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(54) **COMPOSITIONS AND METHODS OF DELIVERY OF PHARMACOLOGICAL AGENTS**

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See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,425,319 A	1/1984	Yokoyama et al.
4,645,660 A	2/1987	Takahashi et al.
5,272,171 A	12/1993	Ueda et al.
5,362,478 A	11/1994	Desai et al.
5,399,363 A	3/1995	Liversidge et al.
5,439,686 A	8/1995	Desai et al.
5,498,421 A	3/1996	Grinstaff et al.
5,505,932 A	4/1996	Grinstaff et al.
5,508,021 A	4/1996	Grinstaff et al.
5,512,268 A	4/1996	Grinstaff et al.
5,560,933 A	10/1996	Soon-Shiong et al.
5,616,330 A	4/1997	Kaufman et al.
5,626,862 A	5/1997	Brem et al.
5,635,207 A	6/1997	Grinstaff et al.
5,639,473 A	6/1997	Grinstaff et al.
5,650,156 A	7/1997	Grinstaff et al.

5,651,986 A	7/1997	Brem et al.
5,665,382 A	9/1997	Grinstaff et al.
5,665,383 A	9/1997	Grinstaff et al.
5,681,846 A	10/1997	Trissel
5,714,520 A	2/1998	Jones et al.
5,716,981 A	2/1998	Hunter et al.
5,731,355 A	3/1998	Jones et al.
5,731,356 A	3/1998	Jones et al.
5,886,026 A	3/1999	Hunter et al.
5,916,596 A	6/1999	Desai et al.
5,945,033 A	8/1999	Yen
5,977,163 A	11/1999	Li et al.
5,990,153 A	11/1999	Wood et al.
5,994,341 A	11/1999	Hunter et al.
5,997,904 A	12/1999	Magdassi et al.
6,028,108 A	2/2000	George
6,096,331 A	8/2000	Desai et al.
6,100,302 A	8/2000	Pejaver et al.
6,120,805 A	9/2000	Spenlehauer et al.
6,143,276 A	11/2000	Unger
6,147,122 A	11/2000	Mirejovsky et al.
6,150,423 A	11/2000	Carpenter
6,177,477 B1	1/2001	George et al.
6,197,051 B1	3/2001	Zhong
6,197,349 B1	3/2001	Westesen et al.
6,204,054 B1	3/2001	Sutton et al.
6,306,993 B1	10/2001	Rothbard et al.
6,310,039 B1	10/2001	Kratz
6,326,406 B1	12/2001	De Tommaso
6,362,234 B1	3/2002	Handler
6,399,087 B1	6/2002	Zhang et al.
6,441,025 B2	8/2002	Li et al.
6,458,373 B1	10/2002	Lambert et al.

(Continued)

FOREIGN PATENT DOCUMENTS

EP 0 227 593 A1 7/1987
(Continued)

OTHER PUBLICATIONS

Altmayer, P. et al. (1995). "Propofol Binding to Human Blood Proteins," *Arzneimittel Forschung Drug Research* 45(II)(10):1053-1056.

(Continued)

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ABSTRACT

The present invention relates to a pharmaceutical composition comprising a pharmaceutical agent and a pharmaceutically acceptable carrier, which carrier comprises a protein, for example, human serum albumin and/or deferoxamine. The human serum albumin is present in an amount effective to reduce one or more side effects associated with administration of the pharmaceutical composition. The invention also provides methods for reducing one or more side effects of administration of the pharmaceutical composition, methods for inhibiting microbial growth and oxidation in the pharmaceutical composition, and methods for enhancing transport and binding of a pharmaceutical agent to a cell.

