DEVELOPMENT AND VALIDATION OF A LC METHOD FOR THE DETERMINATION OF SIX CORTICOSTEROIDS, SALICYLIC ACID AND PARABENS IN DIFFERENT PHARMACEUTICAL FORMULATIONS

R. Marini, A. Pantella, M.A. Bimazubute, P. Chiap, Ph. Hubert and J. Crommen.

Dept. of Analytical Pharmaceutical Chemistry, Institute of Pharmacy, University of Liège, CHU, B36, B-4000 Liège 1, Belgium.

Esters of corticosteroids such as clobetasol propionate, clobetasone butyrate, betamethasone dipropionate, betamethasone valerate, triamcinolone acetonide and hydrocortisone acetate are widely prescribed in the topical treatment of psoriasis. They are mainly used alone or combined with salicylic acid in dermatological formulations containing mixtures of methyl- and propylhydroxybenzoates as preservatives.
Up to now, few methods have been described for the simultaneous determination of corticosteroids and salicylic acid.
The objectives of this study is to develop and validate a LC method which can be used for the determination of these compounds in several pharmaceutical formulations (cream, lotion, gel...).
Due to the large difference in polarity between these different compounds, a gradient elution was applied in order to separate them on the same chromatogram and reduce the analysis time.
An adequate separation was obtained by using the DryLab optimisation software. The gradient conditions (gradient range and gradient time), the optimal pH of the mobile phase buffer and the column temperature could be predicted on the basis of a limited number of experiments.
An analytical column (250 x 4.6mm ; i.d.) packed with Superspher octadecyl silica was used. The mobile phase consisted of a mixture of acetonitrile and pH 3.5, 25mM phosphate buffer. The proportion of organic modifier was increased from 30 % to 45 % in 9.9 minutes, then from 45 % to 96 % in 19 minutes. The flow rate was 1.5 ml/min and the column temperature was set at 61°C. The detection was performed at 240 nm.
The developed method was then validated. Very good results with respect to relationship between response and concentration (linearity), selectivity, precision and accuracy were obtained.
The proposed LC method for the analysis of six corticosteroids, acid salicylic as well as methyl- and propylhydroxybenzoates seems to be particularly advantageous in terms of resolution and analysis time.