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(54) Title: COMPOSITION COMPRISING (-)- Δ^9 -TRANS-TETRAHYDROCANNABINOL

(57) Abstract: A composition comprising a tetrahydrocannabinol compound, a solvent and an acid, wherein the tetrahydrocannabinol compound may be Δ^8 tetrahydrocannabinol, (-)- Δ^9 -trans-tetrahydrocannabinol or a side chain alkyl derivative of either compound, the solvent may be an oil or C₁-C₄ alcohol (e.g. sesame oil or ethanol), and the acid may be an organic acid or a mineral acid.



WO 2008/055992 A1

**COMPOSITION COMPRISING (-)- Δ^9 -TRANS-
TETRAHYDROCANNABINOL**

The present invention relates to a composition comprising (-)- Δ^9 -trans-tetrahydrocannabinol or related compounds.

The compound (-)- Δ^9 -trans-tetrahydrocannabinol is the active ingredient in marijuana. It is used therapeutically as an inhalant or an oral drug for stimulation of appetite among AIDS and cancer chemotherapy patients. Tetrahydrocannabinols (THCs) can be isolated from marijuana (a mixture of leaves and flowering heads of the plant *Cannabis Sativa*). Alternatively, THCs can be obtained by synthetic routes, e.g. as described in WO 02/096899.

Pure (-)- Δ^9 -trans-tetrahydrocannabinol that has been produced synthetically and purified is unstable and is liable to degrade to products such as cannabinol (which is inactive) and Δ^8 -tetrahydrocannabinol (which is less potent). Although Δ^8 -tetrahydrocannabinol has similar activity to as (-)- Δ^9 -trans-tetrahydrocannabinol it is only approx. 75% as potent and also tends to degrade to other compounds including cannabinol. Dissolving the (-)- Δ^9 -trans-tetrahydrocannabinol in a solvent or carrier improves the stability, but it is still usual to store the solutions under refrigerated conditions, e.g. at 5°C, to prevent degradation. The present inventors have sought to improve the stability of solutions of (-)- Δ^9 -trans-tetrahydrocannabinol and Δ^8 -tetrahydrocannabinol.

WO 2006/063109 (Insys Therapeutics Inc) discloses a gel capsule comprising a cannabinoid, such as (-)- Δ^9 -trans-tetrahydrocannabinol, dispersed in oil that they claim is stable for at least a year. This application lists a range of different types of compound that might be used as anti-oxidants in the gel capsules. The patent application exemplifies a range of suitable anti-oxidants including weak acids and weak bases. The stability of the compositions of WO 2006/063109 was assessed using the compendial (USP) HPLC method (see paragraph [0216]), i.e. the compositions were not assessed against pure substances but instead used branded products that would have been less than 100% pure.

Accordingly, the present invention provides a composition comprising:

- (a) a tetrahydrocannabinol compound chosen from Δ^8 tetrahydrocannabinol, (-)- Δ^9 -trans-tetrahydrocannabinol and side chain alkyl derivatives of either compound,
- (b) a solvent chosen from oils and C₁-C₄ alcohols, and
- (c) an acid,

wherein the composition is in liquid form and the acid is added in an amount effective to improve the stability of the composition.

By side chain alkyl derivatives of either compound we mean compounds with the structure of either of the compounds depicted in the Figure, in which R represents an alkyl side chain. Of particular interest, are compounds in which R is 1,1 dimethylheptyl.

The Figure shows the chemical structures for alkyl substituted (-)- Δ^8 -trans-tetrahydrocannabinol derivatives and (-)- Δ^9 -trans-tetrahydrocannabinol derivatives.

The inventors have found that the addition of the acid improves the stability of the composition, i.e. there is less degradation of the tetrahydrocannabinol compound during prolonged storage of the composition.

The composition includes a solvent. The solvent may be chosen from oils and C₁ - C₄ alcohols. Suitable examples of oils include sesame oil, olive oil, canola oil and combinations thereof. Suitable examples of C₁ - C₄ alcohols include methanol, ethanol, propanol, iso-propanol and butanol.

