Such a formulation would be particularly suitable for pediatric patients and also for adults who have difficulty swallowing solids.

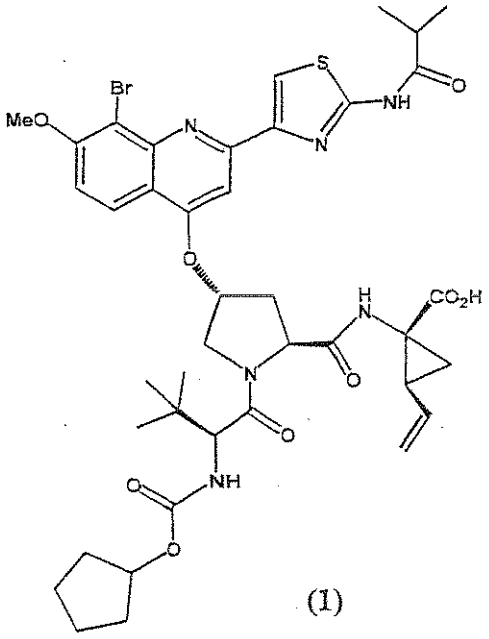
Thus, it is the object of the present invention to provide such a liquid formulation of Compound (1).

BRIEF SUMMARY ~~OF THE INVENTION~~

The present disclosure~~invention~~ provides a pharmaceutically acceptable oral formulation of Compound (1), or a pharmaceutically acceptable salt thereof, in the form of a solution for oral administration.

In one aspect, there is provided a liquid pharmaceutical composition which comprises:

(a) less than or equal to 4.6% by weight of Compound (1), or a pharmaceutically acceptable salt thereof:



(1)

;

(b) at least one 10% to 30% by weight of surfactant; and

(c) at least one 60% to 90% by weight of a pharmaceutically acceptable solvent;

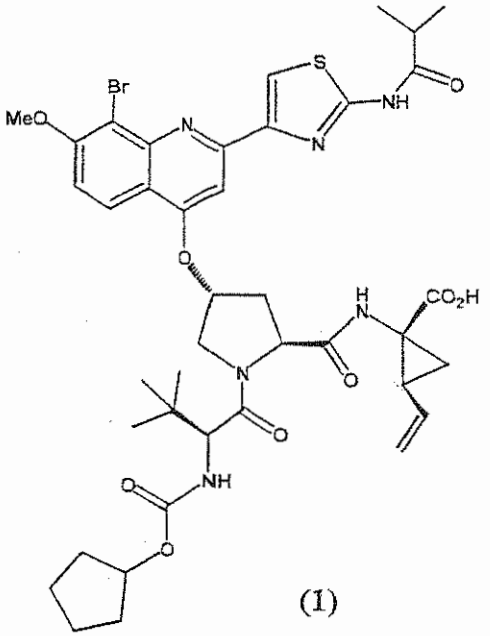
wherein the weight ratio of surfactant to Compound (1) or pharmaceutically acceptable salt thereof is greater than or equal to 2.7;

and wherein the composition comprises less than or equal to 5% by weight of lipid,

and wherein the composition forms a clear dispersion having a mean particle size of less than 1 μm upon dilution in simulated gastric fluid.

In another aspect, there is provided a liquid pharmaceutical composition which comprises:

(a) less than or equal to 6.3% by weight of Compound (1), or a pharmaceutically acceptable salt thereof;



(I)

;

(b) at least one 10% to 30% by weight of surfactant; and

(c) at least one 60% to 90% by weight of a pharmaceutically acceptable solvent;

wherein the weight ratio of surfactant to Compound (1) or pharmaceutically acceptable salt thereof is greater than or equal to 4.3;

and wherein the composition comprises less than or equal to 5% by weight of lipid, and wherein the composition forms a clear dispersion having a mean particle size of less than 1 μm upon dilution in similuated gastric fluid.

Based upon the physicochemical characteristics of the drug substance, the scope for the development was to formulate a solution with the ability to form an emulsion, microemulsion or micellar solution upon contact with aqueous media. The formulation comprises at least one solvent to enhance solubility of the drug and at least one surfactant with a hydrophilic/lipophilic balance (HLB) > 10 added to maintain the drug substance in a dissolved state upon dilution in simulated GI fluids. The formulation of the disclosure~~invention~~ can further contain water as a co-solvent and taste masking components, such as sweeteners and flavors. An antioxidant may be added to prevent drug substance oxidation. Two examples of composition of this formulation, in two different strengths, are shown in Table I.

Table I. Compound (1) NA Oral Solution Formulation (F330 and 335)

Ingredient	F 330 % w/w	F 335 % w/w	Function
Compound (1) sodium salt	2.2	4.4	Drug Substance
Polyethylene Glycol 400	36.5	34.3	Solvent
Propylene Glycol	5.4	5.4	Solvent

Vitamin E Polyethylene Glycol Succinate	29.6	29.6	Surfactant
Water, Purified	22.4	22.4	Solvent
Sucralose	1.9	1.9	Sweetening agent
Butter toffee	2.0	2.0	Flavor
Total Weight	100.0	100.0	

Sometimes due to physicochemical characteristics, the drug substance in combination with the surfactant may solidify or may not be fluid enough for oral administration. One of the objects of the embodiments disclosed herein~~present invention~~ was to obtain a solution well adapted for oral administration in an unencapsulate form. It is preferred that such formulation would be flowable at room temperature, thereby rendering it suitable for oral administration in a liquid form and to facilitate dosing. It has been found that the addition of at least one cosolvent in combination with the surfactant helps to maintain the present formulation as a liquid flowable solution at room temperature, thereby achieving the advantages mentioned above.

The drug substance compound is present in the composition at a concentration level such as to provide flexibility of dosing by allowing one to change the dose administered by changing the volume. This flexibility with respect to dosing provides a wide range of dosing from a low dose for administration to small children to a high dose for adults who are unable to swallow a solid dosage form.

DETAILED DESCRIPTION OF THE INVENTION

The liquid composition of the present invention comprises:

(a) Compound (1), or a pharmaceutically acceptable salt thereof: