Therapeutic Index Calculation

From these experiments, a therapeutic index (TI) was determined for each compound by dividing the threshold dose for inducing emetic episodes by the ED_{50} value for inhibiting the pulmonary neutrophilia. The TI calculation is summarized in Table IV. Compound A had a TI of 12, causing no emetic episodes at an anti-inflammatory dose of 1 ms/kg.

TABLE IV

Summary of the effective doses (ED_{50}) for inhibition of LPS-induced pulmonary neutrophilia and induction of emesis and the therapeutic index derived from these values.

Compound	Inhibition of LPS-induced neutrophilia (ED_{50} mg/kg)	Threshold emetic dose (mg/kg)	Therapeutic Index
Compound A	0.8	10	12

5.10. Example 9

200 mg Dosage Capsule

Table V illustrates a batch formulation and single dosage formulation for a 200 mg Compound A single dose unit, i.e., about 40 percent by weight, in a size #0 capsule.

TABLE V

Formulation for 200 mg capsule

Material	Percent By Weight	Quantity (mg/tablet)	Quantity (kg/batch)
Compound A	40.0%	200 mg	16.80 kg
Pregelatinized Corn Starch, NF5	9.5%	297.5 mg	24.99 kg
Magnesium Stearate	0.5%	2.5 mg	0.21 kg
Total	100.0%	500 mg	42.00 kg

The pregelatinized corn starch (SPRESS B-820) and Compound A components are passed through a 710 μm screen and then are loaded into a Diffusion Mixer with a baffle insert and blended for 15 minutes. The magnesium stearate is passed through a 210 μm screen and is added to the Diffusion Mixer. The blend is then encapsulated in a size #0 capsule, 500 mg per capsule (8400 capsule batch size) using a Dosator type capsule filling machine.

5.11. Example 10

100 mg Oral Dosage Form

Table VI illustrates a batch formulation and a single dose unit formulation containing 100 mg of Compound A.

TABLE VI

Formulation for 100 mg tablet

Material	Percent by Weight	Quantity (mg/tablet)	Quantity (kg/batch)
Compound A	40%	100.00	20.00
Microcrystalline Cellulose, NF	53.5%	133.75	26.75
Pluronic F-68 Surfactant	4.0%	10.00	2.00

TABLE VI-continued

Formulation for 100 mg tablet

Material	Percent by Weight	Quantity (mg/tablet)	Quantity (kg/batch)
Croscarmellose Sodium Type A, NF	2.0%	5.00	1.00
Magnesium Stearate, NF	0.5%	1.25	0.25
Total	100.0%	250.00 mg	50.00 kg

The microcrystalline cellulose, croscarmellose sodium, and Compound A components are passed through a #30 mesh screen (about 430μ to about 655μ). The Pluronic F-68® (manufactured by JRH Biosciences, Inc. of Lenexa, Kans.) surfactant is passed through a #20 mesh screen (about 457μ to about 1041μ). The Plutonic F-68® surfactant and 0.5 kgs of croscarmellose sodium are loaded into a 16 qt. twin shell tumble blender and are mixed for about 5 minutes. The mix is then transferred to a 3 cubic foot twin shell tumble blender where the microcrystalline cellulose is added and blended for about 5 minutes. The thalidomide is added and blended for an additional 25 minutes. This pre-blend is passed through a roller compactor with a hammer mill attached at the discharge of the roller compactor and moved back to the tumble blender. The remaining croscarmellose sodium and magnesium stearate is added to the tumble blender and blended for about 3 minutes. The final mixture is compressed on a rotary tablet press with 250 mg per tablet (200,000 tablet batch size).

8.12. Example 11

Aerosol Dosage Form

A concentrate is prepared by combining Compound A, and a 12.6 kg portion of the trichloromonofluoromethane in a sealed stainless steel vessel equipped with a high shear mixer. Mixing is carried out for about 20 minutes. The bulk suspension is then prepared in the sealed vessel by combining the concentrate with the balance of the propellants in a bulk product tank that is temperature controlled to 21° to 27° C. and pressure controlled to 2.8 to 4.0 BAR. 17 ml aerosol containers which have a metered valve which is designed to provide 100 inhalations of the composition of the invention. Each container is provided with the following:

Compound A	0.0120 g
trichloromonofluoromethane	1.6939 g
dichlorodifluoromethane	3.7175 g
dichlorotetrafluoroethane	1.5766 g
total	7.0000 g

While the invention has been described with respect to the particular embodiments, it will be apparent to those skilled in the art that various changes and modifications may be made without departing from the spirit and scope of the invention as defined in the claims. Such modifications are also intended to fall within the scope of the appended claims.

What is claimed is:

1. A method of treating psoriasis, which comprises orally administering to a patient having psoriasis about 10 mg to about 200 mg per day of stereomerically pure (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acety-