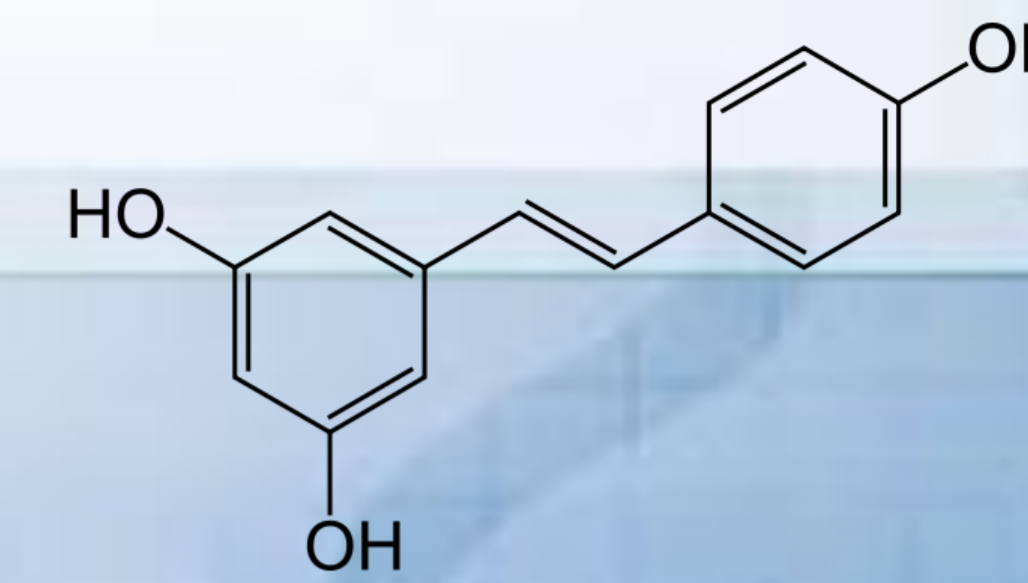


Solumer™ Bioperformance

Resveratrol – BCS Class IV representative



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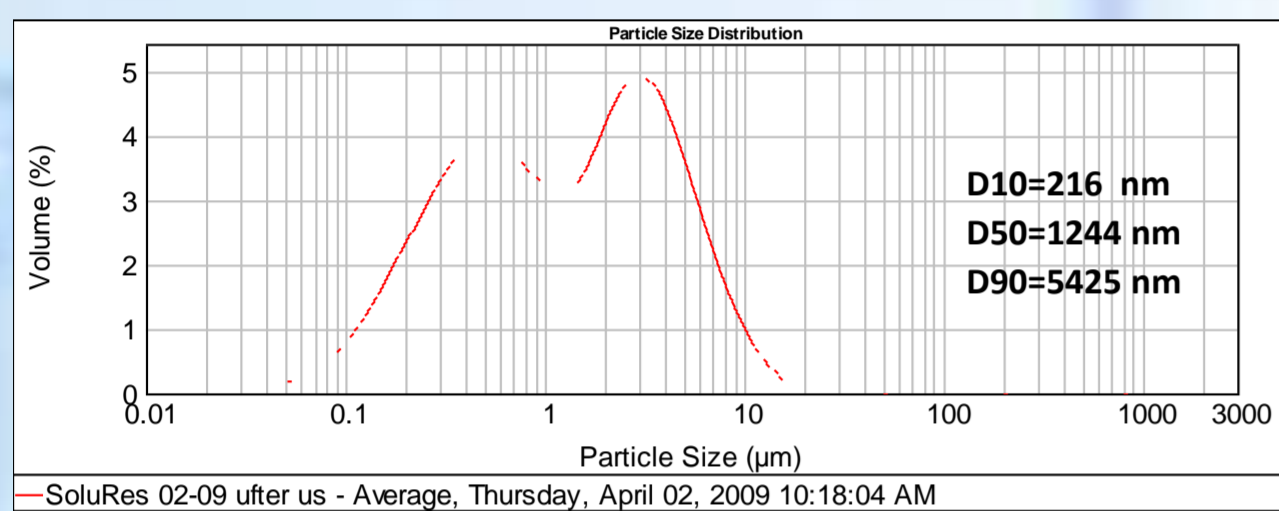


