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DEVELOPMENT OF ORAL DELIVERY SOLID DISPERSION NANOPARTICLE USING ULTRASONIC SPRAY DRYING METHOD

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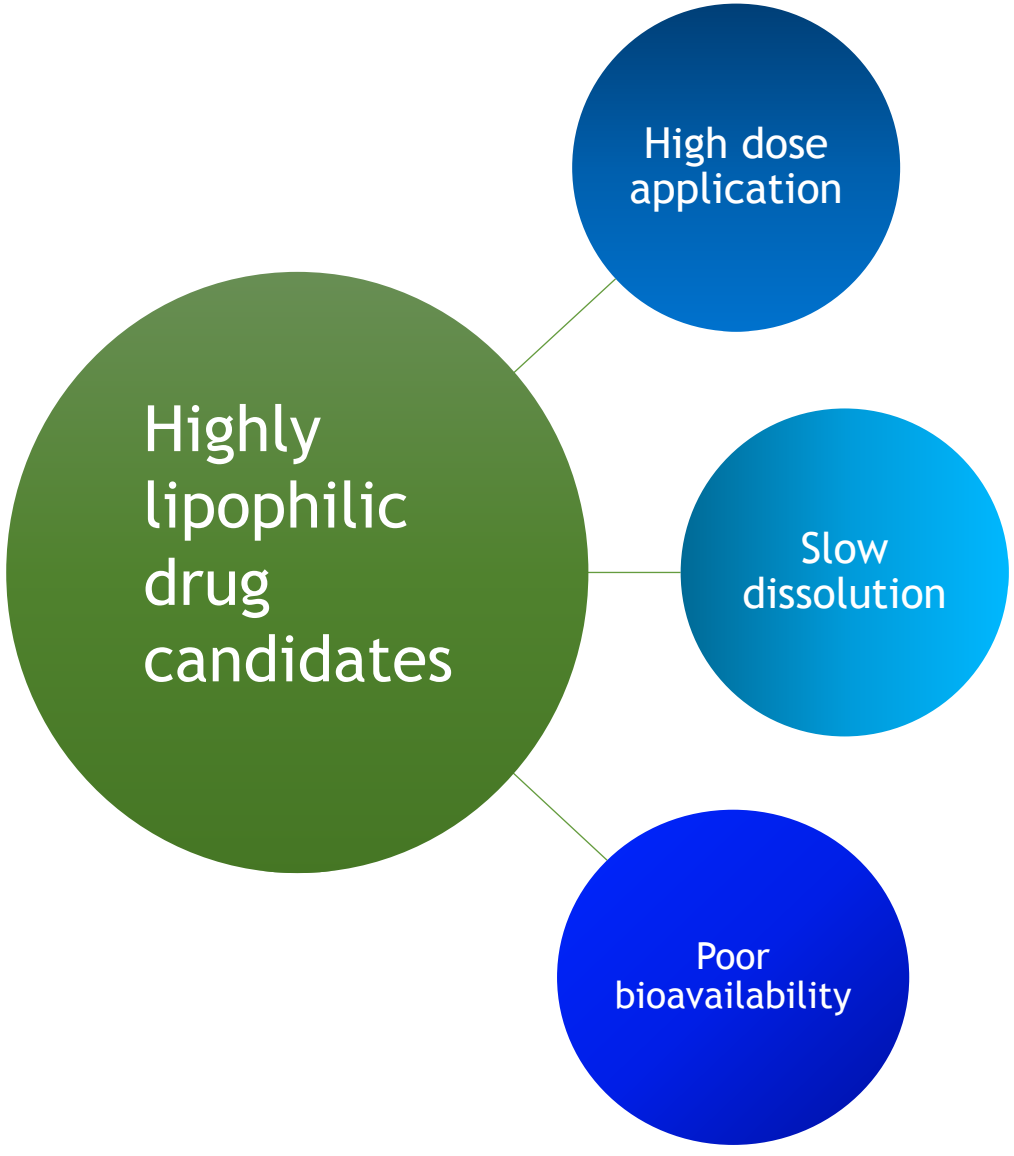
INTRODUCTION



Modern drug discovery techniques result in the development of an increasing number of highly lipophilic drug candidates.

