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Short communication

Following-up skin penetration of lidocaine from different vehicles by Raman spectroscopic mapping

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ABSTRACT

The application of local anesthetics, usually administered by subcutaneous injection, is common in the course of diagnostic, therapeutic, and cosmetic dermatology procedures. The effective dermal delivery of lidocaine could offer a solution to many adverse effects caused by needle insertion, such as pain, local reactions or toxicity, and additionally, it avoids the disruption of anatomical landmarks. Therefore, novel dermal formulations of local anesthetics are needed to overcome the barrier function of the skin and provide sufficient and prolonged anesthesia. In our study, we aimed to investigate and compare the penetration profiles of four different lidocaine containing formulations (hydrogel, oleogel, lyotropic liquid crystal and nanostructured lipid carrier) by Raman microscopic mapping of the drug. The application of Raman spectroscopy provided information about the spatial distribution of lidocaine in the skin *ex vivo*. The penetration of lidocaine from lyotropic liquid crystal and nanostructured carrier reached deeper skin layers and a higher amount of the drug was diffused into the skin, compared with hydrogel and oleogel. This study confirmed that nanostructured carriers can improve skin penetration properties of lidocaine and proved the applicability of Raman spectroscopy in the research of dermatological preparations ex vivo as a nondestructive, relatively easy and fast technique.

1. Introduction

Dermal drug delivery systems are getting increasingly more attention these days because their application is beneficial in many conditions. Dermal application is advantageous due to a decrease in potential adverse reactions and the avoidance of first pass metabolism. However, the skin penetration of drugs is a really complex process because many factors have an impact on it, *e.g.* the physicochemical properties of the API, the carrier system, occlusion, concentration, dosage regimen, skin site on the body, *etc.* [1]. Furthermore, the stratum corneum (SC), which is the outermost layer of the skin, is almost impermeable and it provides a rate-limiting step in the penetration process [2]. The exact knowledge of drug distribution in the skin would be indispensable for the optimization of dermal formulations by revealing their penetration pathways. Widely used techniques for following-up drug penetration, such as diffusion cells and tape-stripping method, are destructive, labor intense, lacking accuracy and have many issues with establishing adequate experimental conditions [3–5].

Spectroscopic methods can provide molecular information about the structure of skin specimens. Raman spectroscopy is an upcoming spectroscopic technique based on detecting the characteristic vibrational energy levels of a molecule irradiated by laser beam and it provides information about the molecular structure of tissue components without the use of fluorescent labels or chemical stains [6–10]. Therefore, this technique is suitable for detecting changes in the structure of skin components and also for following-up the penetration of exogenous materials [8]. In recent times, Raman microscopy has evolved as an important technique to better understand skin structure and percutaneous drug delivery [4,8,11,12].

In this work, we aimed to track the penetration of lidocaine (LID) from different carrier systems in human skin. We used Raman microscopy to obtain images of the spatial distribution of the drug in *ex vivo* human skin. Lidocaine is a local anesthectic agent used in pharmacological pain control and management. The site of action for LID is the dermis, which contains the free nerve endings respon-

Abbreviations: LID, lidocaine; LID-B, lidocaine base form; LID-HCl, lidocaine hydrochloride; LLC, lyotropic liquid crystal; NLC, nanostructured lipid carrier; SC, stratum corneum.

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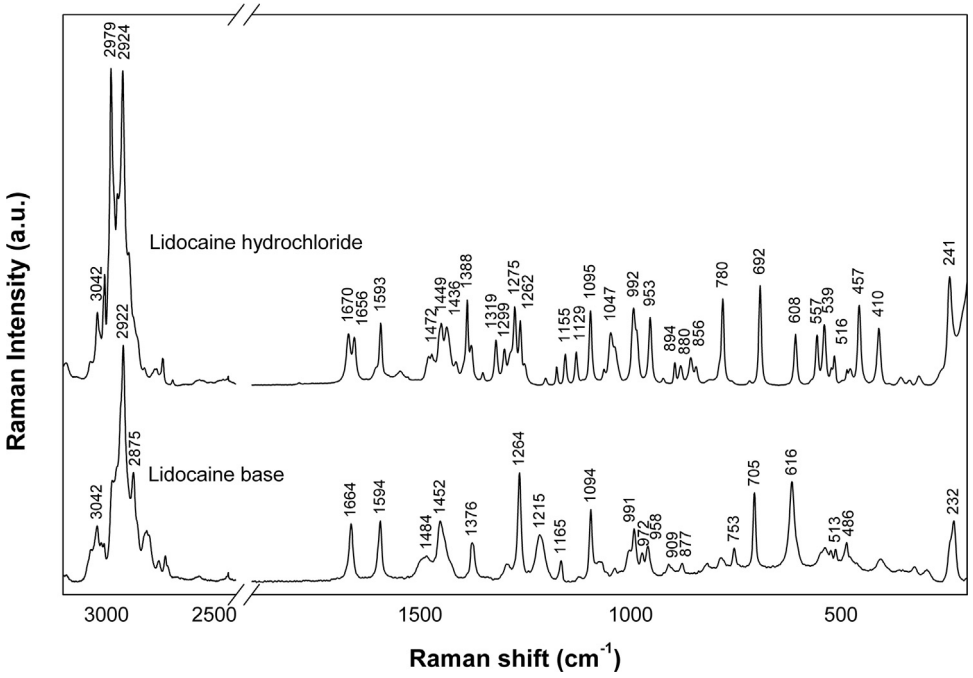

Fig. 1. Raman spectra of the lidocaine base and hydrochloride salt forms with indication of the peak positions.

