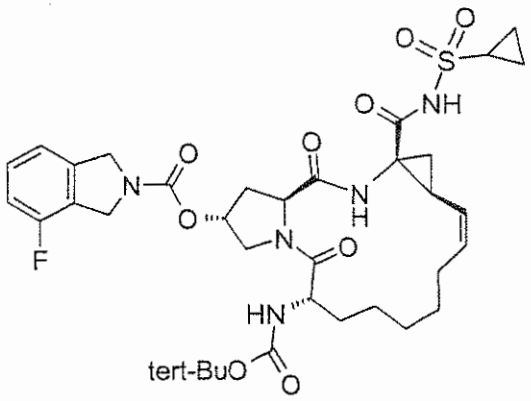
dissociates forming the amorphous free acid. Owing to hydrophobicity, these amorphous particles aggregate to minimize surface contact with the aqueous media. This loose association rapidly leads to particle agglomeration and the formation of larger particulate structures. This phenomena results in a marked reduction in the surface area of compound I in the aqueous environment and consequently a decrease in dissolution rate.

It is this particle interaction in aqueous media that primarily limits the bioavailability of compound I. There is therefore a need for a formulation approach which can overcome this problem in order to improve oral absorption and therapeutic efficacy of compound I.

Surprisingly, it was found by the present inventors that a granular pharmaceutical composition comprising compound I drug particles and at least one poloxamer overcomes the afore-described disadvantages in the art and provides for an improved dispersability of compound I, which ultimately results in an enhanced pharmacokinetic performance, i.e. greater and less variable oral absorption of compound I. The present ~~invention~~disclosure provides thus a solid pharmaceutical composition of compound I with improved pharmacokinetic performance, i.e., enhanced bioavailability, reduced variability, and reduced food effect. The dissolution rate of compound I in aqueous media from poloxamer containing formulations is surprisingly independent of the drug particle size. This is contrary to the previous understanding in the art that dissolution rate and bioavailability of poorly water soluble drugs from crystalline particulate dispersions in a poloxamer or similar hydrophilic matrices are strongly dependent on API particle size.

Manufacturing technologies such as wet or dry granulation, fluid bed granulation, hot melt extrusion, spray drying, spray congealing, solvent evaporation and high shear granulation are useful approaches to obtain the granular pharmaceutical composition according to the present ~~invention~~disclosure by intimate mixing. In one embodiment of the present ~~invention~~disclosure, the granular pharmaceutical composition is manufactured by means of hot melt extrusion. Surprisingly, it has been found that hot melt extrusion resolves a number of manufacturing and powder flow difficulties which are typical for a granulation process of aggregating flocculent and poorly compressible powders like compound I drug substance. Hot melt extrusion achieves optimal results with respect to manufacturability, stability, bioavailability, and patient convenience of the granular pharmaceutical composition according to the present ~~invention~~disclosure.

In a first aspect, there is provided a granular pharmaceutical composition comprising a compound of formula (I)



I

or a pharmaceutically acceptable salt thereof and at least one poloxamer, wherein the at least one poloxamer is poloxamer 188.

In a second aspect, there is provided an oral dosage form comprising the composition as defined above.

In a third aspect, there is provided the composition as defined above for use in the treatment of HCV infections.

In a fourth aspect, there is provided the use of a composition as defined above in the manufacture of a medicament for the treatment of HCV infections.

In a fifth aspect, there is provided the oral dosage form as defined above for use in the treatment of HCV infections.

As used herein, the following terms have the meanings set out below.