US007037528B2

(12) **United States Patent**
**Kipp et al.**

(10) **Patent No.: US 7,037,528 B2**
(45) **Date of Patent: *May 2, 2006**

(54) **MICROPRECIPITATION METHOD FOR PREPARING SUBMICRON SUSPENSIONS**

(75) Inventors: **James E. Kipp**, Wauconda, IL (US); **Joseph Chung Tak Wong**, Gurnee, IL (US); **Mark J. Doty**, Grayslake, IL (US); **Christine L. Rebbeck**, Algonquin, IL (US)

(73) Assignee: **Baxter International Inc.**, Deerfield, IL (US)

( * ) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **09/874,499**

(22) Filed: **Jun. 5, 2001**

(65) **Prior Publication Data**

US 2002/0168402 A1 Nov. 14, 2002

**Related U.S. Application Data**

(60) Provisional application No. 60/258,160, filed on Dec. 22, 2000.

(51) **Int. Cl.**

| | |
|---|---|
| ***A61K 9/14*** | (2006.01) |
| ***A61K 9/10*** | (2006.01) |
| ***B01J 13/00*** | (2006.01) |

(52) **U.S. Cl.** ..... **424/489**; 424/400; 424/450; 264/4; 264/4.1; 264/5

(58) **Field of Classification Search** ..... 424/400, 424/450, 489; 264/4, 4.1, 5

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

| | | | | |
|---|---|---|---|---|
| 2,745,785 | A | 5/1956 | Bruce et al. | |
| 4,056,635 | A | 11/1977 | Glen et al. | 424/346 |
| 4,073,943 | A | 2/1978 | Wretlind et al. | 424/358 |
| 4,452,817 | A | 6/1984 | Glen et al. | 424/346 |
| 4,540,602 | A | 9/1985 | Motoyama et al. | 427/213.31 |
| 4,606,940 | A | 8/1986 | Frank et al. | |
| 4,608,278 | A | 8/1986 | Frank et al. | |
| 4,622,219 | A | 11/1986 | Haynes | 424/38 |
| 4,725,442 | A | 2/1988 | Haynes | 424/490 |
| 4,798,846 | A | 1/1989 | Glen et al. | 514/713 |
| 4,826,689 | A | 5/1989 | Violanto | |
| 4,973,465 | A | 11/1990 | Baurain et al. | 242/406 |
| 4,997,454 | A | 3/1991 | Violante et al. | |
| 5,023,271 | A | 6/1991 | Vigne et al. | 514/458 |
| 5,049,322 | A | 9/1991 | Devissaguet et al. | |
| 5,078,994 | A | 1/1992 | Nair et al. | 424/501 |
| 5,091,187 | A | 2/1992 | Haynes | 424/450 |
| 5,091,188 | A | 2/1992 | Haynes | 424/450 |
| 5,100,591 | A | 3/1992 | Leclef et al. | 264/4.6 |
| 5,118,528 | A | 6/1992 | Fessi et al. | |
| 5,122,543 | A | 6/1992 | Khanna | |
| 5,133,908 | A * | 7/1992 | Stainmesse et al. | 264/4.1 |
| 5,145,684 | A | 9/1992 | Liversidge et al. | 424/489 |
| 5,151,264 | A | 9/1992 | Samain et al. | |
| 5,152,923 | A | 10/1992 | Weder et al. | 252/312 |
| 5,174,930 | A | 12/1992 | Stainmesse et al. | |
| 5,188,837 | A | 2/1993 | Domb | 424/450 |
| 5,246,707 | A | 9/1993 | Haynes | 424/450 |
| 5,250,236 | A | 10/1993 | Gasco | 264/4.4 |
| 5,269,979 | A | 12/1993 | Fountain | |
| 5,298,262 | A | 3/1994 | Na et al. | 424/489 |
| 5,302,401 | A | 4/1994 | Liversidge et al. | 424/501 |
| 5,314,506 | A | 5/1994 | Midler, Jr. et al. | |
| 5,318,767 | A | 6/1994 | Liversidge et al. | |
| 5,326,552 | A | 7/1994 | Na et al. | 424/4 |
| 5,336,507 | A | 8/1994 | Na et al. | 424/489 |
| 5,340,564 | A | 8/1994 | Illig et al. | 424/9 |
| 5,346,702 | A | 9/1994 | Na et al. | 424/490 |
| 5,352,459 | A | 10/1994 | Hollister et al. | 424/489 |
| 5,354,563 | A | 10/1994 | Toyotama | |
| 5,389,263 | A | 2/1995 | Gallagher et al. | 210/729 |
| 5,399,363 | A | 3/1995 | Liversidge et al. | 424/490 |
| 5,417,956 | A | 5/1995 | Moser | |
| 5,429,824 | A | 7/1995 | June | 424/489 |
| 5,447,710 | A | 9/1995 | Na et al. | 424/9.455 |
| 5,466,646 | A | 11/1995 | Moser | |
| 5,470,583 | A | 11/1995 | Na et al. | 424/489 |
| 5,474,989 | A | 12/1995 | Hashimoto et al. | |
| 5,494,683 | A | 2/1996 | Liversidge et al. | 424/490 |
| 5,510,118 | A | 4/1996 | Bosch et al. | 424/489 |
| 5,518,187 | A | 5/1996 | Bruno et al. | |
| 5,518,738 | A | 5/1996 | Eickhoff et al. | 424/493 |
| 5,534,270 | A | 7/1996 | De Castro | 424/490 |
| 5,543,133 | A | 8/1996 | Swanson et al. | 424/9.45 |
| RE35,338 | E | 9/1996 | Haynes | |
| 5,552,160 | A | 9/1996 | Liversidge et al. | 424/489 |
| 5,560,932 | A | 10/1996 | Bagchi et al. | |
| 5,560,933 | A | 10/1996 | Soon-Shiong et al. | 424/489 |

(Continued)

FOREIGN PATENT DOCUMENTS

| | | |
|---|---|---|
| EP | 0379 379 B1 | 1/1990 |

(Continued)

OTHER PUBLICATIONS

US 5,849,884, 12/1998, Woiszwillo et al. (withdrawn)
PCT/US01/49737 Written Opinion.

(Continued)

*Primary Examiner*—Thurman K. Page
*Assistant Examiner*—Simon J. Oh
(74) *Attorney, Agent, or Firm*—Michael C. Mayo

(57) **ABSTRACT**

The present invention provides a method for preparing submicron sized particles of an organic compound, the solubility of which is greater in a water-miscible first solvent than in a second solvent which is aqueous, the process including the steps of: (i) dissolving the organic compound in the water-miscible first solvent to form a solution, (ii) mixing the solution with the second solvent to define a pre-suspension; and (iii) adding energy to the pre-suspension to form particles having an average effective particle size of 400 nm to 2 microns.

**19 Claims, 7 Drawing Sheets**