TECHNICAL REPORT

XyliFos®

Evaluation of the Safety and Toxicological Profile of XyliFos® in the Nasal Mucosa

Abstract: The nasal cavity is a promising site for drug delivery and intranasal preparations are thus commonly dispensed to treat conditions such as chronic, recurrent or resistant sinus. XyliFos is a proprietary powder excipient used in pharmaceutical compounding for nasal nebulization or nasal and wound irrigation. This study was conducted to evaluate the safety and toxicological profile of XyliFos using the EpiAirway™ Tissue Model, a three-dimensional (3D) model that resembles the human nasal mucosa. Results have demonstrated that XyliFos is potentially as safe as sterile water for injection since cell viability was greater than 100% for XyliFos at various concentrations (20%, 15% and 10%). XyliFos may therefore be considered a safe powder excipient to be used in compounding when formulating intranasal preparations.

Introduction:

The nasal cavity is a promising site for drug delivery as it is easily accessible to patients, has a large surface area (due to the presence of microvilli), contains a thin nasal epithelium, and it can bypass first-pass metabolism [1]. XyliFos is a proprietary powder excipient used in pharmaceutical compounding for nasal nebulization or nasal and wound irrigation. It was developed to be combined with active pharmaceutical ingredients and to be dispensed as capsules or sachets, which are opened and mixed with saline or sterile water prior to use. XyliFos contains a unique patent-pending epigallocatechingallate (EGCg)-cyclodextrin complex [2].

The aim of this study was to examine the safety and toxicological profile of XyliFos using the EpiAirway™ Tissue Model (MatTek Corporation), a 3-dimensional (3D) model developed to closely resemble the structure and functionality of the human nasal mucosa [3].

Methodology:

The EpiAirway tissue model consists of normal human-derived tracheal/bronchial epithelial cells, cultured and differentiated to resemble the pseudostratified epithelium of the nasal mucosa [3] (Figure 1). Following tissue preparation, XyliFos 20%, 15%, and 10% (diluted with sterile water for injection) were applied to tissue samples of the EpiAirway model, in duplicate, and incubated for 3 hr at a temperature of 37°C, 5% carbon dioxide and ≥90% humidity. Sterile water for injection was used in this study as a negative control. After 3 hr of incubation, each tissue sample was rinsed 3 times with Phosphate Buffered Saline (PBS) to remove any residual XyliFos. Afterwards, 300 µL of MTT (3-[4,5-dimethylthiazol-2yl]-2,5-diphenyltetrazolium bromide) solution was applied and the tissue samples were incubated for another period of 3 hr. MTT was used as an indicator of cell viability. Succinate dehydrogenase enzymes within the mitochondria of viable cells have the ability to reduce soluble yellow tetrazonium salt of MTT to an insoluble purple formazan derivative [4].

Following incubation, tissues were rinsed with PBS and immersed in 2 mL of extraction solution. Tissues were then sealed in a plastic bag and soaked overnight at room temperature. Once extraction was completed, extra liquid was decanted and the 200 µL aliquot of the extractant solution was examined using a Molecular Device SpectraMax M5 Microplate Reader to determine the absorbance potential of the extract at 570 nm, a wavelength absorbed by the formazan derivative [4].

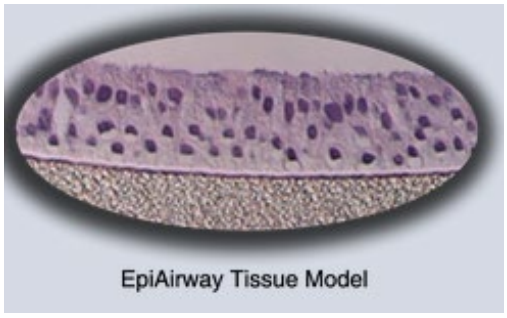

Figure 1. *Illustration of the EpiAirway™ Tissue Model.*

Results and Discussion:

The safety and toxicological profile of XyliFos was evaluated by determining the percent absorbance of the extract (formazan derivative). The greater the percent absorbance, the greater the amount of MTT reduced by succinate dehydrogenase, and the higher the percent cell viability within the tissue [4].

The percent cell viability for sterile water for injection was 100%. For tissues treated with XyliFos 20%, 15%, and 10%, cell viability after 3 hr of exposure was 109%, 106%, and 111%, respectively (Figure 2). These results demonstrate that XyliFos was not toxic to the tissues of the nasal mucosa as percent viability of the tissues was greater than 100% for all three XyliFos samples.

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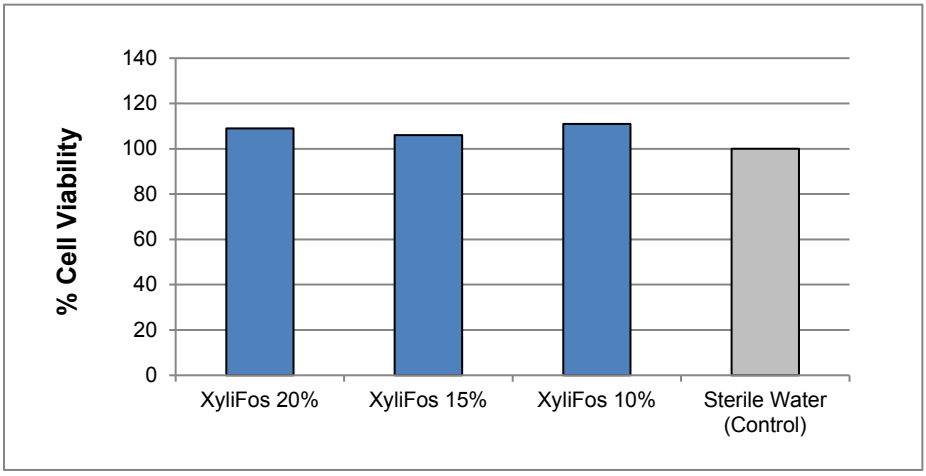

Figure 2. *Percent cell viability after 3 hr of exposure to XyliFos 20%, 15%, and 10%, and sterile water (negative control).*

In the treatment of nasal conditions such as chronic, recurrent or resistant sinus, XyliFos may be combined with the powder excipient LoxaSperse to enhance drug delivery and absorption of active pharmaceutical ingredients [2]. The *in vitro* evaluation of the safety and toxicological profile of XyliFos is very important taking into account the intimate contact of the powder excipient with the nasal mucosa. An ideal powder excipient for nasal administration should be non-toxic and non-irritating to the nasal mucosal tissue.

Study results have demonstrated that cell viability was greater than 100% for all three concentrations of XyliFos (20%, 15% and 10%), making it an ideal delivery system with a safety and toxicological profile similar to that of water.

Conclusions:

XyliFos has demonstrated to be a safe powder excipient to be used in compounding for nasal nebulization or nasal and wound irrigation. Compounding pharmacists may then safely utilize this excipient when formulating intranasal preparations.

References:

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