

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
29 November 2001 (29.11.2001)

PCT

(10) International Publication Number
WO 01/89679 A2

(51) International Patent Classification⁷: **B01J 2/20**,
2/22, A61K 9/16, A61J 3/00

Morris Plains, NJ 07950 (US). **SHAH, Umang** [IN/US];
Warner-Lambert Consumer Group, 201 Tabor Road,
Morris Plains, NJ 07950 (US).

(21) International Application Number: PCT/US01/15597

(22) International Filing Date: 14 May 2001 (14.05.2001)

(74) Agents: **FEDERMAN, Evan, J.**; Warner-Lambert Com-
pany, 201 Tabor Road, Morris Plains, NJ 07950 et al. (US).

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
09/576,373 22 May 2000 (22.05.2000) US

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
ZW.

(71) Applicant (*for all designated States except US*):
WARNER-LAMBERT COMPANY [US/US]; 201
Tabor Road, Morris Plains, NJ 07950 (US).

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **GHEBRE-SEL-
LASSIE, Isaac** [US/US]; Warner-Lambert Consumer
Group, 201 Tabor Road, Morris Plains, NJ 07950 (US).
MOLLAN, Matthew, J., Jr. [US/US]; Warner-Lambert
Consumer Group, 201 Tabor Road, Morris Plains, NJ
07950 (US). **PATHAK, Nitin** [IN/US]; Warner-Lambert
Consumer Group, 201 Tabor Road, Morris Plains, NJ
07950 (US). **LODAYA, Mayur** [US/US]; Warner-Lam-
bert Consumer Group, 201 Tabor Road, Morris Plains,
NJ 07950 (US). **FESSEHAIE, Mebrahtu** [ER/US];
Warner-Lambert Consumer Group, 201 Tabor Road,

Published:

— *without international search report and to be republished
upon receipt of that report*

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: CONTINUOUS PRODUCTION OF PHARMACEUTICAL GRANULATION

(57) Abstract: A single pass, continuous, automated system for producing a pharmaceutical granulation includes multiple feeders to feed powders and liquids, a twin screw processor to granulate, a radio frequency or microwave based drying apparatus to dry the granulation, and at least one mill to process the dried granulation to desired particle sizes. The system incorporates means for monitoring key process parameters on-line. The granulation produced can be compressed into a tablet or incorporated into a capsule, both having a uniform distribution of the active ingredient. The system produces product having consistent properties even when production is scaled up for manufacture of the tablet in commercial volume. A single pass, continuous, automated system for producing a high dose pharmaceutical granulation from a low density active ingredient, includes multiple feeders to feed powders and liquids, a twin screw processor to granulate, a radio frequency or microwave based drying apparatus to dry the granulation, and at least one mill to process the dried granulation to desired particle sizes. The system produces product having consistent properties even when production is scaled up for manufacture of the tablet in commercial volume. The twin screw processor has first and second conveying elements, with a mixing element in between the conveying elements, and the second conveying element has at least one pitch less than at least one pitch of the first conveying element. The system also permits the optimization of a number of other design parameters, such as a location and feed rate of a side stuffer and a liquid feeder, the rotational speed of the granulator itself, and the final granulation size. The system is particularly suitable for producing a granulation of nelfinavir mesylate along with excipients, including calcium silicate, for a high dose product.

WO 01/89679 A2