



US009060976B2

(12) **United States Patent**  
**Wright et al.**(10) **Patent No.:** **US 9,060,976 B2**  
(45) **Date of Patent:** **Jun. 23, 2015**

- (54) **PHARMACEUTICAL FORMULATION CONTAINING GELLING AGENT**
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- (\* ) 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.: **13/726,324**
- (22) Filed: **Dec. 24, 2012**
- (65) **Prior Publication Data**  
US 2013/0217716 A1 Aug. 22, 2013

3,133,132 A 5/1964 Loeb et al.  
3,173,876 A 3/1965 Zobrist et al.  
3,260,646 A 7/1966 Paulsen et al.  
3,276,586 A 10/1966 Rosaen  
3,541,005 A 11/1970 Strathmann et al.  
3,541,006 A 11/1970 Bixler et al.  
3,546,876 A 12/1970 Fokker et al.  
3,845,770 A 11/1974 Theeuwes et al.  
3,916,889 A 11/1975 Russell  
3,965,256 A 6/1976 Leslie  
3,980,766 A 9/1976 Shaw et al.  
4,063,064 A 12/1977 Saunders et al.  
4,070,494 A 1/1978 Hoffmeister et al.  
4,088,864 A 5/1978 Theeuwes et al.  
4,160,020 A 7/1979 Ayer et al.  
4,175,119 A 11/1979 Porter  
4,200,098 A 4/1980 Ayer et al.  
4,235,870 A 11/1980 Leslie  
4,285,987 A 8/1981 Ayer et al.  
4,293,539 A 10/1981 Ludwig et al.  
4,366,310 A 12/1982 Leslie  
4,385,057 A 5/1983 Bjork et al.  
4,389,393 A 6/1983 Schor et al.  
4,424,205 A 1/1984 LaHann et al.  
4,443,428 A 4/1984 Oshlack et al.  
4,457,933 A 7/1984 Gordon et al.  
4,459,278 A 7/1984 Porter  
4,588,580 A 5/1986 Gale et al.  
4,599,342 A 7/1986 LaHann

(Continued)

**Related U.S. Application Data**

- (63) Continuation of application No. 13/349,449, filed on Jan. 12, 2012, now Pat. No. 8,337,888, which is a continuation of application No. 12/653,115, filed on Dec. 8, 2009, now abandoned, which is a continuation of application No. 10/214,412, filed on Aug. 6, 2002.
- (60) Provisional application No. 60/310,534, filed on Aug. 6, 2001.
- (51) **Int. Cl.**  
*A61K 31/439* (2006.01)  
*A61K 31/485* (2006.01)  
*A61K 31/167* (2006.01)  
*A61K 9/20* (2006.01)  
*A61K 9/00* (2006.01)  
*A61K 47/38* (2006.01)  
*A61K 47/36* (2006.01)  
*A61K 47/10* (2006.01)  
*A61K 45/06* (2006.01)
- (52) **U.S. Cl.**  
CPC ..... *A61K 31/167* (2013.01); *A61K 9/2013* (2013.01); *A61K 9/205* (2013.01); *A61K 9/2054* (2013.01); *A61K 9/0002* (2013.01); *A61K 31/439* (2013.01); *A61K 31/485* (2013.01); *A61K 47/38* (2013.01); *A61K 47/36* (2013.01); *A61K 47/10* (2013.01); *A61K 45/06* (2013.01)
- (58) **Field of Classification Search**  
None  
See application file for complete search history.

- (56)
- References Cited**

## U.S. PATENT DOCUMENTS

3,065,143 A 11/1962 Christenson et al.

## FOREIGN PATENT DOCUMENTS

EP 0318262 A1 5/1989  
EP 0661045 7/1995

(Continued)

## OTHER PUBLICATIONS

Moroni, et al., "Application of Poly(oxyethylene) Homopolymers in Sustained Release Solid Formulations", Drug Dev. and Indus. Pharmacy, 21(12), 1411-28 (1995).

Apicella, et al., "Poly(ethylene oxide) (PEO) Constant Release Monolithic Devices," Polymers in Medicine: Biomedical and Pharmaceutical Applications, Chapter 3 (1992).