APPLICATION OF SOLID DISPERSION NANOPARTICLES

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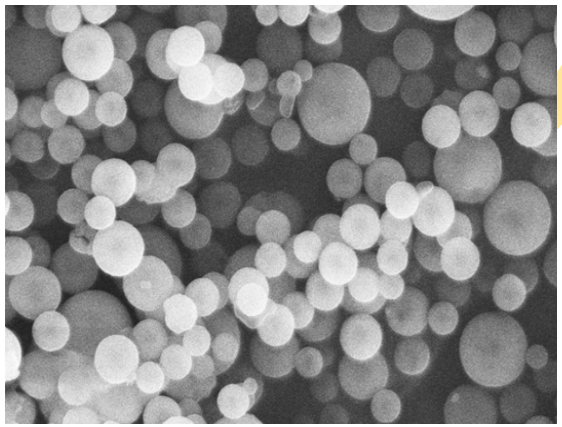
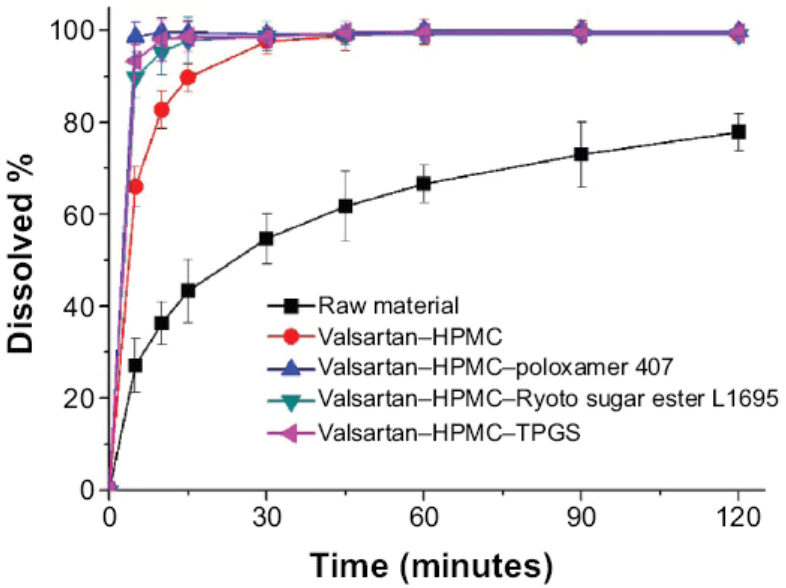


Solid dispersion nanoparticles

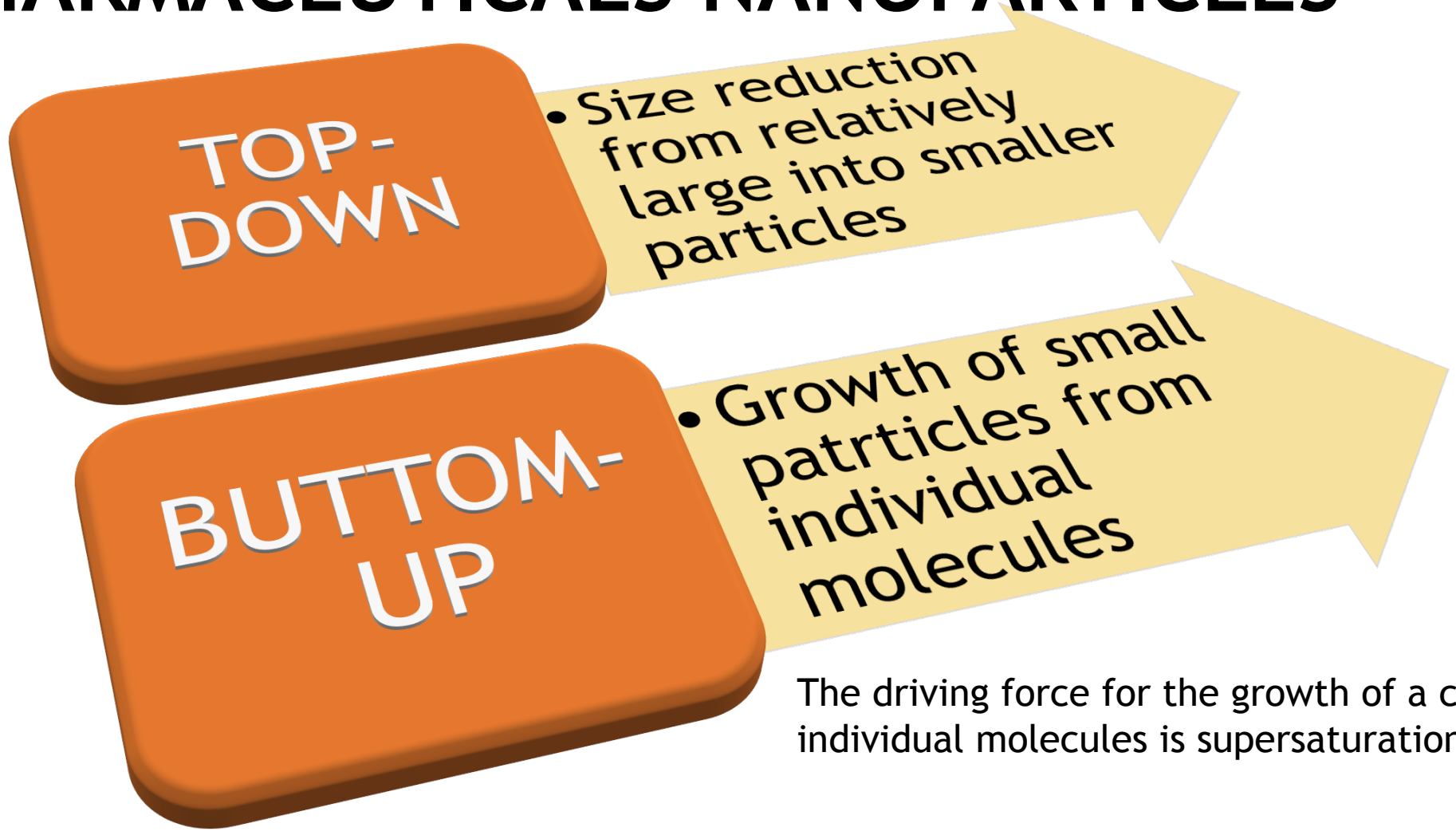
Increase surface area available for dissolution

