

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Inventor(s): Sundaram, Srikanth, et al.	Docket No.: 009423.010US1
App. No.: 15/958,854	Conf. No.: 1051
Filed: 2018-04-20	Art Unit: 1615
Title: Storage Stable Sincalide Formulations	Examiner: AL-AWADI, DANA H. J.

VIA EFS-WEB

AMENDMENT & RESPONSE TO NON-FINAL OFFICE ACTION

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Attention: Commissioner for Patents:

The following amendments and remarks are submitted in response to the November 19, 2018 Office Action. This paper is being submitted on or before February 19, 2019, thereby making this a timely response.

Amendments to the Specification begins on page 2 of this paper.

Amendments to the Claims are reflected in the listing of claims that begins on 5 of this paper.

Remarks begin on page 12 of this paper.

Amendments to the Specification

Please replace paragraph [0043] with the following amended paragraph:

[0043] A surfactant/solubilizer is used to generally reduce the interfacial tension or aid in solubilization thus preventing or reducing denaturation and/or degradation at air/liquid or liquid/solid interfaces of a peptide in solution. As described herein, the compositions comprise sincalide, lack a buffer in solid form or optionally lack a buffer in liquid form, and optionally also lack a surfactant/solubilizer. Accordingly, as described herein, the compositions may comprise sincalide and a surfactant/solubilizer, and lack a buffer. In some embodiments, a composition described herein comprises sincalide and optionally a surfactant/solubilizer, is storage stable, and lacks a buffer, *e.g.*, dibasic potassium phosphate. A surfactant/solubilizer as described herein may be selected from the group consisting of free fatty acids; esters of fatty acids with polyoxyalkylene compounds like polyoxypropylene glycol and polyoxyethylene glycol; ethers of fatty alcohols with polyoxyalkylene glycols; esters of fatty acids with polyoxyalkylated sorbitan; soaps; glycerol-polyalkylene stearate; glycerol-polyoxyethylene ricinoleate; homo- and copolymers of polyalkylene glycols; polyethoxylated soya-oil and castor oil as well as hydrogenated derivatives; ethers and esters of sucrose or other carbohydrates with fatty acids, fatty alcohols, these being optionally polyoxyalkylated; mono-, di- and triglycerides of saturated or unsaturated fatty acids; glycerides or soya-oil and sucrose; sodium caprolate; ammonium sulfate; sodium dodecyl sulfate (SDS); Triton-100 and anionic surfactants containing alkyl, aryl or heterocyclic structures; and any combination thereof. In some embodiments, a composition as described herein comprises sincalide, is storage stable, lacks a buffer (*e.g.*, dibasic potassium phosphate) and comprises or lacks a surfactant/solubilizer selected from the group consisting of a pluonic (*e.g.*, Lutrol F68, Lutrol F127), Poloxamers, SDS, Triton-100, polysorbates such as TWEEN[®] 20 and TWEEN[®] 80, propylene glycol, PEG and similar compounds, Brij58 (polyoxyethylene 20 cetyl ether), cremophor EL, cetyl trimethylammonium bromide (CTAB), dimethylacetamide (DMA), NP-40 (Nonidet P-40), and N-methyl-2-pyrrolidone (Pharmasolve), ~~glycine and other amino acids/amino acid salts~~ and anionic surfactants

containing alkyl, aryl or heterocyclic structures, and cyclodextrins. In some embodiments, a composition as described herein comprises sincalide, is storage stable, lacks a buffer (*e.g.*, dibasic potassium phosphate) and comprises or lacks a surfactant/solubilizer, wherein the surfactant/solubilizer is a polysorbate. In some embodiments, a solid composition as described herein comprises sincalide, is storage stable, lacks a buffer (*e.g.*, dibasic potassium phosphate), and lacks or comprises a surfactant/solubilizer, wherein the surfactant/solubilizer is a polysorbate 20.

