SUMMARY

~~This invention thus relates to~~In one aspect, there is provided a self-preserved oil dispersion including a dispersed oil phase, an aqueous phase and at least one surfactant, wherein said oil dispersion comprises boric acid or salt thereof, in an amount ranging from 0.005% to 0.075% in weight of the total weight of the oil dispersion, wherein said amount of boric acid ~~being~~ is a preservative effective amount so that the oil dispersion ~~has a preservative activity~~is self-preserved, and wherein the dispersion is free of sorbic acid.

According to one embodiment, the oil dispersion of the ~~invention~~disclosure has a sufficient preservative activity to comply with USP and/or Ph. Eur. preservative efficacy requirements, said pharmacopeias being herein incorporated by reference. In an embodiment, compliance with USP and/or Ph. Eur. means that the dispersion shall have sufficient preservative activity to inhibit the growth and decrease the population of Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Candida albicans, Aspergillus niger or Aspergillus.

According to one embodiment, the oil dispersion of the ~~invention~~disclosure is an oil-in-water emulsion.

According to one embodiment, the amount of boric acid in the oil dispersion of the ~~invention~~disclosure ranges from 0.008 to 0.05%, preferably from 0.01 to 0.05%, more preferably from 0.01 to 0.02% w/w.

According to one embodiment, boric acid, in the meaning of this ~~invention~~disclosure, include any form of boric acid or salt thereof, especially sodium borate, sodium metaborate, calcium borate, borax, tricopper diborate, trioleyl borate, lithium borate, tris(trimethylsilyl) borate, ethyl borate, potassium tetrafluoroborate, disodium dihydrogen borate, manganese borate, oleyl borate, tripentyl borate, tributyl borate, trimethyl borate, tridodecyl borate, triazanium borate or a mixture thereof.

According to one embodiment, the oil phase comprises an oil selected from mineral oil such as petrolatum or liquid paraffin; medium chain triglycerides (MCT); triglycerides oils, vegetable oils such as castor oil, corn oil, olive oil, soybean oil, sesame oil, cotton seed oil, sweet almond oil or any suitable vegetable oil; fatty acid, isopropyl myristate,

oily fatty alcohols, esters of sorbitol and fatty acids, oily sucrose esters or a mixture thereof.

According to one embodiment, the oil dispersion of the ~~invention~~disclosure comprises a cationic surfactant.

According to one embodiment, the cationic surfactant is selected from cetalkonium chloride (CKC), benzethonium chloride, cetrimide, cationic lipids, oleylamine, stearylamine, DOTAP (N-[1-(2,3-dioleoyloxy) propyl]-N,N,N trimethylammonium) chloride, DOPE (dioleoyl phosphatidylethanolamine), poly(ethylenimine) (PEI), poly-L-lysine (PLL) or a mixture thereof.

According to one embodiment, the oil dispersion of the ~~invention~~disclosure comprises a non-ionic surfactant.

According to one embodiment, the non-ionic surfactant is selected from tyloxapol, poloxamer such as poloxamer 282 or poloxamer 188 or Pluronic F-68LF or Lutrol F68, polysorbate such as polysorbate 20 or polysorbate 80, solutol, polyoxyethylene fatty acid esters such as Emulphor, polyoxyethylene alkyl ethers, polyoxyethylene castor oil derivatives such as Cremophor EL or Cremophor RH, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene stearates, sodium lauryl sulfate, sorbitan esters, vitamin E derivatives such as vitamin E-tocopheryl polyethylene glycol succinate or a mixture thereof.

According to one embodiment, the oil dispersion of the ~~invention~~disclosure further comprises a therapeutically active agent.

According to one embodiment, the therapeutically active agent is selected from antiallergenics such as sodium cromoglycate, antazoline, methapyriline, chlorpheniramine, cetirizine, olapatadine, ketotifen, azelastine, epinastine, emedastine, levocabastive, terfenadine, astemizole and loratadine, pyrilamine or prophenpyridamine; synthetic glucocorticoids and mineralocorticoids and more generally hormones forms derivating from the cholesterol metabolism (progesterone, estrogens, androgenic hormones such as testosterone DHEA and their derivatives); anti-inflammatories such

cholinesterase inhibitors such as physostigmine, echothiophate; antivirals, such as idoxuridine, trifluorotymidine, acyclovir, valaciclovir, ganciclovir, cidofovir and interferon; antibiotics such as aminoglycosides, carbacephem, carbapenems, cephalosporins, glycopeptides, penicillins, polypeptides, quinolones, sulfonamides, tetracyclines, chlortetracycline, bacitracin, neomycin, polymyxin, gramicidin, cephalexin, oxytetracycline, chloramphenicol, kanamycin, rifampicin, tobramycin, gentamycin, ciprofloxacin, aminosides, erythromycin, ceftazidime, vancomycine, imipeneme; antifungals such as polyene antibiotics, azole derivatives, imidazole, triazole, allylamines, amphotericin B and miconazole; antibacterials such as sulfonamides, sulfadiazine, sulfacetamide, sulfamethizole and sulfisoxazole, nitrofurazone and sodium propionate; and/or their derivatives; and/or their prodrugs; and/or their precursors; and/or acceptable salts thereof; alone or in combination.

~~According to one embodiment~~In another aspect, there is provided an ~~the~~ oil dispersion ~~of the invention is~~as defined above for use in the treatment of an eye disease or eye condition.

~~The present invention also relates to~~In another aspect, there is provided a process of manufacturing of ~~the~~ an oil dispersion ~~of the invention~~as defined above, comprising the steps of emulsifying and mixing the aqueous phase and the oil phase with surfactant.

~~The present invention also relates to~~In another aspect, there is provided a multi-dose container including the oil dispersion ~~of the invention~~as defined above. The present ~~invention~~ disclosure also relates to a mono-dose container including the oil dispersion of the ~~invention~~disclosure.

~~The present invention also relates to~~In another aspect, there is provided use of boric acid in an oil dispersion, in an amount ranging from 0.005% to 0.075% in weight of the total weight of the oil dispersion~~, for use~~ as a preservation promoter.

DEFINITIONS

In the present invention, the following terms have the following meanings:

- "**a composition with a preservative activity**" or "**a preserved composition**" refers to a composition that is protected from microbial and/or fungal contamination