According to one embodiment, the solvent is sesame oil. The sesame oil may be refined or unrefined, but is preferably refined (the US Food and Drug Administration standards require that refined sesame oil is used in pharmaceutical products). The composition may further comprise other solvents, but preferably comprises only sesame oil as the solvent. According to an alternative embodiment, the solvent is ethanol.

In one embodiment the composition comprises an oil and a C₁ - C₄ alcohol.

The acid used in the composition may be an organic acid. When an organic acid is used, the organic acid is suitably chosen from citric acid, ascorbic acid, malic acid, oxalic acid, succinic acid and tartaric acid, and is preferably citric acid.

The acid used in the composition may be a mineral acid. When a mineral acid is used, the mineral acid is suitably chosen from phosphoric acid, hydrochloric acid, nitric acid and sulphuric acid, and is preferably phosphoric acid.

In one embodiment the composition comprises a combination of different acids, optionally a combination of at least one organic acid with at least one mineral acid.

Weak acids have an especially positive stabilizing effect on (-)- Δ^9 -trans-tetrahydrocannabinol and its derivatives, forming a stabilized composition. If the amount or concentration of strong acid is too large, the Δ^9 -isomer degrades to the Δ^8 -isomer.

The acid may be added to the other constituents either as a separate component, or the acid may be formed in a solution of the other constituents. An example of the latter is the use of dissolved CO₂ in ethanol, which also stabilizes the Δ^9 -isomer, probably due to formation of carbonic acid.

The amount of acid is suitably from 0.01-2% as a weight percentage of the composition, preferably from 0.02-1% and most preferably from 0.05-0.5%.

The amount of (-)- Δ^9 -trans-tetrahydrocannabinol in the composition is suitably from 0.1-15% as a weight percentage of the composition, preferably from 1 to 10%.

The composition may further comprise antimicrobial agents such as methyl paraben or propyl paraben. The composition may further comprise preservatives such as alpha-tocopherol or butylated hydroxytoluene (BHT). The composition may further comprise antioxidants. The antimicrobial agents, preservatives and antioxidants may be used alone or in combination.

In a preferred embodiment, the composition of the invention consists essentially of a tetrahydrocannabinol compound, an oil or a C₁-C₄ alcohol, and 0.01-2wt% of an acid chosen from the group consisting of citric acid, ascorbic acid, malic acid, oxalic acid, succinic acid, tartaric acid, phosphoric acid, hydrochloric acid, nitric acid and sulphuric acid. Additional components (e.g. antimicrobial agents, preservatives, antioxidants) may comprise up to 1wt% of the solution. In an especially preferred embodiment, the composition of the invention consists essentially of (-)- Δ^9 -trans-tetrahydrocannabinol, sesame oil and 0.05-0.5wt% citric acid or phosphoric acid, wherein additional components may comprise up to 1wt% of the solution.

Compositions according to the invention may be prepared by adding the acid to a solution of a tetrahydrocannabinol compound in sesame oil or a C₁-C₄ alcohol and mixing. Solutions of (-)- Δ^9 -trans-tetrahydrocannabinol in sesame oil may be prepared by dissolving pure (-)- Δ^9 -trans-tetrahydrocannabinol in sesame oil, or by mixing sesame oil with a solution of (-)- Δ^9 -trans-tetrahydrocannabinol in ethanol, and then distilling off the ethanol.

The following examples are illustrative but not limiting of the invention.

Composition Preparation: Sesame oil solvent

Sesame oil was degassed under vacuum distillation and blanketed with nitrogen. The sesame oil was refined sesame oil from Jeen International (Compositions 1-2, 7-17) or Dipasa (Compositions 3-6). A solution of (-)- Δ^9 -trans-tetrahydrocannabinol in ethanol was added to the sesame oil and the acid was also added. The solution was mixed and the ethanol was removed using a rotary evaporator.

