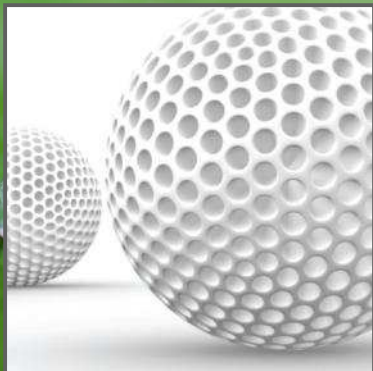
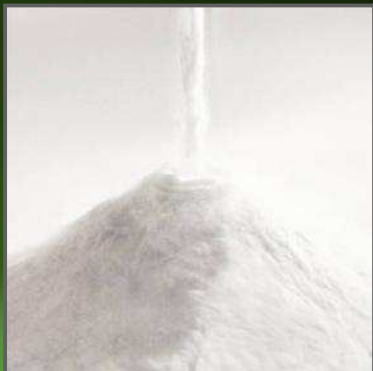




Syloid® FP Silica

Expect More From Your Excipient



Grace Davison
Discovery Sciences

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Raising Expectations for Excipients



Syloid® FP Silica

In the Past...

An excipient was considered any compound other than the active ingredient

Excipient's role was mainly used to improve the stability of the end product.

- Inert inactive ingredients (not API)
- Interactions:
 - Physical interactions
 - Chemical interactions



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Raising Expectations for Excipients



Syloid® FP Silica

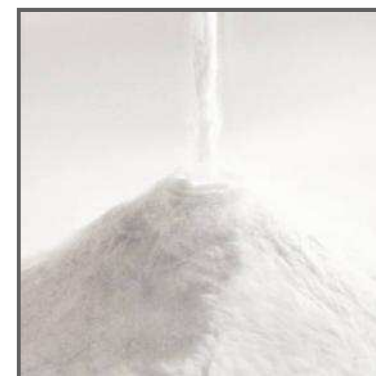
Today:

More than 70% of formulations contain excipients in higher concentrations than the drug.

Greater awareness for the value excipients bring to formulations

Increasing need for understanding excipients

- Chemical interactions (new developments)
- Physical interactions (glidant, anti caking, ...)
- Physiological & biopharmaceutical interactions
- Interaction between ALL ingredients



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Raising Expectations for Excipients



Syloid® FP Silica

There is an increased demand for new excipients

But, do we understand existing excipients?

- Increasing need for understanding excipients and their QUALITY
- Interaction between ALL ingredients and API
- What activity or functionality to the API
- More communication between user/researcher and manufacturer will bring value to the industry

“Quality, however you want to define it (QbD, Six Sigma, GMP) is a constant journey, not a destination”



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Not All Silicon Dioxides are the Same



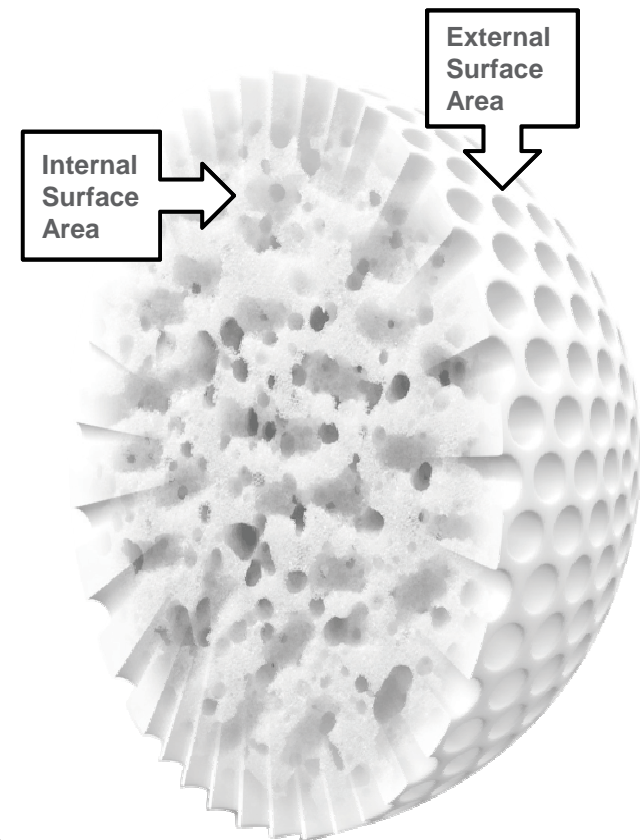
SYLOID® FP is an Amorphous Micronized Multi-functional “Meso-porous” Silica Gel