Increase dissolution rate



Kim and Baek, 2014

TOP-DOWN AND BOTTOM-UP TECHNIQUES TO PRODUCE PHARMACEUTICALS NANOPARTICLES



The driving force for the growth of a crystal from individual molecules is supersaturation.

RECENT DEVELOPMENT ON BOTTOM-UP TECHNIQUE

Hot-melt	• In 1960s, Sekiguchi et al. prepared a solid dispersion of the poorly soluble sulfathiazole embedded in urea. The small particles were prepared by melting the drug and matrix and subsequently cooling this mixture in an ice bath.
Solvent evaporation	• A method developed by Tachibani et al. to prepare solid dispersions. The drug and matrix are dissolved in a common solvent (e.g. chloroform), after which the solvent is evaporated under vacuum.
Precipitation (Hydrosol technique)	• A technique developed by List and Sucker. The lipophilic drug is first dissolved in an organic solvent (e.g. ethanol) and then mixed with a large amount of anti-solvent that is miscible with the organic solvent, usually water.

RECENT DEVELOPMENT ON BOTTOM-UP TECHNIQUE

Supercritical fluid technologies	• Current development processes to prepare drug nanoparticles based on **supercritical fluid technologies**: *gas anti-solvent recrystallization (GAS), rapid expansion of supercritical solutions (RESS), and supercritical anti solvent technique (SAS)*
Freeze-drying	• More recently, a *freeze drying technique* to prepare drug nanocrystals, *controlled crystallization* during freeze- drying (CCDF) and a *spray freeze-drying technique (SFD)* were developed.

DISADVANTAGES

Although there are many promising in-vitro results published, only a few of these efforts resulted in a marketed product.

- possible decomposition of the drug (hot melt method)
- contamination from toxic organic solvents (solvent evaporation method)
- difficulty controlling the size of the drug crystals (hydrosol),
- limited solubility of the drug in the solvent (supercritical fluid technologies)
- long processing times and expensive cooling (CCDF)
- nozzle clog (SFD)

ULTRASONIC SPRAY-DRYING METHOD

- The latest study found that there is an increase in the dissolution rate of fenofibrate in nanoparticles developed by spray-freeze drying method, and there was no significant change in chemical stability when the sample has been put into storage for 27 days in different temperature (27°C, 40°C, 55°C and 70°C).
- However, it showed that a batch-to-batch difference in powder was yield, and the clogged nozzle was suggested to be the cause of this difference.

(Avanti *et al.*, 2014)

We therefore develop
solid dispersion nanoparticles
by ***ultrasonic spray drying method***

ULTRASONIC SPRAY-DRYING METHOD

- Several studies reported that frequency and amplitude will create an unstable movement in the liquid surface lead to droplets formation.
- It also reported that increasing frequency will decrease the droplet's diameter into nano-size. (Sindayihebura *et al*. 1997).
- Ultrasonic spray dryer that will be developed in this study is a modification of spray dryer and ultrasonic atomizer.
- The advantage of ultrasonic spray drying is the absence of expensive cooling (dries quickly without nitrogen fluid and freeze dryer). (Dalmoro *et al*. 2012)