(Continued)

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- (57)
- ABSTRACT**

Disclosed in certain embodiments is a controlled release oral dosage form comprising a therapeutically effective amount of a drug susceptible to abuse together with one or more pharmaceutically acceptable excipients; the dosage form further including a gelling agent in an effective amount to impart a viscosity unsuitable for administration selected from the group consisting of parenteral and nasal administration to a solubilized mixture formed when the dosage form is crushed and mixed with from about 0.5 to about 10 ml of an aqueous liquid; the dosage form providing a therapeutic effect for at least about 12 hours when orally administered to a human patient.

**1 Claim, No Drawings**

(56)

References Cited

U.S. PATENT DOCUMENTS

4,610,870 A	9/1986	Jain et al.	5,730,716 A	3/1998	Beck et al.	
4,612,008 A	9/1986	Wong et al.	5,741,524 A	4/1998	Staniforth et al.	
4,666,705 A	5/1987	DeCrosta et al.	5,762,963 A	6/1998	Byas-Smith	
4,764,378 A	8/1988	Keith et al.	5,843,480 A	12/1998	Miller et al.	
4,765,989 A	8/1988	Wong et al.	5,849,240 A *	12/1998	Miller et al. ....	264/460
4,769,372 A	9/1988	Kreek	5,866,164 A	2/1999	Kuczynski et al.	
4,785,000 A	11/1988	Kreek et al.	5,879,705 A	3/1999	Heafield et al.	
4,806,341 A	2/1989	Chien et al.	5,891,471 A *	4/1999	Miller et al. ....	424/468
4,812,446 A	3/1989	Brand	5,891,919 A	4/1999	Blum et al.	
4,834,984 A	5/1989	Goldie et al.	5,914,131 A	6/1999	Merrill et al.	
4,844,909 A	7/1989	Goldie et al.	5,958,452 A	9/1999	Oshlack et al.	
4,861,598 A	8/1989	Oshlack	5,958,459 A	9/1999	Chasin et al.	
4,957,681 A	9/1990	Klimesch et al.	5,965,161 A	10/1999	Oshlack et al.	
4,970,075 A	11/1990	Oshlack	5,965,163 A *	10/1999	Miller et al. ....	424/468
4,990,341 A	2/1991	Goldie et al.	5,968,551 A	10/1999	Oshlack et al.	
5,026,556 A	6/1991	Drust et al.	6,024,982 A	2/2000	Oshlack et al.	
5,059,600 A	10/1991	Gawin et al.	6,120,751 A	9/2000	Unger	
5,069,909 A	12/1991	Sharma et al.	6,124,282 A	9/2000	Sellers et al.	
5,111,942 A	5/1992	Bernardin	6,136,864 A	10/2000	Nichols et al.	
5,114,942 A	5/1992	Gawin et al.	6,143,322 A	11/2000	Sackler et al.	
5,130,311 A	7/1992	Guillaumet et al.	6,153,621 A	11/2000	Hamann	
5,149,538 A	9/1992	Granger et al.	6,162,467 A *	12/2000	Miller et al. ....	424/468
5,169,645 A	12/1992	Shukla et al.	6,223,075 B1	4/2001	Beck et al.	
5,202,128 A	4/1993	Morella et al.	6,228,863 B1	5/2001	Palermo et al.	
5,215,758 A	6/1993	Krishnamurthy	6,245,357 B1	6/2001	Edgren et al.	
5,225,199 A	7/1993	Hidaka et al.	6,277,398 B1	8/2001	Caruso	
5,232,934 A	8/1993	Downs	6,294,194 B1	9/2001	Horhota et al.	
5,240,711 A	8/1993	Hille et al.	6,309,668 B1	10/2001	Bastin et al.	
5,266,331 A	11/1993	Oshlack et al.	6,348,469 B1 *	2/2002	Seth .....	514/254.02
5,273,758 A	12/1993	Royce	6,352,721 B1	3/2002	Faour	
5,273,760 A	12/1993	Oshlack et al.	6,375,957 B1 *	4/2002	Kaiko et al. ....	424/400
5,286,493 A	2/1994	Oshlack et al.	6,403,056 B1	6/2002	Unger	
5,290,816 A	3/1994	Blumberg	6,419,954 B1	7/2002	Chu	
