

# The Solumer™ Platform



**Solubest**



# HIGHLIGHTS

- Industry VALIDATED
- PROPRIETARY Platform
- FAST turnaround
- Standardized process, CUSTOMIZABLE formulations
- SIMPLE & COST EFFECTIVE implementation
- EASY to scale up
- Micron sized particles constructed from non-amorphous API interwoven within a polymer matrix:
  - High SOLUBILITY
  - High STABILITY
  - Bypass current IP

# Unmet Needs in Drug Solubilization Market

## Issue

Active Ingredients in development are *poorly soluble*

- Poor solubility has become a *major challenge in drug delivery* as 90%<sup>1</sup> of the active ingredients have at least some solubility issues ; this proportion is still growing
- *This implies that drug solubilization techniques could potentially impact up to 90% of R&D*

## Effect on R&D

*Time and cost* involved with screening for salts

- *Hydrophobic nature of the New Chemical Entity (NCE)* prompts for screening of its various salts with the aim of identifying one with similar safety and efficacy and a better solubility/bioavailability
- *Salt selection is a time consuming process* and delays drug development, *adding to the development cost of a drug*

## Effect on Pipeline

*Failure* of drugs to move from preclinical to phase I

- Nearly 75% of preclinical stage drugs do *NOT* move to phase I
- Around 39%<sup>3</sup> of these failures are attributed to *poor drug-like properties of the drugs (significant among them- low solubility)*

## Impact on Market Size

Increase in number of *poorly soluble drugs on the market*

- About 40%<sup>2</sup> of *drugs currently on the market* exhibit poor solubility leading to poor dissolution kinetics and suboptimal bioavailability, *i.e. low product efficacy and reduced commercial success due to poor patient/physician perceptions*

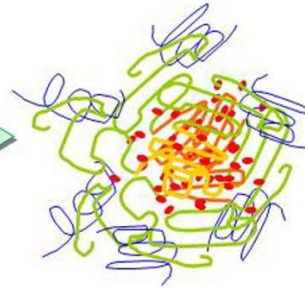
# SoluBest's solution: Solumer™

## Creation of Self-Assembled Multipolymer-Drug Complex

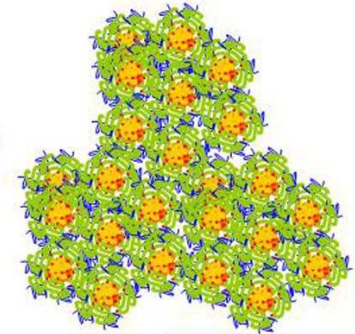
Initial interactions starting in homogeneous solution



Drying



Drying and aggregation

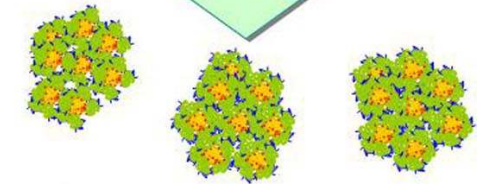


Solid dispersion comprising drug with modified properties

- Drug molecules
- Hydrophilic polymer (H)
- Hydrophobic segments of amphiphilic polymer (A)
- Hydrophilic segments of amphiphilic polymer (A)

Self-assembly with induced hydrophilic-hydrophobic gradient

Aqueous media



Colloidal dispersion



# The Solumer Technological Platform

- Robust & versatile: applicable to wide range of small molecules
- Short feasibility screening times (up to 4 weeks per project)

## The Process:

- 2 steps: liquid feed followed by spray drying
- Bottom-Up : Components self assemble
  - Initial noncovalent interactions between polymers and lipophilic drug occur in the liquid feed
  - Subsequent drying process ensures a strengthening of these interactions resulting in a self-assembled polymer-drug complex in powder form



# The Solumer Technological Platform (cont.)

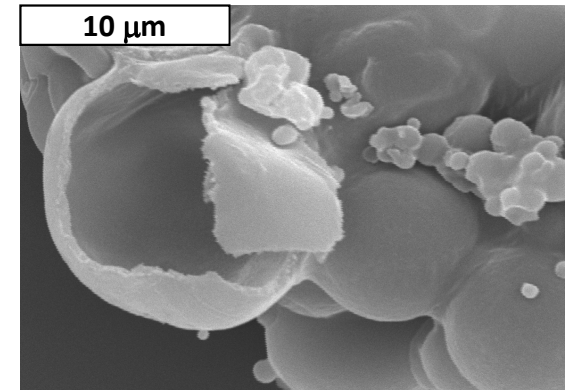
Polymer-drug constructs give the API unique physico-chemical properties

