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Short communication

Development of Lidocaine-Containing NLCs Combined with 3D printed solid microneedle

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Introduction

Lidocaine is a widely utilized as local anesthetic in medical and dental procedures due to its effectiveness and low toxicity. In recent years, there has been a growing interest in the development of lidocaine formulations that can enhance drug delivery and provide prolonged analgesia. One such approach involves the utilization of nanostructured lipid carriers (NLCs) containing lidocaine base. NLCs, which belong to the category of lipid nanoparticles, offer advantages such as improved drug solubility, stability, and bioavailability (Suto et al., 2015).

The objective of the study was to prepare and optimize formulation parameters by selecting appropriate lipids and surfactants in conjunction with lidocaine base. Subsequently, a comprehensive evaluation of in vitro drug release and drug permeation through the skin was conducted. Furthermore, the study aimed to develop a method for investigating a drug delivery system combined with solid microneedles to enhance the penetration of lidocaine.

Materials and methods

The NLC formulation were prepared using ultrasonication with a Hielscher UP200S compact ultrasonic homogenizer (Hielscher Ultrasonics GmbH, Teltow, Germany).

Based on a 2^3 full factorial design, 8 different NLC formulations were prepared, varying the concentration of lidocaine (A), cooling process (B), and concentration of surfactant (Kolliphor RH40) (C). The dependent parameters assessed were zeta potential and particle size. These parameters were analyzed using photon correlation spectroscopy (PCS) with a Zetasizer Nano ZS instrument (Malvern Instruments, Malvern, UK).

Additional tests were conducted on the formulation, including the evaluation of thermal behavior using differential scanning calorimetry (DSC 3+, Mettler Toledo, Switzerland), and the determination of crystalline characteristics using X-ray powder diffraction (XRPD) with a D8 Advance diffractometer (Bruker AXS GmbH, Germany).

Biopharmaceutical investigations were carried out to assess in vitro release (using a synthetic membrane) and permeation (using heat-separated human epidermis) studies. These studies were conducted using a vertical Franz diffusion cell system (Phoenix RDS Automated Diffusion Testing System, Teledyne Hanson, USA). The permeation depth into the skin was investigated using Raman spectroscopy with a DXR Dispersive Raman spectrometer (Thermo Fisher Scientific Inc, USA).

The 3D printed solid microneedle arrays were fabricated using a biocompatible resin through stereolithography technology. Specifically, a Projet 6000 HD Stereolithography printer (3D Systems, Rock Hill, USA) was utilized for the fabrication process. The printed microneedles were subsequently examined and analyzed using a light microscope, (LEICA DM6 B model manufactured by Leica Microsystems GmbH, Germany).

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Results and discussion

The particle size (Z ave) values of the NLC systems ranged from 63.9 nm to 278.4 nm, indicating the size distribution of the particles. The Zeta potential of the NLC systems ranged from -14.3 to -79.5 mV, reflecting the surface charge of the particles (Table 1). The polydispersity index (PDI) values for all samples were below 0.3, indicating a narrow size distribution and uniformity within each formulation.

Table 1. Values of the independent and dependent factors examined in the factorial design formulation of the NLCs.

	A (%)	B (°C)	C (%)	Zeta potential (mV)	Z ave (nm)
NLC1	1	0	1	-79.5	262.6
NLC2	1	25	1	-52.9	250.2
NLC3	1	0	5	-15.4	85.16
NLC4	1	25	5	-32.3	67.19
NLC5	2	0	1	-44.8	265.4
NLC6	2	25	1	-48.6	278.4
NLC7	2	0	5	-14.3	63.9
NLC8	2	25	5	-23.9	71.45

The obtained results were analyzed using Statistica for Windows software version 13 (Fig. 1). Based on the results, the surfactant concentration had significant effect on the dependent factors.

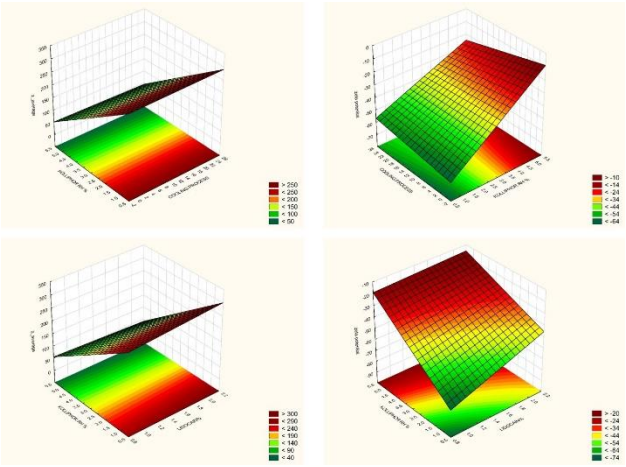

Fig. 1 Zeta potential and particle size as a function of the independent factors surfactant, lidocaine, and cooling process.

Among the various NLC formulations, NLC 6 was selected for further investigation, specifically to determine thermal behaviour, crystalline characteristics and biopharmaceutical profile of the drug delivery system.
In addition, the microneedles were prepared using SLA technology and designed in a spherical shape with a diameter of 1 cm. The microneedles exhibited a conical shape, measuring 1000 µm in height and 500 µm in base diameter. The spacing between the needles was set at 955 µm, while each needle's tip had a size of 50 µm (Elahpour et al., 2021). Microscopic examination was conducted to assess the suitability of these microneedles for dermal applications (Fig. 2).

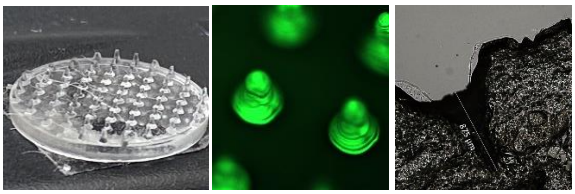

Fig. 2 Visual representation of the microneedle patch, providing an insight into the unique forms and structures of the needles, and screening in the skin.

Conclusion

In conclusion, factorial-made lidocaine containing NLCs was successfully developed and evaluated. 3D printed solid microneedles were fabricated and tested for further investigation. Hereafter, we would like to combine the NLC drug delivery system with solid microneedle and investigate the efficacy and potential of these formulations for enhanced drug delivery into the skin.

Our findings shed light on the distinct advantages and potential applications of each approach, providing valuable insights for the development of optimized drug delivery systems in the field of local anesthesia.

References

Elahpour, N., Pahlevanzadeh, F., Kharaziha, M., Bakhsheshi-Rad, H.R., Ramakrishna, S., Berto, F., 2021. 3D printed microneedles for transdermal drug delivery: A brief review of two decades. Int. J. Pharm., 597, 120301. doi.org/10.1016/j.ijpharm.2021.120301

Sütő, B., Weber, S., Zimmer, A., Farkas, G., Kelemen, A., Budai-Szűcs, M., Berkó, S., Szabó-Révész, P., Csányi, E., 2015. Optimalization and design of an ibuprofen-loaded nanostructured lipid carrier with a 2^3 full factorial design. Chem. Eng. Res. Des. 104, 488-496. doi.org/10.1016/j.cherd.2015.09.010