

A powerful carrier adapted for HME process to formulate stable ASD's while avoiding downstream process



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INTRODUCTION

Hot melt extrusion (HME) is generally applied for the formulation of amorphous solid dispersions (ASD) aiming to enhance the solubility of poorly water-soluble drugs [1,2]. The aim of this work was to evaluate the use of an innovative dry carrier - Sepitrap™ 80 (S80) in a HME process, to assess its capability to formulate ASD's and for solubility enhancement of BCS class II drug like indomethacin (IND) and further cutting down the downstream process after HME, which may lead to recrystallization of the API [3-7].

Different parameters can influence the properties of ASD. A previous work was done to find the optimal concentration of surfactant and porosity of the carrier to obtain promising ASD.

In this work, different concentrations of IND were tested to evaluate their influence on active amorphisation and solubility enhancement of the API.

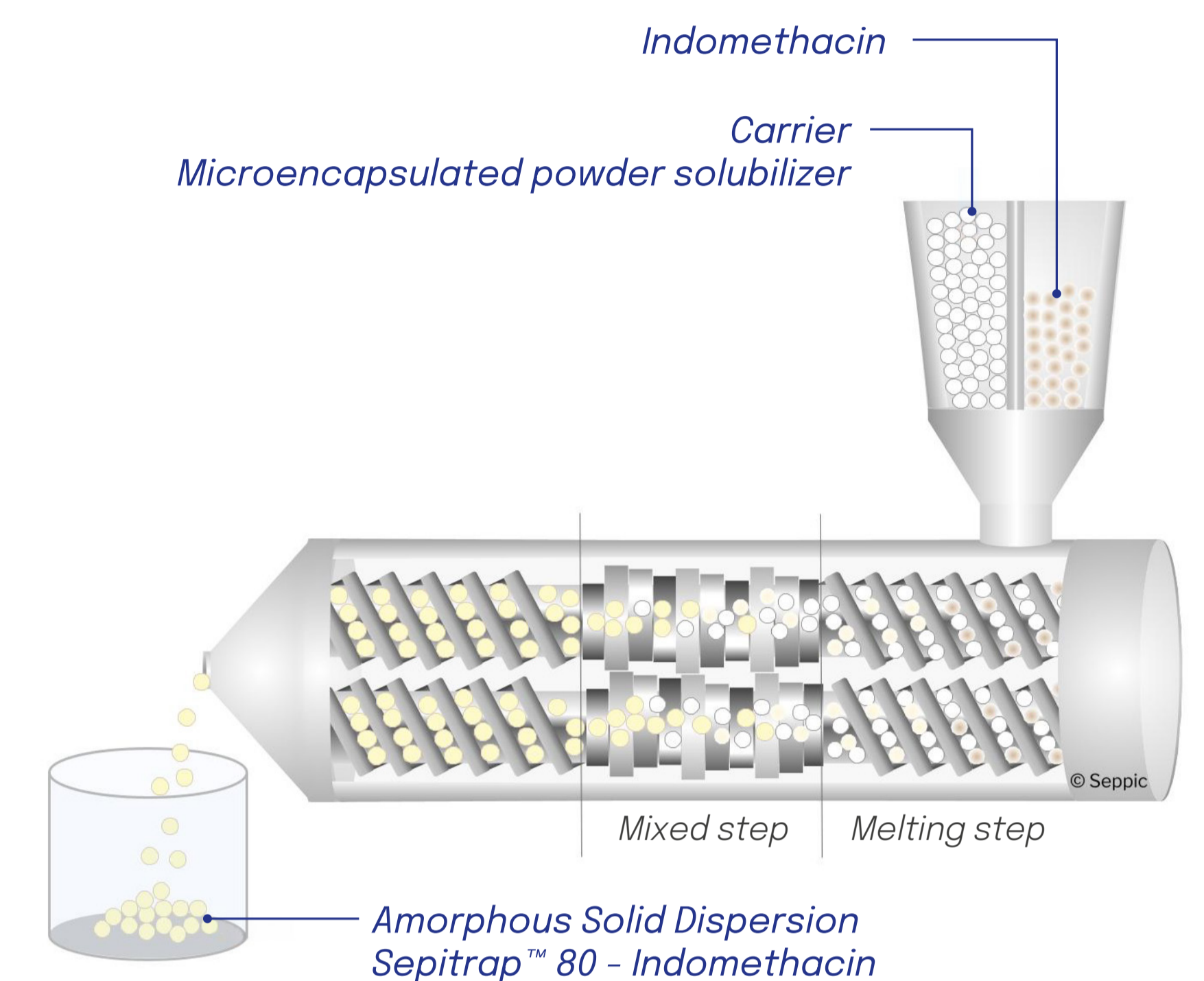
MATERIALS & METHODS

S80 [50 wt% of polysorbate 80 (PS80) onto a porous magnesium aluminosilicate (pMA)], as a solid carrier for ASD, was loaded at different IND concentration:

- 14.9%wt (S80 / IND = ASD1),
- 31.2%wt (S80 / IND = ASD2),
- 43.8%wt (S80 / IND = ASD3).

A Hot Melt Extruder, Pharma 16 from Thermofisher, was used to produce ASD.

- ASD morphology was analyzed by Scanning Electron Microscopy (SEM).
- The crystallinity of the samples was determined by X-ray Diffraction (XRD), Fourier Transform Infra-Red Spectrometry (FTIR) and Differential Scanning Calorimetry (DSC).
- The solubility and dissolution profiles of samples were evaluated in a phosphate buffer (pH 7.2) at 37 °C.



RESULTS

1 Carrier of interest for HME

According to SEM image, the particles possess a uniform and mostly spherical shape.

