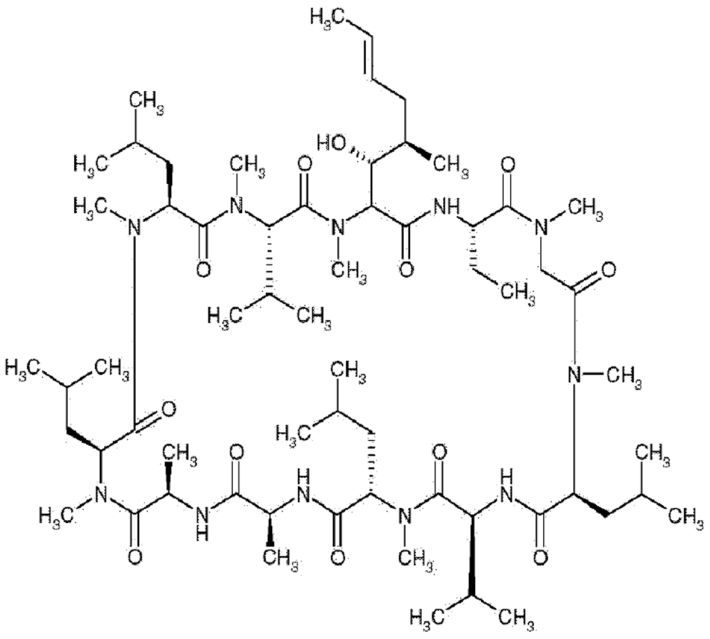
identified. The use of cyclosporine A and cyclosporine A derivatives to treat the ophthalmic conditions set forth above has been the subject of various patents, for example Ding et al U.S. Pat. No. 5,474,979; Garst U.S. Pat. No. 6,254,860; and Garst U.S. Pat. No. 6,350,442, the disclosure of each of which is incorporated in its entirely herein by reference. With respect to its solid state chemistry, cyclosporine A (CsA) is known to exist in an amorphous form, liquid crystal form, tetragonal crystalline form (Form 1), and an orthorhombic form (Form 3).

SUMMARY

The present disclosure provides a new crystalline form of CsA, with unique and novel properties suitable for pharmaceutical development.

In one aspect, provided herein is cyclosporine A having the structure in crystalline form 2 as represented by the formula



.X H_2O;

wherein X is the number of molecules of water and varies from 0 to 3, wherein said crystalline form has an X-ray powder diffraction pattern with major peaks at about (2θ) 7.5, 8.8, 10.2, 11.3, 12.7, 13.8, 14.5, 15.6 and 17.5.

In another aspect, provided herein is cyclosporine A in the crystalline form defined herein for use in therapy.

In another aspect, provided herein is a use of cyclosporine A in the crystalline form defined herein in the manufacture of a medicament for treating an aqueous deficient dry eye state, uveitis, phacoanaphylactic endophthalmitis, or keratoconjunctivitis sicca (KCS) in an eye, wherein the medicament is to be administered to a subject in need thereof.

In another example of the disclosure, there are provided pharmaceutical compositions including a therapeutically effective amount of cyclosporine A in a new crystalline form in an ophthalmically acceptable carrier.

In another example there are provided methods for treating an aqueous deficient dry eye state, uveitis or phacoanaphylactic endophthalmitis in an eye. Such methods can be performed, for example, by administering to a subject in need thereof cyclosporine A in crystalline form 2 in an ophthalmically acceptable carrier.

BRIEF DESCRIPTION OF THE FIGURES

FIG. **1** depicts characteristic X-ray powder diffraction (XRPD) patterns of CsA in a new crystalline form (designated as Form 2 herein), tetragonal form (designated as Form 1 herein), and orthorhombic form (designated as Form 3 herein).

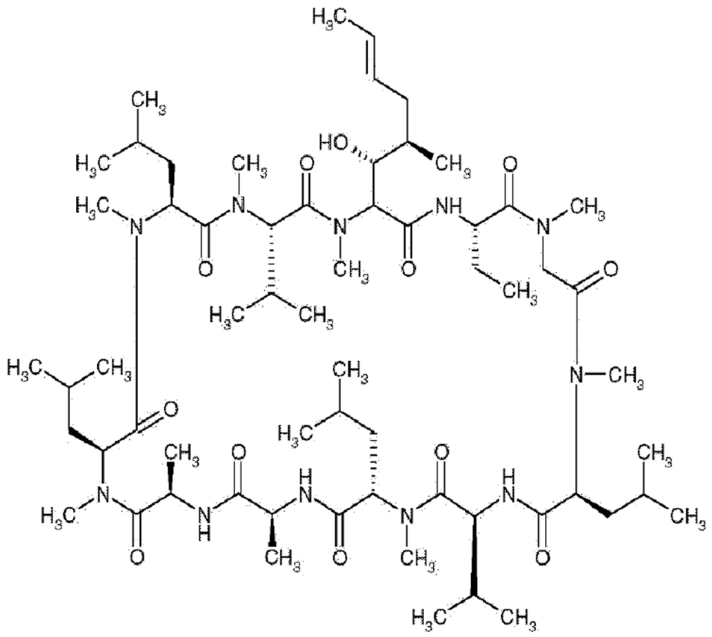
FIG. **2** depicts the XRPD diffractogram of CsA crystalline Form 2.

