Patentability of Product Based on Dissolution Data

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5th Annual Intl. Conf.
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INDIA

June 08, 2017

Intellectual Property [IP]

Refers to creations of the mind which includes INVENTIONS

Two Categories –

- Industrial Property
- Copyright

There are several compelling reasons to **PROMOTE** and **PROTECT** IP through efficient and equitable IP System

1967: WIPO provided list of subject matter protected by IP rights

- SCIENTIFIC WORKS
- SCIENTIFIC DISCOVERIES

The pharmaceutical products including, but not limited to, formulations, processes, medical devices, diagnostic kits, etc., for example, **resulting from scientific works and discoveries have been protected by IP rights by issuance and grant of Patent to the generator (innovator) of IP**.

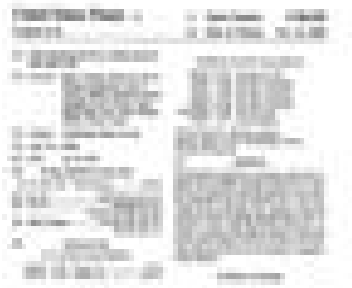
INTELLECTUAL PROPERTY [IP]

- Creation/Generation of NEW knowledge
- Novel
- Innovative

novelty + *innovation* → **PATENT**

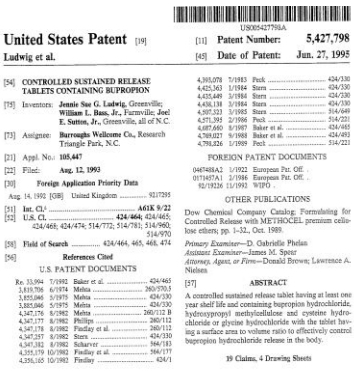
- Protection of IP --→ **PATENT**

!! IP → WORTH !!



US Patent 4,786,505 [*2007*]

PRILOSEC $ > 1.2B



United States Patent [19]
Ludwig et al.

US005427798A
[11] Patent Number: 5,427,798
[45] Date of Patent: Jun. 27, 1995

[54] CONTROLLED SUSTAINED RELEASE TABLETS CONTAINING BUPROPION

[75] Inventors: Jennie Sue G. Ludwig, Greenville; William L. Bass, Jr., Farmville; Joel E. Sutton, Jr., Greenville, all of N.C.

[73] Assignee: Burroughs Wellcome Co., Research Triangle Park, N.C.

[21] Appl. No.: 105,447

[22] Filed: Aug. 12, 1993

[30] Foreign Application Priority Data
Aug. 14, 1992 [GB] United Kingdom 9217295

[51] Int. Cl.[6] A61K 9/22
[52] U.S. Cl. 424/464; 424/465; 424/468; 424/474; 514/772; 514/781; 514/960; 514/970
[58] Field of Search 424/464, 465, 468, 474

[56] References Cited
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92/19226	11/1992	WIPO .

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Primary Examiner—D. Gabrielle Phelan
Assistant Examiner—James M. Spear
Attorney, Agent, or Firm—Donald Brown; Lawrence A. Nielsen

[57] ABSTRACT

A controlled sustained release tablet having at least one year shelf life and containing bupropion hydrochloride, hydroxypropyl methylcellulose and cysteine hydrochloride or glycine hydrochloride with the tablet having a surface area to volume ratio to effectively control bupropion hydrochloride release in the body.

19 Claims, 4 Drawing Sheets

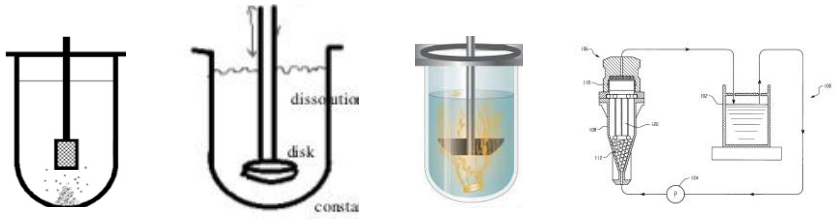
US Patent 5,427,798 [*2013*]

