MANUFACTURE OF DISSOLVING MICRONEEDLE LOADED WITH NANOSUSPENSION: POTENTIAL FOR PROLONGED LOCAL ANTI-INFLAMMATORY EFFECTS

QUEEN'S UNIVERSITY BELFAST

Mingshan Li [1], Lalitkumar Vora[1], Alejandro Paredes[1], Ryan F. Donnelly [1]

[1] School of Pharmacy, Queen's University Belfast, BT9 7BL, United Kingdom

Introduction

Nonsteroidal anti-inflammatory drugs (NSAIDs) are some of the most commonly used drugs at present. Approximately 30 million people consume NSAIDs every day around the world [1]. NSAIDs block the effect of cyclo-oxygenase (COX) enzymes to ease the pain and inflammation. Diclofenac (2-(2,6-dichloranilino) phenylacetic acid) belongs to NSAIDs and it is prominently used in osteoarthritis, ankylosing spondylitis, rheumatoid arthritis treatments and some post-operative pain management [2].

Aim

This project involves loading diclofenac nanosuspensions into dissolving microneedles (MNs) to achieve anti-inflammatory effects.

Method

Diclofenac nanosuspension (NS) was manufactured by beads milling methods [3]. A 7 mL glass vial contains 5 mL polymer blends composed of 9-10 kDa poly (vinyl alcohol) (PVA) and K-29/32 poly (vinyl pyrrolidone) (PVP). 200 mg of diclofenac drug powder and 2 mL of 0.1 mm beads were added into the glass vial. Four 12x6 mm stir bars in the vessel rotated at 1200 rpm.

Figure 1. The schematic diagram of beads milling method which is used to manufacture the DCF nanosuspensions.

Following the milling process, water was removed from the NS by freeze-drying the formulation.

Dissolving MNs were cast through a two-step process.

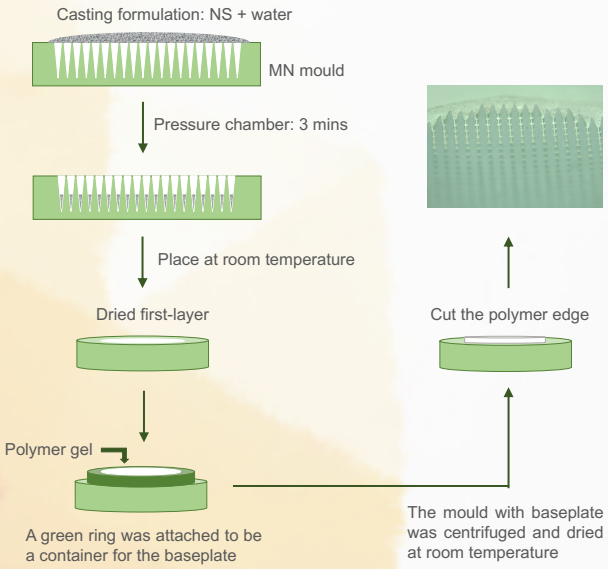

Figure 2. The schematic diagram of two-step casting method.

In the insertion study, MNs were placed into 37 ℃ oven for more than 30 mins and then were applied on the full-thickness porcine skin for 30 seconds. Insertion performances were observed under OCT.

Result and Discussion

The diclofenac drug powder had a particle size of 114 microns. During the milling process, after 3 hours, diclofenac NS had a particle size of 281.97±21.99 nm (n=10) and after 6 hours had a particle size of 241.53±11.87 nm (n=10). After 20 hours, the particle size of diclofenac NS decreased to 192.85±12.86 nm.

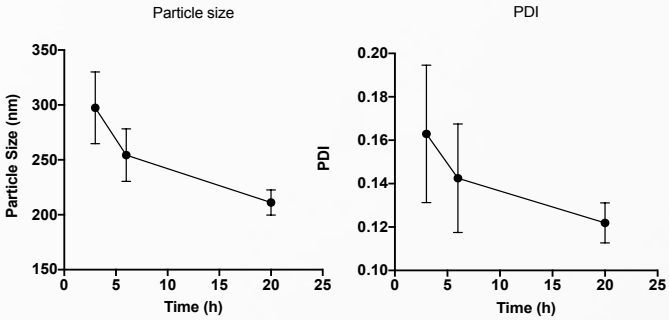

Figure 3. The particle size and polydispersity index of diclofenac were decreased with the milling time. (Mean ± SD, N =10)

Particle size was retained during freeze-drying. All four types of MNs were well-formed and successfully inserted into the porcine skin. The drug content of round MNs (750μm) was 2.3mg (n=5) and it could increase to 3.1mg (n=3). For 14x14 MNs (500μm), the drug content was 1.3mg (n=6). 19x19 MNs (500μm) had 1.2mg (n=6) drug loading and 16x16 MNs (850μm) had 2.3mg (n=6) drug loading.

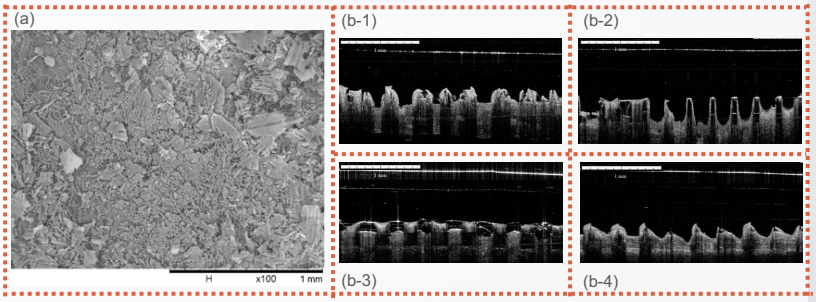

Figure 4. (a) The SEM photo of freeze-dried diclofenac NS. (b) The porcine skins were observed under the OCT after the insertion of MNs. (b-1) The applied MN patch was composed of 600 pyramidal needles with a height of 750 μm. (b-2) The applied MN was cast by the 16x16 silicone moulds with pyramidal needles (850 μm). (b-3) The applied MN was cast by the 14x14 moulds with conical needles (500 μm). (b-4) The applied MN was cast by the 19x19 moulds with pyramidal needles (500 μm).

Conclusion

NS of diclofenac were successfully fabricated *via* beads milling method and significantly decreased the particle size of diclofenac. Four types of dissolving MNs with two different baseplates were well-formed and could successfully inserted. The MN contained 600 pyramidal needles (750 μm) had the highest drug loading.

References

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