FIG. **3** depicts the water sorption/desorption profile of CsA Form 2.

FIG. **4** depicts MDSC analysis of CsA Form 2 recovered from 0.04% formulation with 1% PS80.

WHAT IS CLAIMED IS:

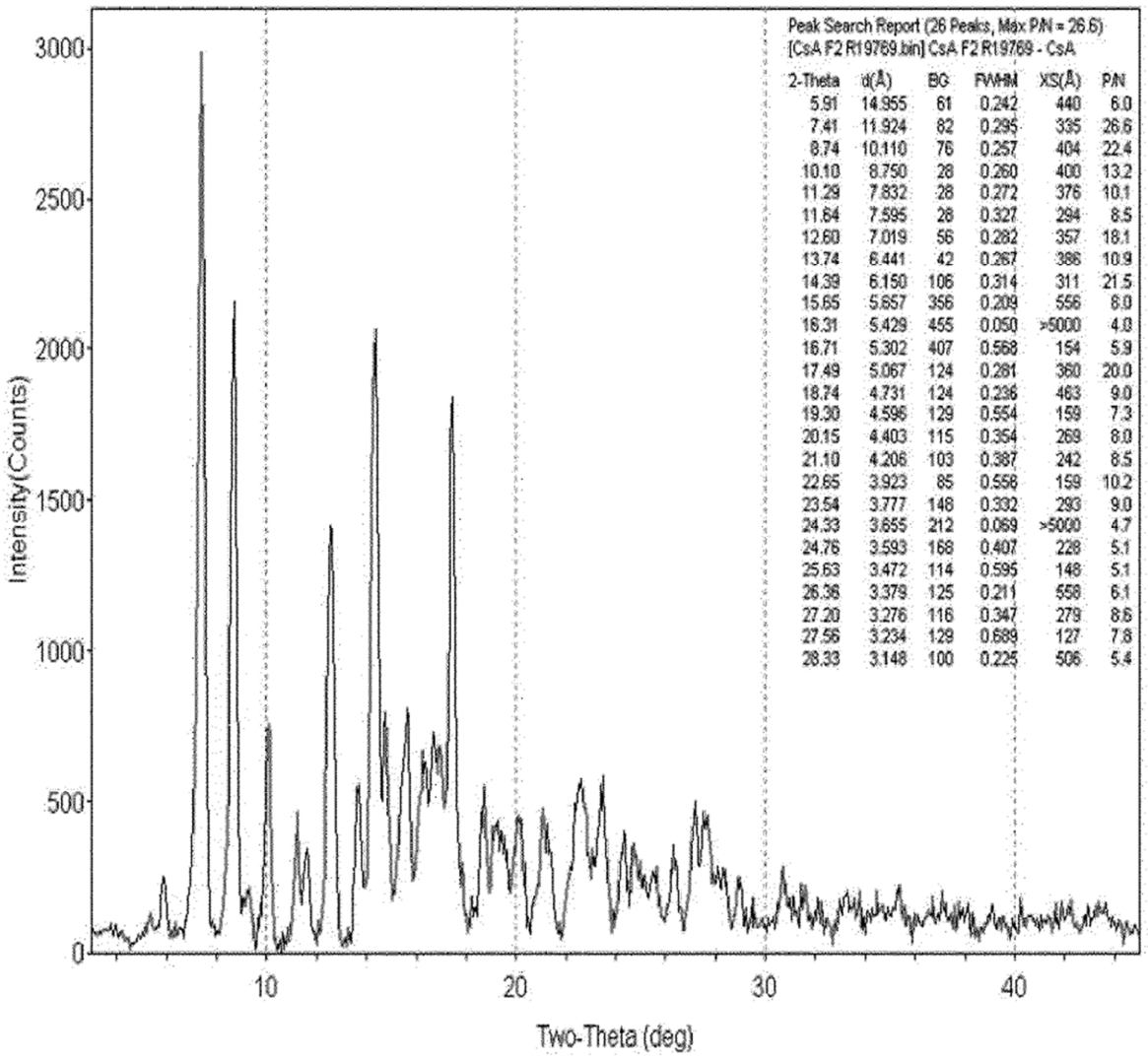
1. Cyclosporine A having the structure in crystalline form 2 as represented by the formula



