

Syloid® FP Silica

Pharmaceutical Excipient

2-Step Mixing Application Note

formulation
and delivery

An Improved 2-Step Process for Moisture Sensitive Drugs Using Syloid® FP Silicas

Keywords: Moisture-sensitive APIs, moisture protection, Direct compression, Two-step mixing process

Introduction: Several APIs are sensitive to moisture, and formulating these drugs into stable oral dosage forms can pose quite a challenge to formulators. There are several potential problems associated with moisture sensitive drugs, such as caking and poor flow properties, chemical degradation, changes in dissolution rates, and decrease in shelf life of the drug.

Before considering special packaging to protect moisture sensitive formulations, one should first consider selecting the right excipients and formulation techniques to help stabilize moisture sensitive APIs. Porous silica gel, such as Syloid® FP silicas, can help improve the stability of moisture sensitive APIs by adsorbing moisture in the final formulation.

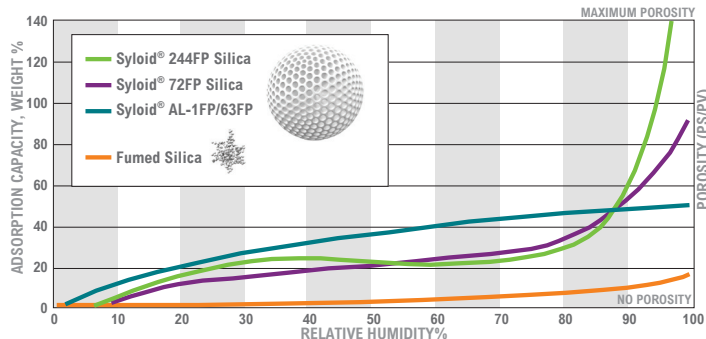


Figure 1. The higher surface area and internal porosity gives Syloid® FP silicas greater moisture adsorption than other silicon dioxide excipients. Having a range of adsorption capacities makes Syloid® FP silicas the ideal choice for both stages of two-step mixing.

Direct compression is another technique that is recommended for moisture sensitive APIs, as it does not involve heat, moisture, and long blending times, unlike other techniques such as wet and dry granulation methods. Therefore, using porous silicas in direct compression formulations can potentially provide the maximum benefits to moisture sensitive drugs.

Porous silica gel, such as Syloid® 244FP silica, is typically used in formulations as a glidant in small amounts (up to 2%). For adequate moisture protection, such low quantities would not be sufficient. Another grade of porous silica, Syloid® AL-1FP/63FP silica, is particularly effective for providing moisture protection, and can be incorporated into formulations in larger amounts, depending on the % CRH as well as nature and amount of API in the formulation.

Here, we demonstrate that addition of the two different grades of porous silicas (Syloid® AL-1FP/63FP and Syloid® 244FP silica) through a two-step mixing process can provide the combined benefits of moisture protection and flow improvement to a formulation. We also demonstrate that greater quantities of porous silica (5-20%) required to provide moisture protection can be used, while maintaining compressibility of the formulation mixture.

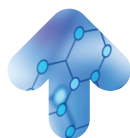
Using Syloid® AL-1FP/63FP Silica to Protect Moisture Sensitive APIs...

In Formulation: Moisture sensitive APIs are prone to caking, flow issues, and inconsistent dissolution



For Shelf Life: Moisture sensitive APIs can degrade quickly, reducing their shelf life if not protected from moisture