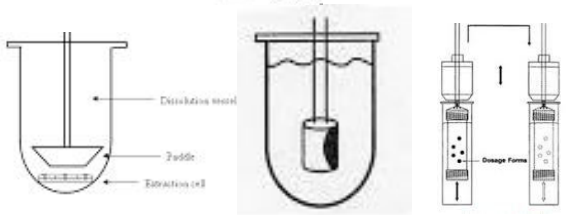
WELBUTRIN XR $ > 900M

US Patent 6,663,720 [*2020*]

LIALDA $ = 1B

PATENTABILITY





US006419960B1

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

(10) **Patent No.: US 6,419,960 B1**
(45) **Date of Patent: Jul. 16, 2002**

(54) **CONTROLLED RELEASE FORMULATIONS HAVING RAPID ONSET AND RAPID DECLINE OF EFFECTIVE PLASMA DRUG CONCENTRATIONS**

(75) Inventors: **Thinnayam N. Krishnamurthy**, Scarborough; **Andrew Darke**, Newmarket, both of (CA)

(73) Assignee: **Euro-Celtique S.A.**, Luxembourg (LU)

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

(21) Appl. No.: **09/465,159**

(22) Filed: **Dec. 16, 1999**

Related U.S. Application Data

(60) Provisional application No. 60/112,617, filed on Dec. 17, 1998.

(51) **Int. Cl.**[7] **A61K 9/16**; A61K 9/14; A61K 9/20; A61K 9/22; A61K 9/26

(52) **U.S. Cl.** **424/490**; 424/461; 424/464; 424/489; 424/490; 424/494; 424/468; 424/469

(58) **Field of Search** 424/461, 464, 424/484, 489, 490, 494, 468, 469

(56) **References Cited**

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WO	WO9703673	2/1997	..... A61K/31/445
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* cited by examiner

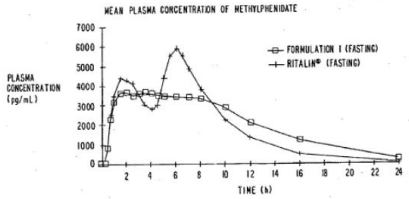
Primary Examiner—Thurman K. Page
Assistant Examiner—S. Tran
(74) *Attorney, Agent, or Firm*—Davidson, Davidson & Kappel, LLC

(57) **ABSTRACT**

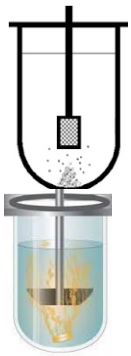
The invention is directed to oral modified/controlled release drug formulations which provide a rapid initial onset of effect and a prolonged duration of effect. Preferably, the peak concentration is lower than that provided by the reference standard for immediate release formulations of the drug, and the duration of effect falls rapidly at the end of the dosing interval.

18 Claims, 8 Drawing Sheets

MEAN PLASMA CONCENTRATION OF METHYLPHENIDATE



IVIVC



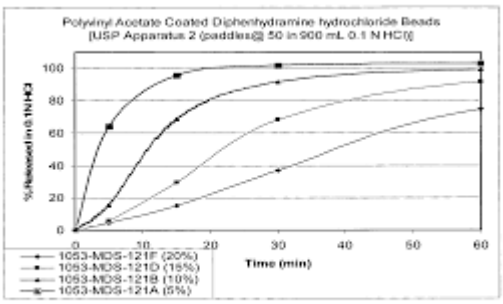
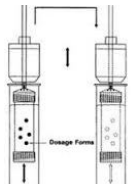
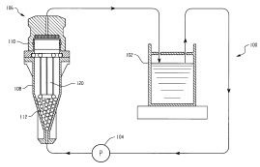
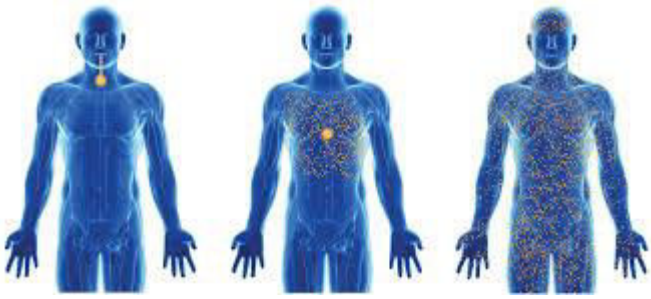
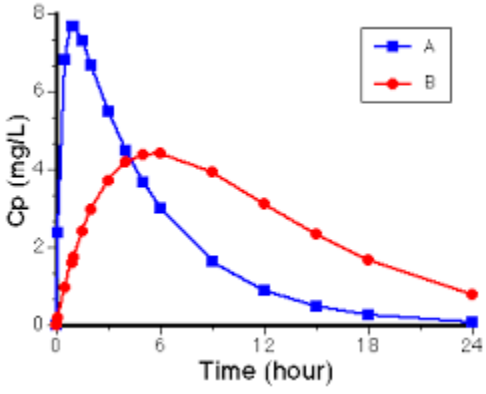

