

STANDARD OPERATING PROCEDURE



Liquid Loading with SYLOID® XDP Silica

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PHARMACEUTICAL SOLUTIONS

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Grace has developed and introduced a patented silica-based carrier, SYLOID® XDP silica [1], to directly convert liquid ingredients into various solid dosage forms. With a combination of exceptionally high internal pore volume and high bulk density, SYLOID® XDP silica carrier is designed to provide optimum performance in liquisolid formulations. The key properties of SYLOID® XDP silica associated with loading are provided below. For detailed information on the properties of SYLOID® XDP silica, please refer to the technical data sheet [2].

Table 1. Key properties of SYLOID® XDP silica.

SYLOID® XDP silica	
Bulk density	~ 0.26 g/ml
Tapped bulk density	~ 0.28 g/ml
Loading capacity	up to 1.65 ml liquid per gram silica

The following provides a general guideline and some examples for the liquid loading with SYLOID® XDP silica.

1. General Procedure and Mechanism

The general procedure is given as an overall guideline and describes the fundamental mechanism of liquid loading with SYLOID® XDP silica. Liquid loading with SYLOID® XDP silica includes distribution of the liquid in the silica powder and absorption of the liquid into the pores of each individual silica particle. Distribution of the liquid and the absorption usually occur simultaneously for optimum results and process efficiency.

Distributing liquid in silica powder is typically achieved by mixing when the liquid is continuously added to the powder bed. Conventional mixing equipment, such as a rapid mixer granulator and planetary mixer, can be used

for this purpose. Though not required, for liquid that is sprayable, mixing can be accelerated by atomizing the liquid prior to contacting the powder bed. For small lab scale experimentation, liquid can be added with a burette and manual mixing can be used to distribute the liquid.

The mixing action described above brings the liquid into proximity of each porous silica particle so the liquid can be efficiently absorbed into the pores of the particle. Absorption of the liquid into the pores of each individual silica particle is driven by capillary action. Capillary action is the ability of a liquid to flow into narrow spaces without assistance. The controlled and uniform pore size of SYLOID® XDP silica allows rapid absorption of various liquids into the pores.

The time required to achieve complete absorption may vary for liquids with different viscosities. Liquids with high viscosity may require longer time to be fully absorbed into the pores. Some ingredients, such as waxes, are solid at ambient temperature and need to be liquefied before loading. For both viscous liquids and waxy ingredients, increasing the temperature of the raw materials as well as the loading process through heat jacketed equipment can be considered to liquefy the ingredient and lower its viscosity to accelerate the absorption. Operation temperature is selected also in consideration of the thermolabile nature of the ingredients.

Up to 1.65 ml of liquid can be loaded for every gram of SYLOID® XDP silica, while maintaining good powder flow property. For typical liquids with density of 0.9 g/ml to 1 g/ml, this equals to about 1.5 g of liquid loading per gram of silica. The silica powder loaded with liquid maintains good powder flow properties and provides dense powder packing. The combination of high absorption capacity and powder packing density maximize the amount of liquid active ingredient in tablets or capsules [3].

1. Fred H. Monsuur, "Porous Silica Gel as a Carrier for Liquid Technologies" U. S. Patent US 10,660,856, issued on May 26, 2020
2. Technical Data Sheet: SYLOID® XDP Silica – Solution for Liquisolid Formulations
3. SYLOID® XDP Technical Information Sheet

2. Examples of Loading with Various Equipment

Loading can be conducted with various conventional equipment used for the processing of pharmaceutical and nutraceutical ingredients. In the sections below, one lab scale and two pilot scale examples are provided for demonstration purposes. The choice of equipment is not limited by the examples. Vitamin E oil (tocopherol)[4] is selected as the exemplary active liquid ingredient to be converted into free-flowing powder and SYLOID® XDP 3150 silica is selected as the exemplary silica carrier. The subsequent formulation into various solid dosage forms is described in Grace application notes and thus not included in this document.