- Grades include 244FP, 72FP, and 63FP
- Since 2001 > 40 patents on Syloid® FP

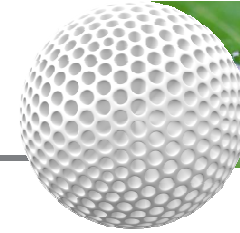
Benefits to Manufacturing

For varying relative humidity conditions Syloid® FP silicas can improve flow properties for direct compression and prevent valve blockage during manufacturing.

- Improves glidant properties and homogeneity
- Decreases friability, capping, and lamination
- Acts as an anti-static agent and reduces API loss
- Eliminates or reduces need for sieving prior to use
- Increases tablet hardness at lower compression force



Security and Compliance



Syloid® FP Silica

- **FCC:** SYLOID® silica gels meet FCC standards for silicon dioxide
- **USP/NF:** SYLOID® FP silica gel meets the standards for **Silicon Dioxide**
- **EP:** SYLOID® 244FP meets the monograph for **Colloidal Silica Hydrated**
- **JPE:** All SYLOID® FP silica gels meet the monograph for **Hydrated Silicon Dioxide**
- **FDA:** SYLOID® FP silica gels comply with numerous citations in Title 21 of the CFR for direct and indirect food applications and are Generally Recognized as Safe. Assigned Master File No.932
- **CTFA:** SYLOID® silicas are classified as Hydrated Silica in INCI



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World Leading Quality



Syloid® FP Silica

Grace Baltimore, USA manufacturing facility



*Syloid® FP silicas are
manufactured in Worms,
Germany, Baltimore, USA,
and Sorocaba, Brazil.*

Grace receives first ever IPEC GMP certification



*Our commitment to quality is further
demonstrated by our ISO 9001 plant
certifications and Six Sigma culture of
continuous improvement.*

**Working with an original manufacturer with accredited quality
can help you meet your QbD goals**

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Dosage Forms



Examples:

- Oral: Tablets, Capsules, Suppositories, Drops, Granules, Powders
- Topical: Gels
- Transdermal Systems
- Solutions: Suspensions, & Emulsions



Aspirin Tablets -330mg

- | | |
|------------------------|-------|
| ■ Aspirin | 85.0% |
| ■ Stearic Acid | 0.5% |
| ■ Starch | 12.0% |
| ■ SYLOID® 244FP silica | 2.5% |



What is a Formulation?



The successful formulation depends on the careful selection of those excipients that are added to promote the **consistent release and **bioavailability** of the drug and **protect it from degradation**.**

Handbook of pharmaceutical granulation technology - Dilip Parikh from Synthon pharmaceuticals USA

Due to the advanced porosity of Syloid® FP silica:

- Better uptake of water (moisture sensitive drugs/antibiotics = desiccant) and oils (odor, taste, keeping drug in suspension)
- Better wetting of the tablet: better release/uptake of the drug (= disintegrant)
- Higher density = lower dust
- Liquids can easily be transformed into powders (= carrier)

Example: Magnesium stearate is very often used

- Reduction of friction between powder and metal surface
- Hydrophobic nature
- Negative effect on disintegration

Syloid® FP silica has excellent wetting properties – and gives better disintegration