Each composition contained 6.65wt% (-)- Δ^9 -trans-tetrahydrocannabinol based on the weight of the composition. The additional components in each composition were as shown in Table 1 below:

Table 1 Compositions 1-18 in Sesame Oil Solvent

	Acid	Other components
Composition 1	None	None
Composition 2	0.1wt% citric acid	None
Composition 3	None	None
Composition 4	0.1wt% citric acid	None
Composition 5	None	Methyl paraben, Propyl paraben, Alpha tocopherol, BHT
Composition 6	0.1wt% citric acid	Methyl paraben, Propyl paraben, Alpha tocopherol, BHT
Composition 7	None	None
Composition 8	0.1wt% ascorbic acid	None
Composition 9	0.1wt% acetic acid	None
Composition 10	0.1wt% citric acid	None
Composition 11	0.1wt% lactic acid	None
Composition 12	0.1wt% fumaric acid	None
Composition 13	0.1wt% malic acid	None
Composition 14	0.1wt% oxalic acid	None
Composition 15	0.1wt% succinic acid	None
Composition 16	0.1wt% salicylic acid	None
Composition 17	0.1wt% tartaric acid	None
Composition 18	0.1wt% phosphoric acid	None

Composition Preparation: Ethanol solvent

Citric acid was added to 2ml samples of a solution of (-)- Δ^9 -trans-tetrahydrocannabinol in ethanol (the concentration of the (-)- Δ^9 -trans-tetrahydrocannabinol was 66.6mg/ml). The solutions were mixed. The amount of citric acid in each solution is shown in Table 2 below:

Table 2 Compositions 18-23 in Ethanol Solvent

	Amount of citric acid (mg)	Weight % of citric acid compared to the weight of Δ^9 -THC
Composition 19	0.00	0.0%
Composition 20	2.51	1.9%
Composition 21	2.01	1.5%
Composition 22	0.50	0.4%
Composition 23	0.25	0.2%
Composition 24	0.13	0.09%

Stability: Sesame Oil solvent

The stability of the sesame oil compositions (compositions 1-18) was assessed at three different conditions: 5°C or Normal Storage (Refrigerated) Conditions; 25°C/60% Relative Humidity or Accelerated Conditions; and 40°C/75% Relative Humidity or High Temperature/High Humidity Conditions. The degradation of the (-)- Δ^9 -trans-tetrahydrocannabinol was monitored using a High Performance Liquid Chromatography (HPLC) method with ultraviolet detection at 228nm. Each detected impurity peak was measured using percent peak area (% PA) with respect to the peak area counts for (-)- Δ^9 -trans-tetrahydrocannabinol for each chromatogram, i.e. the degradation of the composition was assessed against (-)- Δ^9 -trans-tetrahydrocannabinol not against a branded product containing (-)- Δ^9 -trans-tetrahydrocannabinol. Each impurity peak was identified with a relative retention time (RRT) relative to the (-)- Δ^9 -trans-tetrahydrocannabinol peak elution time from each chromatogram. Impurity peaks measuring above 0.05% PA were recorded.

The impurities that are attributed to the degradation of (-)- Δ^9 -trans-tetrahydrocannabinol elute from the HPLC column at a RRT window of 0.56 to 0.95 and at a RRT of 1.06. The impurities cannabinol and Δ^8 - tetrahydrocannabinol elute from the column at RRTs of 0.95 and 1.06 respectively.

Table 3 shows the results of the stability tests for compositions 1-18. The period of time after which the degradation of the composition was assessed is indicated beside each table.

Table 3 - Stability tests for compositions 1-18

Composition 1, 1 month

Condition	% Peak Areas according to Relative Retention Time (RRT)												
	0.56	0.57	0.58	0.61	0.63	0.66	0.67	0.70	0.74	0.78	0.90	0.95	1.06
Initial													0.28
25°C/60%RH		4.13	4.45	0.96	3.11	10.2	2.35	0.22		0.36	1.46	4.06	5.33
40°C/75%RH		8.09	5.35	2.43	4.91	0.29	15.62	0.28			0.49	1.86	2.99

Composition 2, 3 months

Condition	% Peak Areas according to Relative Retention Time (RRT)												
	0.56	0.57	0.58	0.61	0.63	0.66	0.67	0.70	0.74	0.78	0.90	0.95	1.06
Initial													
5°C			0.08	0.05								0.05	
25°C/60%RH	0.18			0.13		0.07		0.07			0.16	0.37	0.29
40°C/75%RH	1.96		0.22	0.91	0.17	0.45	0.36	0.3		0.05	1.25	4.16	2.17