- Drug homogeneously interwoven into a polymer construct
- Increased Surface Area
- Depressed  $T_m$
- Depressed Enthalpy
- Formation of colloidal dispersions in contact with aqueous media  
= **Enhanced dissolution**

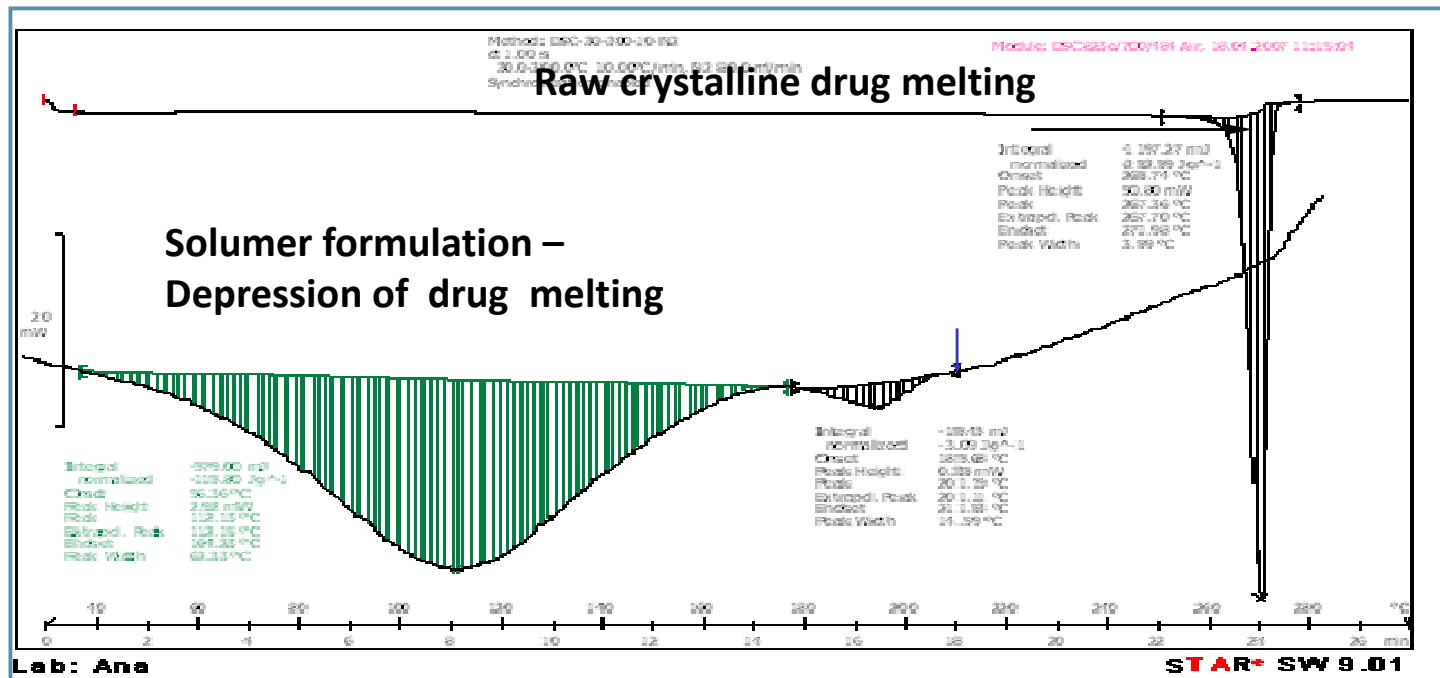
# SoluBest Technological Capabilities

- Powder Development
  - Powder optimization and characterization
  - Stability testing
  - Scale up: to lab and pilot scale (outside facility); up to Industrial scale
- Dosage form prototype development
  - Milling/ Granulation
  - Capsule prototype development
  - Tablet prototype development