DEVELOPMENT OF FENOFIBRATE NANOCRYSTALS USING USD METHOD

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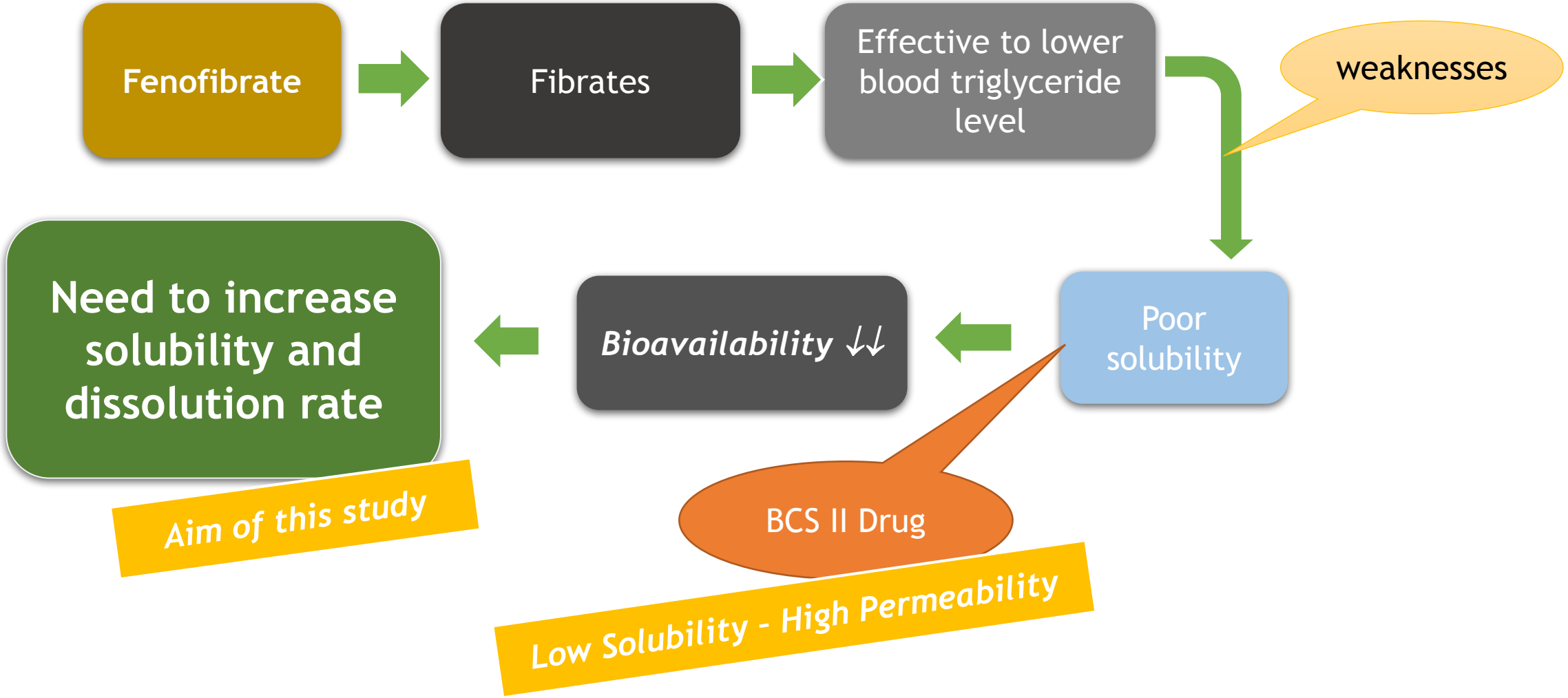
- Manitol has been chosen as a dispersed medium as it provide a high glass transition temperature (T_g) that can be used to increase kinetic stability of the drugs and/or influenced the dissolution rate.
- Fenofibrate has a low T_g, which has a very high risk to uncontrolled crystallization.
- fenofibrate-manitol (10% drug load) has been made into nanometer size solid dispersion by ultrasonic spray drying.
- The physical characteristic observed by several test, such as: FTIR,, X-Ray Powder Diffractometer, Scanning Electron Microscope, and Dissolution test

WHY FENOFIBRATE?