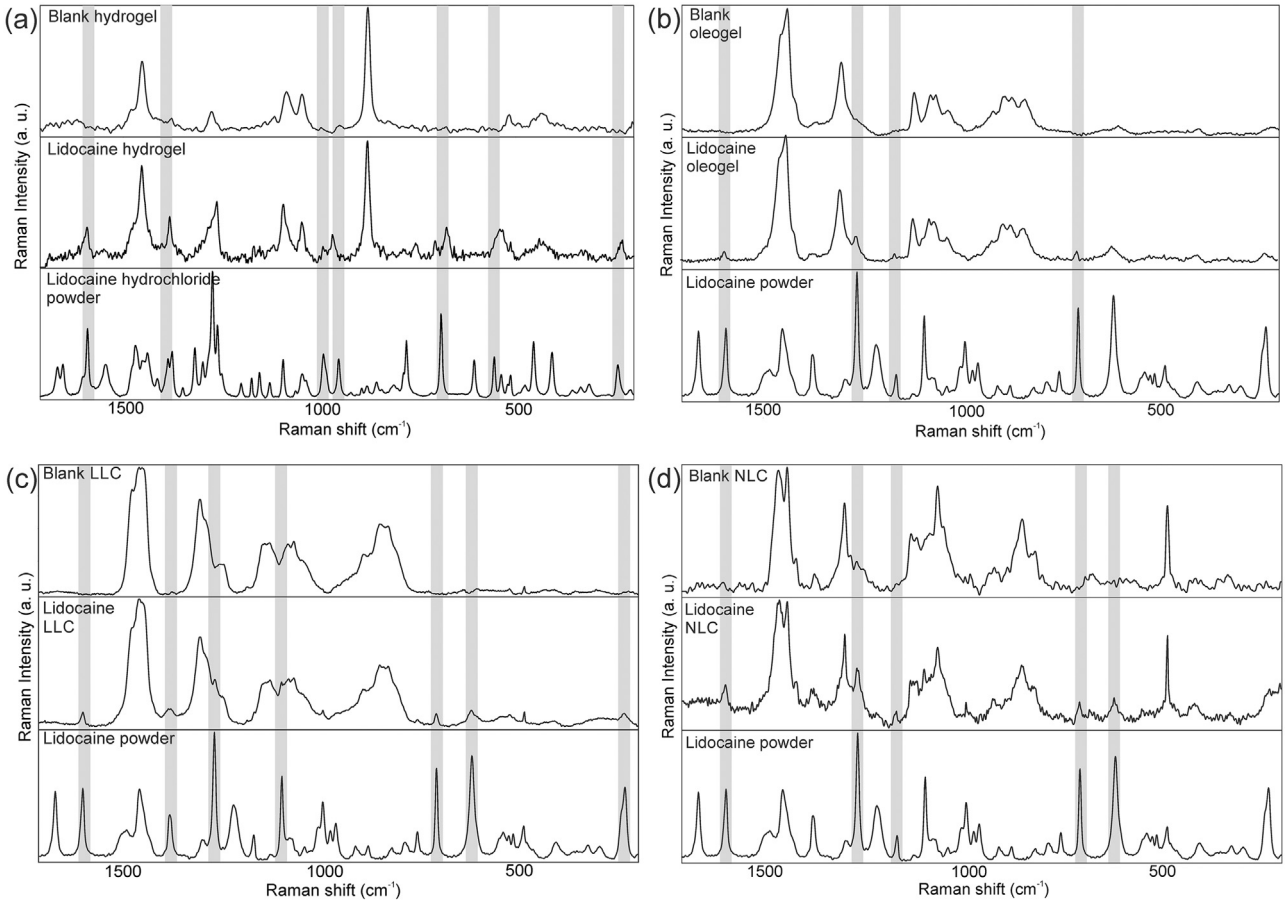

Fig. 2. Raman spectra of hydrogel (a), oleogel (b), LLC (c) and NLC (d) formulations.

sible for pain sensation [2]. However, the topical application of this drug is not as effective as administration by subcutaneous injection because its penetration into the dermal layers is limited owing to the barrier function of SC. Using a vehicle which maximizes drug delivery into the skin seems to be a good strategy for optimizing the percutaneous permeation of topically applied drugs. So there