5,321,012 A	6/1994	Mayer et al.	6,436,441 B1	8/2002	Sako et al.	
5,324,351 A	6/1994	Oshlack et al.	6,440,464 B1	8/2002	Hsia et al.	
5,330,766 A	7/1994	Morella et al.	6,488,963 B1	12/2002	McGinity	
5,356,467 A	10/1994	Oshlack et al.	6,491,949 B2	12/2002	Faour et al.	
5,368,852 A	11/1994	Umemoto et al.	6,559,159 B2	5/2003	Carroll et al.	
5,376,705 A	12/1994	Leys et al.	6,572,885 B2	6/2003	Oshlack et al.	
5,378,474 A	1/1995	Morella et al.	6,593,367 B1	7/2003	Dewey et al.	
5,403,868 A	4/1995	Reid et al.	6,627,635 B2	9/2003	Palermo et al.	
5,409,944 A	4/1995	Black et al.	6,696,088 B2	2/2004	Oshlack et al.	
5,411,745 A	5/1995	Oshlack et al.	6,733,783 B2	5/2004	Oshlack et al.	
5,422,123 A	6/1995	Conte et al.	6,808,720 B2	10/2004	Unger	
5,436,265 A	7/1995	Black et al.	6,995,169 B2	2/2006	Chapleo et al.	
5,472,712 A	12/1995	Oshlack et al.	7,141,250 B2	11/2006	Oshlack et al.	
5,472,943 A	12/1995	Crain et al.	7,144,587 B2	12/2006	Oshlack et al.	
5,474,995 A	12/1995	Ducharme et al.	7,157,103 B2	1/2007	Sackler	
5,478,577 A	12/1995	Sackler et al.	7,201,920 B2	4/2007	Kumar et al.	
5,500,227 A	3/1996	Oshlack et al.	7,332,182 B2	2/2008	Sackler	
5,502,058 A	3/1996	Mayer et al.	7,727,557 B2	6/2010	Sackler	
5,505,959 A	4/1996	Tachon et al.	7,776,314 B2	8/2010	Bartholomaeus et al.	
5,508,042 A	4/1996	Oshlack et al.	7,842,307 B2 *	11/2010	Oshlack et al. ....	424/450
5,510,368 A	4/1996	Lau et al.	7,943,174 B2	5/2011	Oshlack et al.	
5,514,680 A	5/1996	Weber et al.	8,017,148 B2	9/2011	Sackler	
5,521,213 A	5/1996	Prasit et al.	8,075,872 B2	12/2011	Arkenau-Maric	
5,536,752 A	7/1996	Ducharme et al.	8,101,630 B2	1/2012	Kumar et al.	
5,549,912 A	8/1996	Oshlack et al.	8,114,383 B2	2/2012	Bartholomaeus	
5,550,142 A	8/1996	Ducharme et al.	8,114,384 B2	2/2012	Arkenau	
5,552,422 A	9/1996	Gauthier et al.	8,192,722 B2	6/2012	Arkenau-Maric	
5,556,838 A	9/1996	Mayer et al.	8,309,060 B2	11/2012	Bartholomaeus et al.	
5,580,578 A	12/1996	Oshlack et al.	8,337,888 B2	12/2012	Wright et al.	
5,593,695 A	1/1997	Merrill et al.	8,377,453 B2 *	2/2013	Han et al. ....	424/400
5,593,994 A	1/1997	Batt et al.	8,389,007 B2	3/2013	Wright et al.	
5,604,253 A	2/1997	Lau et al.	8,524,275 B2	9/2013	Oshlack et al.	
5,604,260 A	2/1997	Guay et al.	8,529,948 B1	9/2013	Wright et al.	
5,616,601 A	4/1997	Khanna et al.	8,609,683 B2	12/2013	Wright et al.	
5,639,476 A	6/1997	Oshlack et al.	8,652,497 B2	2/2014	Sackler	
5,639,780 A	6/1997	Lau et al.	8,652,515 B2	2/2014	Sackler	
5,656,295 A	8/1997	Oshlack et al.	8,871,265 B2	10/2014	Wright et al.	
5,667,805 A	9/1997	Merrill et al.	2003/0004177 A1 *	1/2003	Kao et al. ....	514/282
5,672,360 A	9/1997	Sackler et al.	2003/0021841 A1	1/2003	Matharu et al.	
5,679,650 A	10/1997	Fukunaga et al.	2003/0026838 A1	2/2003	Farrell	
5,681,585 A	10/1997	Oshlack et al.	2003/0035839 A1	2/2003	Hirsh et al.	
5,695,781 A	12/1997	Zhang et al.	2003/0054027 A1	3/2003	Unger	
			2003/0059471 A1	3/2003	Compton et al.	
			2003/0064099 A1	4/2003	Oshlack et al.	
			2003/0064122 A1	4/2003	Goldberg et al.	
			2003/0068276 A1	4/2003	Hughes et al.	

