How to Find the Appropriate In Vitro Dissolution Test Method for Solid Solutions Based on Soluplus®
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Purpose
Danazol does not dissolve from Soluplus® based amorphous dispersions and the poor in-vitro dissolution profile would have led to a dramatic underestimation of the oral bioavailability improvement. A few other active ingredients show an equally poor in-vitro performance in simulated gastric fluid when they are formulated with Soluplus®. It was the aim of this study to develop a dissolution test method, which allows to evaluate the super-saturating performance of Soluplus® - based formulations and to establish a better correlation with in-vivo results.

Methods
Soluplus®-based amorphous dispersions (relation 20:80) were prepared with twelve different poorly soluble actives by melt extrusion in a 16 mm twin screw extruder equipped with a 3 mm die (Polylab, ThermoFisher,) at 200 rpm, 1000 g/h and at ~10°C above the melting point of the API. Dissolution tests were conducted with an USP apparatus 2 (paddle) operating at 100 rpm and using 100 mg active and 700 mL hydrochloric acid (0.08 molar) with and without the addition of sodium lauryl sulfate (SDS).

Results
Soluplus® based amorphous dispersions with active ingredients could be grouped into two clusters: The first group of extrudates (itraconazole or fenofibrate), was soluble in 0.08N HCl and a cumulative drug release of more than 80% was obtained during 120 minutes dissolution testing. The addition of surfactants to the medium had a negative effect (recrystallization).

The second group of extrudates (celecoxib or danazol) did not dissolve in 0.08N HCl and the cumulative drug release was less than 50%. In this case, the addition of 0.1% SDS to the medium allowed discrimination between crystalline substance (max 25% release after 120 min) and extrudate (min. 80% after 120 min).

Conclusion
The proposed rapid solubility test helps to select a suitable dissolution test method for Soluplus® based solid dispersions in early formulation screening. The results correlate well with published bioavailability studies for itraconazol, fenofibrate and danazol.