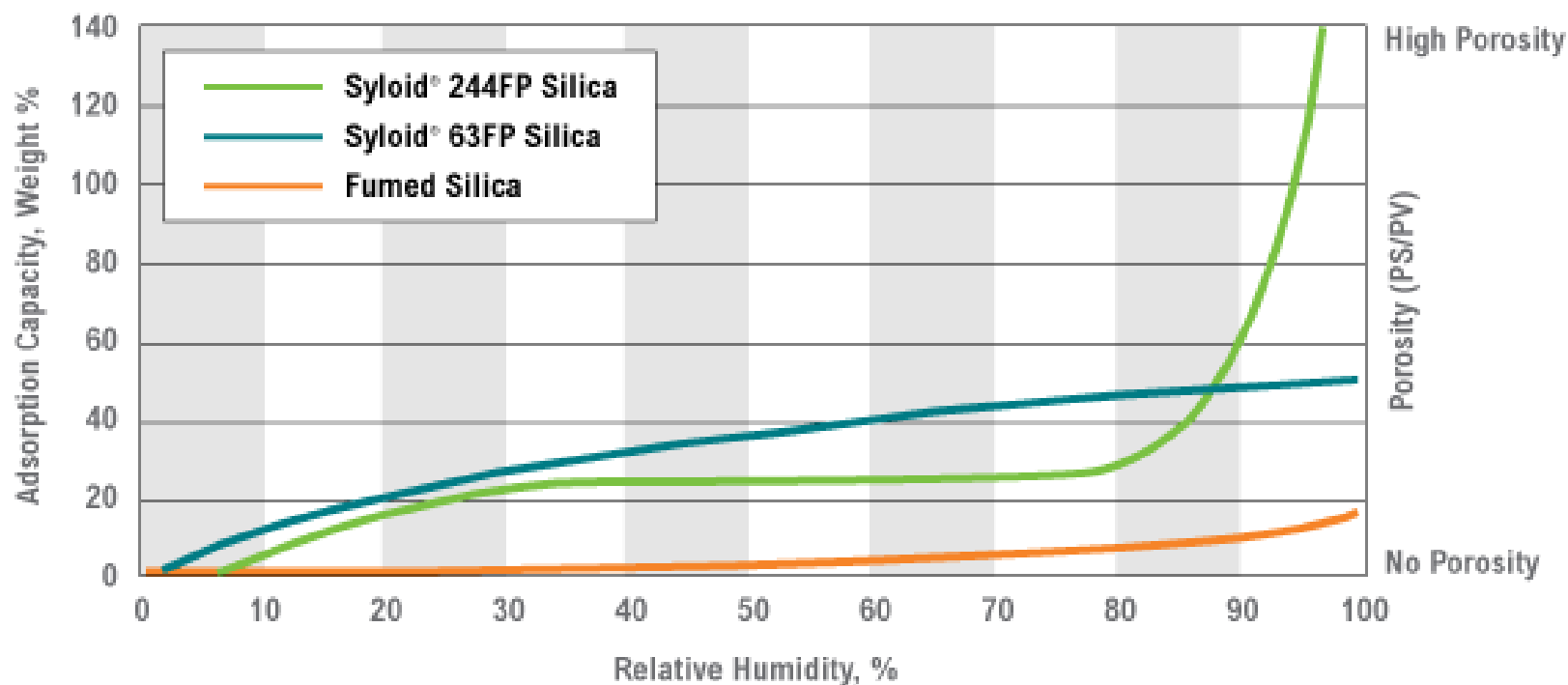
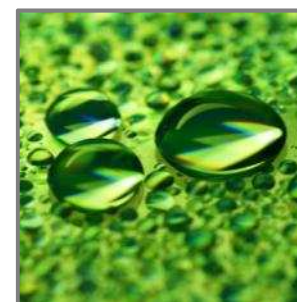
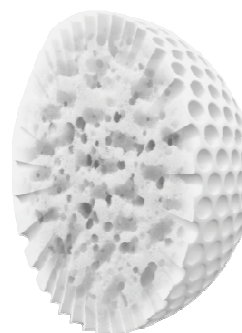
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Adsorptive Capacity