Composition 3, 3 months

Condition	% Peak Areas according to Relative Retention Time (RRT)												
	0.56	0.57	0.58	0.61	0.63	0.66	0.67	0.70	0.74	0.78	0.90	0.95	1.06
Initial						0.12							
5°C	0.29	0.51		0.29	0.13	3.96	0.22		0.35	1.89		0.15	0.08
25°C/60%RH	0.85	0.74	1.97	1.23	0.72	6.13	1.81	0.06	0.23	2.55	0.44	2.03	0.64
40°C/75%RH	0.16	0.52	0.31	0.65	0.74	3.72	0.45	0.02	0.08	1.02	1.96	1.46	0.7

Composition 4, 3 months

Condition	% Peak Areas according to Relative Retention Time (RRT)												
	0.56	0.57	0.58	0.61	0.63	0.66	0.67	0.70	0.74	0.78	0.90	0.95	1.06
Initial													
5°C												0.05	
25°C/60%RH	0.19			0.10							0.10	0.20	0.14
40°C/75%RH	1.96			0.15	0.53	0.29	0.30	0.17			1.11	2.62	0.41

Composition 5, 3 months

Condition	% Peak Areas according to Relative Retention Time (RRT)												
	0.56	0.57	0.58	0.61	0.63	0.66	0.67	0.70	0.74	0.78	0.90	0.95	1.06
Initial									1.54				
5°C	0.05	0.12			0.08	0.06			1.36	0.05	0.09		0.30
25°C/60%RH	0.40	0.65	0.2	0.13	0.41	0.50	0.37	0.14	0.92	0.12	0.27	0.48	1.00
40°C/75%RH	1.05	0.63	0.23	0.11	0.91	0.62	0.22		1.07	0.11	0.54	1.63	1.74

Composition 6, 3 months

Condition	% Peak Areas according to Relative Retention Time (RRT)												
	0.56	0.57	0.58	0.61	0.63	0.66	0.67	0.70	0.74	0.78	0.90	0.95	1.06
Initial				0.05					1.54				
RF 5°C				0.06					1.52			0.11	0.05
25°C/60%RH	0.09			0.06		0.07			1.52			0.53	0.3
40°C/75%RH	0.97	0.21	0.15	0.52	0.25	0.32	0.2	0.18	1.57		0.63	2.96	1.96

Composition 7, 4 weeks

Condition	% Peak Areas according to Relative Retention Time (RRT)												
	0.56	0.57	0.58	0.61	0.63	0.66	0.67	0.70	0.74	0.78	0.90	0.95	1.06
Initial		0.03	0.03				0.02			0.01			0.02
5°C	0.01					0.11	0.02		0.04	0.04	0.01		0.05
25°C/60%RH	0.19	0.16		0.13	0.11	1.76			0.51	0.22	0.01	0.05	0.05
40°C/75%RH	0.23	0.21	0.46	1.41	0.67	5.60	0.22	0.07	1.00	0.81	0.29	0.56	0.05

Composition 8, 4 weeks

Condition	% Peak Areas according to Relative Retention Time (RRT)												
	0.56	0.57	0.58	0.61	0.63	0.66	0.67	0.70	0.74	0.78	0.90	0.95	1.06
Initial	0.01		0.01			0.01				0.01			0.02
5°C			0.02								0.01		0.02
25°C/60%RH			0.03	0.03							0.02	0.01	0.02
40°C/75%RH	0.02	0.01	0.06	0.11	0.03				0.02	0.02	0.04	0.05	0.06

Composition 9, 4 weeks

Condition	% Peak Areas according to Relative Retention Time (RRT)												
	0.56	0.57	0.58	0.61	0.63	0.66	0.67	0.70	0.74	0.78	0.90	0.95	1.06
Initial	0.02					0.04	0.03						0.02
5°C	0.17	0.10	0.02	0.1	0.02	0.67	0.16		0.15	0.15		0.02	0.05
25°C/60%RH	0.13	0.23	0.36	1.00	0.09	3.18	0.46	0.02	0.58	0.59	0.1	0.68	0.14
40°C/75%RH	0.65	1.25	0.29	2.95	0.32	2.99	1.71	0.04	0.30	0.12	0.49	3.69	0.7