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synthesis
intermediates



purification
technologies

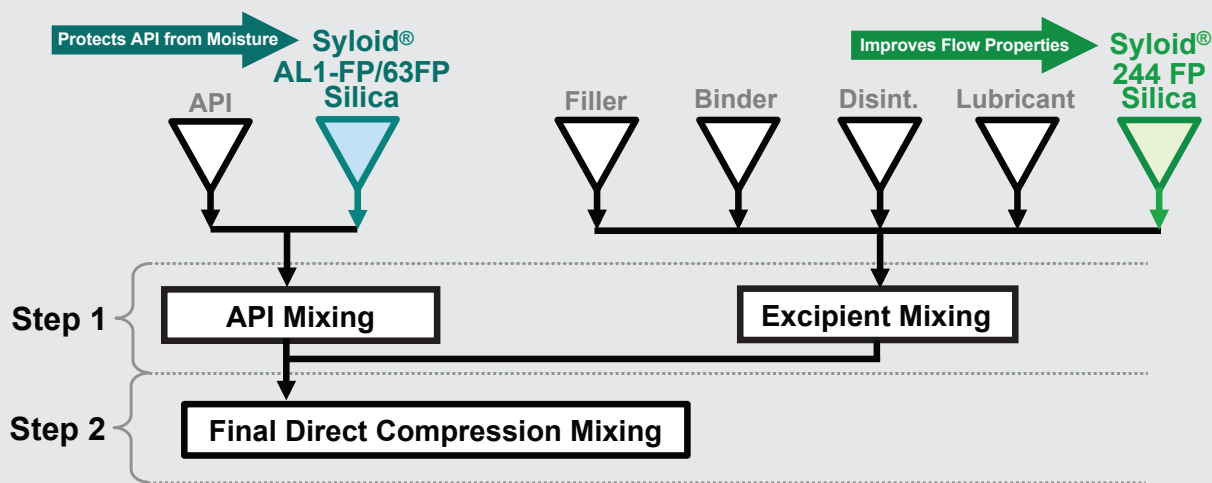


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Figure 2: Two-Step Mixing Process Using Syloid® FP Silicas



Hygroscopic products, such as plant related API's, anti-infectives, lyophilized products, probiotica, and many others can adsorb moisture from the air and adhere together. Caking can also occur when powders are not completely dry or when moisture migrates towards the outer surface after drying in wet granulation. The high porosity of Syloid® FP silica can adsorb a considerable amount of moisture, keeping the product dry and improving the stability.

Figure 2: Two-Step Mixing Process: Syloid® 244FP silica is used as a glidant in the excipient part of the formulation. It also has the capacity to take up excessive moisture from the other excipients while keeping the plasticising properties available. Syloid® AL-1FP/63FP silica, which is effective for moisture control of sensitive molecules, is mixed with the API to adsorb moisture and provide maximum stability to the formulation mix.

Ascorbic acid was used as a model drug in a direct compression formulation to demonstrate the effects of different amounts of silica on flow and tablet parameters. We evaluated the effect of different amounts of Syloid® AL-1FP/63FP silica on the flow behavior and the compressibility of the final formulation, with both 10% and 40% drug loading. Syloid® 244 FP silica is used at 1% in all the formulations to provide optimum glidant benefits. The amount of Syloid® AL-1FP/63FP silica was varied from 5-20% of the formulation.

We first tested the flow parameters of the final mixture with and without Syloid® AL-1FP/63FP silica at different percentages. The mixtures were then compressed into tablets by direct compression. The resulting tablets were evaluated for such as hardness, friability, weight uniformity, etc. The tablets maintained favorable properties with respect to weight uniformity, hardness, friability and disintegration, with both 10% and 40% API loading. The tablet hardness was between 6 kg/cm² and 12.50 kg/cm² with 5-20% Syloid® AL-1FP/63FP silica and weight uniformity (RSD) is not more than 0.82% for 10% API loading. The tablet hardness is less with 20% Syloid® AL-1FP/63FP silica at 40% API loading. However, the tablet hardness can be improved by increasing compression force during tableting

Chart 1. Effect of Syloid® AL-1 FP/63FP silica on flow properties

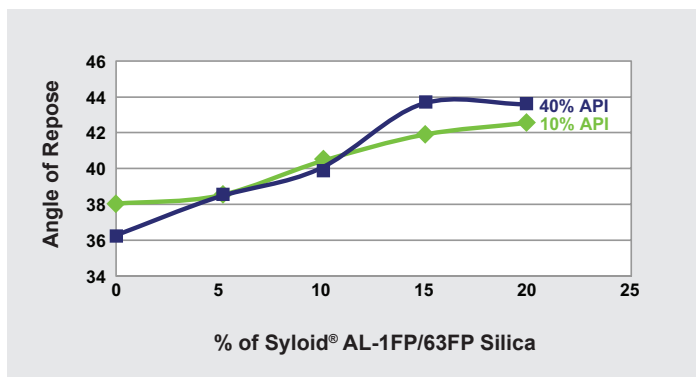
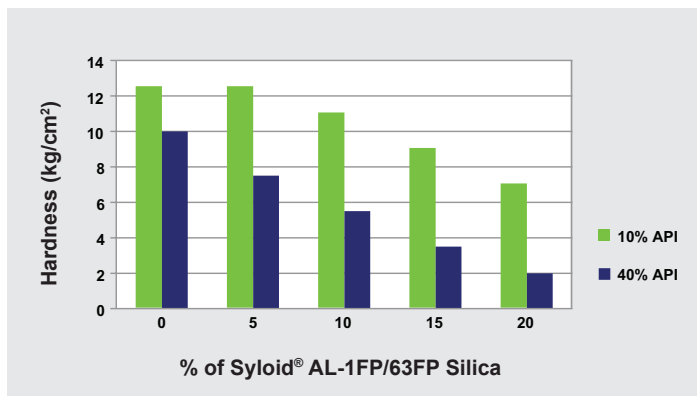