Syloid® FP Silica

Advanced internal porosity gives greater adsorptive capacity



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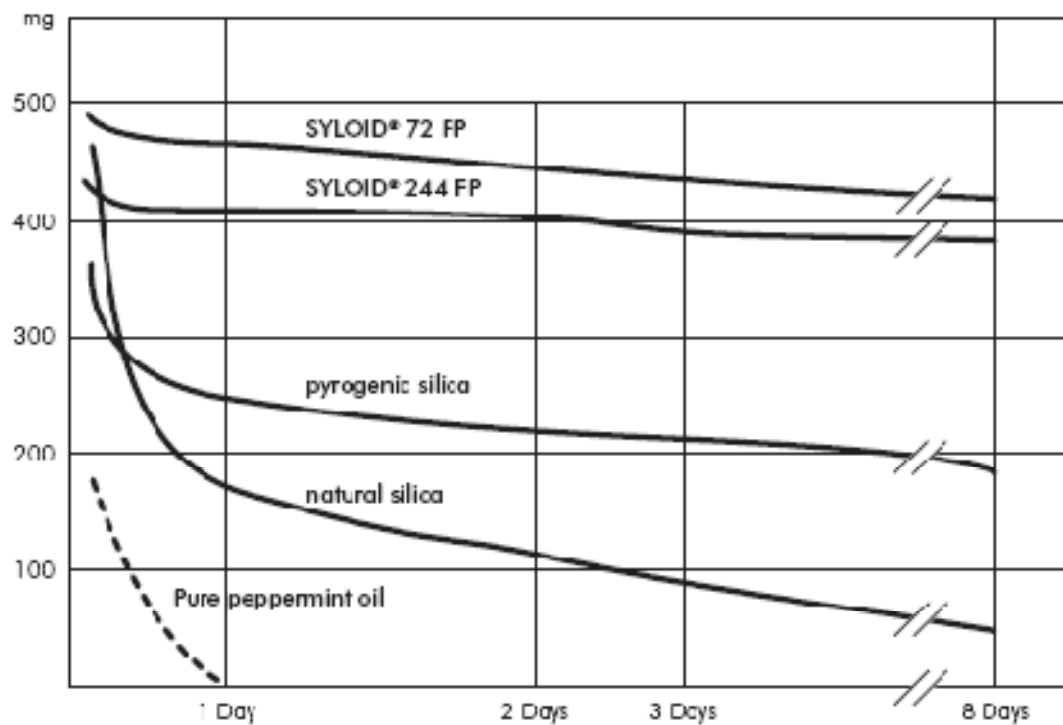
Oil Adsorption



Syloid® FP Silica

- Creates a better suspension
- Improves storage of aroma

Evaporation of Peppermint Oil from Various Silica Gels



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Dosage Forms



Capsules:

- As carrier and also as matting agent
- Soft gelatine capsules

Granules, Tablets:

- As a carrier
- Improved flow during tableting
- Anti tacking
- Unique dessicant properties for anti-Infectives
- Permeabilizing agent + antistatic agent (ODT's)



Liquids:

- As a carrier and for increasing the viscosity (syrup)
- Converting liquids to powders = higher adsorption capacity



Silica Gel vs. Colloidal (Fumed) Silica



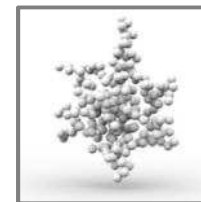
Syloid® FP Silica

- Low dust
- Easy to disperse/handle
- Porosity is developed intra-particle
- Porosity available after compression
- Higher available surface area