Introduction:

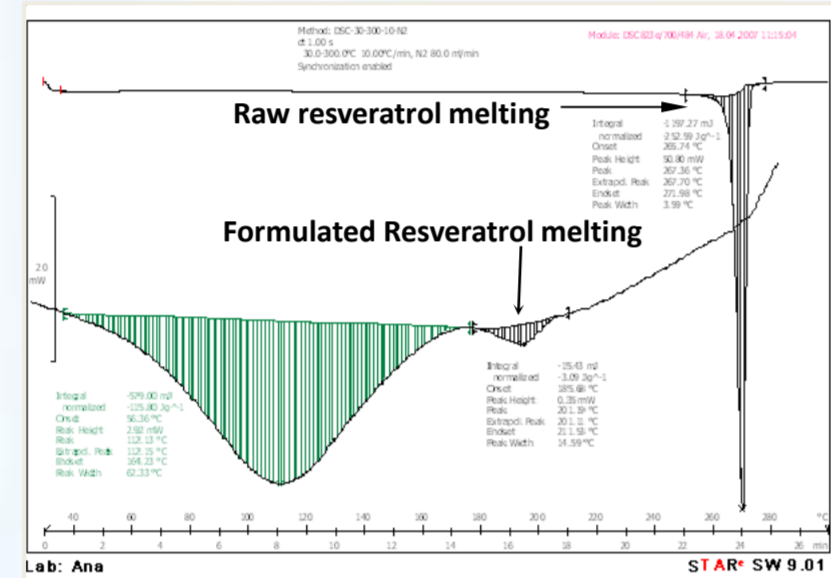
Resveratrol (RSV) is a natural polyphenol, a small molecule activator of Sirtuin 1 (Sirt1), protein that controls age-related disorders: obesity, metabolic syndrome, type II diabetes mellitus, etc. RSV is practically insoluble in aqueous media and is characterized by a very low bioavailability and rapid, extensive metabolism. Therefore, only trace amounts of the un-metabolized resveratrol reach the systemic circulation following oral administration.

Solumer™ Resveratrol characteristics

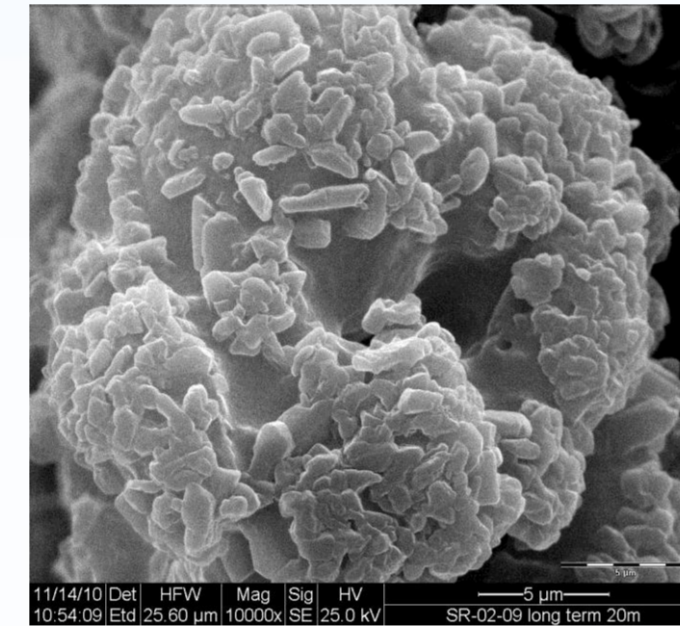
Utilizing Solumer™ technology, Solubest developed a highly bio-available Solu-RSV formulation of resveratrol with improved parameters.



