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A Comparison of Oil-In-Water and Water-In-Oil Microemulsions for Enhancing Piroxicam Permeation Through Skin

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SUMMARY. **Microemulsions consisting of vitamin E acetate (oil phase), Labrasol® and Plurol Oleique® (surfactant phase) were developed for transdermal delivery of a water insoluble non-steroidal anti-inflammatory drug (NSAID) piroxicam. Oil-in-water (o/w) and water-in-oil (w/o) microemulsions were formulated and their physicochemical properties were determined prior to *in vitro* skin permeation studies using Wistar rat skin in a modified Franz diffusion cell. The optimal o/w and w/o microemulsion contained vitamin E acetate (14% and 19%), 3:1 of Labrasol®:Plurol Oleique® (56% and 73%), and water (30% and 8%), respectively. To compare, o/w microemulsions exhibited similar piroxicam loading to w/o microemulsions (0.4 mg/g) but smaller droplet size (66 nm vs 157 nm) and higher drug incorporation efficiency (86% vs 75%). Drug permeation in rat skin following topical application of o/w microemulsions was found to be significantly greater (763 µg/cm²) than that obtained using w/o microemulsion (411 µg/cm²) and piroxicam solution in water (459 µg/cm²) ($p < 0.05$). The release profile of piroxicam from microemulsions fitted the zero order model while the profile for piroxicam solution followed first-order kinetics. Both types of piroxicam microemulsion were stable on storage at room temperature for at least three months. These findings demonstrate that o/w microemulsions offer significant potential as transdermal delivery systems for piroxicam in the treatment of acute and chronic rheumatoid arthritis.**

RESUMEN. Se desarrollaron microemulsiones conteniendo acetato de vitamina E (fase oleosa), Labrasol® y Plurol Oleique® (fase surfactante) para la administración transdérmica del fármaco antiinflamatorio no esteroideo insoluble en agua (AINE) piroxicam. Se formularon microemulsiones de aceite en agua (o/w) y agua en aceite (w/o) y se determinaron sus propiedades fisicoquímicas antes de los estudios de permeación cutánea *in vitro* usando piel de ratas Wistar en una célula de difusión de Franz modificada. La microemulsión optima de o/w y w/o contenía acetato de vitamina E (14% y 19%), 3:1 de Labrasol®: Plurol Oleique® (56% y 73%) y agua (30% y 8%), respectivamente. Las microemulsiones de o/w mostraron una carga similar de piroxicam a microemulsiones w/o (0,4 mg/g) pero un tamaño de gota más pequeño (66 nm frente a 157 nm) y una mayor eficacia de incorporación de fármaco (86% frente a 75%). La permeabilidad del fármaco en la piel de rata después de la aplicación tópica de microemulsiones o/w fue significativamente mayor (763 µg/cm²) que la obtenida usando una microemulsión w/o (411 µg/cm²) y una solución de piroxicam en agua (459 µg/cm²) ($p < 0.05$). El perfil de liberación de piroxicam a partir de microemulsiones se ajustó al modelo de orden cero mientras que el perfil para la solución de piroxicam siguió una cinética de primer orden. Ambos tipos de microemulsión de piroxicam se mantuvieron estables durante el almacenamiento a temperatura ambiente durante al menos tres meses. Estos hallazgos demuestran que las microemulsiones o/w ofrecen un potencial significativo como sistemas de administración transdérmica para el piroxicam en el tratamiento de la artritis reumatoide aguda y crónica.

KEY WORDS: microemulsions, NSAID, piroxicam, rheumatoid arthritis, skin permeation, transdermal drug delivery.

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