ULTRASONIC SPRAY DRYER SKETCH

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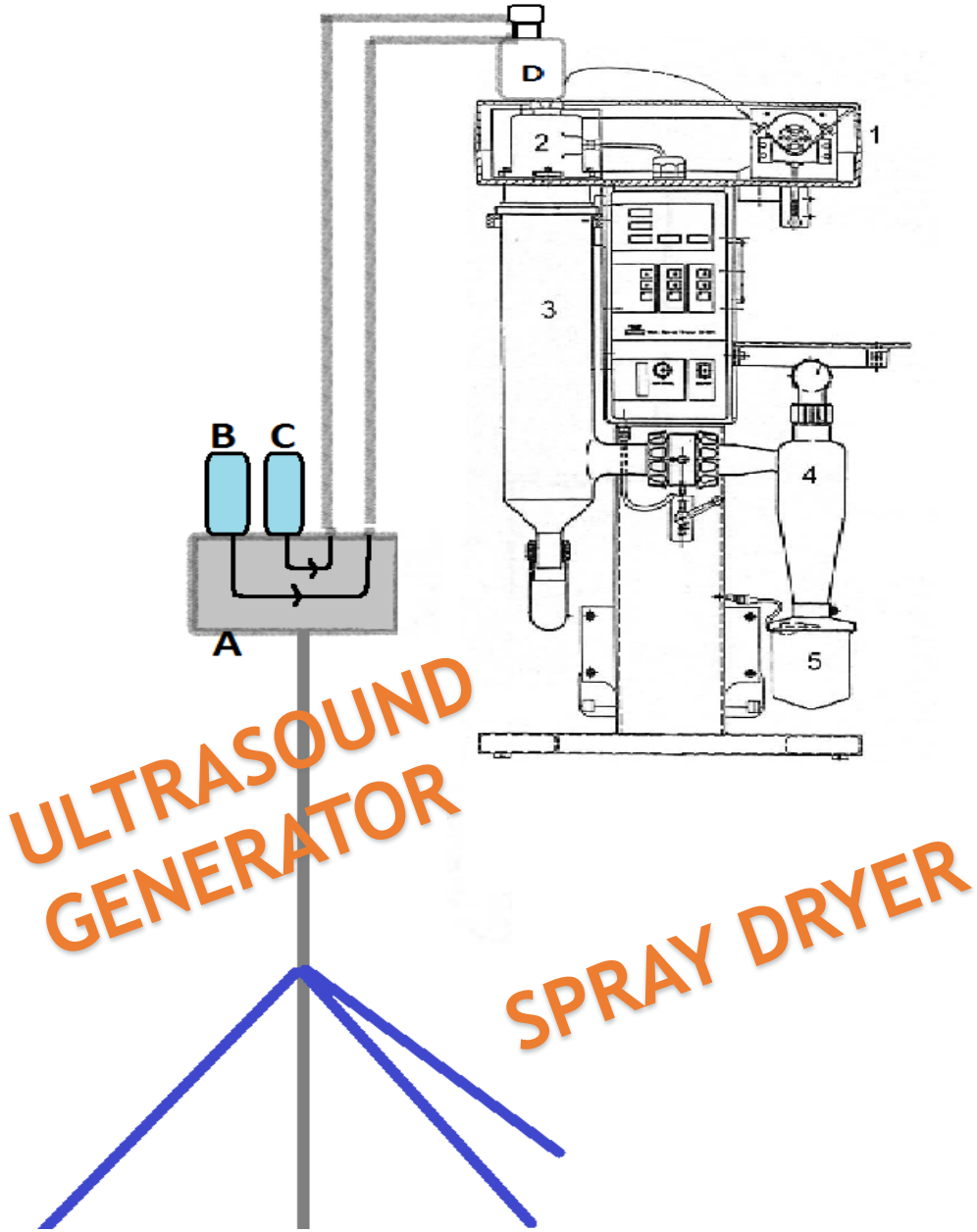
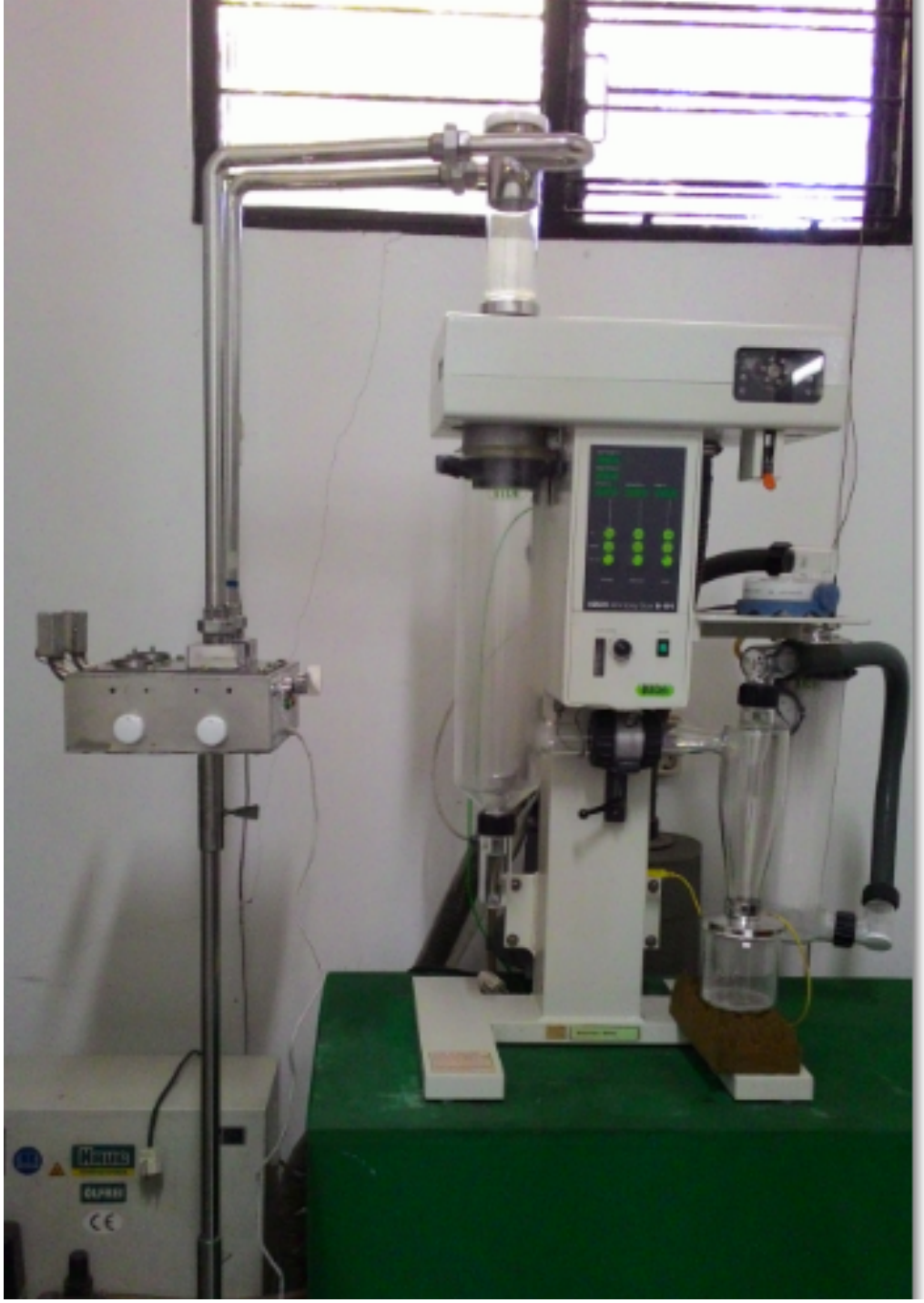
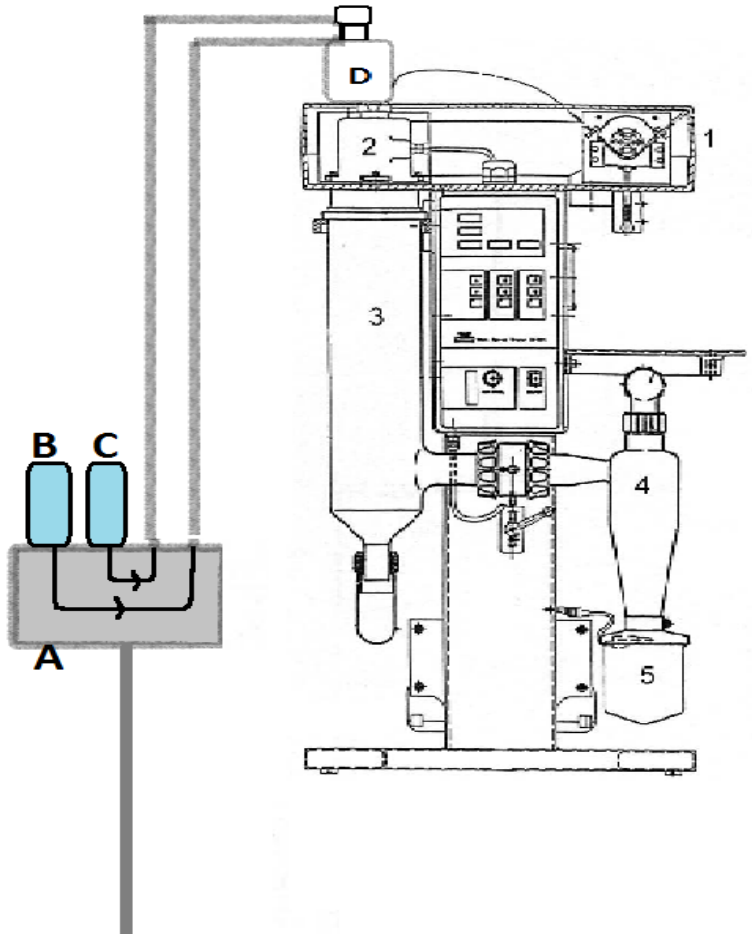