# SoluDrug Formulation



... With a unique thermal behavior fingerprint



Example: Resveratrol

# Solumer Fingerprints

API			Formulation		
	$T_{\text{melt}} (^{\circ}\text{C})$	$\Delta H_{\text{melt}} (\text{J/g})$	$T_{\text{melt}} (^{\circ}\text{C})$	$\Delta H_{\text{melt}} (\text{J/g}_{\text{drug}})$	Partical size nm
<i>Resveratrol</i>	267.4	253.6	199.1	14.0	1224
<i>Hesperetin</i>	231	166.2	No peak of melting		1310
<i>Nifedipine</i>	172.4	113.4	140.9	8.4	749
<i>Fenofibrate</i>	81.5	74.3	64.4	9.3	669
<i>Tacrolimus</i>	135.0	60.5	118.0	52.0	836
<i>Clarithromycin</i>	227.6	70.2	207.9	40.1	1190
<i>Albendazole</i>	215.2	209.7	161.4	31.2	555
<i>Fenbendazole</i>	239.2	166.3	203.7	8.9	892
<i>Itraconazole</i>	169.7	84.4	155.6	21.9	910

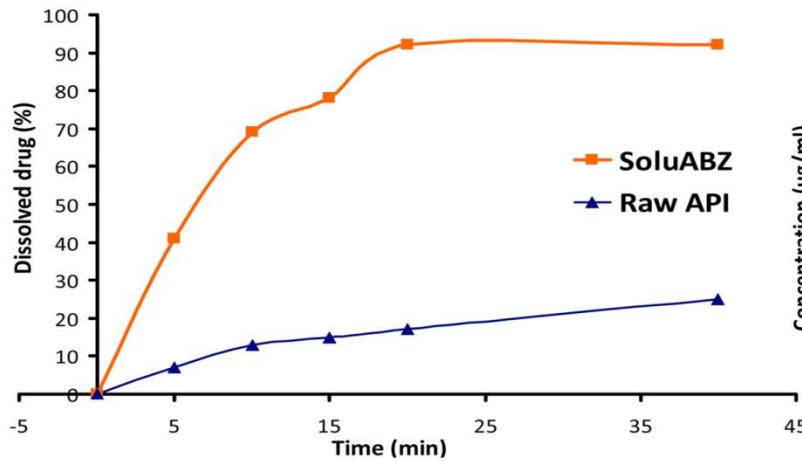
Formulating lipophilic crystalline drugs results in a self-assembled drug-polymer complex possessing two features required for improved bioavailability:

- **Depression of melting temperature and energy**
- **Formation of colloidal dispersions upon contact with aqueous media**

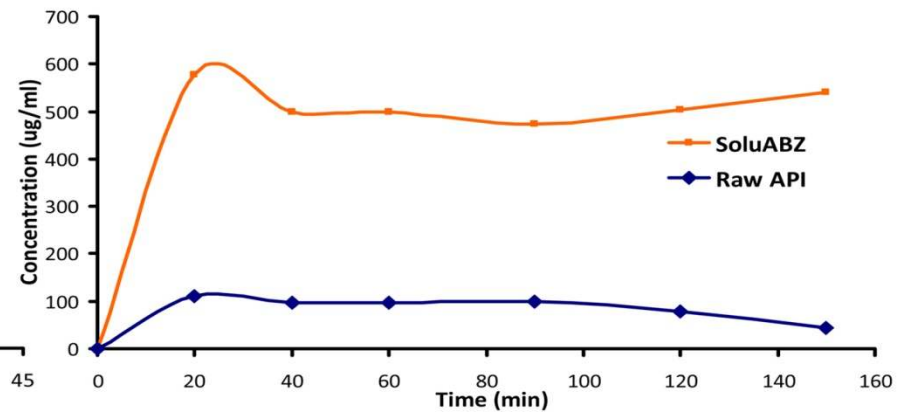
# Better Dissolution= Higher Bioavailability