16 Claims, No Drawings

US 7,923,536 B2

Page 2

U.S. PATENT DOCUMENTS

6,469,069	B1	10/2002	Mirejovsky et al.
6,506,405	B1	1/2003	Desai et al.
6,528,067	B1	3/2003	Magdassi et al.
6,537,579	B1	3/2003	Desai et al.
6,565,842	B1	5/2003	Sojomihardo et al.
6,652,884	B2	11/2003	Falciani
6,743,826	B1	6/2004	Hegedus et al.
6,749,868	B1	6/2004	Desai et al.
6,753,006	B1	6/2004	Desai et al.
6,759,431	B2	7/2004	Hunter et al.
7,119,124	B2	10/2006	Hegedus et al.
7,332,568	B2	2/2008	Trieu et al.
7,771,751	B2	8/2010	Desai et al.
7,820,788	B2	10/2010	Desai et al.
2003/0185894	A1	10/2003	Zenoni et al.
2003/0187062	A1	10/2003	Zenoni et al.
2003/0199425	A1	10/2003	Desai et al.
2005/0004002	A1	1/2005	Desai et al.
2005/0009731	A1	1/2005	Desai et al.
2005/0064028	A1	3/2005	Hegedus et al.
2006/0263434	A1	11/2006	Desai et al.
2007/0082838	A1	4/2007	De et al.
2007/0087022	A1	4/2007	Desai et al.
2007/0092563	A1	4/2007	Desai et al.
2007/0093547	A1	4/2007	Desai et al.
2007/0116774	A1	5/2007	Desai et al.
2007/0117133	A1	5/2007	Trieu et al.
2007/0117744	A1	5/2007	Desai et al.
2007/0129448	A1	6/2007	Desai et al.
2007/0166388	A1	7/2007	Desai et al.
2008/0063724	A1	3/2008	Desai et al.
2008/0280987	A1	11/2008	Desai et al.
2009/0048331	A1	2/2009	Soon-Shiong et al.
2009/0098210	A1	4/2009	Desai et al.
2009/0196933	A1	8/2009	De et al.
2009/0263483	A1	10/2009	Desai et al.
2009/0304805	A1	12/2009	Desai et al.
2010/0035800	A1	2/2010	Desai et al.
2010/0048499	A1	2/2010	Desai et al.
2010/0112077	A1	5/2010	Desai et al.
2010/0166869	A1	7/2010	Desai et al.
2010/0183728	A1	7/2010	Desai et al.
2010/0215751	A1	8/2010	Desai et al.
2010/0291673	A1	11/2010	Harper et al.
2010/0297243	A1	11/2010	Desai et al.

FOREIGN PATENT DOCUMENTS

EP	0 544 292	A2	6/1993
EP	0 544 292	A3	6/1993
FR	2 775 900	A1	9/1999
RU	2127606	C1	3/1999
WO	WO-92/07259	A1	4/1992
WO	WO-94/13300	A1	6/1994
WO	WO-94/18954	A1	9/1994
WO	WO-94/20072	A1	9/1994
WO	WO-95/03036	A1	2/1995
WO	WO-96/40829	A1	12/1996
WO	WO-97/10850	A1	3/1997
WO	WO-98/07410	A1	2/1998
WO	WO-98/14174	A1	4/1998
WO	WO-98/14175	A1	4/1998
WO	WO-99/00113	A1	1/1999
WO	WO-99/13914	A1	3/1999
WO	WO-99/39696	A1	8/1999
WO	WO-00/06152	A1	2/2000
WO	WO-00/23117	A1	4/2000
WO	WO-00/64437	A1	11/2000
WO	WO-00/71079	A2	11/2000
WO	WO-00/71079	A3	11/2000
WO	WO-01/49268	A1	7/2001
WO	WO-01/89522	A1	11/2001
WO	WO-02/087545	A1	11/2002
WO	WO-03/096944	A1	11/2003
WO	WO-2004/007520	A2	1/2004
WO	WO-2004/007520	A3	1/2004

