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Abstract

Study on In Vitro Release and Permeation of Oxymetazoline Hydrochloride from Topical Cream and Hydrogel Vehicles †

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Background:

Oxymetazoline is a selective α1A adrenergic receptor agonist and α2A adrenergic receptor partial agonist, and it belongs to the group of vasoconstrictor drugs, for which an anti-inflammatory effect was also demonstrated. In the last fifteen years, oxymetazoline, as a water-soluble hydrochloride salt, has been used off-label as a topical therapy effective in reducing persistent facial erythema associated with rosacea, through cutaneous vasoconstriction [1,2]. In 2017, the Food and Drug Administration approved a topical cream containing 1% oxymetazoline hydrochloride (brand name Rhofade® by Allergan, Dublin, Ireland) for topical treatment of persistent facial erythema of rosacea [2]. However, because Rhofade® is not available in all European countries, oxymetazoline hydrochloride is prescribed for this indication in the form of extemporaneous preparations. The selection of the vehicle for topical extemporaneous preparations is very important for a successful therapy, as the excipients used significantly impact the properties of the preparations, including drug release and permeation profiles [3]. Several recently published studies revealed the safety, tolerability, and efficacy of some cream matrices containing 1% oxymetazoline hydrochloride, but without any data about their in vitro drug release and permeation.

Objective:

The present study aimed to evaluate the in vitro release and permeation of oxymetazoline hydrochloride from different topical semisolid matrices in correlation with their composition. Methods. The solubility of oxymetazoline hydrochloride in two receptor media (citrate buffer with pH 4.5, and sodium chloride isotonic solution) was measured by the saturation shake-flask method. The experimental formulations were prepared by dissolving 1% oxymetazoline hydrochloride in the aqueous phase of three semisolid matrices: a hydrophilic cream (OCR) based on liquid paraffin and cethylstearyl alcohol and stabilized with Cremophor® A6 and Cremophor® A25 (BASF, Ludwigshafen, Germany); a hydroxypropylmethylcellulose-based hydrogel (OHPMC); and a poloxamer 407-based hydrogel (OP407). The prepared formulations where evaluated in terms of drug content,

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in vitro drug release, and permeation through a synthetic membrane and pig ear skin, respectively, using vertical diffusion cells.

Results:

As the solubility of oxymetazoline hydrochloride was higher in the citrate buffer (pH 4.5) than in the sodium chloride isotonic solution, the first was selected as the receptor medium for in vitro release and permeation tests. The drug content of the tested formulations ranged between 99.78 ± 1.17% and 101.29 ± 0.69%, revealing the uniform distribution of oxymetazoline hydrochloride in the systems. Through the synthetic membrane, the hydrogels rapidly released (first 2 h) over 90% oxymetazoline hydrochloride, whereas the cream slowly released (over 7 h) only 21% of drug; all the release profiles fitted best with the Korsmeyer–Peppas model. When using pig ear skin as a semipermeable membrane, the oxymetazoline hydrochloride permeation from the cream was higher (66.25%) than that from the hydrogels (32.02% for OHPMC and 48.96% for OP407); the zero order and Korsmeyer–Peppas models described better the drug permeation.

Conclusions:

Compared to the cream formulation, the hydrogels presented greater ability for oxymetazoline hydrochloride in vitro release through a synthetic hydrophilic membrane, but a lower drug permeation when using a biological membrane. All tested formulations can be considered for the optimization formulation study.

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