Polyvinyl Acetate Coated Diphenhydramine hydrochloride Beads
(USP Apparatus 2 (paddles)@ 50 in 900 mL 0.1 N HCl)
% Released in 0.1N HCl
100
80
60
40
20
0
0
10
20
30
40
50
60
Time (min)
1053-MDS-121F (20%)
1053-MDS-121D (15%)
1053-MDS-121B (10%)
1053-MDS-121A (5%)

FIG. 3








8
6
4
2
0
Cp (mg/L)
0
6
12
18
24
Time (hour)
A
B

IP ⟶ PATENT

- **NOVELTY**
- **INNOVATION**
- **(*non*)OBVIOUS**
- **(*non*)INHERENT**
- **OTHERS**

DISSOLUTION

The process by which a solid substance enters into the solvent to yield a solution. It is the process by which a solid substance dissolves.

PATENTS

An official document granting a right or privilege to an inventor for a term of years the only right to make, use or sell his or her invention

Terms/Terminology ….1

Novelty ----

First time ever …..

Innovation ----

First time for what is already known

Both are required to support a patent claim

Intellectual Property

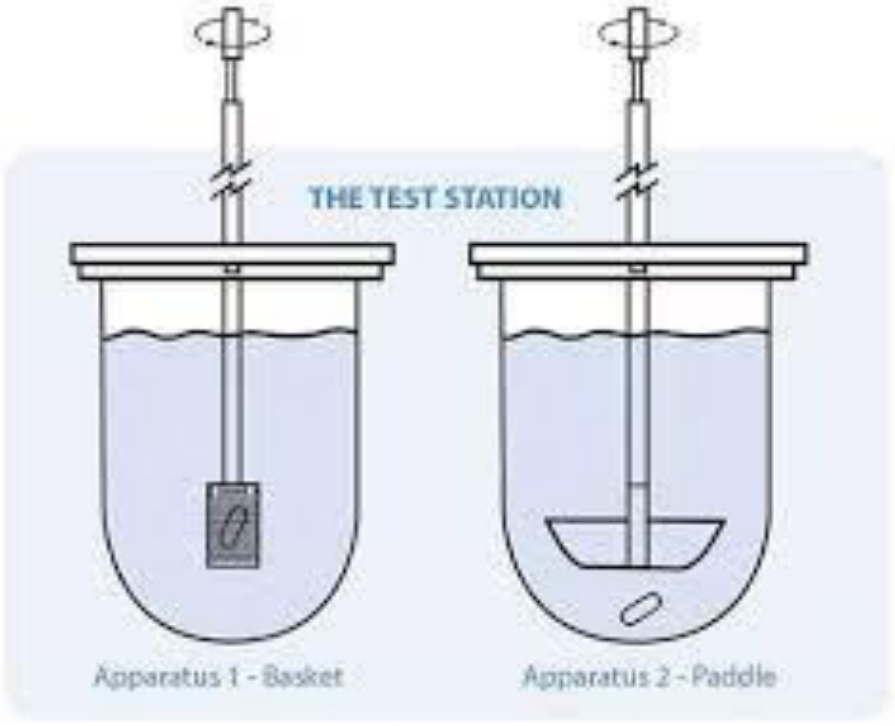
Claims !

Claims !!

CLAIMS !!!

CLAIMS !!!!

DISSOLUTION TESTING



Intellectual Property [IP]

US006344215B1

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

(10) **Patent No.: US 6,344,215 B1**
(45) **Date of Patent: Feb. 5, 2002**

(54) **METHYLPHENIDATE MODIFIED RELEASE FORMULATIONS**

(75) Inventors: **Marie J. Bettman**, Clayton; **Phillip J. Percel**, Troy; **Dan L. Hensley**, Huber Heights; **Krishna S. Vishnupad**; **Gopi M. Venkatesh**, both of Dayton, all of OH (US)

(73) Assignee: **Eurand America, Inc.**, Vandalia, OH (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.