e.g. Albendazole

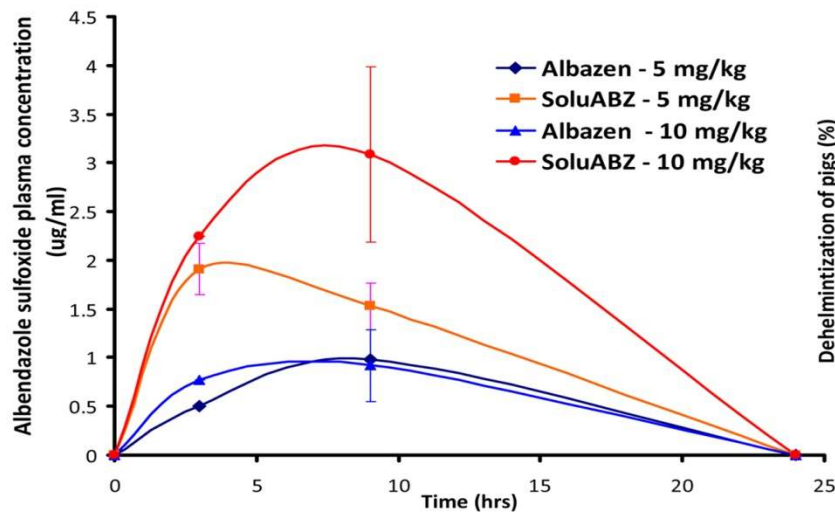
**A** Dissolution of Solu-Albendazole vs. Raw crystalline API in 0.05M SLS



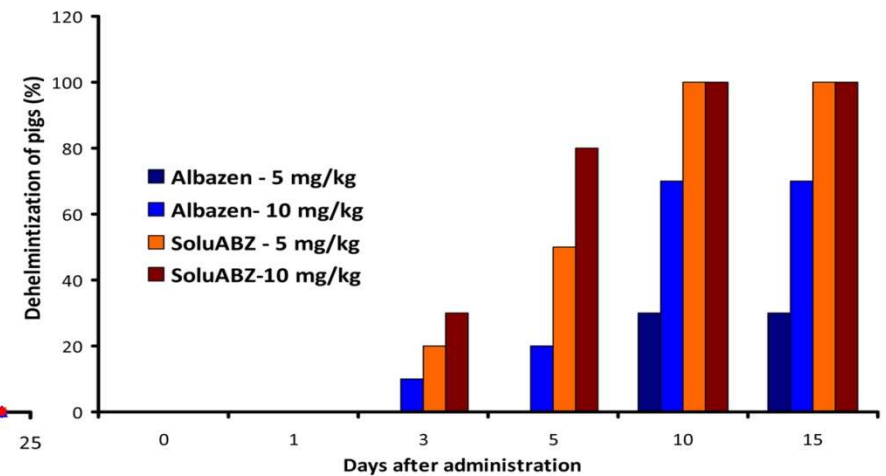
**B** Saturation Solubility of Solu-Albendazole vs Raw API in FaSSIF



