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BergaCare smartLipids® lidocaine – increased dermal anesthetic potency & duration of action at reduced risk of serious adverse reactions

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Lidocaine ointments with a high drug content of up to 20% are commonly used to anesthetize the skin sufficiently prior a painful and invasive skin treatment such as tattooing or lasering. Two formulation problems occur: Firstly, the lidocaine ointment has only a short shelf life of less than one week since such a large quantity of lidocaine cannot be completely dissolved even in a highly lipophilic ointment such as petroleum jelly. Consequently Ostwald ripening progresses leading to formation of sharp needle-like crystals irritating the skin and impair the penetration. Secondly, lipophilic ointments cannot be entirely removed from skin without soap or alcohol. Because both should be avoided prior to an invasive skin treatment, non-removed lidocaine can enter the blood circulation unhindered increasing the risk of serious adverse reactions e.g. tremor, dizziness, respiratory depression and cardiac arrhythmia. To overcome this problem a hydrophilic, better removable lidocaine formulation is required. However, just dissolving the lidocaine directly in a hydrophilic base at skin pH would form single charged cations which only poorly penetrate the skin, thus decreasing distinctly the bioavailability. Therefore lidocaine was loaded into smartLipids® and then incorporated into easily removable hydrogels.

smartLipids® are the optimized 3rd generation of lipid nanoparticles after the solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC). Strictly speaking, they are a specialized version of the NLC. The special about smartLipids® is their clearly increased drug loading capacity with firm drug inclusion during storage. The difference is in the lipid composition. The lipid matrix of the SLN typically consisted of only 1 solid lipid, the NLC of 1 solid lipid combined with 1 liquid lipid. In contrast, the smartLipids® matrix is composed of multiple lipids, e.g. 5 to 10 lipids causing a “chaotic” particle matrix structure. The many imperfections and less ordered lipids allow a higher drug loading, which was exploited for formulating lidocaine. The lidocaine showed an initial maximum loading of 15% in SLN and 25% in NLC, but the lidocaine was expelled from the NLC matrix after only 2 weeks of storage at room temperature. In contrast, lidocaine at 40% could be loaded in the optimized smartLipids® matrix consisting of Polyglyceryl-2 Dipolyhydroxystearate, Octyldodecanol, Carnauba (Carnauba Wax), Candelilla Cera (Candellila Wax), Cera Alba (Beeswax), Cetearyl Glucoside, Cetearyl Alcohol and MCT (medium chain triglycerides).

A particle suspension composed of 20% lipid-drug matrix, 2% Plantacare 810 UP, 1% Sisterna PS 750C and 77% distilled water was produced by high pressure homogenization (500 bar, 3 cycles, at 75°C). A small skin-adhesive particle size of 143 nm was achieved and the formulation showed no drug expulsion with stable particle size over 3 months up to now.

To transfer the suspension into a dermally applicable form, hydroxypropyl cellulose was used to from a hydrogel containing 8% lidocaine. Physical stability of the particles in the gel was shown at both 5°C and room temperature over 3 months up to now.

The potency and duration of action of new developed hydrogel was compared with a 20% lidocaine petroleum jelly formulation in a double blind and triply performed in-vivo orientating study. 50 mg formulation was applied on 2cm x 8cm sized area at the inner side of the forearm and in short intervals the treated area was pricked with a blunt needle. The numbness had to be evaluated from 0% to 100%, where 100% represented the totally numbness. Regarding the potency lidocaine smartLipids® hydrogel was clearly superior with a maximum numbness of 60% reached already after 15 minutes, were the standard formulation never exceed 20% during the whole test period although having a 2.5 times higher lidocaine concentration. With regard to the analgesic duration, the hydrogel showed again considerable advantage with a long lasting numbing effect of 35 minutes compared to the standard formulation with duration of only 20 minutes. After 40 minutes of exposure time the hydrogel dried out completely forming a thin and elastic film which was removed by pulling off in one piece. In contrast, the standard formulation was wiped off with a tissue conventionally done in laser centers. Afterwards, the relative reminding lidocaine content on the skin surface was investigated. Even after removing the standard formulation very carefully from the skin, 2% of applied lidocaine amount remained, whereas less than 0.1% and thus 20 times lower amount of lidocaine was detected on the skin surface treated with the lidocaine smartLipids® hydrogel.

To sum up, lidocaine smartLipids® hydrogel was developed having a 12 times prolonged shelf life with three times increased potency. The duration of action almost doubled compared to the standard formulation, which had even 2.5 times higher lidocaine concentration. In addition, the removability of the formulation from skin is 20 fold improved and thus the safety of the formulation regarding serious adverse reactions is distinctly increased.