PURPOSE

To investigate the percutaneous penetration of nortriptyline chlorhydrate (NTH) from film matrices of (hydroxypropyl)methylcellulose (HPMC) for transdermal drug delivery.

EXPERIMENTAL METHODS

Film preparation:

NTH was dissolved in a mixture of PG (15%), PEG 400 (1%) in distilled water at 0.2% (Film I), 1% (Film II), 2% (Film III), 4% (Film IV) and 6% (Film V). HPMC (2%) was then incorporated. Once gel consistency was obtained, the mixture was dried over night on a glass plate (BIO-RAD, Segrate (MI) Italy). Film VI was obtained by addition of chitosan microparticles (NTH, 4% w/w to HPMC gel with NTH (6%).

Microparticle preparation:

Chitosan solutions in acetic acid (1%, w/w) were homogenized (Teflon pestle, 1000 rpm) and left to stand for 24 h at room temperature. NTH (8%, w/w) in PG (15%, w/w) (50 g) was added to chitosan solution (50 g) and pH was adjusted to 5.5. Spray-drying (Minispray Dryer, Büchi 190, Switzerland) was used). The size distribution was determined by the laser light scattering technique (Zetasizer Nano Series, Malvern Instruments, United Kingdom).

The morphology of the microparticles was observed with a scanning electron microscope (SEM, S-4100; Hitachi Co., Ltd, Tokyo, Japan). Spherical morphology was observed, with a size of 3.6 ±1.7 µm. The drug content was of 3.89 ± 0.23 % and the loading efficacy was of 97.5%.

RESULTS AND DISCUSSION

NTH released at 24 h was higher than 88 % of the dose for Films I to V, for Film VI was 79 %. Kd values were similar for the patches from I to V and they show significant differences (P<0.05) with respect to Film VI, for which the diffusion constant was 12.47 mg/cm².h. This fact could be attributed to the microparticles, which act as a reservoir.

Lag time calculated for film VI is smaller than those obtained with the other films. It could be attributed to the effect of PG, what is present in the sheet and also in the microparticles.

CONCLUSION

Film VI (4.6 cm x 4.6 cm) should used for the initial dosage regimen in smoking cessation and 8 cm x 8 cm for the maintenance dose. Optimisation of the patch can be possible by incorporation of penetration enhancers (i.e. ethanol, oleic acid, polysorbate 80) in the films.