

# Transdermal permeation study of a 5% cetirizine nanoemulsion

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Skin Forum 12th Annual Meeting: APV International Association for Pharmaceutical Technology

28<sup>th</sup> to 29<sup>th</sup> March 2011 in Frankfurt, Germany.

## INTRODUCTION

Cetirizine dihydrochloride is a second generation H1 antihistamine, with no sedating characteristics. At the site of action it causes vasoconstriction leading to a decreased vascular permeability. It also diminishes redness, swelling and *pruritus* associated with allergic reactions. Nanoemulsions are kinetically stable dispersions of oil and water, forming transparent and translucent systems, with a droplet size range from 20 to 100 nm. At present, there are no semisolid formulations with cetirizine for topical administration. An alternative treatment for skin allergic reactions could be developed, consisting of a nanoemulsion applied directly onto the affected area.

## EXPERIMENTAL METHODS

### Material

| Ingredients             | Formulation (%) |
|-------------------------|-----------------|
| Cetirizine Chlorhydrate | 5               |
| Propilenglycol          | 5               |
| Transcutol® P           | 20              |
| Purified water          | 17              |
| Labrasol®               | 19              |
| Plurol® Oleique         | 19              |
| Isostearyl isostearate  | 5               |
| Limoneno                | 10              |

**Elaboration method:** The formulation was prepared by weighing and mixing of different components and agitation by vortex shaker.

### Characterization of the nanoemulsions:

- **Nanoemulsion droplet size analysis:** Zeta-Sizer Malvern Instruments, Spain.
- **Rheological study:** Rotational viscosimeter (Haake VT 500) was used for flow curves evaluation.
- **Skin permeation:** Franz-type diffusion cells (Crown Glass Co. Sommerville, N.J., USA) with a diffusion area of 2,54 cm<sup>2</sup> and abdominal human skin from Hospital de – SCIAS (Barcelona, Spain).
- **Determination and quantification of Cetirizine HCl:** A Waters (Milford, Mass., USA) LC module I plus instrument.
- **Nanoemulsion stability:** was determined by measuring the droplet size as a function of time, both at 4°C and 25°C.
- **Statistic data analysis:** non-parametric statistical assay (Kruskal-Wallis Z, p<0,05), using GraphPad for Windows 2008.
- **Permeation parameters** (Steady state concentration): non-linear adjustment from the equation of transdermal penetration LAPLACE®.

