Ethosomal Gel for Topical Administration of Dimethyl Fumarate in the Treatment of HSV-1 Infections

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The infections caused by the HSV-1 virus induce lesions on the lips, mouth, face, and eye. In this study, an ethosome gel loaded with dimethyl fumarate was investigated as a possible approach to treat HSV-1 infections. A formulative study was conducted, evaluating the effect of drug concentration on size distribution and dimensional stability of ethosomes by photon correlation spectroscopy. Ethosome morphology was investigated by cryogenic transmission electron microscopy, while the interaction between dimethyl fumarate and vesicles, and the drug entrapment capacity were respectively evaluated by FTIR and HPLC. To favor the topical application of ethosomes on mucosa and skin, different semisolid forms, based on xanthan gum or poloxamer 407, were designed and compared for spreadability and leakage. Dimethyl fumarate release and diffusion kinetics were evaluated in vitro by Franz cells. The antiviral activity against HSV-1 was tested by plaque reduction assay in Vero and HRPE monolayer cells, while skin irritation effect was evaluated by patch test on 20 healthy volunteers. The lower drug concentration was selected, resulting in smaller and longer stable vesicles, mainly characterized by a multilamellar organization. Dimethyl fumarate entrapment in ethosome was 91% w/w, suggesting an almost total recovery of the drug in the lipid phase. Xanthan gum 0.5%, selected to thicken the ethosome dispersion, allowed to control drug release and diffusion. The antiviral effect of dimethyl fumarate loaded in ethosome gel was demonstrated by a reduction in viral growth both 1 h and 4 h post-infection. Moreover, the patch test demonstrated the safety of the ethosomal gel applied on the skin.

Słowa kluczowe

dimethylfumarate, cryogenic transmission electron microscopy, HSV-1, infection control, in vitro diffusion

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