TECHNICAL REPORT

XyliFos®

Characterization of the Physical and Microbiological Properties of XyliFos®

Abstract: XyliFos is a proprietary powder excipient used in compounding for nasal nebulization or nasal and wound irrigation. The purpose of this study is to characterize the physical and microbiological properties of XyliFos, alone and in combination with 10% LoxaSperse, using three laboratory experiments as follows: static laser light scattering, optical microscopy, and water activity. Results of this study show that XyliFos has a relatively narrow particle size distribution with the ability to potentially improve the aqueous solubility of itraconazole when used in conjunction with 10% LoxaSperse. In addition, water activity results for XyliFos show that this excipient base does not support microbial growth ($a_w \leq 0.60$ with desiccant). These characteristics favor the use of XyliFos in compounded preparations for nasal nebulization and/or nasal and wound irrigation.

Introduction:

XyliFos and LoxaSperse are proprietary powder excipients used in compounding for nasal nebulization or nasal and wound irrigation. Multiple active ingredients are often combined with these excipients in the form of capsules or sachets to be mixed with saline or sterile water prior to use. XyliFos contains a unique patent-pending epigallocatechingallate (EGCg)-cyclodextrin complex [1], while LoxaSperse consists of a proprietary blend of xylitol and poloxamer [2]. The purpose of this study is to characterize the physical and microbiological properties of XyliFos, alone and in combination with 10% LoxaSperse.

Methodology:

The physical and microbiological properties of XyliFos, alone and in combination with LoxaSperse were characterized using three types of laboratory experiments as follows: static laser light scattering, optical microscopy, and water activity (a_w).

Physical properties: static laser light scattering and optical microscopy

Static laser light scattering was used to determine the particle size distribution of XyliFos. In this technique, as XyliFos powders flow through the light beam, size of the particles were measured based on the intensity of scattered light. Higher intensity of scattered light is equivalent to larger particle size, while lower intensity equates to smaller particle size [3].

Microscopic examination is also suitable for determining the distribution of particles of inhalable size [4] and therefore, optical microscopy was performed to examine the effects of XyliFos and LoxaSperse combination on the particle size distribution of itraconazole, an antifungal medication. A Nikon eclipse FS 100 microscope with Nikon Ds-FI2 Digital Camera and NIS-Elements BR 4.30.02 software was used for photographic characterization of itraconazole 1% in sterile water, with and without XyliFos (15%) and LoxaSperse (10%), at 100x magnification. This test was performed in accordance with the respective 'Physical Test' of the US Pharmacopeia [5], and was repeated with PCCA Formula #11625.

Microbiological property: water activity

To estimate microbiological growth in XyliFos, a_w of this powder excipient base was determined with and without desiccant, after 90 days of storage at the following temperature / humidity conditions: 4°C ± 1°C, 25°C / 50% humidity, and 40°C / 75% humidity.

Results and Discussion:

Results from static laser light scattering, optical microscopy, and water activity tests are discussed in the following text.

Static laser light scattering

Within a powder sample, particles exist in various shapes and sizes, and therefore, no single value can adequately represent the particle size of a powder excipient. Rather, distribution of particle size is often utilized to characterize a powder sample. The static laser light scattering test provides a weighed distribution which shows the contribution of each particle size to the volume in the sample [3, 6]. XyliFos exhibits a narrow distribution of particles (Figure 1), with the majority of particles having a size of 77.267 µm. The narrow distribution of particle size is a favorable physical characteristic to have as it potentially correlates to a more uniform powder sample.

