tube contained 0.9 mL Tween 80 in 5 mL ethanol. To establish homogeneity, 200 mg MP was added and agitated for 15 minutes. The solution was baked at 40-45°C for 3 days to evaporate the ethanol. Drop-by-drop magnetic stirring (1200 rpm) combined deionized water with nanoparticles in ambient settings. This produced 5 mL of clear MP-NM.[11,12]

Evaluation of the mupirocin-loaded nanomicelles

Globular diameter and polydispersity index analysis

Photon correlation spectroscopy (Zetasizer NanoZS, Malvern Instrument, UK) measured MP-NM mean spherical diameter and polydispersity index (PDI). Brownian particle motions analyze light scattering fluctuation in the spectrometer.[13] Using filtered deionized water, MP-NM samples were diluted to 1:10 and 1:5 ratios. At 25°C and 173° angle of detection, globule diameters were measured.[14] Samples were analyzed three times.

Measurement of pH

Following calibration of an Inolab (Germany) pH meter using standard buffer solutions with pH values of 4, 7 and 9, a sample of MP-NM was placed immediately in contact with the electrode for analysis at a temperature of 25˚C. Three pH readings were taken in order to compute the mean value.[15]

Efficient entrapment

Entrapment efficiency was measured using a 5 cm dialysis membrane strip (3.5 Kd cut-off) as closed-ended tape (EE). 1 mL MP-NM, containing 40 mg MP, was put on the membrane and centrifuged at 6000 rpm for 45 minutes to separate the free MP. Using a solvent system, these drops were decanted and diluted. Sample absorbance was measured by UV-vis spectrometry at 222 nm.[16] The MP calibration curve's absorbance plot determined the supernatant's free MP concentration.

TEM

TEM (Supra-55VP Zeiss, Germany) was used to determine MP-NM sample shape, features, and globular dimensions. The material was diluted 1:1 and 1:10 with filtered deionized water.[17]

Insulin gel preparation

A hot plate magnetic stirrer was used to gradually dissolve 5 g HPMC polymer in 100 ml boiling deionized water to create a homogeneous gel.[18] After cooling, 0.1 mL soluble insulin was added to 4.84 mL gel to make insulin-loaded gel. 5.06 mL MP-NM was added to insulin-based gel to get the 2% final formulation.

In vitro drug release study

An adapted membrane dialysis method, based on the technique described by Schwarzl *et al.* (2017), was used for the *in vitro* drug release assessment. Transfer of the insulin-based gel MP-NM (200 mg MP) onto the dialysis membrane was performed (3.5 Kd cut-off). 1 mL aliquots of the receptor medium, PBS, were extracted at 1, 5, 10, 20, 30, 60, 90, 120 and 180 minutes, and at 24 hours, respectively. The volume was restored with fresh PBS on each occasion. The obtained samples were made up into a solution with 0.11 mL ethanol. UV-vis spectrophotometry was performed at 222 nm three times on each sample.[19,20]

Results and Discussion

Characterisation of mupirocin

Several investigations verified the identity and the purity of the MP powder. The λ max values obtained for MP and Tween 80 were similar to their basic values of 222 nm and 195-234 nm, respectively [Figure 1].[21]

Preparation of mupirocin nanomicelles in insulin-based gel

It has been claimed in a contemporary revision published by Gangwar *et al.* (2021) that in clinical or pre-clinical fields, there have been no nanoparticle preparations which have admixed MP with Tween 80 using NM. The current research is therefore considered to be innovative.[22] The preparation of MP-NM generated

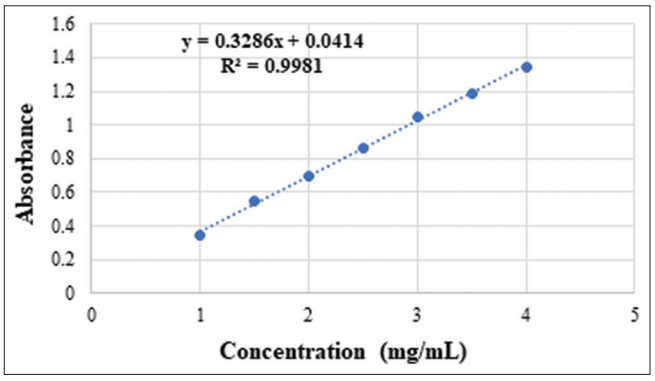

Figure 1: Calibration curve for mupirocin made up to various concentrations in 10% aqueous ethanol

Table 1: Formulation parameters: Globular diameter and polydispersity index. Data presented as mean±standard deviation, (*n*=3)

Formulas	F:D.W (mL:mL)	Diameter (nm)	PDI
F1	Without dilution	10.4±0.25	0.351±0.03
F2	1:5	9.687±0.06	0.276±0.01
F3	1:10	8.648±0.2	0.143±0.003

F=Formula, D.W=Distilled water, PDI=Polydispersity index

in this study was completely clear; the MP was totally dissolved with no visible precipitation of the drug. MP is dissolved by NM through its entrapment within the mixed micellar hydrophobic core; the clear aqueous solution is facilitated by a corona of hydrophilic chains which are directed towards the NM exterior.[23]

The use of the Tween 80 was thought to facilitate the production of the final clear solution and to ensure that the MP was totally dissolved. A polymeric non-ionic surfactant, Tween 80 enhances micelle stability and consequently, the solubilisation of hydrophobic compounds in an aqueous solution.