**C** Preclinical Comparative Study of Albendazole

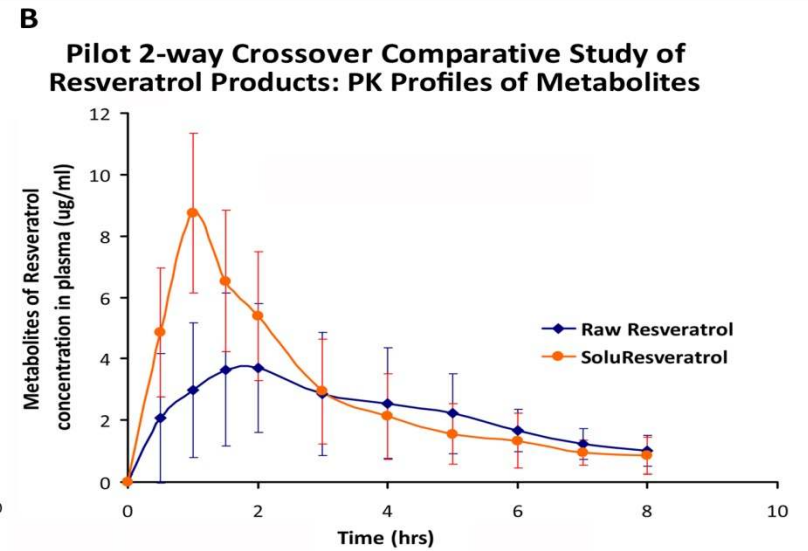
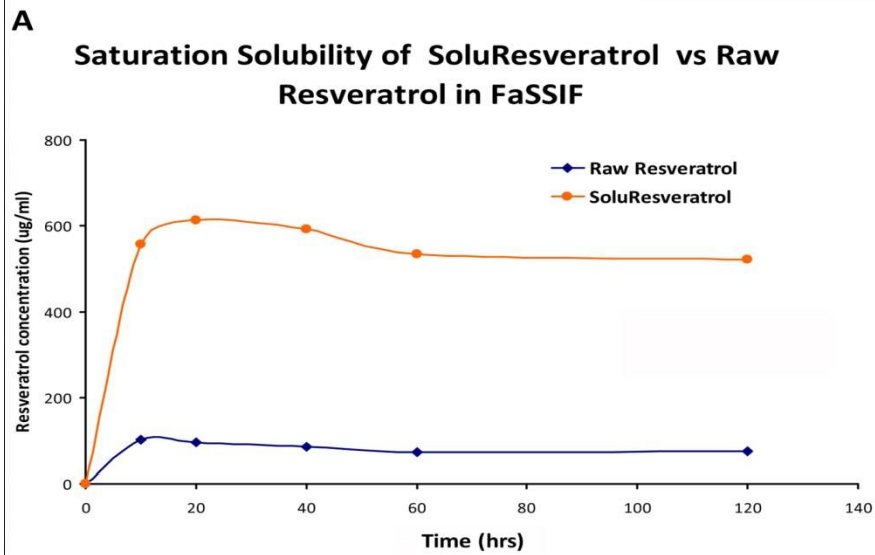


**D** Efficacy of Solu-Albendazole vs Albazen



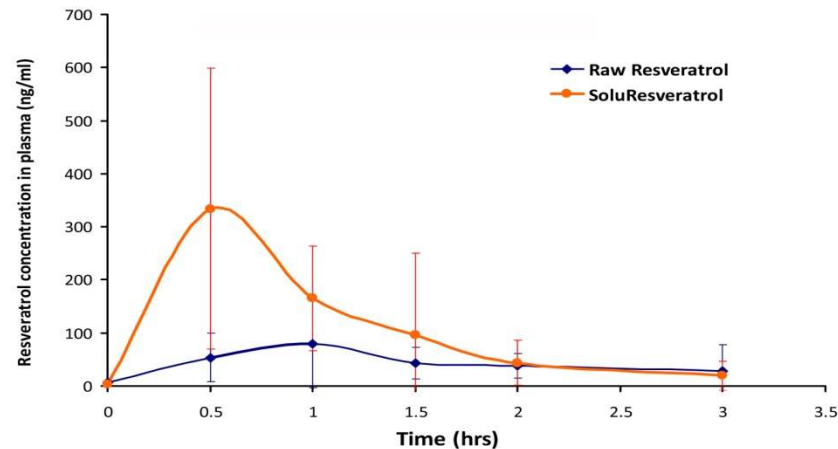
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e.g. Resveratrol



