

DESIGN AND ELABORATION OF METRONIDAZOLE 1% TOPICAL SOLUTION FOR TREATMENT OF ULCERS INFECTED BY ANAEROBIC BACTERIA

3PC-021



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BACKGROUND AND IMPORTANCE

Literature was reviewed in order to elaborate metronidazole 1% topical solution for treatment of ulcers infected by anaerobic bacteria, recommend refrigeration storage. However, the samples elaborated in the Hospital Pharmacy Department presented a crystalline precipitate, which could not be redispersed. Therefore, a compounding improvement was necessary.

AIM AND OBJECTIVES

Design and analyze, by galenic validation, different compounding improvement to increase the solubility of metronidazole in water in three storage environments.



MATERIAL AND METHODS

A bibliographic search was done finding that metronidazole base solubility:

- in water is 10.5 mg/mL (25°C)
- in propyleneglycol is 17 mg/ml (20°C)

The 1% solution in water is a saturated solution that initially presents an oversaturation stage whose intensity and duration are determined by solid particle size and its solubility increases progressively over the time.

We elaborated three metronidazole solutions in different vehicles:

- 1 Water (M1)
- 2 Water + Glycerin (M2)
- 3 Water + Propyleneglycol (M3)

30-DAY FOLLOW-UP:

- ✓ Stored in refrigeration, room-temperature and $T^a > 25^{\circ}\text{C}$.
- ✓ A galenic validation was carried out:
 - organoleptic characteristics,
 - sedimentation time
 - Redispersability
 - Homogeneity
 - crystal growth
 - pH
- ✓ Analysis on days 0,1,5,7,11,14,18,30

RESULTS

The three solutions had a pH=5.5 and showed neither color nor odor throughout the 30-day analysis.

In refrigeration, in less than 24h, the three solutions crystallized and cannot be resuspended

Follow-up was stopped and refrigeration was discarded.



Conservation	Metronidazole in Water (M1)	Metronidazole in Water + Glycerin (M2)	Metronidazole in Water + Propyleneglycol (M3)
Room temperature	<ul style="list-style-type: none">✓ Crystals were observed✓ It was necessary a hand vigorous shaking and heating for several minutes to resuspend them.		<ul style="list-style-type: none">✓ Physical characteristics were maintained✓ It was no longer oversaturated from day = 18.
$T^a > 25^{\circ}\text{C}$	<ul style="list-style-type: none">✓ The three solutions began as an oversaturated solution:<ul style="list-style-type: none">➢ No crystals were observed at any time✓ M3 became a saturated solution on day = 4 and M1/M2 on day=7		



CONCLUSION AND RELEVANCE

- ✓ Metronidazole base in solution cannot be stored in refrigerator due to an irreversible crystallization.
- ✓ Glycerin as a humectant does not provide any advantage compared with water as a single vehicle.
- ✓ Propyleneglycol allows a compounding improvement because it increases the solubility of metronidazole in water, allowing the solution to be preserved at room temperature without crystals formation and to reach the saturation phase quickly at $T^a > 25^{\circ}\text{C}$.
- ✓ The hospital pharmacists knowledge allows to solve compounding difficulties derived from the physicochemical characteristics of raw materials.