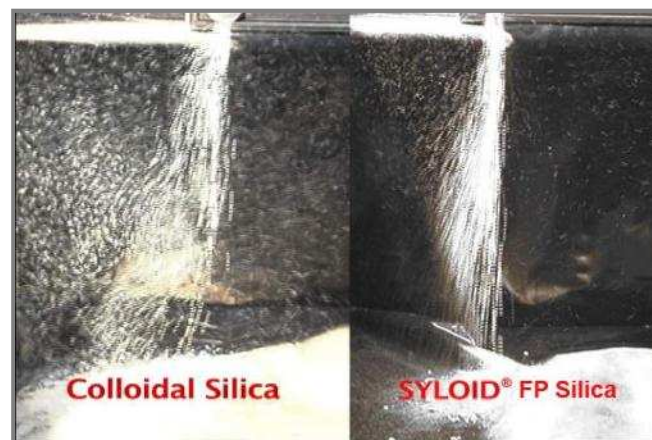
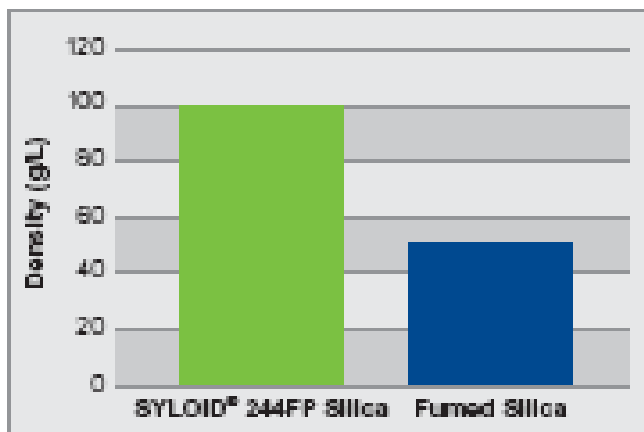


Colloidal (Fumed) Silica

- Very dusty
- Difficult to disperse/handle
- Porosity is developed inter-particle
- Porosity is not available
- Lower available surface area



DENSITY



Syloid® FP Silica is Multi-Functional



Properties

- Very High Purity = Physiological Inert
- High internal porosity and surface area
- High adsorptive capacity
- Tightly controlled particle size distribution
- Unique particle structure and morphology
- Low refractive index, invisible
- More dense than most precipitated and colloidal silicas
- Resulting in “less to no sieving”
- Plastic behavior stay available after compression

Benefits

- Products available to meet USP/NF monograph
- High efficiency low usage levels, lower cost
- Better adsorption – improved water penetration (wetting agent, bursting aid)
- Faster disintegration
- Uniform blending/tabletting – improved product uniformity
- High carrying level
- Protection against moisture pick up
- Less dusting in the manufacturing area = GMP compliance

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Choose the Grade for Your Needs



Carrier of Actives/Delivery (244FP)

- To effectively convert liquids/API's to free-flowing powders by mixing with Syloid® silica (1:1 wt. ratio)
- To improve or aid disintegration
- Better storage of aroma
- To facilitate dry liquid blending/ mixing with other constituents
- To assist active ingredients' release when exposed to moisture vapor and water



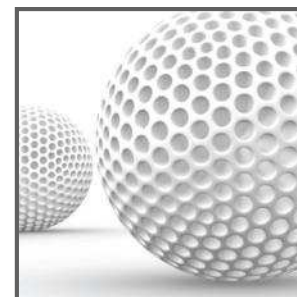
Processing Aid (244FP)

- Keeps powders dry in a free flowing state
- Enables uniform blending, more consistent fill weight, and consistent distribution of the API
- Improves resistance to sticking
- Eliminates or reduces the need for sieving - low dust



Glidant (244FP, 63FP)

- Anti-caking agent
- Improves flow properties and homogeneity



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Choose the Grade for Your Needs



Coating (244FP, 63P)

- Matting agent
- Wetting agent: capillary wetting, aqueous and gastric wetting

Tabletting Aid (244FP, 63FP)

- Improves tablet hardness, tensile strength, structural stability and reduces friability
- Ensures uniform tablet weight



Thickening/Gellation/Suspension Aid (72FP, 244FP)