Table 1. Percentages of excipients used in 2-step formulation

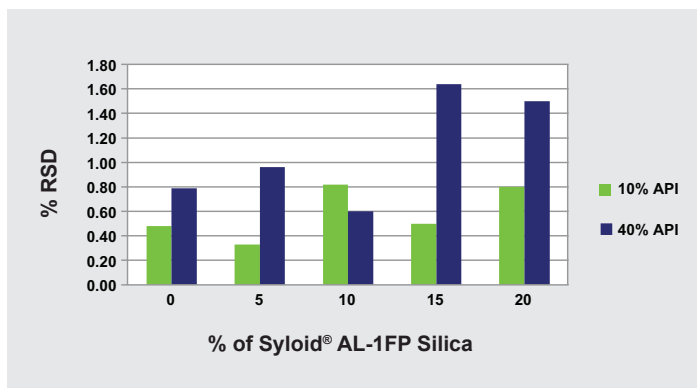
Formulation (%)	A		B		C		D		E	
Syloid® AL-1FP/63 FP Silica	0	40	5	40	10	40	15	40	20	40
Ascorbic acid	10	40	10	40	10	40	10	40	10	40
MCC PH 102	82.3	52.3	77.3	47.3	72.3	42.3	67.3	37.3	62.3	32.3
PVPK 30	2.5		2.5		2.5		2.5		2.5	
Cross Povidone	3.35		3.35		3.35		3.35		3.35	
Syloid® 244 FP Silica	1		1		1		1		1	
Stearic acid	0.85		0.85		0.85		0.85		0.85	
Total	100		100		100		100		100	

Chart 2. Effect of different amounts of Syloid® AL-1FP/63FP silica on tablet hardness

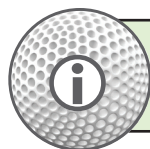


Tablets were compressed at 27-28 KN for 10% API loading; and at 40-42 KN for 40% API loading

Chart 3. Weight uniformity of tablets containing different amounts of Syloid® AL-1FP/63FP silica



*Tablet weight variation is measured as a function of RSD% of the tablet weights. Lower RSD% indicates lower weight variation and better uniformity.



Want More Information on Syloid® FP Silica?
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Conclusions:

We successfully demonstrate that tablets can be prepared by direct compression method using Syloid® AL-1FP/63FP silica from 5-20% at different API loading 10% and 40%.

We found that the tablet properties are very good with 10% API loading at all percentages of Syloid® AL-1FP/63FP silica from 5-20%. For 40% API loading, the tablet properties are good with up to 15% Syloid® AL-1FP/63FP silica.

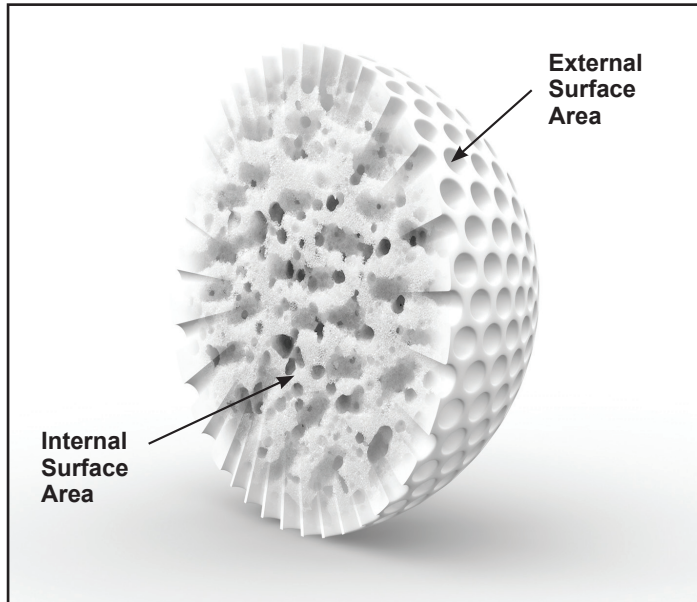
The tablet parameters such as hardness, friability and weight uniformity were found to depend on both percentage of API (10% or 40%) and percentage of Syloid® AL-1FP/63FP silica (5-20%) in the tablets. We are also investigating the effects of larger amounts of silica on other parameters such as disintegration times and dissolution rates.

By optimizing these factors in a formulation for different drugs, sufficient amounts of porous silicas can be incorporated into direct compression formulations, to provide optimal moisture protection to the formulation.

Abbreviations:

CRH Critical Relative Humidity
API Active Pharmaceutical Ingredient
RSD Relative Standard Deviation

The combined external and internal surface area of Syloid® FP silica gives it greater adsorptive capacity.



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