2.1 Lab scale loading with a burette and manual mixing

15 g of vitamin E oil is converted to free-flowing powder by loading into 10 g of SYLOID® XDP 3150 silica. A burette is used to add vitamin E oil while the mixture is continuously mixed manually with a spatula. The experimental set up is shown in Figure 1.

Loading Calculations:

- SYLOID® XDP 3150 silica to oil weight ratio = 1:1.5
- Weight of SYLOID® XDP silica 3150 = 10 g
- Weight of vitamin E oil required = 15 g

Procedures:

- Accurately weigh required amount of vitamin E oil in a glass beaker
- Transfer the oil above into a burette
- Weigh the required quantity of SYLOID® XDP silica in a separate glass beaker
- Add vitamin E oil to SYLOID® XDP 3150 silica with the burette in a dropwise manner
- Thoroughly mix the powder manually using a spatula while adding the oil (Figure 2)
- Once the oil addition is completed, stop the burette and continue mixing the powder until it becomes free-flowing.

Figure 1. Manual oil addition with a burette

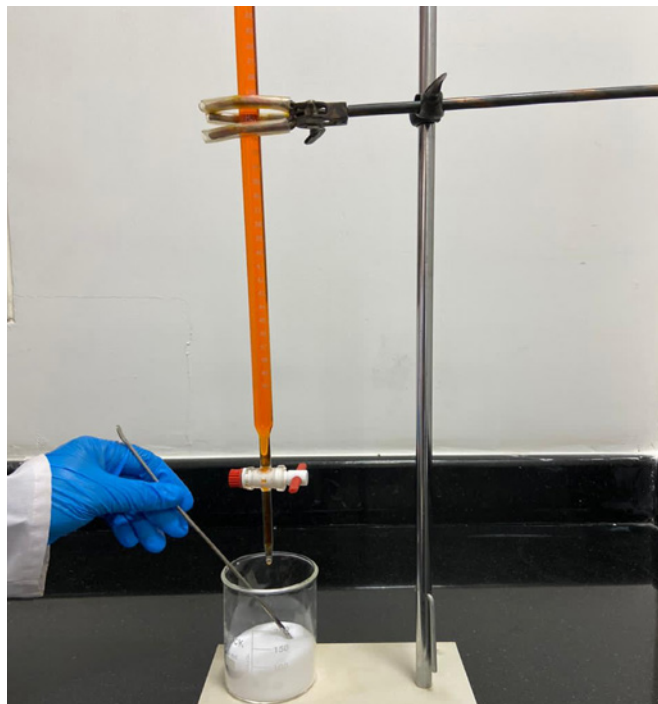
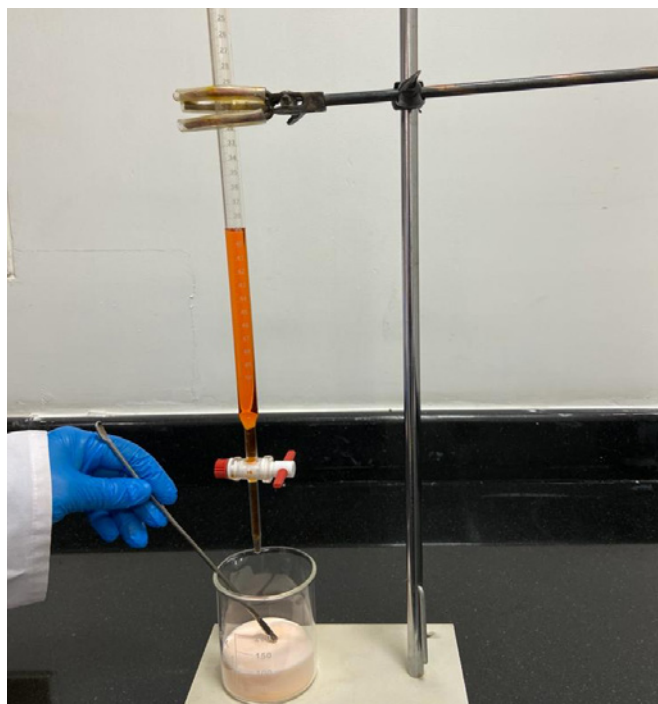


Figure 2. Uniform distribution of oil throughout the powder mixture



4. Vitamin E oil (tocopherol) has a light-yellow color. In order to highlight the distribution of the oil in the powder, a bright sunset yellow color is added to the oil.

