COMPARATIVE STUDY IN VITRO OF THE RELEASE OF METRONIDAZOLE FROM DERMATOLOGICAL PRODUCTS

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INTRODUCTION
Rosacea is a chronic skin disorder characterized by transient or permanent redness of the skin, usually limited to the center area of the face, which may be accompanied by pustules, papules and telangiectasia as well as itching and burning sensation on the skin (1-7). Topical metronidazole is one of the first-line treatments used in this disease. In our country, topical metronidazole is marketed by different pharmaceutical companies as a gel and a cream at 0.75%. It is also prescribed as a compound custom medication in gel form at similar concentration. In this study we evaluated the in vitro release of metronidazole from a compound medication prepared in gel form and two commercial products, a gel and a cream.

MATERIALS AND METHODS
The analytical methodology proposed by the USP 30 for metronidazole was a UV spectrophotometry technique. This was validated in terms of linearity, range, precision, accuracy and specificity (8,9).

We standardized the method to evaluate the release of metronidazole using the modified apparatus 5 of the USP by means of its precision (Category III). For this, the values obtained in each vessel were utilized to obtain the coefficient of variation.

The method used to evaluate the release from metronidazole formulations was a modification of the Apparatus 5 of the USP 30 (paddle over disk), originally used for the evaluation of the release from transdermal patches. The experimental conditions for testing the in vitro release were 50 rpm, 900 mL, 32°C and deaerated distilled water as the dissolution medium.

The kinetic order was calculated using the equation of Peppas. Also other kinetic models (zero order, first order and Higuchi) were studied in order to deepen about the release mechanism of metronidazole from the tested products considering the factor of determination ($r^2$) as a basis for comparison.

The statistical treatment of the values of the constants of average release rate of metronidazole from gels studied ($P_1$ and $P_2$) was conducted using analysis of variance and multiple range test (Statgraphics Plus 5.1 software)

RESULTS
The analytical methodology to quantify metronidazole by UV was validated and met the acceptance criteria outlined in the ICH and USP 30.

The release method was validated with regard only to its precision, as pointed out by the validation recommendations of the USP 30. The results show a similarity between the products $P_1$ and $P_2$ and a noticeable difference with the product $P_3$ (cream).

The results obtained by Peppas equation indicate that the release kinetics of metronidazole given for the three products is approaching a Higuchi model. The release kinetics of metronidazole was adjusted to an apparent first order for the three products studied.

The results showed significant differences between gels and cream. The gel products (reference and compound medicine) turned out to be similar, according to the calculation of the difference factor $f_1$ and $f_2$ similarity factor.

CONCLUSIONS
In this study was compared the in vitro release of metronidazole from a compound medicine prepared in gel form and two commercial products, gel and cream obtaining significant differences between gel and cream products, while products in gel form were similar. These results indicate that the commercial and the compounding gel should have similar efficacy in vivo.
REFERENCES
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