(21) Appl. No.: **09/697,803**

(22) Filed: **Oct. 27, 2000**

(51) **Int. Cl.**[7] **A61K 9/56**; A61K 9/54; A61K 9/58; A61K 9/22; A61K 31/21

(52) **U.S. Cl.** **424/459**; 424/458; 424/462; 424/468; 424/457; 424/451

(58) **Field of Search** 424/451, 457, 424/458, 459, 462, 468

(56) **References Cited**

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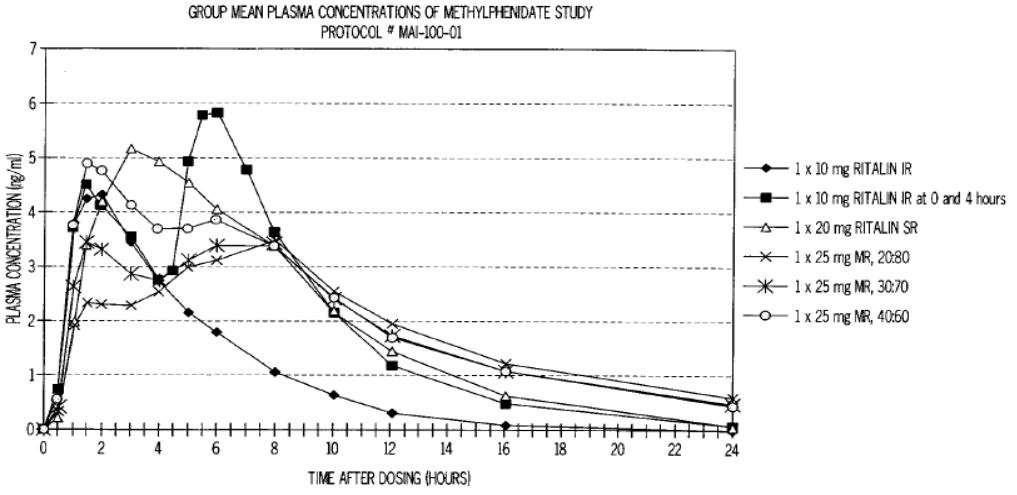
Primary Examiner—Thurman K. Page
Assistant Examiner—Rachel M. Bennett
(74) *Attorney, Agent, or Firm*—Thompson Hine LLP

(57) **ABSTRACT**

A pharmaceutical MR (modified release) multiparticulate dosage form such as a capsule (once-a-day MR Capsule) of Methylphenidate indicated for the treatment of children with attention deficit hyperactivity disorder (ADHD), capable of delivering a portion of the dose for rapid onset of action and the remainder of the dose in a controlled manner for about 12 hours, is composed of a multitude of multicoated particles made of two populations of drug layered beads, IR (immediate release) and ER (extended release) Beads. The IR beads preferably are made by layering an aqueous solution comprising a drug and a binder on to non-pareil sugar spheres and then applying a seal coat to the drug coated cores. The ER Beads are made by applying an extended release coating of a water insoluble dissolution rate controlling polymer such as ethylcellulose to IR Beads. The MR Capsules are manufactured by filling IR and ER Beads in a proper ratio; the dose and the ratio required for an efficacious, cost effective and patient compliant treatment of children with ADHD were determined from extensive clinical investigations and in vitro- in vivo correlations performed as per FDA Guidelines, Guidance for Industry: Extended Release Oral Dosage Forms.

9 Claims, 4 Drawing Sheets



API [Sugar Cube]

US007682628B2

(12) **United States Patent**
Singh

(10) **Patent No.: US 7,682,628 B2**
(45) **Date of Patent: *Mar. 23, 2010**

(54) **COMPOSITIONS FOR DELIVERING HYPNOTIC AGENTS ACROSS THE ORAL MUCOSA AND METHODS OF USE THEREOF**

(75) Inventor: **Nikhilesh N. Singh**, Mill Valley, CA (US)

(73) Assignee: **Transcept Pharmaceuticals, Inc.**, Pt. Richmond, CA (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.: **11/833,323**

(22) Filed: **Aug. 3, 2007**

(65) **Prior Publication Data**

US 2008/0008753 A1 Jan. 10, 2008

4,405,647 A 9/1983 Fisher et al.
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(Continued)

