

XyliFos®

Microbiological Quality of XyliFos® and LoxaSperse® 10% in XyliFos® Dispersions Evaluated by Mikrocount® Combi

Abstract: The incidence of microbial contamination of LoxaSperse and XyliFos formulations containing fluticasone propionate was evaluated for a period of 48 h after the powders were mixed with sterile water under realistic conditions of use by the patient. The resultant dispersions were subjected to total viable microbial count examination using a Mikrocount® Combi kit. Dip-slide tubes coated on both sides with specific media that allow distinguished bacterial and fungal growth were used in determined time intervals in order to assess the microbiological quality of the preparation. Neither microbial contamination nor physical characteristic changes were detected in the LoxaSperse and XyliFos dispersions containing fluticasone propionate throughout the 48 h study time period. The results showed that these non-sterile pharmaceutical preparations in sterile water avoided microbiological contamination in the absence of a preservative for at least 48 h after formulation reconstitution.

Introduction:

LoxaSperse and XyliFos are proprietary powder excipient bases used in compounding for nasal nebulization or nasal and wound irrigation. LoxaSperse corresponds to a blend of specially micronized xylitol with an optimized ratio of micronized poloxamers, designed to improve the dispersability and solubility of active pharmaceutical ingredients (APIs) [1]. XyliFos contains a unique patent-pending epigallocatechingallate (EGCg)-cyclodextrin complex and was developed to boost the performance of LoxaSperse when combined in the same formulation [2]. LoxaSperse and XyliFos mixtures are thus dry powders, formulated as non-sterile capsules or sachets, indicated to be dissolved in purified water or saline prior to administration.

LoxaSperse and XyliFos mixtures are dispensed as powders in capsules or sachets without preservatives. At the time of use, the patient must add a predetermined amount of sterile normal saline or sterile water to an appropriate cup, empty the powder contents into the liquid and mix gently to form a dispersion that will be administered via irrigation or nasal nebulization. From the moment of adding water to the powder, the non-sterile dispersion could possibly become a good environment to support microbial contamination and proliferation.

The aim of this study was to evaluate the capability of the LoxaSperse and XyliFos mixtures to remain exempt of microorganisms for 48 h after the non-sterile preparation was mixed with water under realistic conditions of use by the patient. Fluticasone propionate was the API chosen to be mixed with LoxaSperse and XyliFos due to its ample use as a corticosteroid with topical anti-inflammatory effects against asthma [3].

Methodology:

Mikrocount® Combi was the microbial monitoring system used in the microbiological assay. It is a simple tool applicable to determine the total number of microorganisms present in any pharmaceutical and cosmetic sample, which provides rapid and reliable microbial control. The simple sampling and evaluation of results through different agar medium for bacteria and fungi confers practicability to a wide scope.

Materials: Fluticasone Propionate USP Micronized (lot number C171080) and the excipients XyliFos (lot number 70448981) and LoxaSperse (lot number 6961943) were obtained

from PCCA (Houston, TX, USA). Two capsules size #1 were filled with 3 mg of fluticasone propionate in XyliFos and 3 mg of fluticasone propionate in LoxaSperse 10% in XyliFos, separately, and stored at 4°C. The test dispersions were prepared in medicine plastic cups individually, by adding the contents of each capsule to 10 mL of sterile water (sterile water for injection-USP, Hospira, lot number 49-257-DK). Mikrocount® combi tubes were supplied in a box with 10 units by Schülke Inc. Each tube contains a dip-slide coated on one side with TCC-agar medium (light pink medium - bacterial growth), while on the other side with Rose-bengal-agar (red medium - fungal growth) [4].