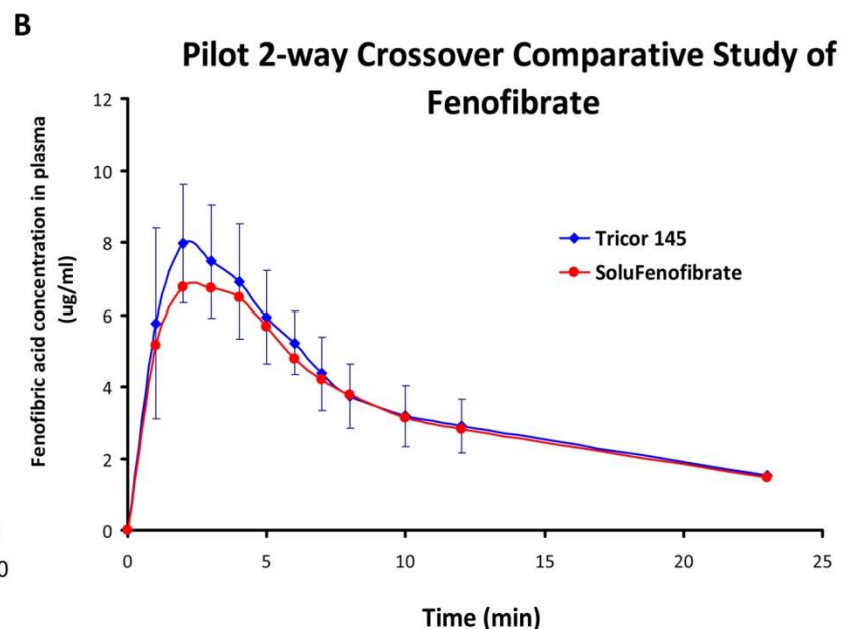
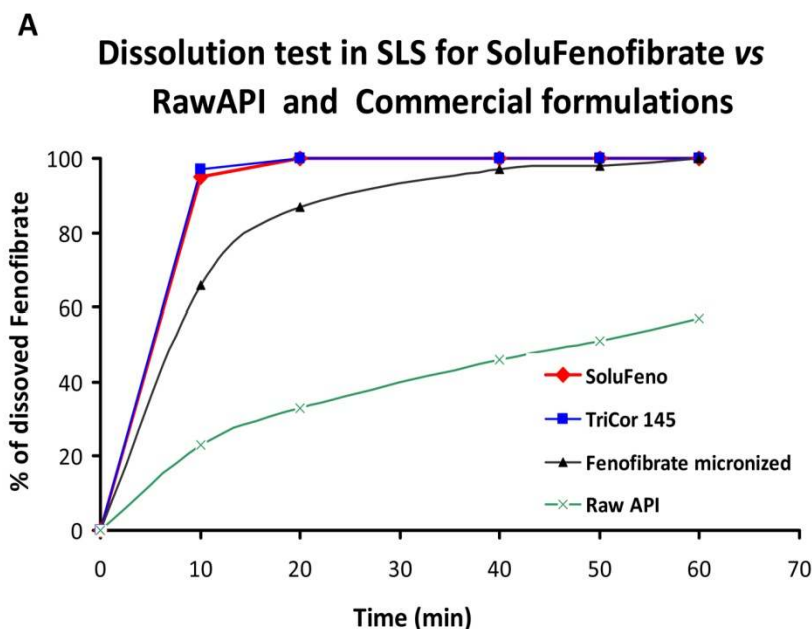
**C**