A clean copy of paragraph [0043] is provided below:

[0043] A surfactant/solubilizer is used to generally reduce the interfacial tension or aid in solubilization thus preventing or reducing denaturation and/or degradation at air/liquid or liquid/solid interfaces of a peptide in solution. As described herein, the compositions comprise sincalide, lack a buffer in solid form or optionally lack a buffer in liquid form, and optionally also lack a surfactant/solubilizer. Accordingly, as described herein, the compositions may comprise sincalide and a surfactant/solubilizer, and lack a buffer. In some embodiments, a composition described herein comprises sincalide and optionally a surfactant/solubilizer, is storage stable, and lacks a buffer, *e.g.*, dibasic potassium phosphate. A surfactant/solubilizer as described herein may be selected from the group consisting of free fatty acids; esters of fatty acids with polyoxyalkylene compounds like polyoxypropylene glycol and polyoxyethylene glycol; ethers of fatty alcohols with polyoxyalkylene glycols; esters of fatty acids with polyoxyalkylated sorbitan; soaps; glycerol-polyalkylene stearate; glycerol-polyoxyethylene ricinoleate; homo- and copolymers of polyalkylene glycols; polyethoxylated soya-oil and castor oil as well as hydrogenated derivatives; ethers and esters of sucrose or other carbohydrates with fatty acids, fatty alcohols, these being optionally polyoxyalkylated; mono-, di- and triglycerides of saturated or unsaturated fatty acids; glycerides or soya-oil and sucrose; sodium caprolate; ammonium sulfate; sodium dodecyl sulfate (SDS); Triton-100 and anionic surfactants containing alkyl, aryl or heterocyclic structures; and any combination thereof. In some embodiments, a composition as described herein comprises sincalide, is

storage stable, lacks a buffer (*e.g.*, dibasic potassium phosphate) and comprises or lacks a surfactant/solubilizer selected from the group consisting of a pluonic (*e.g.*, Lutrol F68, Lutrol F127), Poloxamers, SDS, Triton-100, polysorbates such as TWEEN[®] 20 and TWEEN[®] 80, propylene glycol, PEG and similar compounds, Brij58 (polyoxyethylene 20 cetyl ether), cremophor EL, cetyl trimethylammonium bromide (CTAB), dimethylacetamide (DMA), NP-40 (Nonidet P-40), and N-methyl-2-pyrrolidone (Pharmasolve), anionic surfactants containing alkyl, aryl or heterocyclic structures, and cyclodextrins. In some embodiments, a composition as described herein comprises sincalide, is storage stable, lacks a buffer (*e.g.*, dibasic potassium phosphate) and comprises or lacks a surfactant/solubilizer, wherein the surfactant/solubilizer is a polysorbate. In some embodiments, a solid composition as described herein comprises sincalide, is storage stable, lacks a buffer (*e.g.*, dibasic potassium phosphate), and lacks or comprises a surfactant/solubilizer, wherein the surfactant/solubilizer is a polysorbate 20.

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application.

1. (Currently Amended) A solid composition comprising sincalide, wherein the composition comprises a pH of about 6 to about 8 when reconstituted in a pharmaceutically acceptable diluent,
wherein the composition does not contain a ~~dibasic potassium~~ phosphate buffer, and
wherein the composition is stable in storage.
2. (Currently Amended) The solid composition of claim 1, wherein the composition does not contain any phosphate buffer and also does not contain a buffer selected from the group consisting of phosphoric acid, citric acid, citrate, sulfosalicylate, acetic acid, acetate, methyl boronic acid, boronate, disodium succinate hexahydrate, lactic acid, lactate, maleic acid, maleate, potassium chloride, benzoic acid, sodium benzoate, carbonic acid, carbonate, bicarbonate, boric acid, sodium borate, sodium chloride, succinic acid, succinate, tartaric acid, tartrate, tris-(hydroxymethyl)aminomethane, N-2-hydroxyethylpiperazine, N¹-2-ethanesulfonic acid (HEPES), CHAPS, and any combination thereof.
3. (Currently Amended) The solid composition of claim ~~1~~2, wherein the composition also does not contain polysorbate 20 and/or polysorbate 80.
4. (Currently Amended) The solid composition of claim ~~1~~2, wherein the composition ~~does not contain any surfactant/solubilizer~~further comprises
 - (a) at least one stabilizer,
 - (b) at least one bulking agent/tonicity adjuster,
 - (c) at least one chelator, or
 - (d) any combination of (a)-(c).
5. (Currently Amended) The solid composition of claim 1, wherein the composition does

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