WO	WO-2005/117952	A2	12/2005
WO	WO-2005/117952	A3	12/2005
WO	WO-2006/034147	A2	3/2006
WO	WO-2006/034147	A3	3/2006

OTHER PUBLICATIONS

- Awada, A. (2002) "New Cytotoxic Agents and Molecular-Targeted Therapies in the Treatment of Metastatic Breast Cancer," *Trends in Experimental and Clinical Medicine* 12:4-15.
- Awada, A. et al. (2003). "The Pipeline of New Anticancer Agents for Breast Cancer Treatment in 2003," *Critical Reviews in Oncology/Hematology* 48:45-63.
- Bayes, M. et al. (May 2003). "Gateways to Clinical Trials," *Methods and Findings in Experimental and Clinical Pharmacology* 25(4):317-340.
- Bielen, S. J. et al. (1996). "The Effect of a Cyclodextrin Vehicle on the Cardiovascular Profile of Propofol in Rats," *Anest. Analg.* 82:920-924.
- Briggs, L.P. et al. (1982). "An Adverse Reaction to the Administration of Disoprofop (Diprivan)," *Anaesthesia* 37(7):1099-1101.
- Calabresi, P. et al. (1996). Introduction of "Chemotherapy of Neoplastic Diseases," Section X in Goodman and Gilman's *The Pharmacological Basis of Therapeutics*, 9th ed., McGraw-Hill: New York, pp. 1225-1230.
- Campbell, K. J. et al. (Jul. 2003). "A Phase I Trial of ABI-007 Administered Weekly for Three Doses Every 4 Weeks in Patients With Advanced Non-Hematologic Malignancies," *Proceedings of the American Association for Cancer Research* held on Jul. 11-14, 2003, Washington Convention Center, Washington, D. C., vol. 44(2nd edition), p. 1059, abstract No. R5337.
- Carter, D.C. et al. (1994). "Structures of Serum Albumin," *Advances in Protein Chemistry*. Schumaker, V.N., ed., Academic Press, Inc.: San Diego, CA, 45:153-203.
- Chuang, V. T. G. et al. (May 2002). "Pharmaceutical Strategies Utilizing Recombinant Human Serum Albumin," *Pharmaceutical Research* 19(5):569-577.
- Curry et al. (Sep. 1998). "Crystal Structure of Human Serum Albumin Complexed with Fatty Acid Reveals an Asymmetric Distribution of Binding Sites," *Nat. Struct. Biol.* 5(9):827-835.
- Curry, S. et al. (Nov. 23, 1999). "Fatty Acid Binding To Human Serum Albumin: New Insights From Crystallographic Studies," *Biochim. Biophys. Acta*. 1441(2-3):131-140.
- Damascelli, B. et al. (Nov. 15, 2001). "Intraarterial Chemotherapy with Polyoxethylated Castor Oil Free Paclitaxel Incorporated in Albumin Nanoparticles (ABI-007)," *Cancer* 92(10):2592-2602.
- Damascelli, B. et al. (Jul. 2003). "A Novel Intraarterial Chemotherapy Using Paclitaxel in Albumin Nanoparticles to Treat Advanced Squamous Cell Carcinoma of the Tongue: Preliminary Findings," *AJR Am. J. Roentgenol.* 181(1):253-260.
- Davies, A.F. et al. (Jun. 2002). "Efficacy of Microfiltration in Decreasing Propofol-Induced Pain," *Anaesthesia* 57(6):557-561.
- Desai, N.P. et al. (Apr. 1994). "Controlled and Targeted Drug Delivery With Biocompatible Protein Shell Microspheres," *The 20th Annual Meeting of the Society for Biomaterials*, Boston, MA, Apr. 5-9, 1994, p. 112.
- Desai, N.P. et al. (Oct.-Nov. 1994). "Intravenous Targeted Delivery of Chemo-therapeutic Agents in Protein Microspheres," *XVI International Cancer Progress*, New Delhi, India, Oct. 30-Nov. 5, 1994, p. 275.
- Desai, N.P. et al. (Mar. 1995). "In Vivo Drug Delivery With Biocompatible Protein Shell Microspheres," *The 21st Annual Meeting of the Society for Biomaterials*, San Francisco, CA Mar. 18-22, 1995, one page.
- Desai, N.P. et al. (Aug. 1995). "Protein Microcapsules as Drug Delivery Vehicles," *26th Annual Meeting of the Fine Particle Society*, Chicago, IL, Aug. 22-25, 1995, one page.
- Desai, N.P. et al. (Apr.-May 1997). "Protein-Stabilized Nanoparticles as Drug Delivery Vehicles," *Transactions: 23rd Annual Meeting of the*