- Turn liquids into clear gels, creams or pastes
- Acts as a suspension agent for actives in aerosols and provides uniform dispersion

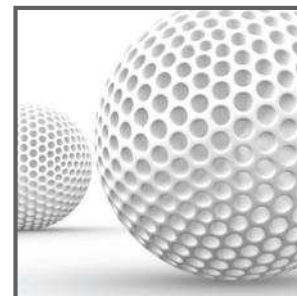


Wetting Agent/Disintegrant Aid (244FP, 63FP)

- Helps tablet break up faster by adsorbing moisture
- Wetting agent: aqueous and gastric wetting, ODT's
- Permeabilising agent

Desiccant/Moisture control (63FP = lowest LOD)

- Insures long term product storage stability
- Adsorbs moisture and oils keeping powders dry to prevent degradation



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Conclusions



SYLOID® FP silica is highly efficient in many pharmaceutical applications

Properties

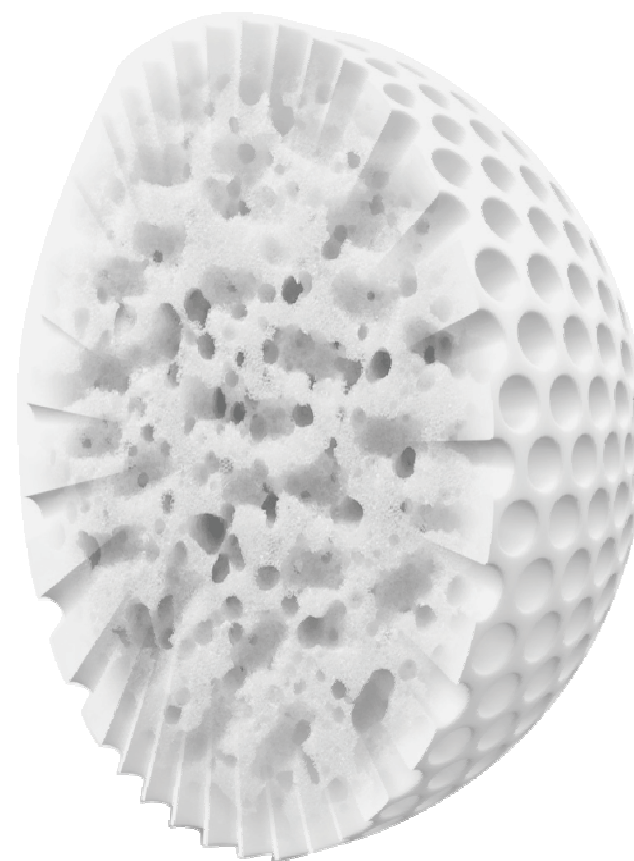
- High internal porosity and surface area
- High adsorptive capacity
- Plastic behavior, pores stay available
- Tightly controlled particle size distribution
- Unique particle structure and morphology

Benefits

- High efficiency – low usage levels, lower cost
- Uniform blending – improved product uniformity
- High carrying level
- Protection against moisture pick up

Applications

- Glidant
- Wetting agent / Permeabilizing agent
- Carrier
- Desiccant / Moisture control
- Anti-tacking



GRACE



Your Partner - From Discovery to Delivery

Discovery

The Reveleris® flash chromatography system combined with Reveleris® cartridges packed with Grace® silica, allows medicinal chemists to detect more, purify more, recover more and submit NCEs faster.



Synthesis

Synthetech customized peptide building blocks and specialty amino acids support clinical development, including regulatory starting materials, advanced intermediates, and early stage APIs.

Purification

Grace offers a broad range of products for pilot and process scale purification, including Davisil® and Vydac® media, Spring® columns, and the Multipacker® column packing station.



Delivery

Syloid® FP silica excipients are specifically cited in numerous patents due to their superior properties that improve the handling, adsorption, and dissolution of many pharmaceutical compounds.



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Enriching Lives, *Everywhere.*™

Grace Davison Discovery Sciences

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