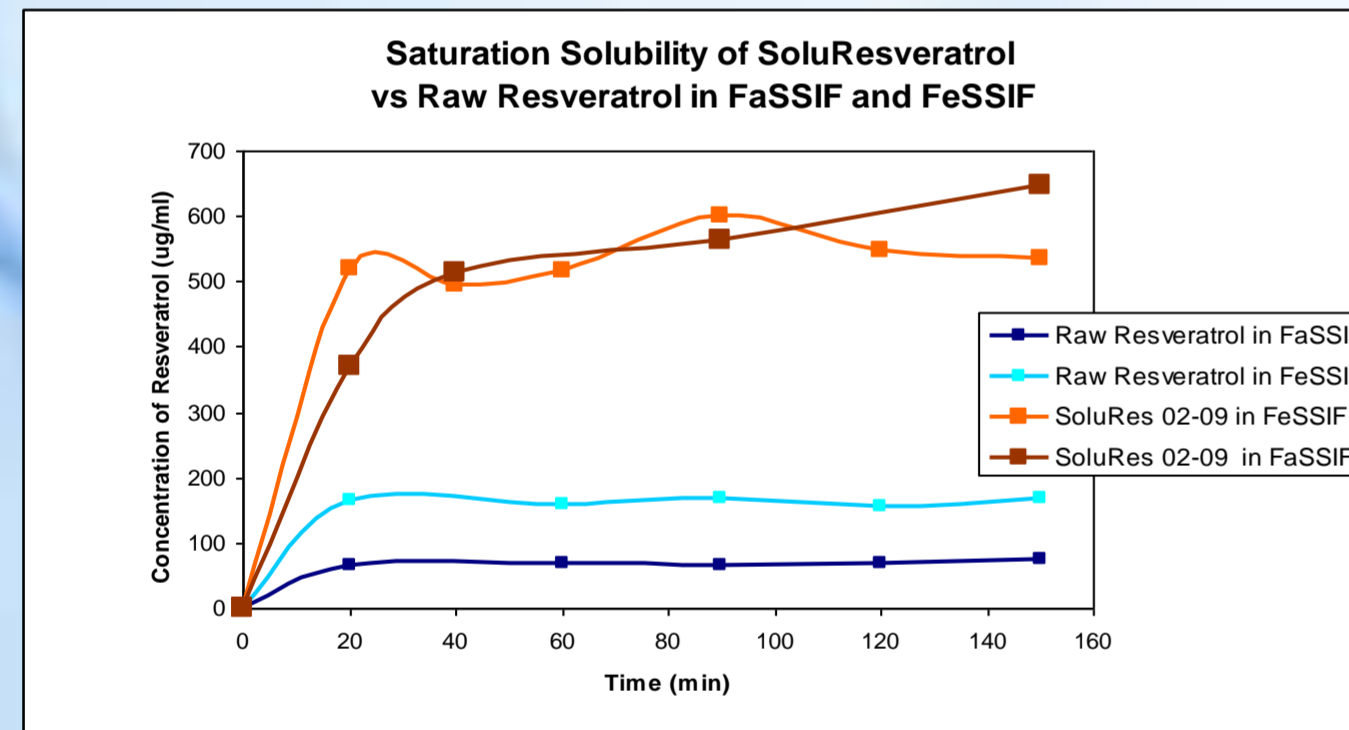
Formation of drug colloids with D50 < 1250



