SILSOL® SILICA-BASED DRUG DELIVERY TECHNOLOGY

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The Bioavailability Challenge

Grace's SILSOL® silica-based drug delivery technology was engineered to bring together advanced silica technologies with challenging active pharmaceutical ingredients (APIs) to effectively formulate a large class of poorly soluble but otherwise promising compounds.

SILSOL® silica drug delivery technology gives pharmaceutical developers a new drug delivery option for enhanced bioavailability of BCS2 (poorly soluble) compounds. BCS2 compounds account for 40 percent of the APIs on the market today, 70 to 80 percent of pharmaceuticals active in the pipeline and those that have been shelved due to solubility issues. In total, BCS2 compounds represent an estimated market opportunity of $5 billion.

The Grace® Silica Advantage

Grace's silicas have been used in pharmaceutical formulations since the 1960's and we continue to innovate today. SILSOL® silica drug delivery technology combines our expertise in mesoporous silica gel, novel application methods, and patented technologies to accelerate the screening and development of solubility enhancing solid dispersions, with the added benefit of doing so with compendial, scalable, and available silicas.

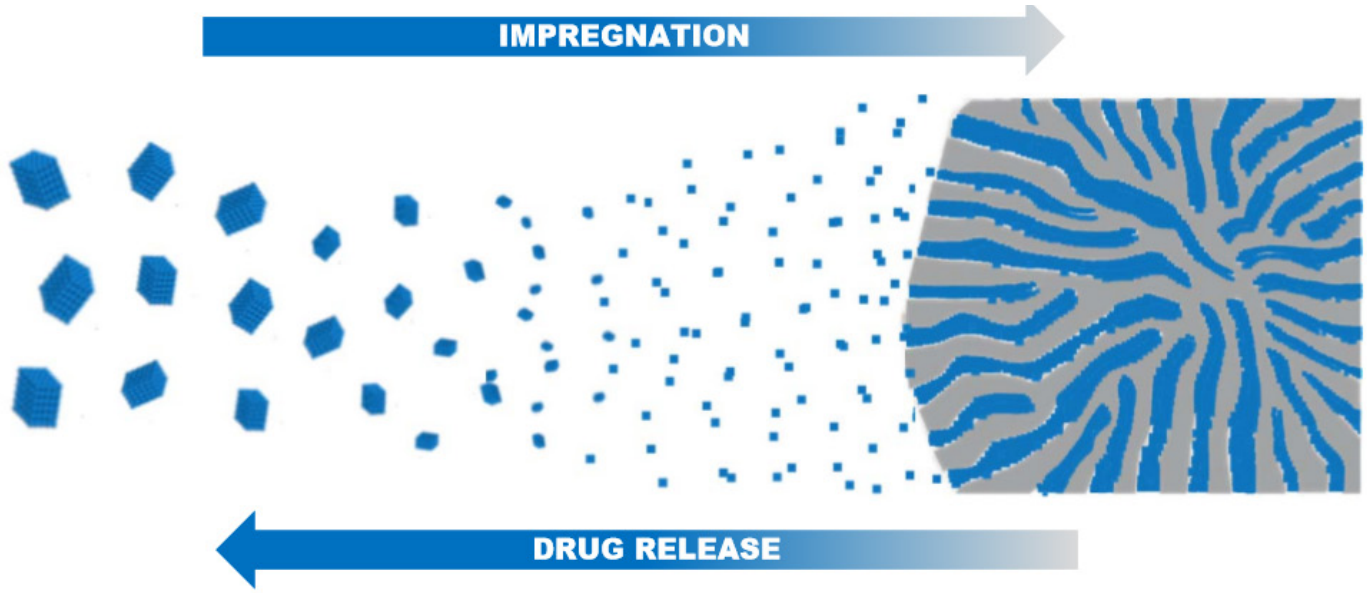
How Does It Work?

Grace's SILSOL® silica drug delivery technology is based on a solvent impregnation technique to create amorphous solid dispersions, as shown in the graphic below.

Solvent Techniques:

- Crystalline API, which is difficult for the body to absorb, is dissolved in a volatile solvent to create a solution of amorphous API.
- Grace's silica material is impregnated with the API-solvent solution.
- The API is deposited into the silica's mesopores.
- The solvent is then evaporated from the particles.
- Silica pores suppress the tendency of the API molecule to re-crystallize.
- The amorphous API is released from the pores and becomes available in the gastrointestinal system.

A solvent-free approach using co-milling API with silica can also be potentially considered. However, very limited work has been done in this area. Ternary systems combining API, silica and polymers is also gaining importance in the drug delivery market.



Grace's SILSOL® Silica Drug Delivery Technology Offers Five Major Benefits

1. **Enhanced Bioavailability –** through delivery of the amorphous form of drugs
2. **Stability –** Amorphous solid dispersions prevent re-crystallization
3. **Pharmacopoeia Acceptance –** GMP manufactured silica conforms to Global monographs
4. **Scalability –** Grams to tons quantities under excipient GMP manufacture
5. **FDA Compliance –** Material is listed on the FDA inactive ingredient database

Grace's Silica Engineering

Through molecular engineering, Grace can modify the pore size and surface characteristics of silica to accommodate various API molecules. The net result is enhanced bioavailability with stability.

The SILSOL® Silica Technology Advantage—Simplicity

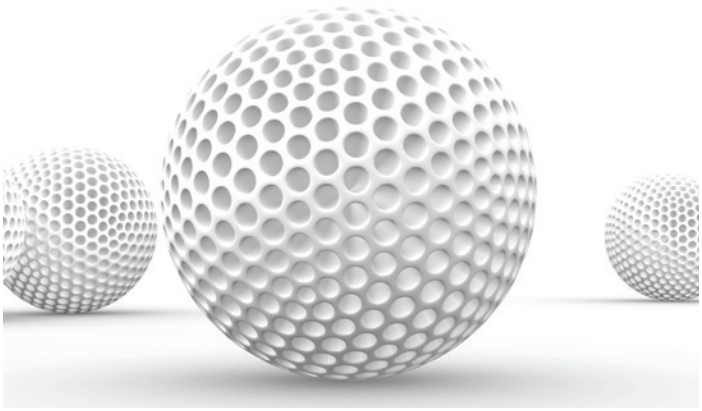
Compared to other bioavailability enhancing techniques such as particle size reduction, complexation, lipid-based systems and polymer-based solid dispersions, Grace's SILSOL® silica technology introduces techniques that are often easier to screen, less complex to make, and require less time when scaling up.

Our technology is:

- Suitable for NCE, life cycle management, reformulations, and repositioning
- Applicable to a broad range of compounds (including all BCS2 poorly solubles)
- Easy and cost effective introduction into established manufacturing units
- Generating stable formulations

Trust Grace

Grace has been a respected provider of silica materials for the pharmaceutical and other industries for more than a century. Laboratory experiments and studies—reported in over 300 scientific publications—have concluded that silica could support bioavailability of difficult-to-absorb APIs.



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