	SIZE			POROSITY	
	D _{v10} (µm)	D _{v50} (µm)	D _{v90} (µm)	Surface area (m ² /g)	Volume mesopores (cm ³ /g)
S80 ▶	3.7 ± 0.1	60.3 ± 0.2	140.0 ± 1.4	36.2	0.24

Table 1. Carrier's characteristics of S80 (granulometry and surface properties)

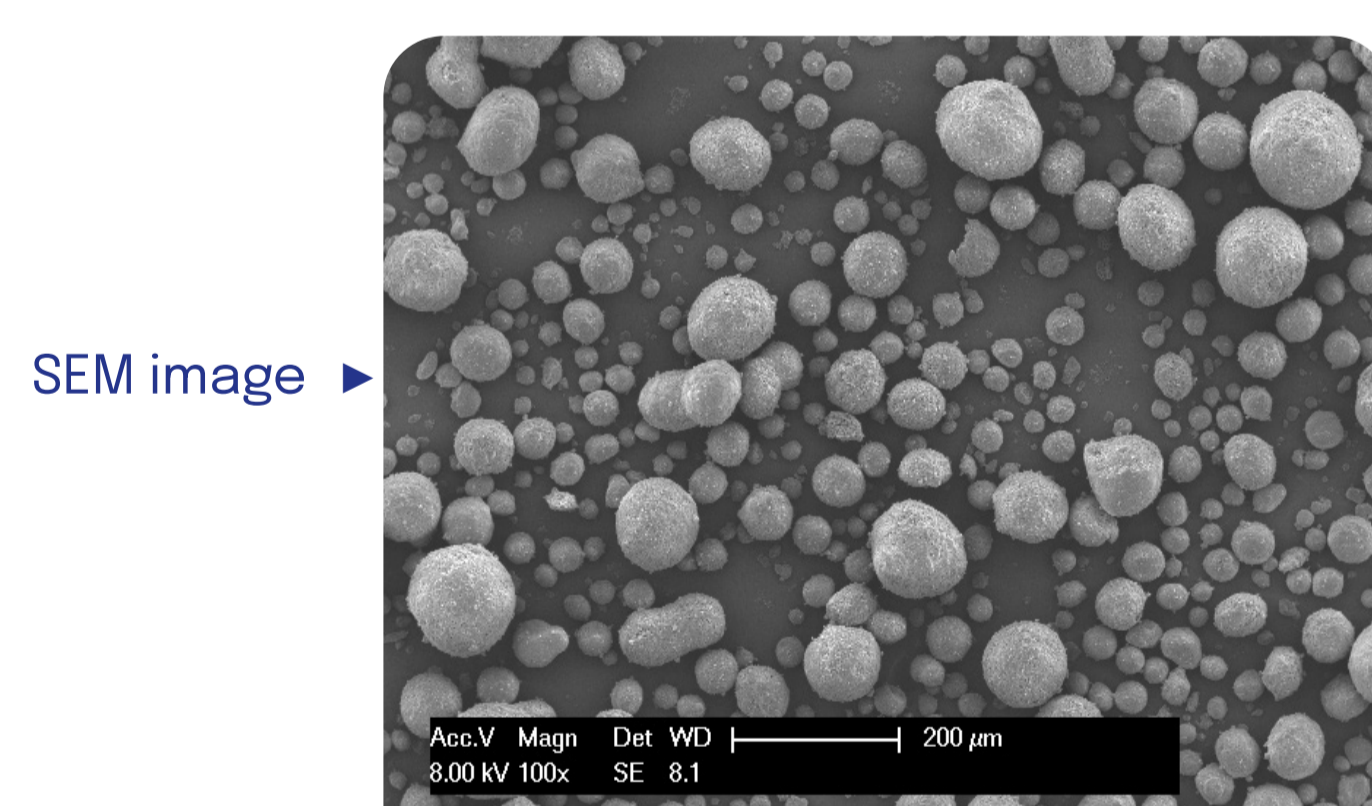


Figure 1. SEM image of S80

2 Extrudates of microencapsulated powder solubilizer and indomethacin

The presence of surfactant, in the pore and at the surface of the particles, probably acts as a lubricant against mechanical friction, confirming the great adaptability of this carrier for HME processes.

Table 2 shows a decrease in specific surface area and pore volumes with increasing IND content in all the ASD's obtained.

Samples	IND CONTENT (%)	SURFACE AREA (m ² /g)	VOLUME MESOPORES (cm ³ /g)
ASD1 ▶	14.9	8.3	0.20
ASD2 ▶	31.2	2.9	0.05
ASD3 ▶	43.8	4.9	0.03

Table 2. BET results obtained by nitrogen sorption at 77K

These results confirm the great capacity of both carriers to absorb a quite huge quantity of API in the pores.

3 Solubility and dissolution kinetics enhancement obtained by amorphisation of the API

The extrudates obtained with S80 and a high load (43.8 wt%) of IND, present essentially the amorphous form of IND [8-10].

Improvement and acceleration of release profile (~70% of amorphous indomethacin released in 5 minutes), compared to commercial IND and physical blends, were directly observed within the first hour of dissolution.

The ASD's obtained (Table 2) are stable at least 6 months at room temperature and for 1 month at 40°C/75% HR.

CONCLUSION

- The choice of an adequate carrier to form a stable amorphous solid dispersion is crucial in HME.
- The research conducted with the poorly water-soluble API, Indomethacin, confirms that the innovative powdered solubilizer, Sepitrap™ 80, can be used as an effective carrier in the HME processes.
- Good extrudability was achieved.
- The amorphous solid dispersion of indomethacin produced showed improved solubility both by the amount of indomethacin dissolved and the rapid dissolution rate.
- Sepitrap™ represents a new range of carriers for amorphous solid dispersions for HME processing, reducing necessary downstream steps such as grinding.

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