

ISSN 0102-6593

caderno de farmácia

Órgão Oficial da Faculdade de Farmácia da Universidade Federal do Rio Grande do Sul
volume 26, Suplemento, 2010

SIMULTANEOUS DETERMINATION OF PERMEATION THROUGH MEMBRANE OF CITRAL ISOMERS BY CENTRAL COMPOSITE DESIGN / SURFACE RESPONSE - PARTIAL LEAST SQUARES (PLS)

¹MIRON, D.; ¹SALES, J.; ³CATEN, C. S. T.; ¹MAYORGA, P.; ²SCHAPOVAL, E. E. S.

¹Laboratório de Controle de Qualidade de Medicamentos, Faculdade de Farmácia, UFRGS;

²Laboratório de Desenvolvimento Galênico, Faculdade de Farmácia, UFRGS;

³Laboratório de Otimização de Produtos e Processos, Escola de Engenharia, UFRGS.

Doutorando: início 2009/1

Introduction Citral is a volatile oil consisting of two geometric isomers - neral (cis) and geranial (trans). The characterization and quantification of volatile oils is challenging as well as the separation and quantification of isomers. The determination of isomers of citral in different matrices is commonly performed by gas chromatography coupled with mass detector or flame ionization. Alternatively, liquid chromatography with UV detection (UV) has been used in both normal phase and reverse phase. The combination method of UV spectrophotometry to mathematical techniques, as the derivative and multivariate analysis, have resolved, in many cases, lack of selectivity of this method. The application of quantitative chemometric methods, particularly the method of partial least squares (PLS) to multivariate analysis of chemical data has been widely applied. Models of permeation are important to optimize the diffusion of drugs from pharmaceutical formulations. Simple, rapid and selective analytical techniques are of great interest in studies of permeation.

Objective: This work describes the application of central composite design - response surface for the selection of the best wavelengths in the UV bands for determination of neral and geranial by PLS. Our research involves the development of formulations containing citral indicated for the treatment of onychomycosis and evaluation of antifungal activity of neral and geranial. Thus, the method by UV - PLS developed was used in the initial evaluation of the membrane permeation of geranial and neral in pharmaceutical formulations.

Materials and Methods: The spectrophotometric analysis was performed on SHIMADZU Spectrophotometer model UV-1601PC controlled by microcomputer, using quartz cells of 10 mm. The acquisition of absorbance was carried out between 200-290 nm using the program UVPC. The data were pretreated in an Excel (2003). The multivariate calibration by the method of Partial Least Squares (PLS), the central composite design and response surface were performed in Minitab 14 software. The range of concentrations used for neral and geranial were 0.1 - 8.8 and 0.1 - 7.9 $\mu\text{g ml}^{-1}$, respectively. The absorption spectra were obtained in the range of 200-290 nm in 1 nm increments, using acetonitrila: water (6:4) as a blank. All absorption data were standardized by centering the mean and the calibration performed with use of two main components.

Results and Discussion: To optimize the lower and upper wavelength, central composite design was employed. As central points were employed factor with lower RMSEP in previous experiments (234 and 258 nm for neral and 234 and 264 nm for geranial). Good fit was obtained between experimental data and the surface response for neral ($r^2=0.942$) and geranial ($r^2=0.967$), using RMSEP as answer. The optimization determined the range of wavelengths of 236-256 nm for quantification of neral and 233-266 nm for geranial. The predictive ability of the optimized methods was evaluated using seven mixtures of isomers of citral. The recovery obtained for both isomers showed accuracy and precision consistent with the sample and technique employed. The use of UV-PLS allowed to characterize the membrane permeation of different formulations of citral.

Conclusions: The mixtures of isomers of citral are complex systems due to large overlap of the absorption spectra in UV of geranial and neral. To overcome the drawback spectral interference and quantify the isomers was applied the multivariate calibration by PLS method. Moreover, the range of wavelength used was determined with the aid of a central composite design associated with analysis by response surface methodology. Good analytical results demonstrate the usefulness of this procedure for determination of neral and geranial in permeation studies. The procedure is an alternative method fast and inexpensive compared with chromatographic techniques.