Total Viable Microbial Count Assay: The microbiological quality of XyliFos and LoxaSperse 10% in XyliFos formulations, after mixture with an appropriate amount of sterile water, was evaluated using the Mikrocount® Combi kit. The assay was undertaken at room temperature for 48 h after the test dispersions were placed in individual medicine plastic cups with free environmental exposure (absence of any protective coverage), according to the kit's instructions. A single dip-slide tube was used for microbial measurement of the test dispersions at each of the following time-points of exposure: 1, 2, 3, 4, 5, 6, 7, 8, 24 and 48 h. The lid of each tube was loosened to remove the slide without touching the agar surfaces. A slide for each test dispersion was wetted for a few seconds by using a plastic disposable pipette to transfer the liquid to both sides. The excess of liquid was drained off the slide, and it was replaced back in the tube, screwing tightly the lid. The bacterial or fungal growth was visually analyzed by colony counting on the respective agar surface, after 48 h (bacteria) or 96 h (fungi) of incubation at 30°C, maintaining the tube sealed. The results can be compared with an evaluation chart in order to characterize in CFU/mL the degree of microbial contamination of the preparation.

Results and Discussion:

The microbiological assay using a microbial test kit (Mikrocount® Combi) revealed no microbial contamination in both LoxaSperse and XyliFos test dispersions containing fluticasone propionate for up to 48 h following preparation. No changes in physical characteristics were observed throughout the study (Figures 1 to 3).

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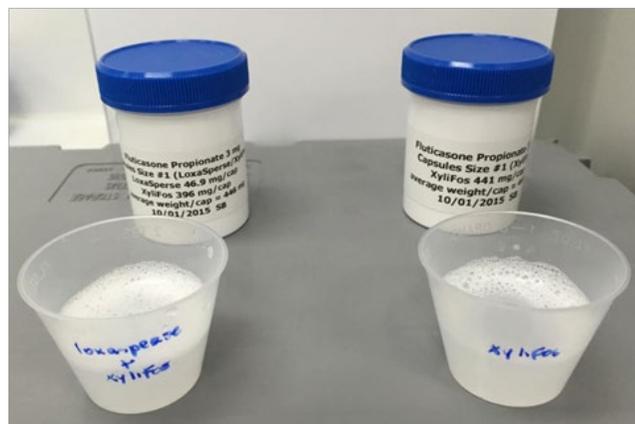


Figure 1. Fluticasone propionate in XyliFos-containing dispersions after formulation reconstitution in the adequate medicine plastic cups.



Figure 3. Representative dip-slide with double agar sides free of microorganisms. This dip-slide was used to test the XyliFos-containing dispersions after 48 h of environment exposure.

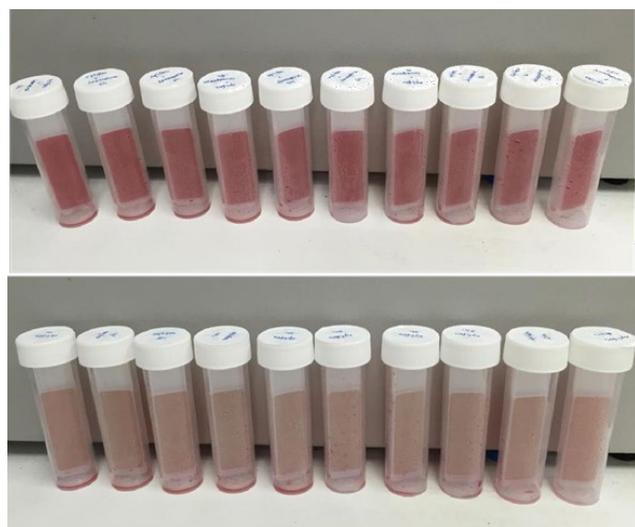


Figure 2. Dip-slide tubes used for testing XyliFos-containing dispersions at 1, 2, 3, 4, 5, 6, 7, 8, 24 and 48 h after the powder contents were mixed with sterile water.

Conclusions:

The LoxaSperse and XyliFos formulations containing fluticasone propionate, as non-sterile pharmaceutical preparations in sterile water used for nasal nebulization/irrigation, are able to prevent microbial contamination up to 48 h and, therefore, are appropriate for immediate use in nasal nebulization/irrigation. The LoxaSperse and XyliFos dispersions, even without a preservative, were free from microbial contamination during the first 48 h after reconstitution under realistic conditions of use by the patient.

References:

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