- Desai, N.P. et al. (Apr. 1998). "Protein Based Nanoparticle Delivery Systems," *28th Annual Meeting of the Fine Particle Society*, Dallas, TX, Apr. 1-3, 1998, one page.
- Desai, N.P. et al. (May 2000). "Protein-Based Nanoparticles for Drug Delivery of Paclitaxel," *Transactions of the Sixth World Biomaterials Congress*, Kamuela, HI, May 15-20, 2000, III(I):199 (one page).
- Desai, N. P. et al. (2002). "Evidenced of Enhanced in Vivo Efficacy at Maximum Tolerated Dose (MTD) of Nanoparticle Paclitaxel (ABI-007) and Taxol in 5 Human Tumor Xenografts of Varying Sensitivity to Paclitaxel," 2002 ASCO Annual Meeting American Society of Clinical Oncology, Orlando, Florida, May 2002, *Proc. Am. Soc. Clin. Oncol.* 21 :Abstract No. 462, 4 pages.
- Desai, N. et al. (Dec. 2002). "Evidence of a Novel Transporter Mechanism for a Cremophor-Free, Protein-Engineered Paclitaxel (ABI-007) and In Vivo Antitumor Activity in MX-1 Human Breast Tumor Xenograft Model," *Breast Cancer Research and Treatment*, 25th Annual San Antonio Breast Cancer Symposium (SABCS), San Antonio, Texas, 76(Suppl. 1) Abstract No. 524, p. S131.
- Desai, N. et al. (Dec. 2002). "Preclinical and Clinical Pharmacokinetics and Safety of ABI-007, a Novel, Cremophor-Free, Protein-Engineered Nanotransfer of Paclitaxel," *Breast Cancer Research and Treatment*, 25th Annual San Antonio Breast Cancer Symposium (SABCS), San Antonio, Texas 76(Suppl. 1) Abstract No. 523, p. S131.
- Desai, N. et al. (Jul. 2003). "Oral Bioavailability of Paclitaxel in a Novel, Cremophor el-Free, Protein-Based Nanoparticle Preparation," *Proceedings of the American Association of Cancer Research (AACR)* 94th Annual Meeting, Jul. 11-14, 2003, Washington Convention Center, Washington D.C. 44(2nd edition), Abstract No. 3673, p. 732.
- Desai, N. et al. (Jul. 2003). "Pulmonary Delivery of a Novel, Cremophor-Free, Protein-Based Nanoparticle Preparation of Paclitaxel," *Proceedings of the American Association for Cancer Research* 44(2nd edition), Abstract No. 3672, p. 731.
- Desai, N. et al. (Dec. 2003). "Evidence of Greater Antitumor Activity and Red Cell Partitioning and Superior Antitumor Activity of Cremophor Free Nanoparticle Paclitaxel (ABI-007) Compared to Taxol," *Breast Cancer Research and Treatment*, 26th Annual San Antonio Breast Cancer Symposium (SABCS), San Antonio, Texas, 82(Suppl. 1): Abstract No. 348, pp. S82-S83.
- Desai, N. et al. (Feb. 15, 2006). "Increased Antitumor Activity, Intratumor Paclitaxel Concentrations, and Endothelial Cell Transport of Cremophor-Free, Albumin-Bound Paclitaxel, ABI-007, Compared With Cremophor-Based Paclitaxel," *Clin. Cancer Res.* 12(4):1317-1324.
- Doenicke, A.W. et al. (1996). "Reducing Pain During Propofol Injection: The Role of the Solvent," *Anesthesia & Analgesia* 82:472-474.
- Dosio, F. et al. (1997). "Preparation, Characterization and Properties In Vitro and In Vivo of a Paclitaxel-Albumin Conjugate," *J. Cont. Rel.* 47:293-304.
- Drugs.com (Jun. 22, 2004). "Deferoxamine (Systemic)," located at <http://www.drugs.com/MMX/Deferoxamine_Mesylate.html>, last accessed Feb. 4, 2005, nine pages.
- Eggleing, S. (2003). "Variation on Percentage Concentration Weight/Volume Percent or Mass/Volume Percent," located at <http://dl.clackamas.cc.or.us/ch105-04/wtvolpct.htm>, last visited on Feb. 4, 2005, one page.
- Erlich, R. et al. (Jun. 2002). "American Society of Clinical Oncology—38th Annual Meeting, May 18-21, 2002, Orlando, FL, USA," *Investigational Drugs Journal* 5(6):497-502.
- Fehske, K. J. et al. (Jan. 1, 1981). "The Location of Drug Binding Sites in Human Serum Albumin," *Biochemical Pharmacology* 30(7):687-692.
- Finlayson, J.S. (1980). "Albumin Products," *Seminars in Thrombosis and Hemostasis*, Mammen, E. F. (ed.), Stratton Intercontinental Medical Book Corporation, New York, NY, 6(2):85-120.