Composition 10, 4 weeks

Condition	% Peak Areas according to Relative Retention Time (RRT)												
	0.56	0.57	0.58	0.61	0.63	0.66	0.67	0.70	0.74	0.78	0.90	0.95	1.06
Initial	0.02						0.01					0.01	0.02
5°C											0.01		0.01
25°C/60%RH			0.04								0.03	0.01	0.02
40°C/75%RH	0.11		0.11	0.02	0.02	0.02	0.02	0.03			0.16	0.12	0.14

Composition 11, 4 weeks

Condition	% Peak Areas according to Relative Retention Time (RRT)												
	0.56	0.57	0.58	0.61	0.63	0.66	0.67	0.70	0.74	0.78	0.90	0.95	1.06
Initial			0.02										0.02
5°C			0.02							0.01	0.02	0.02	0.03
25°C/60%RH	0.02	0.01	0.09			0.01					0.04	0.11	0.07
40°C/75%RH	0.02	0.19	0.12	0.27	0.04	0.16	0.04			0.02	0.33	0.60	0.43

Composition 12, 4 weeks

Condition	% Peak Areas according to Relative Retention Time (RRT)												
	0.56	0.57	0.58	0.61	0.63	0.66	0.67	0.70	0.74	0.78	0.90	0.95	1.06
Initial	0.02		0.01			0.02				0.03			0.01
5°C	0.26	0.10	0.09		0.05	0.42	0.17		0.09	0.12	0.01	0.02	0.06
25°C/60%RH	0.08	0.09	0.12	0.02	0.07	0.38	0.1	0.02	0.04	0.07	0.19	0.19	0.67
40°C/75%RH	0.42	0.11	0.53	0.07	0.16	0.31	0.32		0.07	0.04	0.98	1.41	2.58

Composition 13, 4 weeks

Condition	% Peak Areas according to Relative Retention Time (RRT)												
	0.56	0.57	0.58	0.61	0.63	0.66	0.67	0.70	0.74	0.78	0.90	0.95	1.06
Initial													0.02
5°C											0.01		0.01
25°C/60%RH	0.01		0.02								0.02	0.03	0.03
40°C/75%RH	0.15		0.02	0.06	0.04	0.03		0.03			0.15	0.18	0.18

Composition 14, 4 weeks

Condition	% Peak Areas according to Relative Retention Time (RRT)												
	0.56	0.57	0.58	0.61	0.63	0.66	0.67	0.70	0.74	0.78	0.90	0.95	1.06
Initial	0.01												0.02
5°C			0.05								0.01		0.02
25°C/60%RH			0.16								0.03	0.03	0.02
40°C/75%RH	0.04	0.03	0.35	0.02							0.11	0.12	0.02

Composition 15, 4 weeks

Condition	% Peak Areas according to Relative Retention Time (RRT)												
	0.56	0.57	0.58	0.61	0.63	0.66	0.67	0.70	0.74	0.78	0.90	0.95	1.06
Initial						0.02			0.02		0.01		0.02
5°C											0.01	0.01	0.02
25°C/60%RH			0.03		0.02						0.01		0.03
40°C/75%RH	0.05	0.01	0.25	0.03	0.08	0.08	0.03		0.03		0.11	0.10	0.28

Composition 16, 4 weeks

Condition	% Peak Areas according to Relative Retention Time (RRT)												
	0.56	0.57	0.58	0.61	0.63	0.66	0.67	0.70	0.74	0.78	0.90	0.95	1.06
Initial	0.01		0.04		0.01	0.01	0.02					0.01	0.03
5°C	0.01		0.16		0.03	0.08	0.04		0.05	0.15	0.01	0.22	0.07
25°C/60%RH	0.36	0.1	1.87		0.58	0.63	0.75	0.01	0.19	2.76	0.05	4.27	0.15
40°C/75%RH	0.41	0.27	0.99	0.17	0.45	0.34	0.77	0.05	0.08	2.97	0.64	4.5	0.59