.X H_2O;

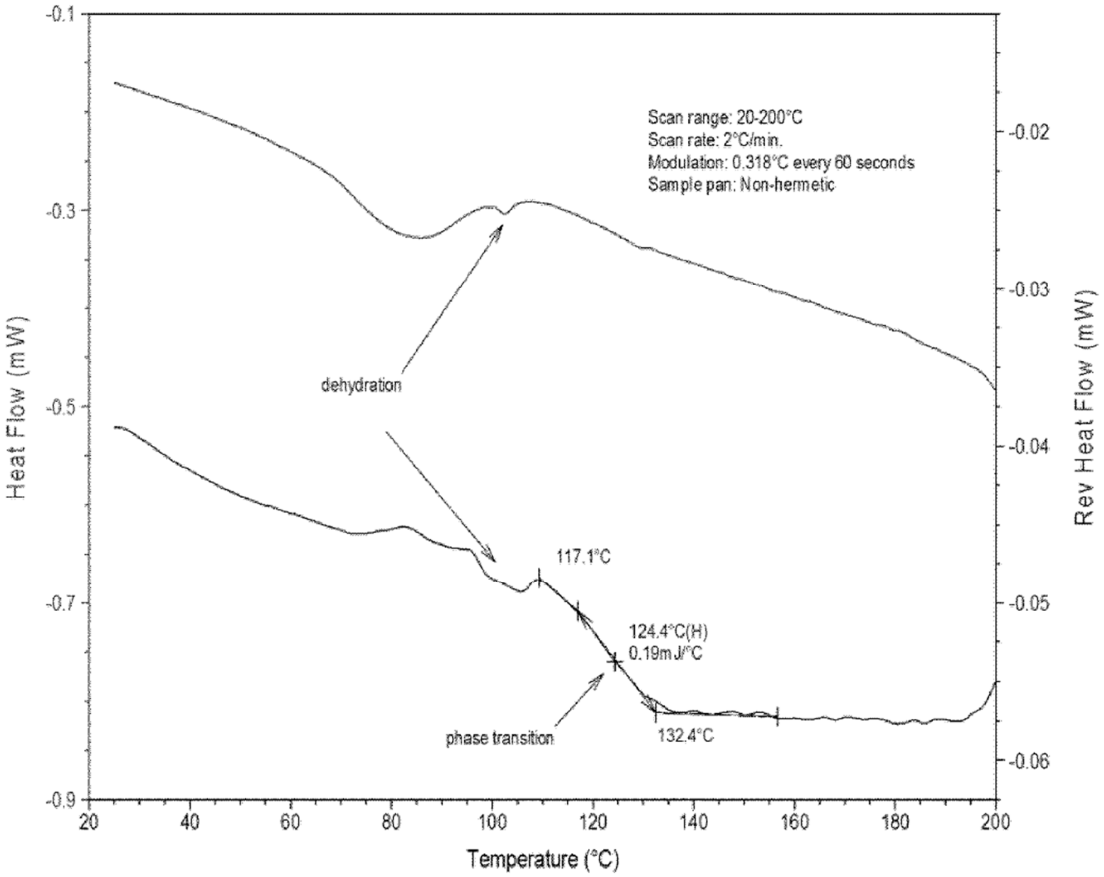
wherein X is the number of molecules of water and varies from 0 to 3, wherein said crystalline form has an X-ray powder diffraction pattern with major peaks at about (2θ) 7.5, 8.8, 10.2, 11.3, 12.7, 13.8, 14.5, 15.6 and 17.5.

2. The crystalline form of claim 1 having the following X-ray diffraction pattern:



3. The crystalline form of claim 1 having a dehydration endotherm at a temperature range of about 65°C to 110°C and a phase transition at 122-125°C in its modulated differential scanning calorimetry profile.

4. The crystalline form of claim 1 having the following MDSC profile:



5. The crystalline form of claim 1 being free of other crystalline forms.

6. The crystalline form of claim 1 which is a nonstoichiometric hydrate of cyclosporine A.

7. The crystalline form of claim 1, wherein X is 2.

8. Cyclosporine A in the crystalline form defined in any one of claims 1-6 for use in therapy.

9. Use of cyclosporine A in the crystalline form defined in any one of claims 1-6 in the manufacture of a medicament for treating an aqueous deficient dry eye state, uveitis, phacoanaphylactic endophthalmitis, or keratoconjunctivitis sicca (KCS) in an eye, wherein the medicament is to be administered to a subject in need thereof.