(56)

References Cited

U.S. PATENT DOCUMENTS

2003/0068370 A1 4/2003 Sackler  
 2003/0068371 A1 4/2003 Oshlack et al.  
 2003/0068375 A1\* 4/2003 Wright et al. .... 424/468  
 2003/0068392 A1 4/2003 Sackler  
 2003/0082230 A1 5/2003 Baichwal et al.  
 2003/0124061 A1 7/2003 Roberts  
 2003/0124185 A1 7/2003 Oshlack et al.  
 2003/0125347 A1 7/2003 Anderson et al.  
 2003/0126428 A1 7/2003 Liu et al.  
 2003/0170181 A1 9/2003 Midha  
 2003/0232081 A1 12/2003 Doshl et al.  
 2004/0047907 A1 3/2004 Oshlack et al.  
 2004/0126428 A1 7/2004 Hughes et al.  
 2004/0131552 A1 7/2004 Boehm  
 2004/0151791 A1 8/2004 Mayo-Alvarez et al.  
 2004/0224020 A1 11/2004 Schoenhard  
 2004/0228802 A1 11/2004 Chang et al.  
 2004/0241234 A1 12/2004 Vilkov  
 2004/0253310 A1\* 12/2004 Fischer et al. .... 424/472  
 2004/0266807 A1 12/2004 Oshlack et al.  
 2005/0020613 A1 1/2005 Boehm et al.  
 2005/0031546 A1 2/2005 Bartholomaeus et al.  
 2005/0063909 A1 3/2005 Wright et al.  
 2005/0106249 A1 5/2005 Hwang et al.  
 2005/0112067 A1 5/2005 Kumar et al.  
 2005/0112201 A1 5/2005 Baichwal et al.  
 2005/0118267 A1 6/2005 Baichwal et al.  
 2005/0158382 A1\* 7/2005 Cruz et al. .... 424/468  
 2005/0163717 A1 7/2005 Anderson et al.  
 2005/0186139 A1 8/2005 Bartholomaeus  
 2005/0214223 A1 9/2005 Bartholomaeus et al.  
 2005/0236741 A1 10/2005 Arkenau et al.  
 2005/0276853 A1 12/2005 Baichwal et al.  
 2006/0002860 A1 1/2006 Bartholomaeus  
 2006/0018837 A1 1/2006 Preston et al.  
 2006/0039864 A1 2/2006 Bartholomaeus  
 2006/0165790 A1\* 7/2006 Walden et al. .... 424/468  
 2006/0188447 A1 8/2006 Arkenau-Maric  
 2006/0193782 A1 8/2006 Bartholomaeus  
 2006/0251721 A1\* 11/2006 Cruz et al. .... 424/468  
 2007/0003616 A1 1/2007 Arkenau-Maric  
 2007/0003617 A1\* 1/2007 Fischer et al. .... 424/468  
 2007/0110807 A1 5/2007 Vergnault et al.  
 2007/0166234 A1 7/2007 Kumar et al.  
 2007/0202049 A1\* 8/2007 Guimberteau et al. .... 424/10.2  
 2007/0264327 A1 11/2007 Kumar et al.  
 2008/0008659 A1\* 1/2008 Guimberteau et al. .... 424/10.1  
 2008/0063725 A1\* 3/2008 Guimberteau et al. .... 424/492  
 2008/0095843 A1 4/2008 Nutalapati et al.  
 2008/0176955 A1 7/2008 Heck et al.  
 2008/0254123 A1\* 10/2008 Fischer et al. .... 424/486  
 2008/0260815 A1\* 10/2008 Hayes et al. .... 424/455  
 2009/0004267 A1\* 1/2009 Arkenau-Maric et al. .... 424/465  
 2009/0011016 A1\* 1/2009 Cailly-Dufestel et al. .... 424/465  
 2009/0081290 A1\* 3/2009 McKenna et al. .... 424/468  
 2009/0169587 A1 7/2009 Baichwal et al.  
 2009/0215808 A1 8/2009 Yum et al.  
 2010/0015222 A1\* 1/2010 Han et al. .... 424/468  
 2010/0015223 A1\* 1/2010 Cailly-Dufestel et al. .... 424/472  
 2010/0221293 A1 9/2010 Cruz et al.  
 2011/0262532 A1 10/2011 Oshlack et al.  
 2012/0164220 A1 6/2012 Huang

