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MICRONEEDLE ASSISTED PERMEATION OF LIDOCAINE HCL FROM A NaCMC:GEL HYDROGEL

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Lidocaine hydrochloride (HCl) is a common local anaesthetic with a short time of drug action and relatively long period of sustained delivery¹. Additional active molecules, such as tetracaine and adrenaline, are used in topical lidocaine ointment to enhance lidocaine HCl delivery. However, these molecules compete with the injected lidocaine HCl². For example, adrenaline is likely to cause a reduced percutaneous delivery of lidocaine HCl^{3,4}. Microneedle assisted delivery of lidocaine HCl involves the creation of artificial pores to bypass the SC layer of skin for delivery of lidocaine HCl⁵. Unlike topical based ointments, injectable lidocaine HCl can produce a burning sensation and is suitable for less sustained percutaneous delivery^{6,7}. However, the time delay between skin surface applications of eutectic mixtures of local anaesthetics (EMLA) to permeating at a depth of 3000 μ m is 60 minutes⁸. In the present work, a pre-fabricated set of stainless steel microneedles with a needle interspacing of 1100 μ m was impacted on dissected porcine skin section at a force of \sim 0.09 N per needle⁵. A novel lidocaine hydrogel was also formulated with approximately half the mass loading of local anaesthetics contained in Lidoderm and EMLA formulation^{5,9,10}. A poke and patch method was adopted in directing the polymeric hydrogel into the microneedles holes on skin. Mild pseudoplasticity resembling an ointment formulation for lidocaine NaCMC:gel hydrogel remained constant when lidocaine HCl loading mass increased. Gelatine (gel) to sodium carboxymethylcellulose (NaCMC) mass ratio of 2.3 resulted in highly favourable zeta potentials when lidocaine HCl 2.4% w/w was loaded. Microneedle assisted lidocaine delivery of gel to NaCMC mass ratio of 2.3 resulted in crossing a minimum therapeutic level at skin depths of \sim 730 μ m before 70 minutes (Fig. 1). The lidocaine permeation flux was 1.7 times greater for gel to NaCMC mass ratio of 2.3 compared with a mass ratio of 1.6 under microneedle assisted delivery (Fig. 2).

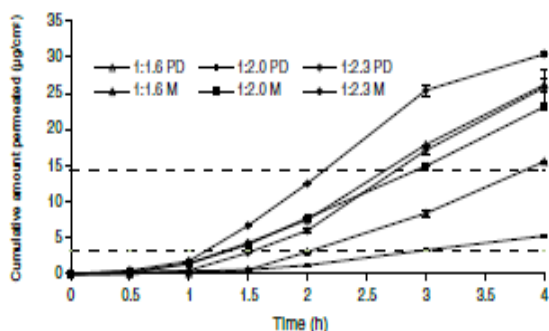


Fig. 1 Example of cumulative amount of lidocaine hydrochloride permeated through skin from NaCMC/GEL within a 4 hour period.

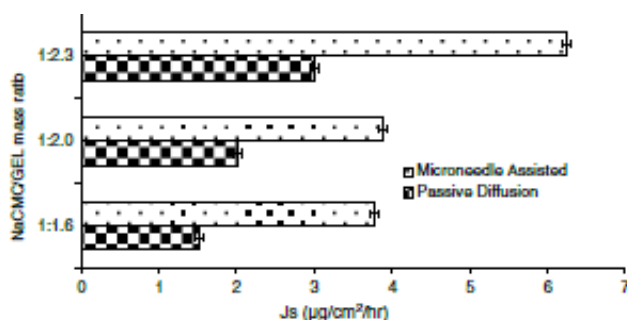


Fig. 2 Example of Lidocaine (2.4% w/w) NaCMC/GEL flux permeation through skin.

References

1. R.G. Loughlin, M.M. Tunney, R.F. Donnelly, D.J. Murphy, Jenkins, P.A. McCarron "Modulation of gel formation and drug-release characteristics of lidocaine-loaded poly(vinyl alcohol)-tetraborate hydrogel systems using scavenger polyol sugars" *Eur. J. Pharm. Sci.*, **69**, 1135–1146 (2008).
2. B.C. Smith and A.H. Wilson, "Topical versus injectable analgesics in simple laceration repair: An integrative review" *J.N.P.*, **9**, 374–380 (2013).
3. M.H. Bekhit, The essence of analgesia and anagesics. Lidocaine for neural blockade, Cambridge University Press, 280-281 (2011).
4. S. Chale, A.J. Singer, S. Marchini, M.J. McBride, D. Kennedy "Digital versus local anesthesia for finger lacerations: A randomized controlled trial" *Acad. Emerg. Med.*, **13**, 1046-1050 (2006).
5. A. Nayak, D.B. Das, G.T. Vladislavljević "Microneedle-assisted permeation of lidocaine carboxymethylcellulose with gelatine co-polymer hydrogel" *Pharm. Res.*, **30**, 1-15 (2013).
6. M.E. Hogan, S. vanderVaart, K. Perampaladas, M. Machado, T.R. Einarson, A. Taddio "Systematic review and meta-analysis of the effect of warming local anesthetics on injection pain" *Ann. Emerg. Med.*, **58**, 86-98 (2011)
7. M.H. Bekhit, The essence of analgesia and anagesics. Lidocaine for neural blockade, Cambridge University Press, 280-281 (2011).
8. S. Tadicherla and B. Berman "Percutaneous dermal drug delivery for local pain control" *Therapeut Clin Risk Manag.*, **2**, 99-113 (2006).
9. A. Nayak, D.B. Das "Potential of biodegradable microneedles as a transdermal delivery for lidocaine" *Biotechnol Lett.*, **35**: 1351-1363 (2013).

10. K.S. Paudel, M. Milewski, C.L. Swadley, N.K. Brogden, P. Ghosh, A.L. Stinchcomb "Challenges and opportunities in dermal/transdermal delivery" *Ther Deliv.*, **1**, 109-131 (2010).