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WO WO 99/16417 4/1999

(Continued)

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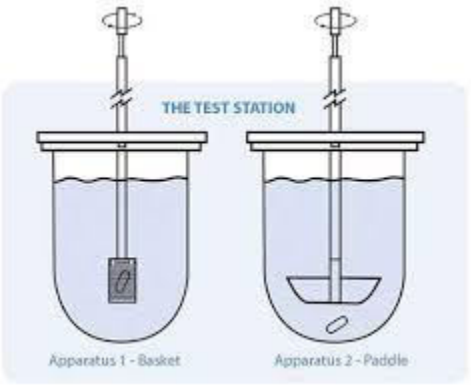
(Continued)

Primary Examiner—Humera N Sheikh
(74) *Attorney, Agent, or Firm*—O'Melveny & Myers LLP

(57) **ABSTRACT**



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(Continued)

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(Continued)

Primary Examiner—Humera N Sheikh
(74) *Attorney, Agent, or Firm*—O'Melveny & Myers LLP

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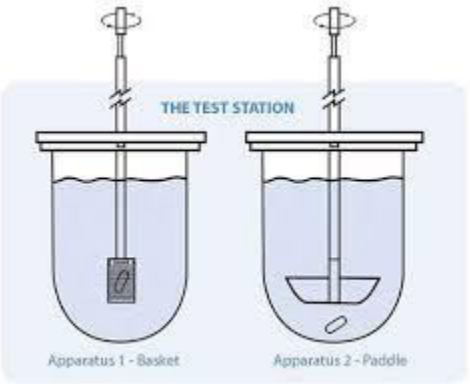

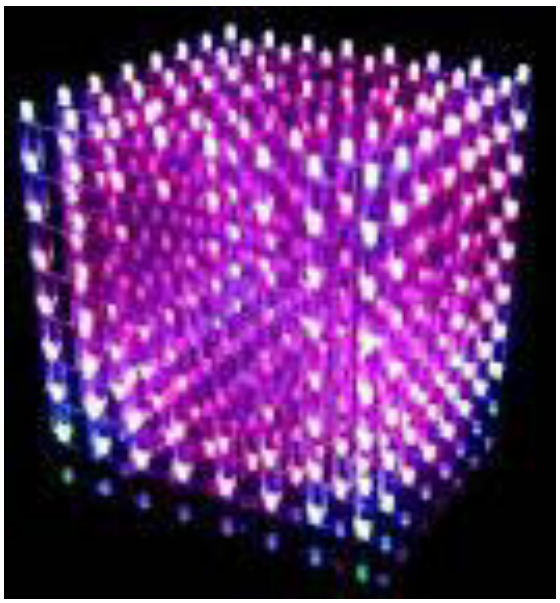

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(Continued)

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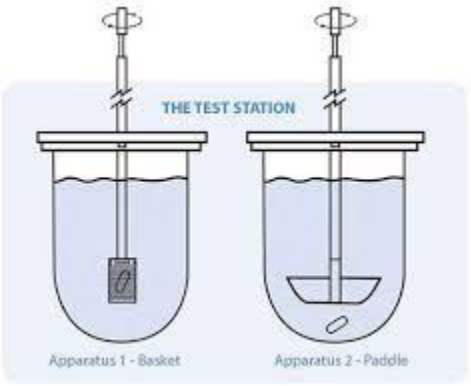
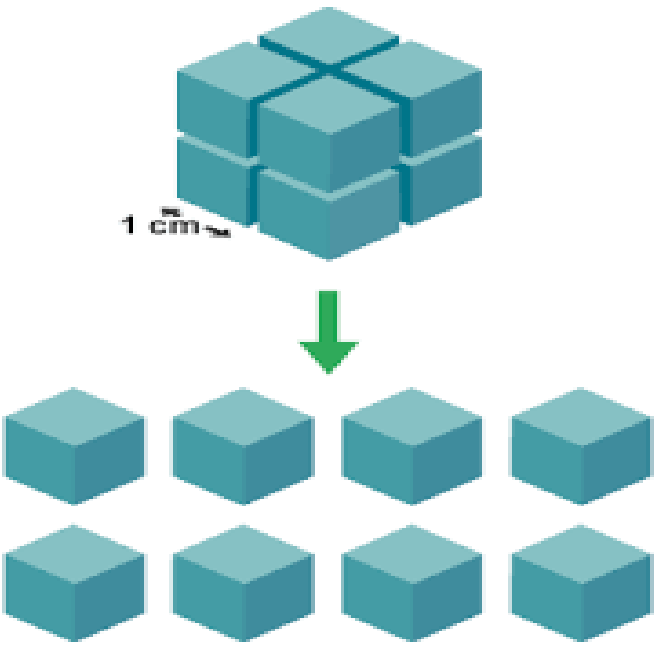
(Continued)