FOREIGN PATENT DOCUMENTS

EP 1293195 A1 3/2003  
 WO 01/07950 6/1991  
 WO 93/10765 5/1993  
 WO 95/20947 8/1995  
 WO WO-95/20947 A1 8/1995  
 WO 97/37689 10/1997  
 WO 97/48385 12/1997  
 WO 97/49384 12/1997  
 WO 99/32120 7/1999

WO WO-99/32119 A1 7/1999  
 WO 00/33835 6/2000  
 WO WO-01/58447 A1 8/2001  
 WO 2002/087558 11/2002  
 WO WO-02/094254 A2 11/2002  
 WO WO-03/015531 A2 2/2003  
 WO 2003/024430 3/2003  
 WO WO-03/026743 A2 4/2003  
 WO 2003/035029 5/2003  
 WO WO-03/092676 A1 11/2003  
 WO WO-2004/026256 A2 1/2004  
 WO WO-2004/026283 A1 4/2004  
 WO WO-2004/037259 A1 5/2004  
 WO WO-2005/053587 A1 6/2005  
 WO 2010078486 7/2010

OTHER PUBLICATIONS

Apicella, et al., "Poly(ethylene oxide)-Based Delivery Systems", Polymeric Drugs and Drug Administration, ACS Symposium Series 545, Chapter 9 (1994).  
 Zhang, F, et al., "Properties of Sustained-Release Tablets Prepared by Hot-Melt Extrusion", Pharmaceutical Development and Technology, vol. 4, No. 2, p. 241-250 (1999).  
 Maggi, L., et al., "Dissolution Behaviour of Hydrophilic Matrix Tablets Containing Two Different Polyethylene Oxides (PEOs) for the Controlled Release of a Water-Soluble Drug", Biomaterials, vol. 23, p. 1113-1119 (2002).  
 The 1997 Physician's Desk Reference ("PDR") entry for Oxycontin ®.  
 Paragraph IV Patent Certification Notice for ANDA 202455 (2013). Complaint 1:13-cv-04606 (Jul. 2, 2013).  
 Paragraph IV Patent Certification Notice for ANDA 202434 (2011).  
 Paragraph IV Patent Certification Notice for ANDA 203235 (2011).  
 Paragraph IV Patent Certification Notice for ANDA 202372 (2011).  
 Paragraph IV Patent Certification Notice for ANDA 202483 (2011).  
 Paragraph IV Patent Certification Notice for ANDA 202762 (2011).  
 Paragraph IV Patent Certification Notice for Amendment to ANDA 202762 (2011).  
 Paragraph IV Patent Certification Notice for ANDA 202455 (2011).  
 Paragraph IV Patent Certification Notice for ANDA 202352 (2011).  
 Woodburn, K.R., et al., "Vascular Complications of Injecting Drug Misuse", British Journal of Surgery, 1996, vol. 83, p. 1329-1334.  
 Kim, C., "Drug Release from Compressed Hydrophilic POLYOX-WSR Tablets", Journal of Pharmaceutical Sciences, vol. 84, No. 3, Mar. 1995, p. 303-306.  
 Apicella, A., "Poly(ethylene oxide) (PEO) and Different Molecular Weight PEO Blends Monolithic Devices for Drug Release", Biomaterials, vol. 14, No. 2, 1993, p. 83-90.  
 Deighan, C.J., et al., "Rhabdomyolysis and Acute Renal Failure Resulting From Alcohol and Drug Abuse", QJ Med, vol. 93, 2000, p. 29-33.  
