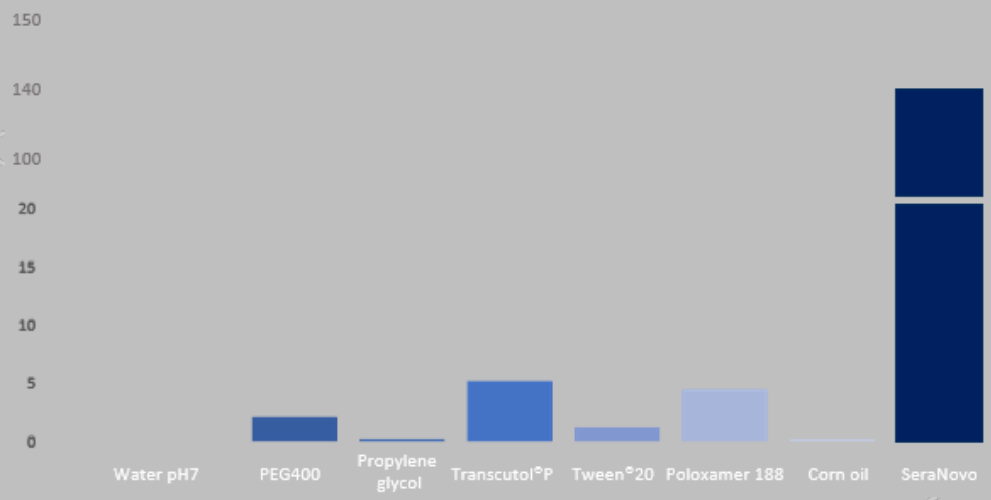
Designing a high-payload liquid formulation for the poorly water-soluble compound Itraconazole using SeraNovo's eutectic formulation technology

Itraconazole

The antimycotic compound itraconazole is extremely poorly water-soluble, which is mainly driven by its high lipophilicity. The oral solution as developed by the originator (Sporanox®, Janssen Pharmaceutica) contains hydroxypropyl-β-cyclodextrin (40%), propylene glycol and hydrochloric acid (pH 2) as solubilising excipients. Despite the cocktail of solubilisation strategies employed (cyclodextrin complexation, cosolvency and pH-adjustment), the total itraconazole concentration in this product is only 10 mg/ml.

Mol. Weight	705.6 g/mol
Melting pt	169 °C
logP	6.2
pKa	2.0 (b), 3.7 (b)

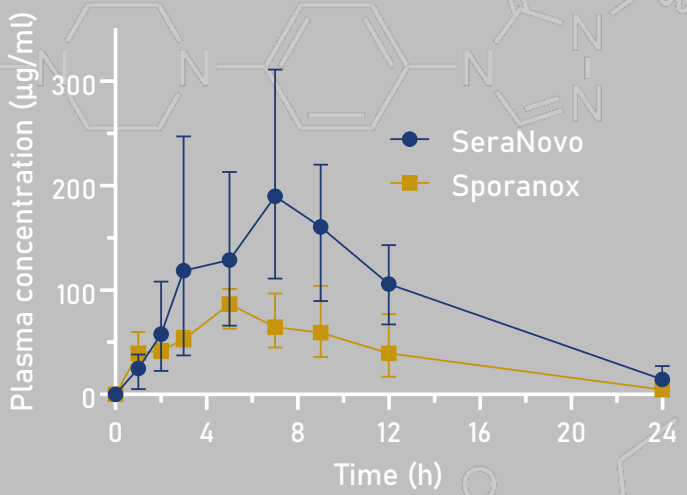
Itraconazole solubility in water and a range of solubilising excipients



Designing a high-payload liquid formulation using our eutectic formulation technology

Using our eutectic formulation technology platform, we have designed a liquid formulation that contains **140 mg/ml** itraconazole. This formulation was based on two small organic molecules that served to form the eutectic solvent with itraconazole, and one polymer that acted as a precipitation inhibitor.

The loading level in our formulation is 14-fold higher than that in the Sporanox® oral solution and two orders of magnitude higher than the solvent capacity in most traditional solubilising excipients (see table above). Oral gavage administration of our formulation to rats resulted in higher bioavailability to the Sporanox® oral solution.



Itraconazole plasma concentration vs time profiles
Rats, n=3 (mean + standard deviation), 1.25 mg dose

Conclusion

Harnessing the potential of our eutectic formulation technology platform, we have designed a formulation that has 14-fold higher loading and greater than 2-fold better biopharmaceutical performance than the marketed oral solution Sporanox®. These findings illustrate the potential of our technology for the development of enhanced oral formulations for very water insoluble compounds.

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