Solution Engine 2.0: Rapid Formulation Development of Amorphous Solid Dispersions by Combined In-Silico Modelling, High-Throughput Screening and in-vivo PK Study

S.Rahimi, F.Asgarzadeh
BioDuro-Sundia

INTRODUCTION

Amorphous solid dispersion (ASD) technology has been successfully utilized to enhance solubility and bioavailability of poorly soluble APIs. The proposed ASD screening platform provides the following benefits for new discovery NCEs:

1. Only 100 to 200 mg to evaluate physical form and in-vivo PK studies
2. In-silico solubility parameters modeling minimizes API use
3. In-vitro and In-vivo studies are completed in 8 to 10 weeks

ACKNOWLEDGEMENT

The authors gratefully acknowledge Amakos, MAK Scientific, and the Center for Drug Discovery (CDD) at Northeastern University and their respective contributors. Authors would also like to thank kind cooperation of Michael Jacobson and Alex Makriyannis.

METHOD(S)

- In-silico modeling of solubility parameters for compound X using the HSPiP and Gibbs free energy calculations allowed selection of miscible pairs with pharma grade polymers
- Polymer and API organic solutions were combined in 2mL micro-centrifuge tubes based on the predicated miscibility levels and vacuum dried (40°C for 1) in a Savant™ SpeedVac™ to produce ASD thin films
- Kinetic solubilities were measured using UV on the reconstituted solution centrifuged supernatant
- PK study was performed on ICR-CD1 mice (30mg/kg)

CONCLUSION(S)

Using this Solution Engine 2.0 platform, a representative compound (x) was formulated into an enabled ASD form with bioavailability improvement up to 12x compared to pure API utilizing only milligram quantities of API.

RESULT(S)

API in HPMCAS-L systems provided the highest API supersaturation concentration. Adding Vitamin E-TPGS and Poloxamer 407 further improved the saturation solubility of API and bioavailability in mice

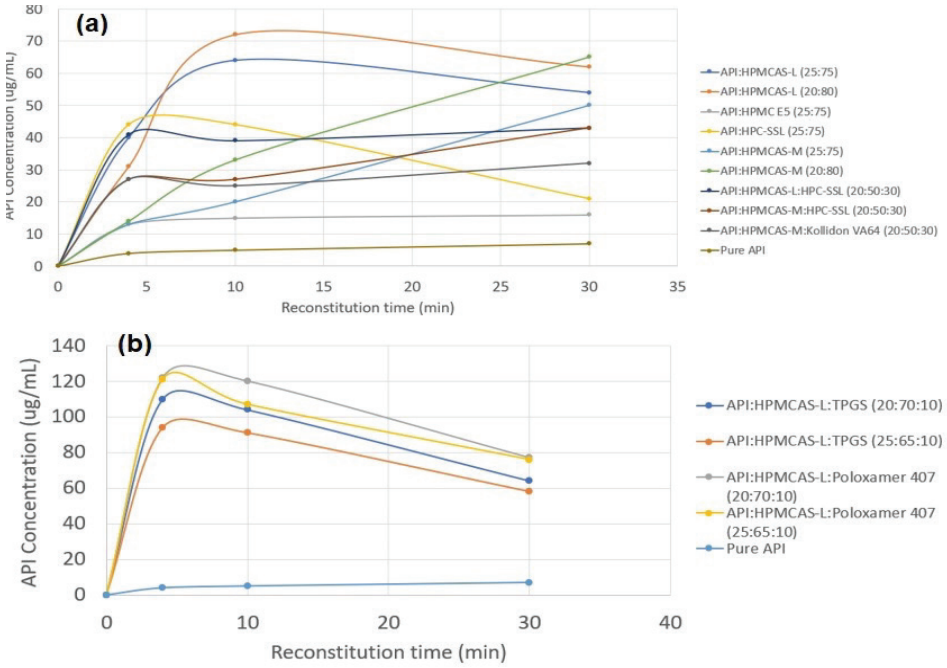

Figure 1: High throughput solubility enhancement screening of Compound X ASDs

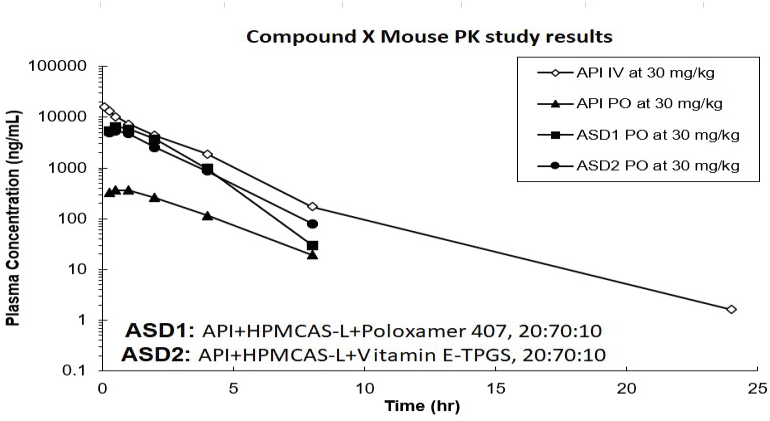

Figure 2: Mouse PK study results (plasma concentrations) for 2 lead ASD prototypes compared to API dosed PO and in IV

*This was presented at Controlled Release Society 2022 by Dr. Firouz Asgarzadeh. Please contact us if you have any questions.