 Kalant, H., et al., "Death in Amphetamine Users: Causes and Rates", CMA Journal, vol. 112, Feb. 8, 1975, p. 299-304.  
 U.S. Pharmacopeia, p. 2206, 1995.  
 Complaint 1:13-cv-01272-SHS (Feb. 25, 2013).  
 Answer and Counterclaims 1:13-cv-01272-SHS (Mar. 8, 2013).  
 Answer to Counterclaims 1:13-cv-01272-SHS (Apr. 1, 2013).  
 Consent Judgement :13-cv-01272-SHS (May 1, 2013).  
 Complaint 1:13-cv-03188-SHS (May 10, 2013).  
 Answer; Affirmative Defenses and Counterclaims 1:13-cv-03188-SHS (Jun. 7, 2013).  
 Complaint 1:13-cv-03374-SHS (May 17, 2013).  
 Answer and Counterclaims 1:13-cv-03374-SHS (Jun. 3, 2013).  
 Complaint 1:13-cv-03372-SHS (May 17, 2013).  
 Written Opinion and International Search Report for International Patent Application No. PCT/IB2011/003152 issued Sep. 19, 2012.  
 U.S. Appl. No. 13/333,560—Non-Final Rejection dated Jan. 29, 2013.  
 U.S. Appl. No. 13/333,560—Amendment/Response dated Apr. 29, 2013.  
 Paragraph IV Patent Certification Notice for ANDA 202352 (2013).  
 Paragraph IV Patent Certification Notice for ANDA 202372 (2013).  
 Paragraph IV Patent Certification Notice for ANDA 202434 (2013).

(56)

**References Cited**

## OTHER PUBLICATIONS

Paragraph IV Patent Certification Notice for ANDA 202483 (2013).  
Paragraph IV Patent Certification Notice for ANDA 203235 (2013).  
Ortho-McNeil-Janssen Pharmaceuticals, Inc. (2010). Prescribing Information for Concerta Extended-Release Tablets.  
Findings of Fact and Conclusions of Law, In re: Oxycontin Antitrust Litigation, Case 1:04-md-01603-SHS, Jan. 14, 2014.  
Opinion & Order filed May 27, 2014, Case 1:04-md-01603-SHS, 24 pgs.  
USPTO Non-Final Rejection for U.S. Appl. No. 13/765,368 dated Oct. 4, 2013.  
USPTO Response for U.S. Appl. No. 13/765,368 dated Jan. 6, 2014.  
USPTO Final Rejection for U.S. Appl. No. 13/765,368 dated Mar. 12, 2014.  
USPTO Response for U.S. Appl. No. 13/765,368 dated Jun. 12, 202014.  
USPTO Advisory Action for U.S. Appl. No. 13/765,368 dated Jul. 1, 2014.  
USPTO Non-Final Rejection for U.S. Appl. No. 13/890,874 dated Dec. 18, 2013.  
USPTO Response for U.S. Appl. No. 13/890,874 dated Feb. 28, 2014.  
USPTO Final Rejection for U.S. Appl. No. 13/890,874 dated Mar. 11, 2014.  
USPTO Response for U.S. Appl. No. 13/890,874 dated Jun. 11, 2014.  
USPTO Advisory Action for U.S. Appl. No. 13/890,874 dated Jun. 19, 2014.  
USPTO Non-Final Rejection for U.S. Appl. No. 13/946,418 dated Sep. 12, 2013.  
USPTO Response for U.S. Appl. No. 13/946,418 dated Dec. 12, 2013.  
USPTO Final Rejection for U.S. Appl. No. 13/946,418 dated Apr. 10, 2014.  
USPTO Response for U.S. Appl. No. 13/946,418 dated Jun. 10, 2014.