Primary Examiner—Humera N Sheikh
(74) *Attorney, Agent, or Firm*—O'Melveny & Myers LLP

(57) **ABSTRACT**





US007682628B2

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(Continued)

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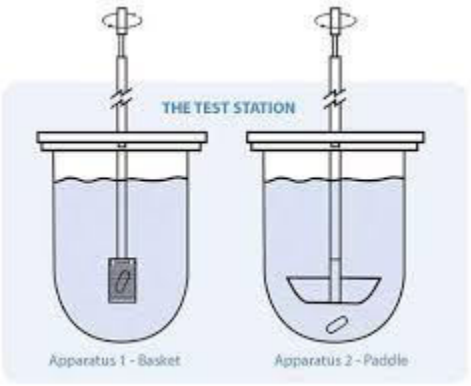
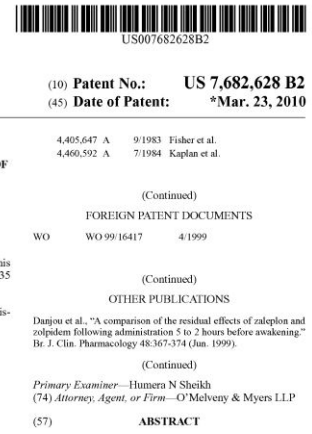
(57) **ABSTRACT**



API DISSOLVED IN DISSOLUTION MEDIUM !!!



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4,460,592 A 7/1984 Kaplan et al.

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(Continued)

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(Continued)

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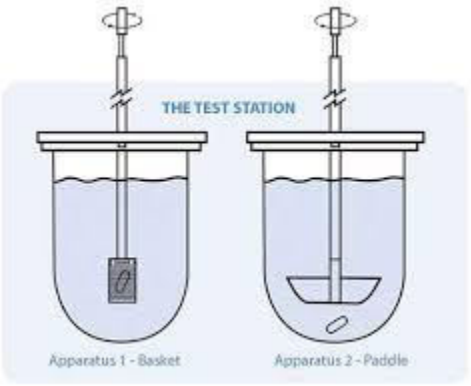
(74) *Attorney, Agent, or Firm*—O'Melveny & Myers LLP

(57) **ABSTRACT**



NOVELTY

INNOVATION

!! INHERENCY !!

IN VITRO DISSOLUTION

!! INHERENT !!

NON PATENTABLE !!

C_{max} Food Effect

Claim language

77. "…wherein upon oral administration of a single dose of the composition to a human subject, the composition provides an oxymorphone C_{max} of at least 50% higher when the dose is administered to the subject under fed as compared to fasted conditions…"

C_{max} Food Effect

Federal Circuit found food effects to be inherent

"Maloney's express teachings render the claimed controlled release oxymorphone formulations obvious, and the claimed 'food effect' adds nothing of patentable consequence"

AUC Food Effect

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PHARMACEUTICAL FORMULATION

API + EXCIPIENTS

Process

PHARMACEUTICAL DOSAGE FORM

DOSAGE FORM

IN VITRO DISSOLUTION OF API FROM DOSAGE FORM

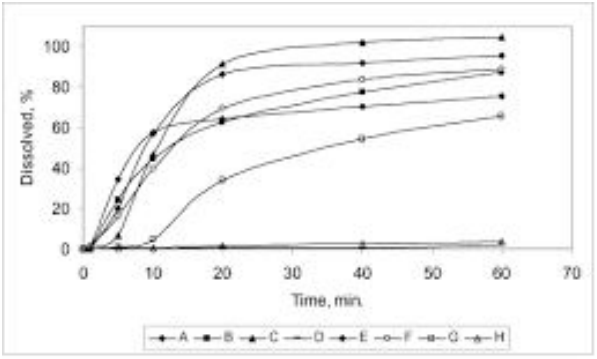


Figure 1 - Dissolution profile of chloramphenicol palmitate obtained from products A, B, C, D, E, F, G and H, for each time interval, in HCl 0.01 N environment. *"Each data point represents the mean of 12 units.*