**Pilot 2-way Crossover Comparative Study of Resveratrol Products: PK Profiles of Resveratrol**

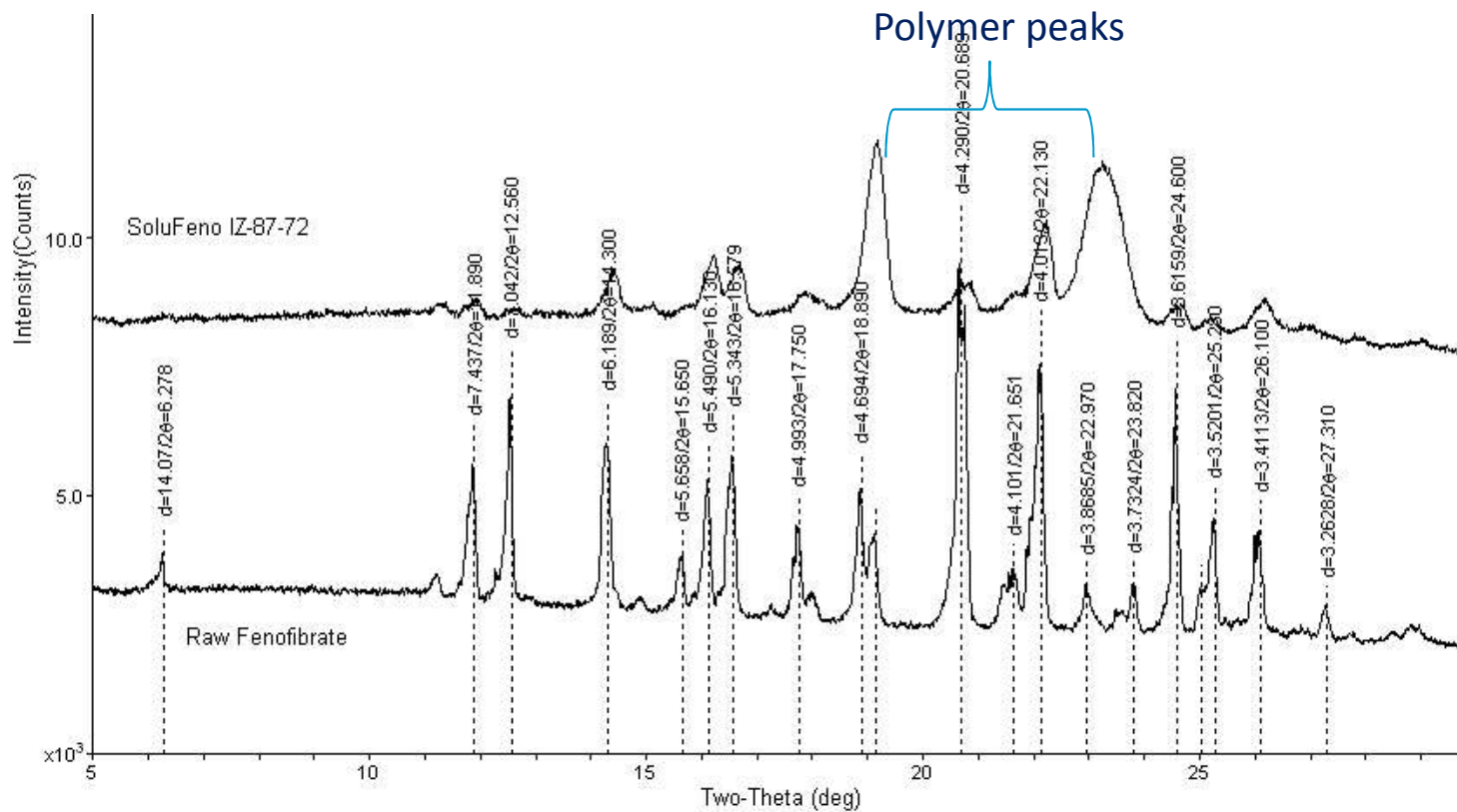


# Better Dissolution= Bioequivalence with leading Nano-formulations

e.g. Fenofibrate



# Different from other SD based methods: non amorphous



Powder X-ray diffraction patterns of raw bulk fenofibrate and SoluBest fenofibrate formulation

# Significant advantage over nano & amorphous: Stability

<i>Batch</i>	<i>Condition of storage</i>	<i>Time in storage (months)</i>	<i>Assay (mg/g)</i>	<i>Melting point (°C)</i>	<i>Melting enthalpy (J/g)</i>	<i>% Dissolved in 15 min</i>
SoluFeno-PR-PD-35	Initial	-	245.0	63.7	3.4	100
	25°C, 60% RH	12	244.2	63.1	3.3	NA
		28	247.8	63.4	2.5	100
	40°C, 75% RH	3	243.5	63.4	2.9	100
		6	245.2	63.4	3.5	100
	SoluABZ-04-08	Initial	-	250.5	180.1	7.2
25°C, 60% RH		17	236.0	179.7	6.2	100
SoluRes-07-08	Initial	-	238.2	193.2	2.6	NA
	5°C	12	245.0	196.1	1.46	NA
	25°C, 60% RH	6	238.0	194.5	2.1	NA



# Technical Considerations

## SoluFeno Process and Product demonstrate:

- Good in-process and post-process stability; three years of monitoring showed no changes in the drug and formulation properties
- Excellent reproducibility, negligible batch-to-batch variability and robustness
- Consistently low residual organic solvent content
- Moisture tolerance (~5% water content in powder)
- Scalable process

# Major Benefits

Feature	Benefit
Superior solubility	Increased Bioavailability Decreased Variability Elimination of Food Effect
No chemical change in drug, FDA approved polymers	Streamlined Regulatory Track, ANDA, 505b2
2 step process: Feed → Spray Drying	Continuous, reproducible and simple manufacturing using readily available equipment
Non-amorphous	On the shelf stability
Modified thermal behavior	Proprietary, Non-infringing products with Superior Dissolution