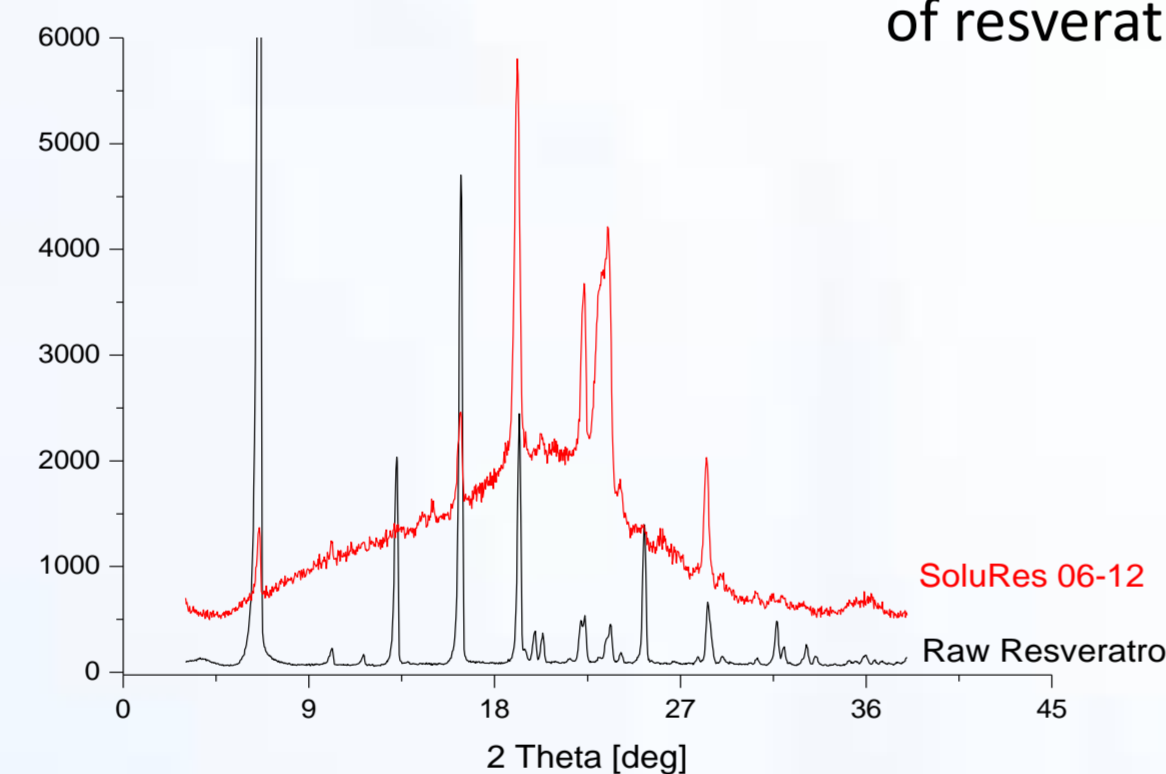
Reduction of melting temperature by 50°C and melting enthalpy 20-folds vs. unformulated raw material



Porous polymer aggregates (100-200 µm) covered by submicron-micron particles of resveratrol (0.5-5 µm)