Q%/T1 ⎫
Q%/T2 ⎬ NOVELTY
Q%/T3 ⎭ ***!! PATENTABLE !!***

US PATENT 6,344,215

1. A **modified release methylphenidate hydrochloride capsule** comprising immediate release (IR) and extended release (ER) methylphenidate-containing beads …… and when the immediate release and the extended release beads are mixed in the amounts shown in the following table and **tested using USP apparatus 2 at 50 rpm in 500 ml Water**, the mixed beads release methylphenidate approximately in the percentages shown in the following table based on the total methylphenidate:

US PATENT 6,344,215

Time, hours	(20 IR/80 ER Beads)	(30 IR/70 ER Beads)	(40 IR/60 ER Beads)	(30 IR/70 ER Beads)	(40 IR/60 ER Beads)
0.0	0.0	0.0	0.0	0.0	0.0
1.0	24.5%	31.6%	42.1%	33.4%	41.3%
2.0	29.8%	37.4%	48.3%	44.9%	50.9%
4.0	57.8%	59.0%	66.3%	66.2%	69.6%
8.0	79.2%	76.3%	83.5%	87.1%	89.2%
12.0	89.1%	84.6%	88.2%	97.1%	98.0%

US PATENT 7,682,268

1. A method for treating insomnia, comprising the steps of: administering a **solid pharmaceutical composition** comprising zolpidem or a pharmaceutically acceptable salt thereof to a subject prone to insomnia, the pharmaceutical composition further comprising a buffer,
wherein the **buffer raises the pH of saliva to a pH of about 7.8** or greater,
wherein zolpidem is absorbed across a permeable membrane of the subject's oral mucosa, and
wherein **at least 75% of the solid pharmaceutical composition dissolved within about 10 minutes** or less within an oral cavity following administration.

US PATENT 7,682,628

The compositions tested were as follows:

1. Zolpidem quick-dissolving tablet (typically dissolves sublingually in about 5 minutes).

2. Zolpidem lozenge (typically dissolves sublingually in about 2-3 minutes).

The experimental conditions were as follows:

Method=USP

Apparatus=USP Apparatus II

Medium=Phosphate Buffer pH 6.8

Volume of the Medium=500 ml

Spindle Speed=25 rpm

Temperature=37° C.

Table 5 below shows the dissolution data and FIG. **2** shows the mean dissolution profiles for a zolpidem quick-dissolving tablet and zolpidem lozenge of the present invention at 5, 10, 15, 20, and 30 minutes in phosphate buffered medium (pH 6.8).