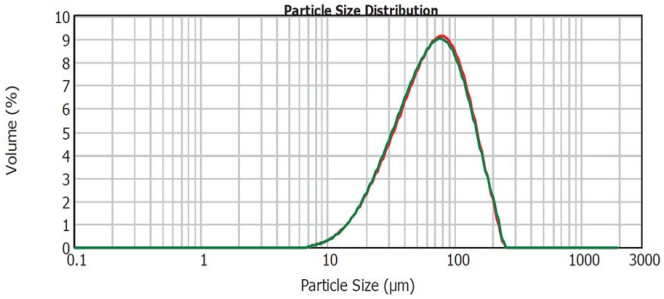

***Figure 1**.Particle size distribution of XyliFos*

Optical Microscopy

Particle size and distribution plays an important role in drug solubility. A reduction in particle size typically increases surface area and solubility of drugs, which could potentially lead to increased bioavailability [7]. The Biopharmaceutics Classification System (BCS) is commonly used to categorize drugs based on their aqueous solubility. Itraconazole is a BCS Class II drug with poor solubility in an aqueous environment, which could lead to erratic drug absorption [8]. The poor aqueous solubility characteristic of itraconazole can be visualized through optical microcopy results of this study as large aggregates of itraconazole formed when this drug was exposed to sterile water (Figure 2). However, the large aggregates were converted into smaller aggregates and single itraconazole particles following the addition of 15% XyliFos and 10% LoxaSperse (Figure 3). Similarly, when optical microscopy was repeated with PCCA Formula #11625 in water, improvements in the distribution of itraconazole particles were also observed as a result of the XyliFos and LoxaSperse content within the formulation (Figure 4). These results demonstrate that XyliFos combined with LoxaSperse, has the ability to optimize the particle size distribution of itraconazole in sterile water.

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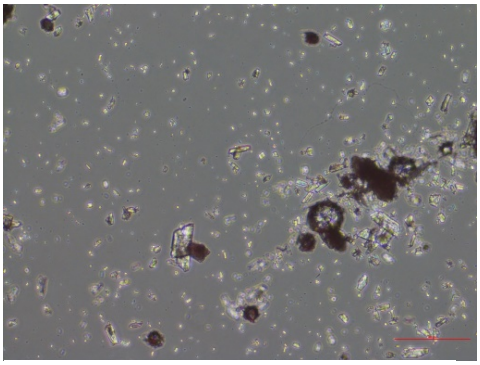

***Figure 2**. Itraconazole 1% in water*

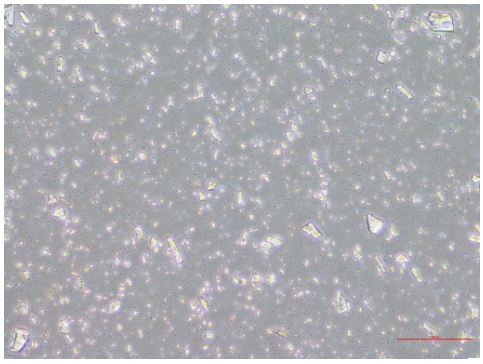

***Figure 3**. Itraconazole 1%, Xylifos 15%, and LoxaSperse 10% in water*

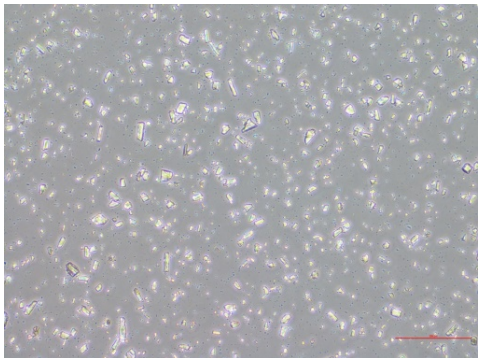

***Figure 4**. PCCA Formula #11625 in water*

Water activity

Water activity is defined as the amount of available or free water in a system, and may be used to measure how efficiently water can take part in a chemical reaction. When compared to total water content, a_w appears to be a more accurate prediction of microbial growth. A reduction in the a_w helps to minimize undesirable chemical reactions and microbial growth as bacteria typically do not grow at $a_w \leq 0.85$, and no microbiological growth is possible at $a_w \leq 0.60$ [9, 10]. The a_w of XyliFos, with and without desiccant, was measured after 90 days of storage at three different temperature / humidity conditions. Results show that the a_w of XyliFos was ≤ 0.60 with desiccant, and ≤ 0.85 without desiccant under all storage conditions, as shown in Table 1. These results demonstrate that this powder excipient does not support the growth of microorganisms (with desiccants).

Temperature (°C) / humidity (%)	a_w (with desiccant)	a_w (without desiccant)
4°C ± 1°C (refrigerated)	0.23	0.65
25°C / 50%	0.34	0.42
40°C / 75%	0.60	0.62

***Table 1.** Water activity of XyliFos, with and without desiccant, after 90 days of storage at three different temperatures*

Conclusions:

XyliFos has a relatively narrow particle size distribution and low water activity that does not support microbial growth (with dessicant). Furthermore, results of this study show that XyliFos could potentially improve the aqueous solubility of itraconazole when used in conjunction with 10% LoxaSperse. These characteristics favor the use of XyliFos in compounded preparations for nasal nebulization and/or nasal and wound irrigation.

References:

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