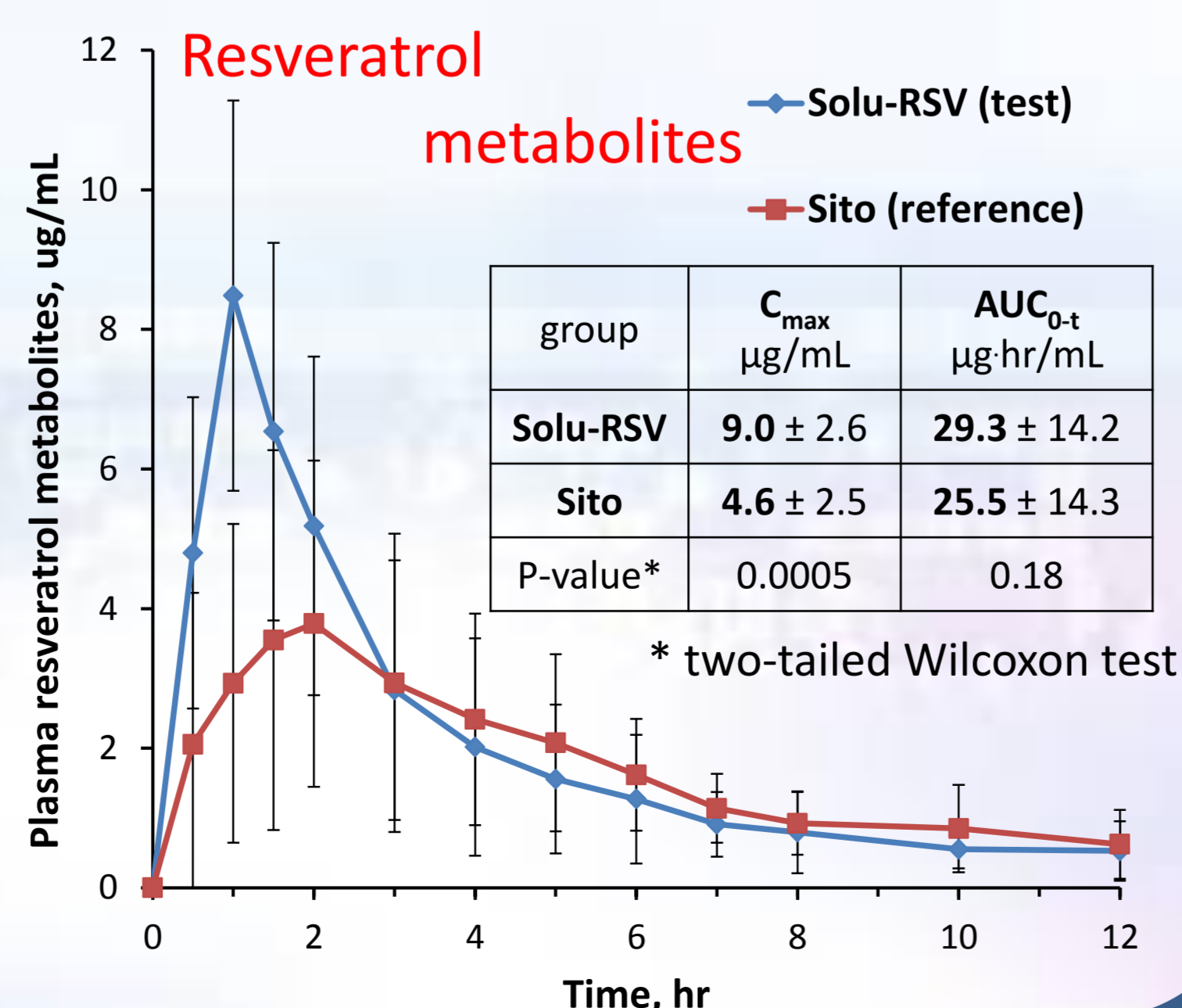
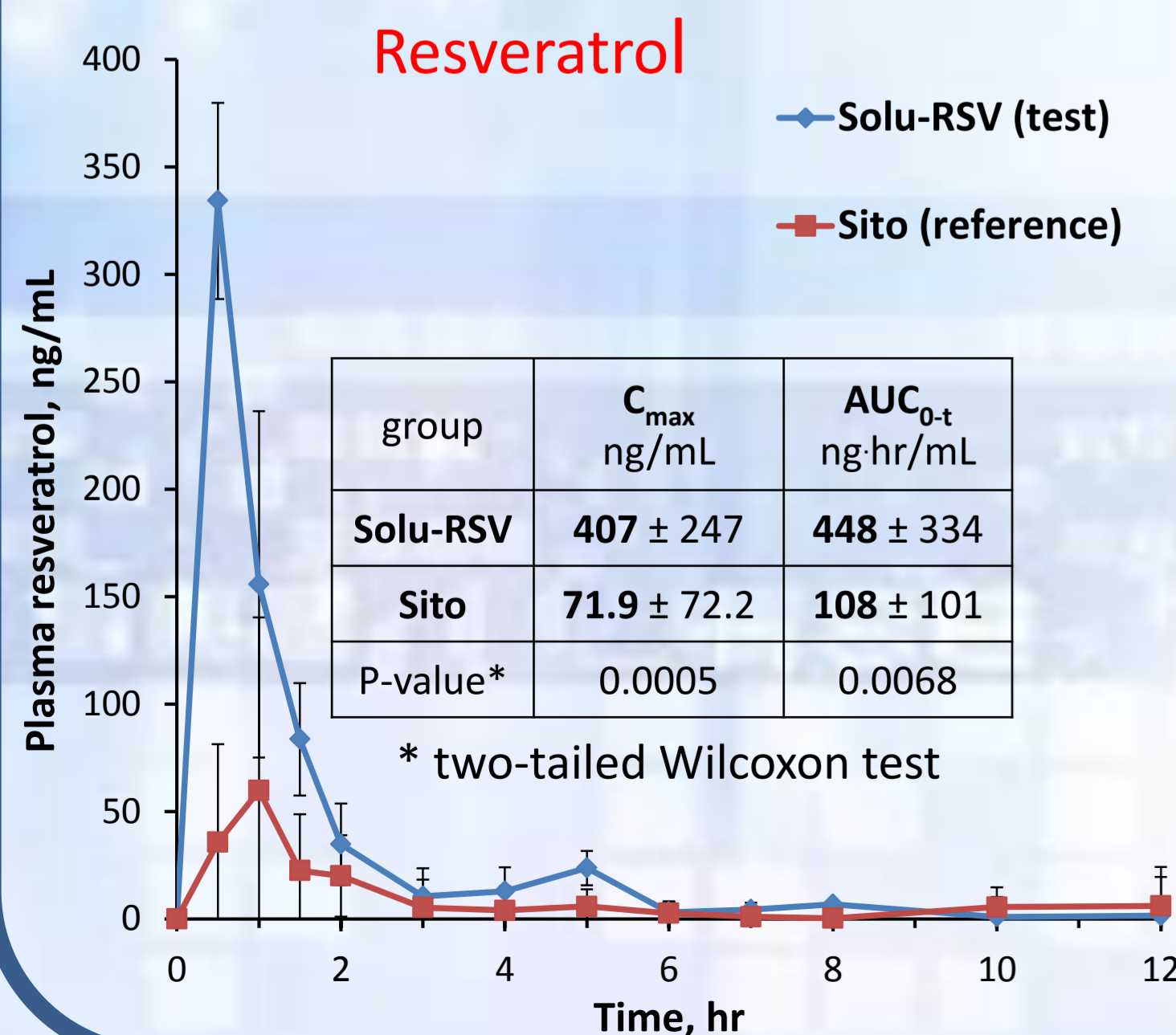