2.2 Pilot scale loading with a rapid mixer granulator

Rapid mixer granulator (RMG) is a common equipment at both pilot and production scales. In the example below, a pilot scale RMG is used to demonstrate the loading of vitamin E oil into SYLOID® XDP 3150 silica. The experimental setup is shown in Figure 3.

The sample bowl capacity of the RMG is 3 liters. Silica powder is loaded into the bowl to achieve 60% occupancy. The calculations for this loading are provided below.

Loading Calculations:

- SYLOID® XDP 3150 silica to oil weight ratio = 1:1.5
- RMG bowl capacity = 3 liters
- Bulk density of SYLOID® XDP 3150 silica = 0.26 g/ml
- Weight of SYLOID® XDP 3150 silica (for 60% bowl occupancy) = 468 g
- Weight of vitamin E oil required = 702 g

Procedures:

- Weigh required amount of vitamin E oil in a suitable container
- Weigh the required quantity of SYLOID® XDP 3150 silica and load into a clean RMG bowl (3-liter capacity)
- Set impeller speed (180 rpm) and chopper speed (400 rpm) to ensure uniform powder mixing in the RMG
- Add the vitamin E oil through a peristaltic pump over 5 minutes while maintaining impeller and chopper speeds
- Once oil addition is completed, further knead the mixture for another 5 minutes at impeller speed of 180 rpm and chopper speed of 400 rpm
- Unload the material from the discharge port of RMG and store in a poly bag for further formulation steps.

Figure 3. Setup for vitamin E loading into SYLOID® XDP 3150 silica using a rapid mixer granulator (RMG-3L, by Saral Engineering company)



2.3 Pilot scale loading with a planetary mixer

Planetary mixer is another common equipment at both pilot and production scales. In the example below, a pilot scale planetary mixer is used to demonstrate the loading of vitamin E oil into SYLOID® XDP 3150 silica (Figure 4). In pilot scale, oil can be added either manually or with a peristaltic pump.

Figure 4. Planetary mixer with SYLOID® XDP 3150 silica in the mixing bowl (MYSA SM-1502 stand mixer by Classique Elements LLP)



The sample bowl capacity of the planetary mixer is 3 liters. Silica powder is loaded into the bowl to achieve 60% occupancy. The calculations for this loading are provided below.

Loading Calculations:

- SYLOID® XDP 3150 silica to oil weight ratio = 1:1.5
- Planetary mixer bowl capacity = 3 liters
- Bulk density of SYLOID® XDP 3150 silica = 0.26 g/ml
- Weight of SYLOID® XDP 3150 silica (for 60% bowl occupancy) = 468 g
- Weight of vitamin E oil required = 702 g

Procedures:

- Weigh required amount of vitamin E oil in a suitable container

- Weigh the required quantity of SYLOID® XDP 3150 silica and load into the clean planetary mixer bowl (3-liter capacity)
- Adjust the mixer speed to ensure uniform powder mixing
- Vitamin E oil can be added manually through a port on the mixer lid (Figure 5)
- Alternatively, vitamin E oil can be added through a peristaltic pump (Figure 6)
- Once oil addition is completed, further knead the mixture until it results in a free-flowing powder
- Discharge the material and store in a poly bag for further formulation for solid dosage forms such as capsules and tablets

Figure 5. Manual oil addition for loading with a planetary mixer (MYSA SM-1502 stand mixer by Classique Elements LLP)



Figure 6. Oil addition with a peristaltic pump for loading with a planetary mixer (MYSA SM-1502 stand mixer by Classique Elements LLP)



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