A : *Ultrasonic transducer*
B : BCS II drug in ethanol
C : Manitol in aqua bidest
D : Mixing Tank
1 : Pump
2 : Nozzle
3 : Dry Column
4 : Cyclone
5 : Collector vessel





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SOLID DISPERSION NANOCRYSTALS

ULTRASONIC SPRAY DRYER

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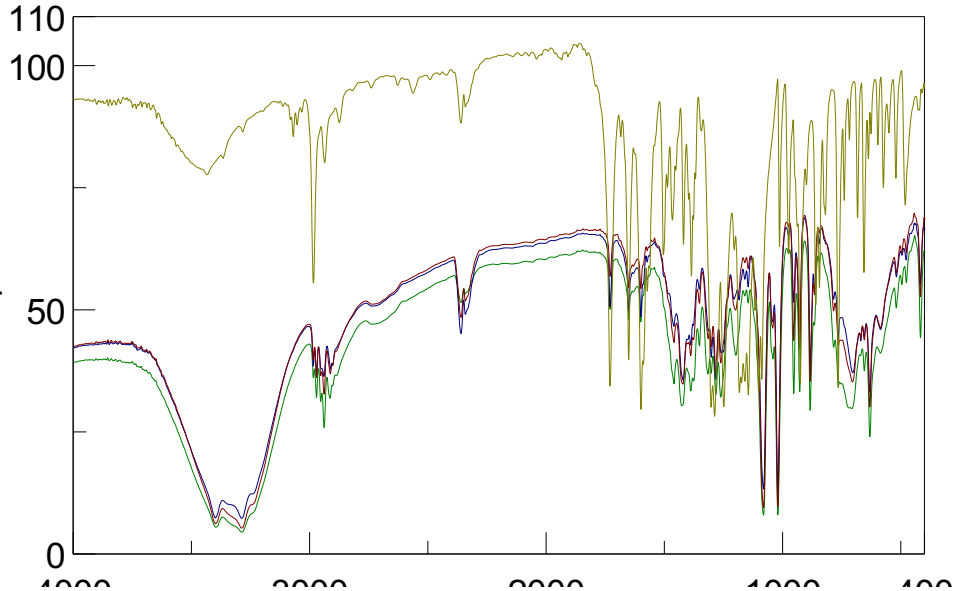
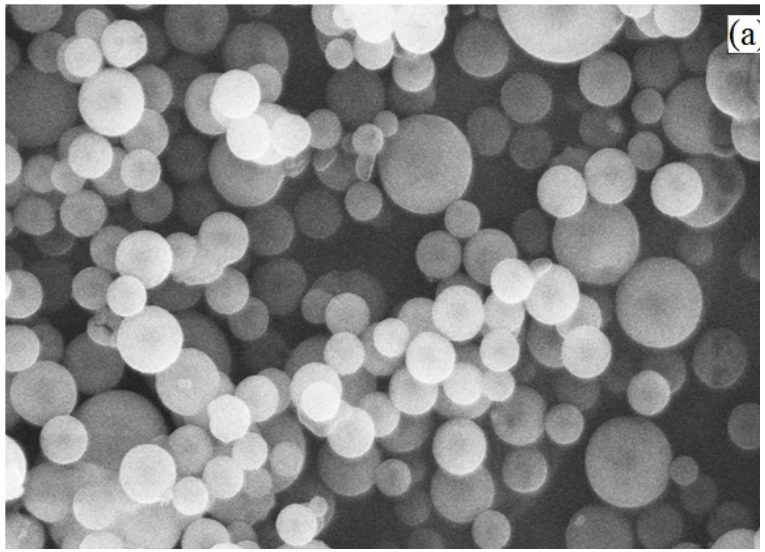
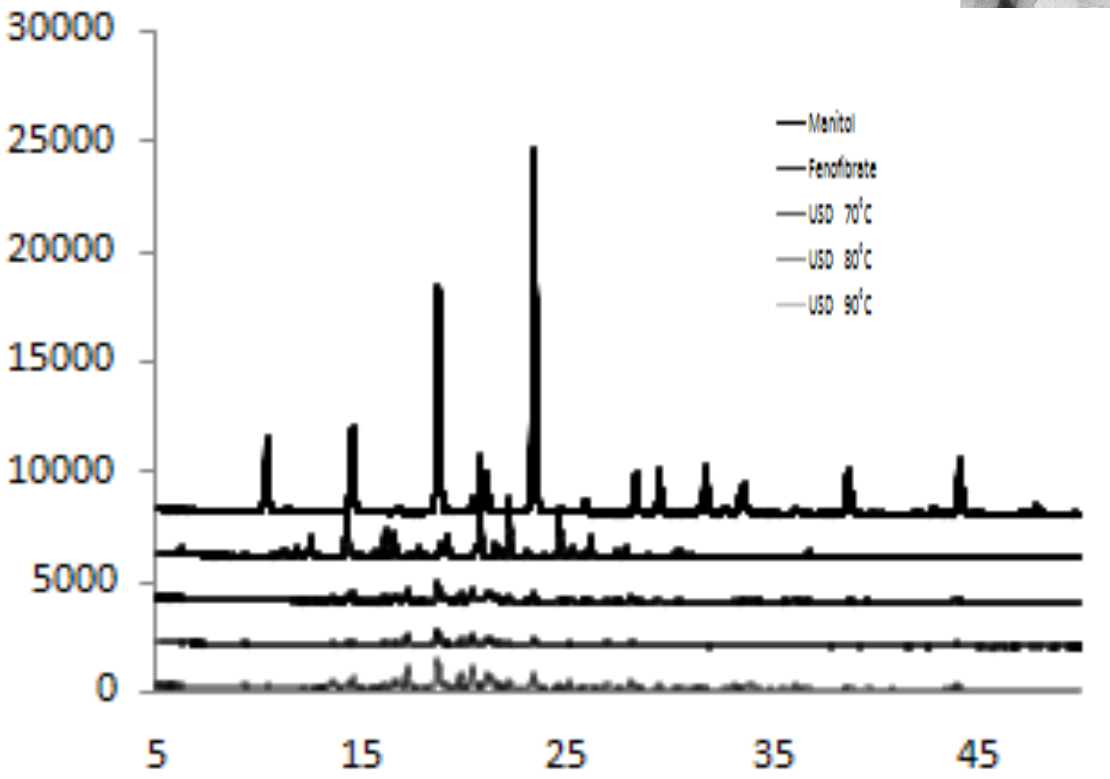
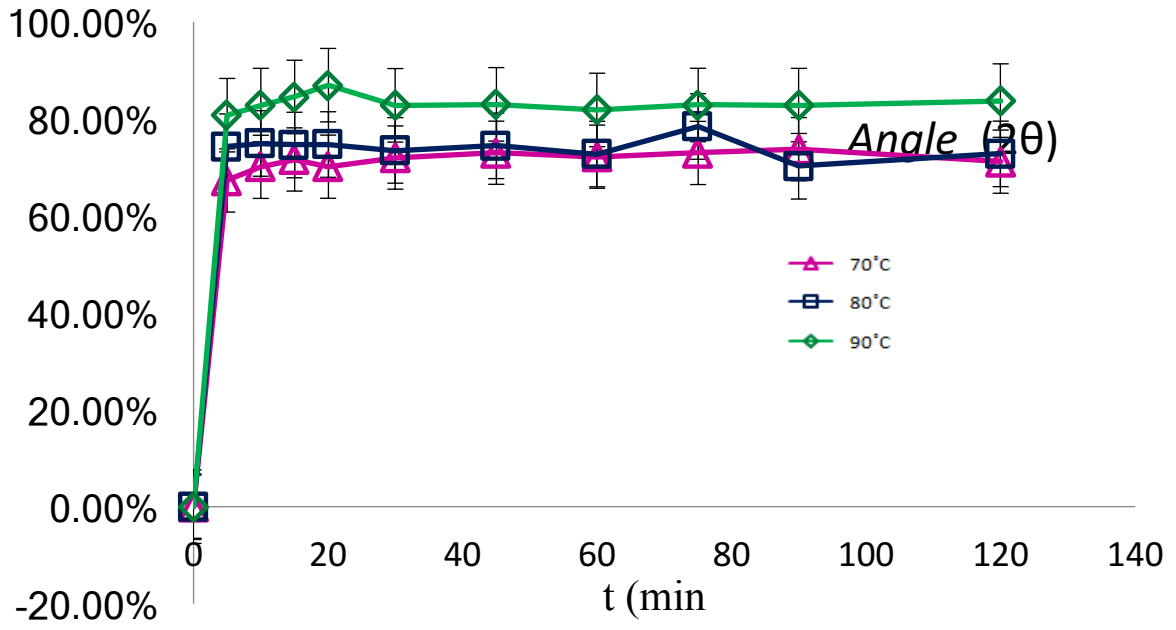
RESULTS





Spherical 200-800 nm





CONCLUSION

- Although there are only a limited number of products based on bottom-up preparation of pharmaceuticals nanoparticles on the market, promising technologies are available.
- Examples of these techniques are hot melt extrusion, supercritical fluid technologies, CCDF. However, products prepared by these or other bottom-up techniques will only reach the market if the industrial production is already kept in mind during lab-scale development.
- Ultrasonic Spray Dryer has been successful to produce nano particle of fenofibrate-manitol solid dispersion and increase the dissolution rate.

THANK YOU

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