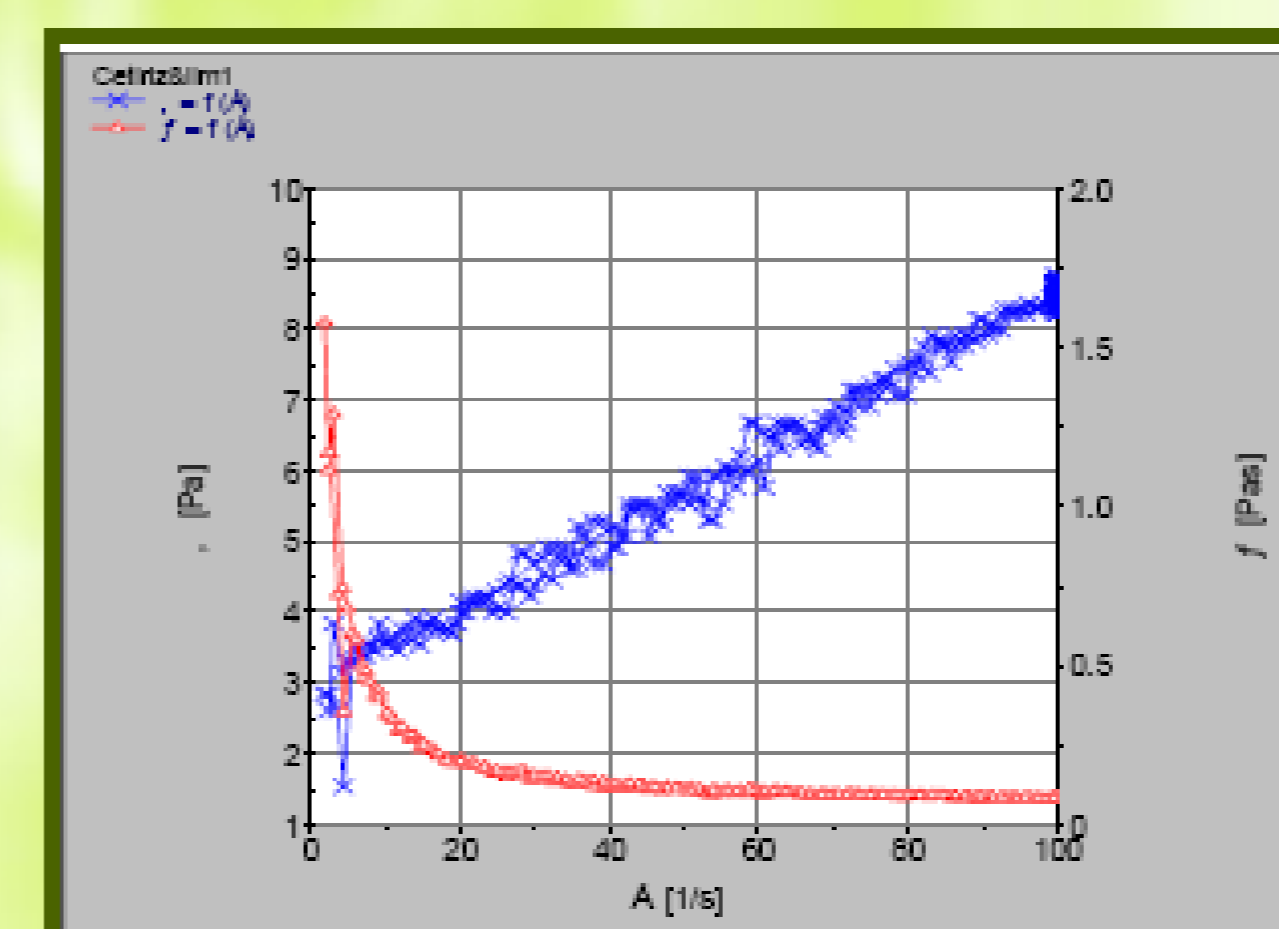
## RESULTS AND DISCUSSION

Droplet size measure and polydispersity in different temperatures:

| Temperature (°C) |                  |                   |                  |                  |                  |
|------------------|------------------|-------------------|------------------|------------------|------------------|
| 4°C              |                  | 25°C              |                  | 40°C             |                  |
| Size (nm)±SD     | Pld (SD)         | Size (nm)±SD      | Pld (SD)         | Size (nm)±SD     | Pld (SD)         |
| 8,55<br>(0,064)  | 0,131<br>(0,020) | 10,08<br>(0,7946) | 0,150<br>(0,019) | 8,622<br>(0,051) | 0,168<br>(0,026) |

The study with changes in temperature, it was seen that particle size and polydispersity measures have remained stable.

### Rheological study: Flow curves



Flow curves and the apparent viscosity show a pseudoplastic feature of the nanoemulsion studied, with a certain structure at rest.

### Transdermal permeation:

The steady state concentration achieved was 5.96 E 10-<sup>5</sup> µg/ml (therapeutic levels: 0.257-0.384 µg/ml). 102.27 µg cetirizine/g of skin per cm<sup>2</sup>, maximum 166.28 and minimum 52.29 (expressed by median) were retained.

| Parameters  | Median               |
|---|----------------------|
| J/sup (µg/h)/cm <sup>2</sup>                                  | 1,58                 |
| Tl (h)  | 17,97                |
| Kp (cm/h)   | 4,64 e <sup>-5</sup> |
| Co (µg/ml)  | 34033,65             |
| Cetirizine retained in the skin (µg/gr piel/cm <sup>2</sup> ) | 102,27               |

## REFERENCES

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## CONCLUSIONS

We have designed a new formulation for topical administration of cetirizine, with particle size of nanometer order. After the nanoemulsions stability study, with changes in temperature, it was seen that particle size and polydispersity measures have remained stable. The transdermal permeation test, opens the possibility to investigate whether or not these quantities are sufficient to cause a local antihistaminic activity. Knowing that antihistamines applied topically usually lead to sensitization of the patient, further biopharmaceutical and toxicological studies are needed.

**Acknowledgements:** To Gatefossé and Reig Jofré for supplying the excipients for the study.