Evaluation of the mupirocin nanomicelles

Globular diameter and polydispersity index

The Formulations with different dilution ratios were considered to be within the nanodimension range. F3 was noted to have an expected homogeneous dispersion and globular size [Table 1, Figure 2].

A relatively high volume of Tween 80 was utilised in order to achieve the current nano-sized particle. Tween 80 showed an excellent behavior when it mixed with drug particles; it promotes the generation of smaller drug particles.[24]

Mupirocin nanomicelles: pH, entrapment efficiency and transmission electron microscopy

The MP-NM insulin-based gel showed a mean pH of 5.043 ± 0.05, which made it appropriate for use as a topical dermatological formulation. A number of intrinsic and extrinsic factors contribute to whether the use of an antibiotics to eradicate a localised skin infection is effective.

The free drug present and EE value obtained were 1.15 ± 0.01% and 98.85 ± 0.01%, respectively. There was successfully entrapment of the MP within the NM; no drug precipitation was seen within the preparation.

The appearance of the MP-NM particles is illustrated in Figure 3.

In vitro mupirocin release from nanomicelles

A high rate of MP release from the NM was observed within the initial 30 minutes; over the following 60 minutes this rate notably slowed until steady-state equilibrium was achieved [Figure 4].

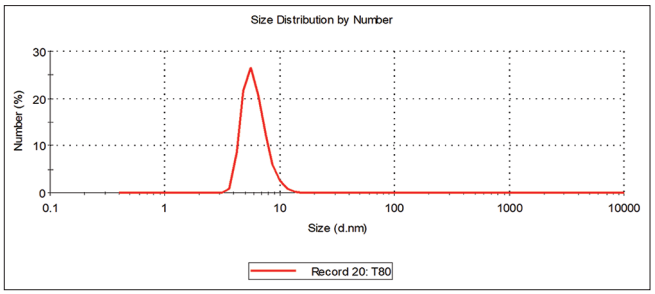

Figure 2: Mupirocin nanomicelles F3 (1:10 dilution ratio):globular diameter according to size distribution by number

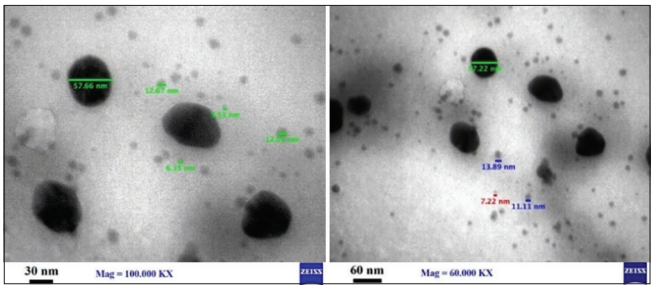

Figure 3: Mupirocin nanomicelles (dilution ratio 1:10), as seen by transmission electron microscopy

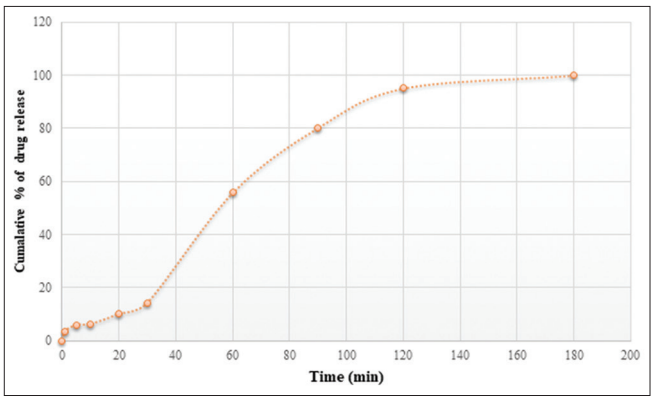

Figure 4: Mupirocin release profile from nanomicelles

Conclusions

The results are encouraging and suggest that this formulation may have applications in pre-clinical and clinical domains. Distinct physicochemical features for the MP-NM were observed which included impressive nanoparticle size and a characteristic homogeneous dispersion. The innovative preparation offered improved release profiles and highly efficacious EE.

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Conflicts of interest

There are no conflicts of interest.

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