acid additive were placed in a tablet grinder (Konishi Seisakusyo Co., Ltd.) and milled to obtain a milled product containing fumaric acid. The milled product containing fumaric acid (1.50 g), a diluent (4.17 g), a disintegrant (0.30 g), and a lubricant (0.030 g) were introduced and mixed in a glass bottle, and then the mixture was compressed using a tableting machine to obtain tablets each weighing 200 mg.

[0052]

Formulation Example 2

Succinic acid ~~Fumaric acid~~ (1 g) was added as an acid additive in place of the fumaric acid ~~succinic acid~~(1 g) of Formulation Example 1, followed by milling to obtain a milled product containing succinic acid ~~fumaric acid~~. Tablets each weighing 200 mg were obtained in the same manner as in Formulation Example 1.

[0053]

Comparative Example 1

As a control, tablets were obtained in the same manner as in Formulation Examples 1 and 2 except that no acid additive was added.

[0054]

Dissolution Test

Regarding Formulation Examples 1 and 2, and Comparative Example 1, the dissolution test was performed at 50 rpm using 900 mL of dissolution test solution 2 (37°C) as a test solution in accordance with the paddle method of the dissolution test methods described in the Japanese Pharmacopoeia, Sixteenth Edition. As measurement equipment, a dissolution tester (Toyama Sangyo Co., Ltd.) and a solution monitor (Otsuka Electronics Co., Ltd.) were used.

The results are shown in Fig. 1 (n=3, average dissolution rate ± SD). In Comparative Example 1, which contained no acid additive, the dissolution rate obtained 15 minutes later was 65%, whereas in Formulation Example 1, which contained fumaric acid, and Formulation Example 2, which contained succinic acid, the dissolution rates obtained 15 minutes later were 93% and 76%,

Table 6

	Formulation Example 7 (mg/tablet)	Comparative Example 3 (mg/tablet)
Compound 1 monohydrate	100	100
Fumaric acid	100	-
Diluent	50	150
Binder	4	4
Disintegrant	13	13
Lubricant	1	1
Total	268	268

[0070]

Example 5: Evaluation of Absorption of Pharmaceutical Preparation Having Different Fumaric Acid Concentration

Tablets of Formulation Examples 8 and 9 were produced. Table 8 shows the formulation of each tablet.

[0071]

Formulation Example 8

Compound 1 monohydrate (42.5 g), fumaric acid (40.9 g), and a diluent (204.4g) were placed in a fluidized bed granulator (Freund Corp.), and the mixture was granulated with spraying a binder solution (123.0 g) to obtain a granulated product. A disintegrant (13.6 g) and a lubricant (1.7 g) were added to the resulting granulated product and mixed, and then the mixture was compressed by using a tableting machine (Kikusui Seisakusyo Ltd.) to obtain tablets each weighing 77.9 mg. A film coating liquid comprising a coating agent (27.0 g), a coloring agent (3.0 g), and puirified water (270.0 g) was sprayed onto the resulting tablets using a coater (Powrex Corp.) to obtain film-coated tablets.

[0072]

Formulation Example 9

A binder solution (108.1 g) was added to the mixture of Compound 1 monohydrate (37.4 g), fumaric acid (71.9 g), and a diluent (179.9 g), and the resulting mixture was granulated to obtain a granulated product. A disintegrant (12.0 g) and a