

Technical Report:

Microbiological Quality of LoxaSperse® Dispersion Evaluated by Mikrocount® Combi



Abstract: LoxaSperse™ is a powder excipient base used for nasal nebulization and irrigation designed to improve dispersibility and solubility of Active Pharmaceutical Ingredients (APIs). PCCA evaluated the incidence of microbial contamination of a LoxaSperse formulation containing fluticasone propionate for a period of 24 h after the powder was mixed with sterile water under realistic conditions for use by the patient. The resultant LoxaSperse dispersion was 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 dispersion containing fluticasone propionate throughout the 24 h study time period. The results showed that this non-sterile pharmaceutical preparation in sterile water avoided microbiological contamination in the absence of a preservative for at least 24 h after formulation reconstitution.

Introduction:

LoxaSperse is a powder excipient base used for nasal nebulization and irrigation. It is 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) (PCCA, 2013). The use of xylitol and poloxamers in nebulization and irrigation is thoroughly referenced in the literature and there is ample evidence of their safety and efficacy (Durairaj *et al.*, 2006; Jagannath *et al.*, 1995; Plataki *et al.*, 2011; Zabner *et al.*, 2000).

LoxaSperse formulations are dispensed as powders in capsules or sachets without preservatives. Due to an extremely low water activity of less than 0.5, microbiological growth cannot occur in this powder (PCCA, 2013). 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 LoxaSperse 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 formulation to remain exempt of microorganisms for 24 h after the non-sterile preparation was mixed with water under realistic conditions for use by the patient, and to draw conclusions about its microbial risk for use in nasal therapy. Fluticasone propionate was chosen as the API in the LoxaSperse formulation tested due to its ample use as a corticosteroid with topical anti-inflammatory effects against asthma (Colice *et al.*, 2013).

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.

Methodology:

Materials: Fluticasone Propionate USP Micronized (lot number C145638) and the excipient LoxaSperse (lot number 5994620) were obtained from PCCA (Houston, TX, USA). A capsule size #1 was filled with 3 mg of fluticasone propionate in LoxaSperse and stored at room temperature. The test dispersion was prepared in a sterile plastic cup by adding the contents of one capsule to 10 mL of sterile water under non-sterile conditions. Mikrocount® Combi tubes were supplied in a 10-unit box 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).

Total Viable Microbial Count Assay:

The microbiological quality of the LoxaSperse formulation after reconstitution with sterile water was evaluated using the Mikrocount® Combi kit. The assay was undertaken at room temperature for 24 h after the test dispersion was placed in a plastic cup open to environmental exposure (absent of any protective cover), according to the kit's instructions. A single dip-slide tube was used for microbial measurement of the test dispersion at each of the following time-points of exposure: 1, 2, 3, 4, 5, 6, 7, 8 and 24 h. The lid of each tube was loosened to remove the slide without touching the agar surfaces. Each slide was dipped into the test dispersion for a few seconds in a way in which both sides stayed completely wet. The excess liquid was drained off the slide, the slide was re-inserted into the tube, and the lid was tightly fixed to close the tube. 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, with the tube remaining sealed. The results can be compared with an evaluation chart in order to characterize in CFU/mL, which represents 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 the LoxaSperse

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dispersion containing fluticasone propionate for at least 24 h after it was mixed with sterile water and placed in an adequate container specified for patient use. No changes in its physical characteristics were observed throughout the study (Figures 1 to 3).

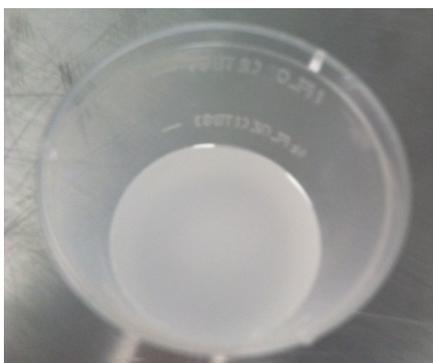


Figure 1. Fluticasone Propionate in LoxaSpers dispersion after the formulation was reconstituted in a sterile plastic cup.

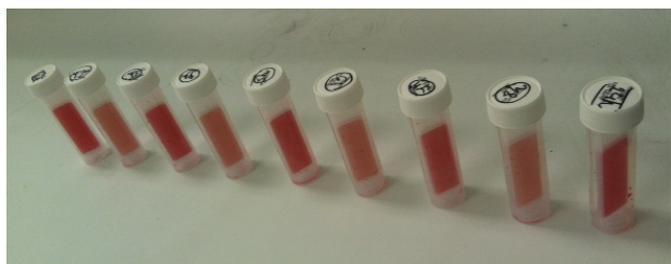


Figure 2. Dip-slide tubes used for testing LoxaSpers dispersion at 1, 2, 3, 4, 5, 6, 7, 8 and 24 h after the powder contents were mixed with sterile water.



Figure 3. Representative dip-slide with double agar sides free of microbial contamination. This dip-slide was used to test the LoxaSpers dispersion for up to 24 h of environmental exposure.

Conclusions:

The LoxaSpers formulation containing Fluticasone Propionate 3 mg, as a non-sterile pharmaceutical preparation in sterile water used for nasal nebulization/irrigation, is able to prevent microbial contamination for up to 24 h, making it appropriate for immediate use in nasal nebulization/irrigation. The LoxaSpers dispersion, even without a preservative in its formulation, was free from microbial contamination during the first 24 h after reconstitution under realistic conditions for use by the patient.

Financial Disclosure: PCCA is the full sponsor of the study.

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