USPTO Advisory Action for U.S. Appl. No. 13/946,418 dated Jun. 23, 2014.  
Bettini et al., "Translocation of drug particles in HPMC matrix gel layer: effect of drug solubility and influence on release rate," *Journal of Controlled Release*, vol. 70, No. 3, Feb. 2001, pp. 383-391.  
Sarkar, N., "Kinetics of thermal gelation of methylcellulose and hydroxypropylmethylcellulose in aqueous solutions," *Carbohydrate Polymers*, vol. 26, No. 3, Jan. 1995, pp. 195-203.  
Wilkins, Jeffrey, N., "Pharmacotherapy of Schizophrenia Patients with Comorbid Substance Abuse", *Schizophrenia Bulletin*, vol. 23, No. 2, 1997, <http://schizophreniabulletin.oxfordjournals.org> pp. 215-228.  
Yang, et al., "Characterization of Compressibility and Compactibility of Poly(ethylene oxide) Polymers for Modified Release Application by Compaction Simulator", *Journal of Pharmaceutical Sciences*, vol. 85, No. 10, Oct. 1996 pp. 1085-1086.  
Paragraph IV Patent Certification Notice for ANDA 203915 (Jul. 26, 2013).  
USPTO Non-Final Rejection for U.S. Appl. No. 14/243,580, dated Oct. 2, 2014.  
USPTO Non-Final Rejection for U.S. Appl. No. 14/460,134, dated Oct. 2, 2014.  
USPTO Non-Final Rejection for U.S. Appl. No. 14/460,170, dated Oct. 2, 2014.  
USPTO Non-Final Rejection for U.S. Appl. No. 14/470,631, dated Oct. 21, 2014.  
USPTO Non-Final Rejection for U.S. Appl. No. 14/470,662, dated Nov. 4, 2014.  
USPTO Non-Final Rejection for U.S. Appl. No. 14/484,077, dated Oct. 22, 2014.  
Sarkar, N., "Thermal Gelation Properties of Methyl and Hydroxypropyl Methylcellulose," *Journal of Applied Polymer Science*, vol. 24, No. 4, Aug. 1979, pp. 1073-1087.  
Findings of Fact and Conclusions of Law, In re: Oxycontin Antitrust Litigation, Case 1:04-md-01603-SHS, Apr. 8, 2015, pp. 1-69.

\* cited by examiner

1

**PHARMACEUTICAL FORMULATION  
CONTAINING GELLING AGENT**

RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 13/349,449, filed Jan. 12, 2012, which is a continuation of U.S. patent application Ser. No. 12/653,115, filed Dec. 8, 2009, which is a continuation of U.S. patent application Ser. No. 10/214,412, filed Aug. 6, 2002, which claims the benefit of U.S. Provisional Application No. 60/310,534, filed Aug. 6, 2001. The contents of these applications are hereby incorporated by reference in their entirety.

BACKGROUND OF THE INVENTION

Opioid analgesics are sometimes the subject of abuse. Typically, a particular dose of an opioid analgesic is more potent when administered parenterally as compared to the same dose administered orally. Therefore, one popular mode of abuse of oral opioid formulations involves the extraction of the opioid from the dosage form, and the subsequent injection of the opioid (using any "suitable" vehicle for injection) in order to achieve a "high." Also, some formulations can be tampered with in order to provide the opioid agonist contained therein better available for illicit use. For example, a controlled release opioid agonist formulation can be crushed in order to provide the opioid contained therein available for immediate release upon oral or nasal administration. An opioid formulation can also be abusable by administration of more than the prescribed dose of the drug.

Opioid antagonists have been combined with certain opioid agonists in order to deter the parenteral abuse of opioid agonists. In the prior art, the combination of immediate release pentazocine and naloxone has been utilized in tablets available in the United States, commercially available as Talwin® Nx from Sanofi-Winthrop. Talwin® Nx contains immediate release pentazocine hydrochloride equivalent to 50 mg base and naloxone hydrochloride equivalent to 0.5 mg base. A fixed combination therapy comprising tilidine (50 mg) and naloxone (4 mg) has been available in Germany for the management of pain since 1978 (Valoron® N, Goedecke). A fixed combination of buprenorphine and naloxone was introduced in 1991 in New Zealand (Temgesic® Nx, Reckitt & Colman) for the treatment of pain.