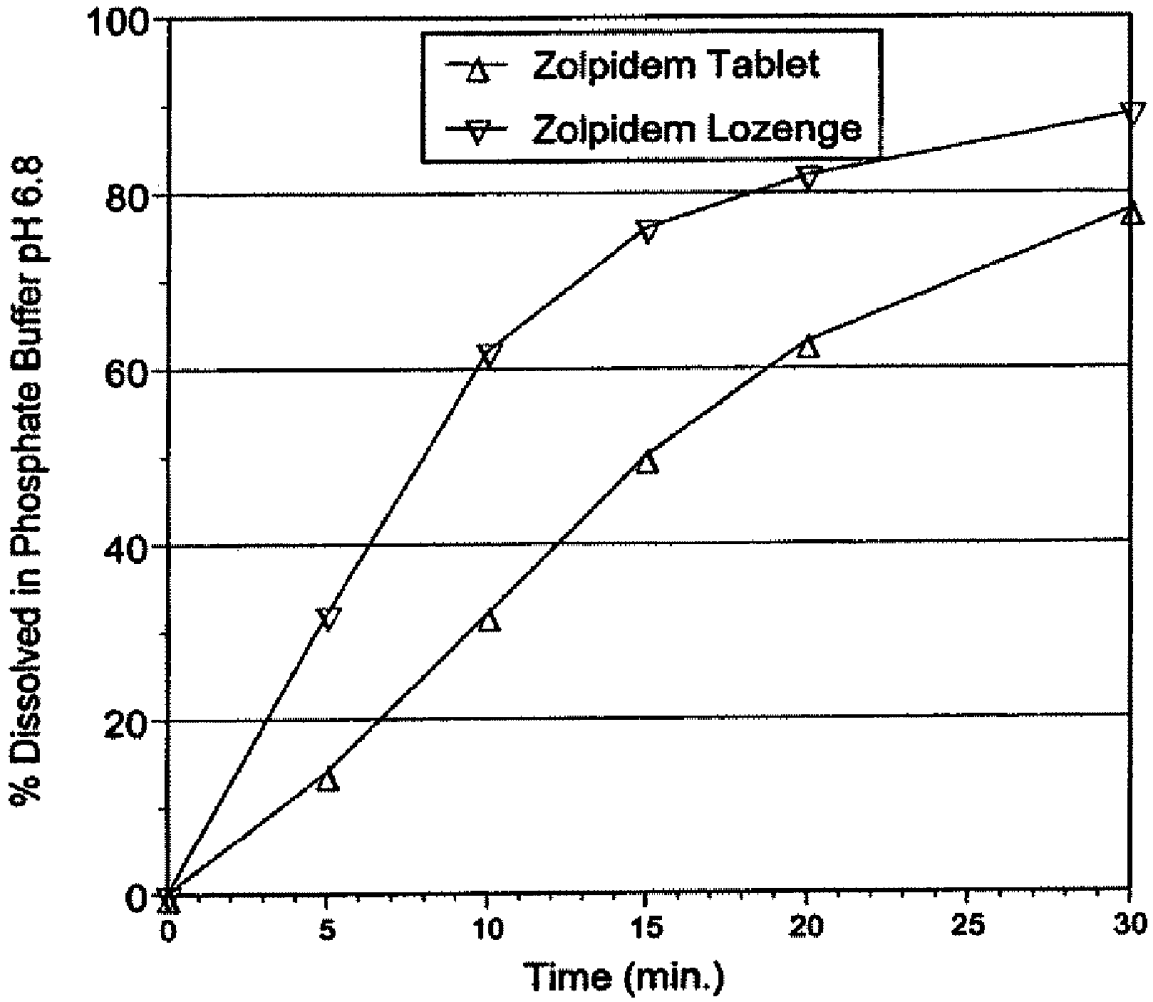
TABLE 5

Dissolution data for the zolpidem quick-dissolving tablet and zolpidem lozenge.

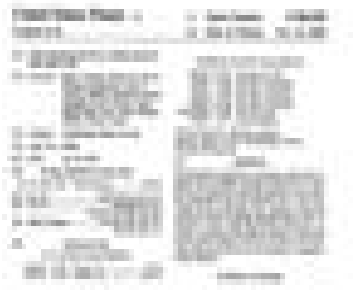
Time (Min.)	Quick-Dissolving Tablet (% Dissolved, RSD[1])	Lozenge (% Dissolved, RSD[1])
5	14.3, 17.7	32.4, 16.2
10	32.8, 14.8	61.7, 8.6
15	50.1, 14.6	75.7, 4.9
20	63, 15.9	82.1, 4.6
30	85.2, 7.9	88.6, 2.8

[1]RSD = Relative Standard Deviation

US PATENT 7,682,628



!! WORTH OF IP !!



US Patent 4,786,505 [*2007*]

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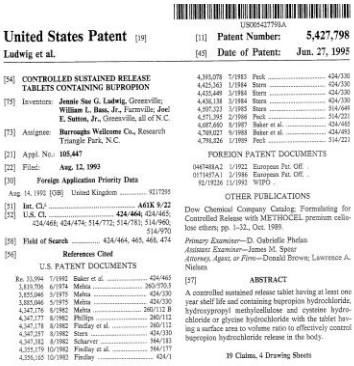

United States Patent [19]

Ludwig et al.

[11] Patent Number: 5,427,798

[45] Date of Patent: Jun. 27, 1995

[54] CONTROLLED SUSTAINED RELEASE TABLETS CONTAINING BUPROPION

US Patent 5,427,798 [*2013*]

WELBUTRIN XR $ > 900M

US Patent 6,663,720 [*2020*]

LIALDA $ = 1B

THANK YOU

DHANYAWAAD !!

धन्यवाद

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Please ….

- ***Only easy/simple questions that I can answer !!!!***

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