5-folds better dissolution in FaSSiF and FeSSiF; similar dissolution profiles in the fed and fasted simulated fluids



Reduction of the crystallites effective sizes

Pharmacokinetic Data Analysis of SoluBest Clinical Study



PK data comparison (based on SoluBest clinical study and literature)

Data source	Resveratrol dosage form	Dose mg	C _{max} , ng/mL	C _{max} /D 10 ⁻⁶ /mL	AUC ng·hr/mL	AUC/D 10 ⁻⁶ hr/mL
Solubest study	Solu-RSV suspension	500	407 ± 247	0.81 ± 0.49	448 ± 334	0.90 ± 0.67
Solubest study	suspension, Sito	500	71.9 ± 72.2	0.14 ± 0.14	108 ± 101	0.22 ± 0.20
Boocock 2007	IR caplets, Royalmount Pharma	500	72.6 ± 35.5	0.15 ± 0.07	224	0.45
Brown 2010	IR caplets, Pharmascience Inc.	500	43.8 ± 39.2	0.09 ± 0.08	175 ± 146	0.35 ± 0.29
Nunes 2009	trans-resveratrol capsules	200	23.5 ± 7.4	0.12 ± 0.04	56 ± 35	0.28 ± 0.18
Almeida 2009	trans-resveratrol capsules	150	24.8 ± 19.7	0.17 ± 0.13	32 ± 20	0.21 ± 0.13

the data are shown as average ± SD

Sito – Raw commercial Resveratrol with mean particle size of 10 microns

Solu-RSV® formulation demonstrate superior pharmacokinetic parameters when compared with raw material and commercially available products. Exposure to higher concentration of intact resveratrol will be reflected in higher bio-potency.

Summary

- Solumer™ technology has been used to generate a new Solu-RSV formulation of resveratrol with improved solubility. Similarity of the solubility in Fed and Fasted intestinal fluids can be translated to the reduction or complete elimination of the food effect.
- Resveratrol from Solu-RSV formulation is more rapidly absorbed and attains significantly higher plasma concentrations, as compared to the control Sito product and other resveratrol products known from the literature. Solu-RSV needs 4-5 times less dosage to get the same bioavailability as other resveratrol products.
- Solumer™ technology can potentially improve the solubility, bioavailability, and efficiency of other BCS class IV drugs that are incompletely absorbed from the gastrointestinal tract.