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<p>(21) International Application Number: PCT/KR99/00341</p> <p>(22) International Filing Date: 28 June 1999 (28.06.99)</p> <p>(30) Priority Data: 1998/24563 27 June 1998 (27.06.98) KR 1999/24437 26 June 1999 (26.06.99) KR</p> <p>(71) Applicant (for all designated States except US): WON JIN BIOPHARMA CO., LTD. [KR/KR]; 1626-2, Socho-dong, Socho-ku, Seoul 137-070 (KR).</p> <p>(72) Inventor; and (75) Inventor/Applicant (for US only): LEE, Beom, Jin [KR/KR]; #501-213 Hyundai 5th Apt., Hupyoung 2-dong, Chunchcheon-si, Kangwon-do 200-162 (KR).</p> <p>(74) Agent: LEE, Won-Hee; Suite 805, Sung-ji Heights II, 642-16 Yoksam-dong, Kangnam-ku, Seoul 135-080 (KR).</p>		<p>(81) Designated States: AU, CA, CN, JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</p> <p>Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>																																				
<p>(54) Title: SOLID DISPERSED PREPARATION OF POORLY WATER-SOLUBLE DRUG CONTAINING OIL, FATTY ACID OR MIXTURES THEREOF</p>																																						
<table border="1"> <caption>Estimated data from the Plasma Concentration graph</caption> <thead> <tr> <th>Time (hour)</th> <th>Top Curve (ng/ml)</th> <th>Middle Curve (ng/ml)</th> <th>Bottom Curve (ng/ml)</th> </tr> </thead> <tbody> <tr><td>1</td><td>2500</td><td>1500</td><td>1000</td></tr> <tr><td>2</td><td>3300</td><td>2000</td><td>1500</td></tr> <tr><td>3</td><td>3500</td><td>2500</td><td>1800</td></tr> <tr><td>4</td><td>3000</td><td>2000</td><td>1500</td></tr> <tr><td>5</td><td>2500</td><td>1800</td><td>1200</td></tr> <tr><td>6</td><td>2500</td><td>1800</td><td>1200</td></tr> <tr><td>7</td><td>2200</td><td>1500</td><td>1000</td></tr> <tr><td>8</td><td>2300</td><td>1500</td><td>1000</td></tr> </tbody> </table>			Time (hour)	Top Curve (ng/ml)	Middle Curve (ng/ml)	Bottom Curve (ng/ml)	1	2500	1500	1000	2	3300	2000	1500	3	3500	2500	1800	4	3000	2000	1500	5	2500	1800	1200	6	2500	1800	1200	7	2200	1500	1000	8	2300	1500	1000
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<p>(57) Abstract</p> <p>Disclosed is a solid dispersed preparation for poorly water-soluble drugs, which is prepared by dissolving or dispersing the poorly water-soluble drugs in an oil, a fatty acid or a mixture thereof, mixing the solution or dispersion in a water-soluble polyol matrix and drying the mixture. The solid dispersed preparation can be formulated into a power formulation or a granule formulation. The solid dispersed preparation is improved in the solubility of poorly water-soluble drugs in the gastro-intestinal tract, resulting in a great increase in the bioavailability of the drugs. In addition, the solid dispersed preparation gives the pharmaceutical solutions to the problems that the conventional semi-solid or liquid preparations possess, enabling medicinally effective, poorly water-soluble compounds to be formulated, molded and processed, quickly and in an economically favorable manner without use of any organic solvent.</p>																																						

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SOLID DISPERSED PREPARATION OF POORLY WATER-SOLUBLE DRUG
CONTAINING OIL, FATTY ACID OR MIXTURES THEREOF

BACKGROUND OF THE INVENTION

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Field of the Invention

The present invention relates to a solid dispersed preparation for poorly water-soluble drugs or biologically active substances. More particularly, this invention relates to a solid dispersed preparation which allows poorly water-soluble drugs to be increased in the uptake efficiency in the gastro-intestinal track and is convenient to make in a pharmaceutical formulation.

15 Description of the Prior Art

A good many drugs poorly dissolve in water. When being administered to a body, these poorly water-soluble drugs have so low solubility and releasing rate in digestive juices as to retard their absorption, resulting the bioavailability decreased. In order to solve this problem, various preparation methods were developed with the aim of solubilizing these poorly water-soluble drugs and increasing their releasing rates. For instance, there have been reported many methods for improving the bioavailability of drugs, including micronization, formation of micelles by use of surfactant, solvent deposition, utilization of dry elixirs, co-precipitation

by use of inert water-soluble carriers, solid-dispersion and formation of inclusion complexes using cyclodextrins.

In conducting these methods, however, the drugs to be administered do not show a constant increase in solubility.

5 Thus, they are problematic in terms of preparation, commercialization, and efficiency.

For the poorly water-soluble drugs, which are also poor in internal uptake, there have been made attempts to enhance their bioavailability upon administration.

10 However, the dosage forms developed thus far, are of semi-solid or liquid form, giving disadvantages in pharmaceuticals, especially in formulating, molding and processing.

15 SUMMARY OF THE INVENTION

We, the inventors made the intensive and thorough research on the formulation of poorly water-soluble drugs, to improve the bioavailability of the drugs upon
20 administration. As a result, we found that the dispersion or solution of the poorly water-soluble drugs in oils, fatty acids or mixtures thereof, followed by mixing with a water-soluble polymer matrix allowed the drugs to efficiently release in the gastro-intestinal tract and the
25 mixture can be formed into a solid form.

Therefore, it is an object of the present invention to provide a solid dispersed preparation which improves the

bioavailability of poorly water-soluble drugs by enhancing the release of the drugs in the gastro-intestinal tract.

It is another object of the present invention to provide a solid dispersed preparation which can be prepared
5 by simple and convenient process with an economical benefit.

According to the present invention, a solid dispersed preparation for poorly water-soluble drugs is prepared by dissolving or dispersing the drugs in an oil, a fatty acid
10 or a mixture thereof, mixing the solution or dispersion in a water-soluble polyol matrix and drying the mixture.

BRIEF DESCRIPTION OF THE DRAWINGS

15 **Fig. 1** is a graph in which the plasma concentration of cyclosporine is plotted against the times after administrating the solid dispersed preparations of the present invention (closed rectangle and closed triangle) and a commercially available preparation (Neoral, closed
20 lozenge);

Fig. 2 is a graph in which the plasma concentration of aceclofenac is plotted against the times after orally administrating aceclofenac powder (closed circle) and the solid dispersed preparation of the present invention (open
25 circle, oleic acid 5%) to rats;

Fig. 3 is a graph in which the plasma concentration of cyclosporine is plotted against the times after

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