Purdue Pharma EP currently markets sustained-release oxycodone in dosage forms containing 10, 20, 40, and 80 mg oxycodone hydrochloride under the tradename OxyContin.

U.S. Pat. Nos. 5,266,331; 5,508,042; 5,549,912 and 5,656,295 disclose sustained release oxycodone formulations.

U.S. Pat. Nos. 4,769,372 and 4,785,000 to Kreek describe methods of treating patients suffering from chronic pain or chronic cough without provoking intestinal dysmotility by administering 1 to 2 dosage units comprising from about 1.5 to about 100 mg of opioid analgesic or antitussive and from about 1 to about 18 mg of an opioid antagonist having little to no systemic antagonist activity when administered orally, from 1 to 5 times daily.

U.S. Pat. No. 6,228,863 to Palermo et al. describes compositions and methods of preventing abuse of opioid dosage forms.

WO 99/32119 to Kaiko et al. describes compositions and methods of preventing abuse of opioid dosage forms.

U.S. Pat. No. 5,472,943 to Crain et al. describes methods of enhancing the analgesic potency of bimodally acting opioid agonists by administering the agonist with an opioid antagonist.

2

U.S. Pat. No. 3,980,766 to Shaw et al., is related to drugs which are suitable for therapy in the treatment of narcotic drug addiction by oral use, e.g., methadone, formulated to prevent injection abuse through concentration of the active component in aqueous solution by incorporating in a solid dosage or tablet form of such drug an ingestible solid having thickening properties which cause rapid increase in viscosity upon concentration of an aqueous solution thereof.

However, there still exists a need for a safe and effective treatment of pain with opioid analgesic dosage forms which are less subject to abuse than current therapies.

All documents cited herein, including the foregoing, art incorporated by reference in their entireties for all purposes.

OBJECTS AND SUMMARY OF THE  
INVENTION

It is an object of certain embodiments of the invention to provide an oral dosage form of an opioid analgesic which is subject to less parenteral abuse than other dosage forms.

It is an object of certain embodiments of the invention to provide an oral dosage form of an opioid analgesic which is subject to less intranasal abuse than other dosage forms.

It is an object of certain embodiments of the invention to provide an oral dosage form of an opioid analgesic which is subject to less oral abuse than other dosage forms.

It is a further object of certain embodiments of the invention to provide an oral dosage form of an opioid analgesic which is subject to less diversion than other dosage forms.

It is a further object of certain embodiments of the invention to provide a method of treating pain in human patients with an oral dosage form of an opioid analgesic while reducing the abuse potential of the dosage form.

It is a further object of certain embodiments of the invention to provide a method of manufacturing an oral dosage form of an opioid analgesic such that it has less abuse potential.

These objects and others are achieved by the present invention, which is directed in part to an oral dosage form comprising an opioid analgesic; and at least one aversive agent for reducing the abuse of the opioid analgesic.

In certain embodiments of the present invention, the oral dosage forms of the present invention comprising an opioid analgesic; and an aversive agent or agents as a component(s) of the dosage form helps to prevent injection, inhalation, and/or oral abuse by decreasing the "attractiveness" of the dosage form to a potential abuser.

In certain embodiments of the present invention, the dosage form comprises an aversive agent such as a bittering agent to discourage an abuser from tampering with the dosage form and thereafter inhaling or swallowing the tampered dosage form. Preferably, the bittering agent is released when the dosage form is tampered with and provides an unpleasant taste to the abuser upon inhalation and/or swallowing of the tampered dosage form.

In certain embodiments of the present invention, the dosage form comprises an aversive agent such as an irritant to discourage an abuser from tampering with the dosage form and thereafter inhaling, injecting, or swallowing the tampered dosage form. Preferably, the irritant is released when the dosage form is tampered with and provides a burning or irritating effect to the abuser upon inhalation, injection, and/or swallowing of the tampered dosage form.

In certain embodiments of the present invention, the dosage form comprises an aversive agent such as a gelling agent to discourage an abuser from tampering with the dosage form and thereafter inhaling, injecting, and/or swallowing the tam-

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