Composition 17, 4 weeks

Condition	% Peak Areas according to Relative Retention Time (RRT)												
	0.56	0.57	0.58	0.61	0.63	0.66	0.67	0.70	0.74	0.78	0.90	0.95	1.06
Initial	0.02						0.01			0.02			0.02
5°C											0.01		0.02
25°C/60%RH			0.02								0.02	0.02	0.02
40°C/75%RH	0.13		0.04	0.04	0.01	0.04		0.03			0.12	0.12	0.17

Composition 18, 16 days

Condition	% Peak Areas according to Relative Retention Time (RRT)												
	0.56	0.57	0.58	0.61	0.63	0.66	0.67	0.70	0.74	0.78	0.90	0.95	1.06
Initial			1.58	0.26	0.55				0.36		0.05		
25°C/60%RH			3.39	0.20	0.17*	0.09				0.09		1.08	
40°C/75%RH			3.39	0.20	0.18*	0.08			0.10			1.08	

* data after 1 week, not 16 days

Compositions 1, 3, 5 and 7 did not contain any organic acid, and the tables show that considerable degradation occurred during the observation period. By contrast, the degradation observed for compositions 2, 4 and 6 (which all contained 0.1wt% citric acid) was considerably less. Compositions 5 and 6 both contained antimicrobial agents and preservatives, yet composition 6 (containing 0.1wt% citric acid) was more stable than composition 5.

Compositions 8-18 contained a variety of acids. Compositions 8, 10, 11, 12, 13, 14, 15, 17 and 18 (containing 0.1wt% ascorbic acid, 0.1wt% citric acid, 0.1wt%

lactic acid, 0.1wt% fumaric acid, 0.1wt% malic acid, 0.1wt% oxalic acid, 0.1wt% succinic acid, 0.1wt% tartaric acid and 0.1wt% phosphoric acid respectively) all showed improved stability compared to composition 7 (containing no organic acid). Compositions 9 and 16 (containing 0.1wt% acetic acid and 0.1wt% salicylic acid) did not show an appreciable improvement compared to composition 7 and it would seem that these acids are less effective at improving stability (although the inventors believe that these acid may provide an improvement if used at another concentration).

Stability: Ethanol solvent

The stability of the ethanol compositions (compositions 19-24) was assessed in substantially the same manner as for the sesame oil compositions except that they were only assessed at only one set of conditions (40°C) and the compositions were analysed after 60 hours and 1 month.

Table 4 shows that the composition that did not contain citric acid (composition 19) showed the greatest degradation and there seems to be a slight correlation between increasing citric acid content and increased stability.

Table 4 - Stability tests for compositions 19-24

	Condition	% Peak Areas according to Relative Retention Time (RRT)												
		0.57	0.58	0.59	0.61	0.63	0.66	0.67	0.70	0.74	0.78	0.82	0.90	0.95
	Initial						0.11							
Composition 19	40°C/60hr	0.04	0.04		0.25	0.02	1.80			0.35		0.02		
	40°C/1mo	0.34	0.34	0.14	8.6	1.58	5.13		0.13	2.33	0.07	1.46	0.52	0.34
Composition 20	40°C/60hr				0.3	0.02						0.04		0.07
	40°C/1mo	0.02			2.38	0.19	0.03	0.06	0.02			0.05	0.01	0.58
Composition 21	40°C/60hr	0.04			0.3	0.02	0.01					0.05		0.08
	40°C/1mo	0.02			2.51	0.2	0.02	0.06	0.02			0.05	0.01	0.6
Composition 22	40°C/60hr				0.35	0.03	0.07					0.11		0.04
	40°C/1mo	0.02			3.37	0.27	0.06	0.06	0.03			0.23	0.02	0.69
Composition 23	40°C/60hr				0.31	0.03	0.11					0.11		0.02
	40°C/1mo	0.02	0.02		3.03	0.25	0.12	0.04	0.03			0.42	0.01	0.51
Composition 24	40°C/60hr	0.02			0.28	0.03	0.16			0.02		0.11		0.02
	40°C/1mo	0.02			1.71	0.14	0.13	0.02	0.03			0.39		0.24

The claims defining the invention are as follows:

1. A composition comprising:
 - (a) a tetrahydrocannabinol compound chosen from Δ^8 tetrahydrocannabinol, (-)- Δ^9 -trans-tetrahydrocannabinol and side chain alkyl derivatives of either compound,
 - (b) a solvent chosen from oils and C₁-C₄ alcohols, and
 - (c) an acid,wherein the composition is in liquid form and the acid is added in an amount effective to improve the stability of the composition.
2. A composition according to claim 1, wherein the derivative of Δ^8 tetrahydrocannabinol or (-)- Δ^9 -trans-tetrahydrocannabinol has a 1,1 dimethylheptyl side chain.
3. A composition according to claim 1 or 2, wherein the solvent is sesame oil.
4. A composition according to claim 1 or 2, wherein the solvent is ethanol.
5. A composition according to any preceding claim, comprising more than one solvent.
6. A composition according to claim 5, comprising an oil and a C₁-C₄ alcohol.
7. A composition according to any preceding claim, wherein the acid is an organic acid.
8. A composition according to claim 7, wherein the organic acid is chosen from the group consisting of citric acid, ascorbic acid, malic acid, oxalic acid, succinic acid and tartaric acid.
9. A composition according to claim 7 or 8, wherein the organic acid is citric acid.

10. A composition according to any of claims 1 to 6, wherein the acid is a mineral acid.
11. A composition according to claim 10, wherein the mineral acid is chosen from the group consisting of phosphoric acid, hydrochloric acid, nitric acid and sulphuric acid.
12. A composition according to claim 10 or 11, wherein the mineral acid is phosphoric acid.
13. A composition according to any preceding claim, wherein the amount of acid is from 0.01-2% as a weight percentage of the composition.
14. A composition according to any preceding claim, wherein the amount of (-)- Δ^9 -trans-tetrahydrocannabinol in the composition is from 0.1-15% as a weight percentage of the composition.
15. A composition according to any preceding claim, further comprising at least one of antimicrobial agents, preservatives and antioxidants.
16. A composition according to any preceding claim, consisting essentially of a tetrahydrocannabinol compound, an oil or a C₁-C₄ alcohol, and 0.01-2wt% of an acid chosen from the group consisting of citric acid, ascorbic acid, malic acid, oxalic acid, succinic acid, tartaric acid, phosphoric acid, hydrochloric acid, nitric acid and sulphuric acid, wherein additional components may comprise up to 1wt% of the solution.
17. A composition according to claim 15, consisting essentially of (-)- Δ^9 -trans-tetrahydrocannabinol, sesame oil and 0.05-0.5wt% citric acid or phosphoric acid, wherein additional components may comprise up to 1wt% of the solution.
18. A composition substantially as described herein with reference to the Examples.

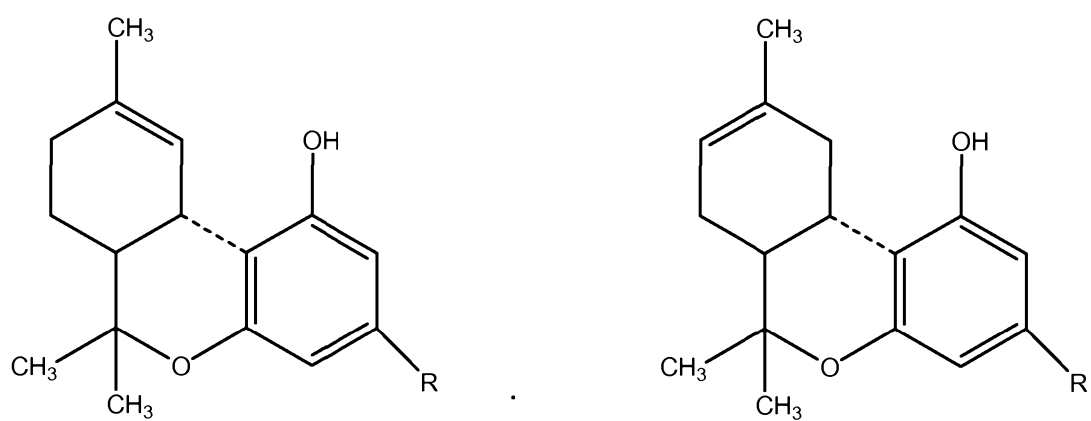


Figure 1