

TABLE 1

Blood Phenytoin Concentrations (in $\mu\text{g/ml}$) after Oral Administration of Commercial Phenytoin Preparations and Activated Phenytoin Preparation																		
subject	Commercial Preparation A					Commercial Preparation B					Activated Preparation of the Present Invention (Example 1)							
	1	2	3	4	0	8	2	3	4	6	8	1	2	3	4	6	8	
1	0	0	0	0	0	0	0	0	0	1.7	1.7	1.7	1.8	4.8	4.6	5.0	4.9	4.2
2	0	0	0	0	0	0	0	0	1.6	1.7	1.8	1.7	<1	2.8	3.6	5.5	4.3	4.4
3	0	0	0	0	0	0	0	0	0	0	1.5	1.6	2.2	4.7	5.9	6.1	5.5	5.5
4	0	0	0	0	0	0	0	0	1.6	2.0	2.2	2.6	4.6	6.4	6.4	5.5	5.5	5.5
5	0	0	0	0	0	0	0	0	1.3	1.7	1.8	<1	4.4	5.8	6.0	5.2	5.1	5.1
6	0	0	0	0	0	0	0	0	1.3	1.7	1.6	1.7	2.8	4.5	5.4	6.0	5.8	4.5
7	0	0	0	0	0	0	0	0	1.2	1.8	2.5	1.2	4.2	5.0	5.5	4.7	4.0	4.0
8	0	0	0	0	0	1.0	0	0	0	1.4	1.9	3.3						
9						0.1			0.4	1.3	1.8	2.1	2.12	4.29	5.24	5.79	5.13	4.74

In this figure, the curves XVI—XVI and XVII—XVII represent the activated preparation of Example 15 and the commercial preparation, respectively.

EXAMPLE 16

In a beaker were placed 160 g of chloramphenicol palmitate, 40 g of hydroxypropyl cellulose (manufactured and sold by Nippon Soda Co., Ltd., Japan) 0.16 g of dioctyl sodium sulfosuccinate, and 1,000 ml of ethanol. Then, the chloramphenicol palmitate was wet-ground for 30 minutes by means of Politron® (manufactured and sold by Kinematica GmbH, Switzerland). The resulting dispersion was dried in a spray dryer (Type FS-20, manufactured and sold by Freund Industrial Co., Ltd., Japan). The dry powder thus obtained exhibited very good redispersibility in water.

The hydroxypropyl cellulose-coated chloramphenicol palmitate powder prepared in this example and a commercial preparation of crystalline chloramphenicol palmitate were separately administered per os to 6 adult male human subjects in a dose of 500 mg (as potency) of chloramphenicol. This test was of the cross-over design in which each subject received the two preparations with an interval of one week. The results thus obtained are illustrated in FIG. 9 where the time (in hours) elapsed after administration is plotted an abscissa and the concentration (in $\mu\text{g/ml}$) of chloramphenicol in the blood as ordinate. In this figure, the curves XVIII—XVIII and XIX—XIX represent the activated preparation of Example 16 and the commercial preparation, respectively.

EXAMPLE 17

Into the pot of a vibration mill similar to that used in Example 14 were charged 50 g of griseofulvin, 5 g of polyethylene glycol (6000), 5 g of methyl cellulose, and 100 ml of water. Then, the griseofulvin was wet-ground by operating the mill for 8 hours. In the same manner as in Example 14, the resulting dispersion was heated to effect gelation of the methyl cellulose. The precipitate so formed was separated from the liquid phase by filtering the dispersion while being kept at that temperature. Thereafter, the precipitate was dried in a hot-air drying oven preheated to 105° C. and then reduced to a powder by means of an atomizer (manufactured and sold by Fuji Powdal Co., Ltd., Japan). The powder thus obtained exhibited very good redispersibility in water, an artificial gastric juice, and an artificial intestinal juice. When measured by electron microscopy, the diameters of most redispersed particles were not greater than 0.5 μ .

EXAMPLE 18

In a beaker were placed 30 g of hydrocortisone acetate, 10 g of ethylene oxide-propylene oxide block copolymer (Pluronic F68), 100 ml of water, and 50 ml of ethanol. Then, the hydrocortisone acetate was wet-ground for 30 minutes by means of Politron® as has been described in Example 16. The resulting dispersion was dried in a spray dryer (Type FS-20, manufactured and sold by Freund Industrial Co., Ltd., Japan). The powder thus obtained was very quickly redispersed in water at 37° C., an artificial gastric juice, and an intestinal juice.

We claim:

1. A process for the preparation of an activated pharmaceutical composition containing a solid drug in the form of finely divided particles substantially not greater than 10 microns in diameter, which comprises the steps of:

- (1) providing a solid drug that is scarcely soluble in water and is soluble in a low-boiling hydrophobic organic solvent;
- (2) dissolving the solid drug in said low-boiling hydrophobic organic solvent;
- (3) emulsifying the resulting solution in water in the presence of a water-soluble, high-molecular weight substance selected from the group consisting of hydroxypropyl cellulose, methyl cellulose, hydroxyethyl cellulose, hydroxypropyl methyl cellulose, hydroxypropyl ethyl cellulose, carboxymethyl cellulose sodium salt, alpha-starch, hydroxypropyl starch, pullulan, gum arabic, tragacanth gum, gelatin, polyvinyl alcohol, polyvinyl pyrrolidone and mixtures thereof; and
- (4) then removing the dispersion medium from the so-formed disperse system.

2. A process for the preparation of an activated pharmaceutical composition containing a solid drug in the form of finely divided particles substantially not greater than 10 microns in diameter, which comprises the steps of:

- (1) providing a solid drug that is scarcely soluble in water and is soluble in a low-boiling hydrophobic organic solvent selected from the group consisting of chloroform, methylene chloride, trichloroethylene, trichloroethane, carbon tetrachloride, benzene, n-hexane, benzene, toluene, ethyl ether, isopropyl ether, methyl ethyl ketone, ethyl acetate and mixtures thereof;
- (2) dissolving the solid drug in said low-boiling hydrophobic organic solvent;