- Flournoy, D.J. (Jul. 1991). "In Vitro Antimicrobial Properties of Deferoxamine Mesylate," *Eur. J. Clin. Microbiol. Infect. Dis* 10(7):597-598.
- Garrido, M.J. et al. (1994). "Caracterización de la Fijación de Propofol a las Proteínas Plasmáticas y Posibles Interacciones," *Rev. Gelderblom, H. et al. (Sep. 2001). "Cremophor EL: the Drawbacks and Advantages of Vehicle Selection for Drug Formulation," *Eur. J. Cancer* 37(13):1590-1598.*
- Gradishar, W. J. et al. (Nov. 1, 2005). "Phase III Trial of Nanoparticle Albumin-Bound Paclitaxel Compared with Polyethylated Castor Oil-Based Paclitaxel in Women With Breast Cancer," *J. Clin. Oncol.* 23(31):7794-7803.
- Green, M. R. et al. (Aug. 2006, e-pub. Jun. 1, 2006). "Abraxane® A Novel Cremophor-Free, Albumin-Bound Particle Form of Paclitaxel for the Treatment of Advanced Non-Small-Cell Lung Cancer," *Ann. Oncol.* 17(8):1263-1268.
- Grinstaff, M.W. et al. (Mar. 1994). "Intravenous Targeted Delivery of Taxol in Protein Microspheres," *Abstracts of Papers 207th National Meeting of the American Chemical Society*, 1994, San Diego, CA, Mar. 13-17, 1994, 207(1-2), Abstract No. 91, one page.
- Gutteridge, J.M.C. et al. (1981). "Iron-Dioxygen-Dependent Changes to the Biological Activities of Bleomycin," *J. Inorg. Biochem.* 15:349-357.
- Gutteridge, J.M.C. (1984). "Streptonigrin-Induced Deoxyribose Degradation: Inhibition by Superoxide Dismutase, Hydroxyl Radical Scavengers and Iron Chelators," *Biochem. Pharm.* 33(19):3059-3062.
- Halliwell, B. (1989). "Protection Against Tissue Damage in Vivo By Desferrioxamine: What Is Its Mechanism of Action?" *Free Radic. Biol. Med.* 7(6):645-651.
- Hauser, C.J. et al. (Jun. 1980). "Oxygen Transport Responses to Colloids and Crystalloids in Critically III Surgical Patients," *Surgery, Gynecology and Obstetrics* 150(6):811-816.
- Hawkins, M. J. et al. (2004). "Rationale, Preclinical Support, and Clinical Proof-of-Concept for Delivery of Water-Insoluble Therapeutics by a Novel Nanoparticle Albumin-Bound (Nab) Technology: Experience With Paclitaxel," *Cancer Invest.* 22(Suppl. 1):vii-xxvii, 1-111. Abstracts from the Chemotherapy Foundation Symposium XXI: Innovative Cancer Therapy for Tomorrow, Nov. 12-15, 2003, New York, New York, USA, vol. 22, Supplement 1, pp. 99-100, Abstract No. 79.
- He, X.M. et al. (Jul. 16, 1992). "Atomic Structure and Chemistry of Human Serum Albumin," *Nature* 358(6383):209-215.
- HealthTouch® Online. (2000). "Deferoxamine (Systemic)," located at <<http://healthtouch.com>>, 5 pages.
- Ibrahim, N.K. et al. (2000). "Phase I Study of Cremophor-Free, Protein-Stabilized, Nanoparticle Formulation of Paclitaxel (Abi-007) in Solid Tumors," *Abstract 609F in Proceedings of Thirty-Sixth Annual Meeting of the American Society of Clinical Oncology*, New Orleans, Louisiana, May 20-23, 2000, p. 155a, Abstract No. 609F.
- Ibrahim, N. K. et al. (May 2002). "Phase I and Pharmacokinetic Study of ABI-007, a Cremophor-Free, Protein-Stabilized, Nanoparticle Formulation of Paclitaxel," *Clin. Cancer Res.* 8(5):1038-1044.
- Ibrahim, N. K. et al. (Dec. 2002). "Efficacy and Dose-Dependent Activity of ABI-007, a Cremophor-Free Nanoparticle Paclitaxel, in First-Line Metastatic Breast Cancer: Integrated Results of 2 Phase II Trials," *Breast Cancer Research and Treatment*, 25th Annual San Antonio Breast Cancer Symposium, 76(Suppl. 1): Abstract No. 522, p. S131.
- Ibrahim, N. K. et al. (Sep. 1, 2005). "Multicenter Phase II Trial of ABI-007, an Albumin-Bound Paclitaxel, in Women With Metastatic Breast Cancer," *J. Clin. Oncol.* 23(25):6019-6026.
- John, M. C. et al. (Mar. 6, 2002). "A Novel Preparation of Systemic Paclitaxel Reduces In-Stent Restenosis in the Rabbit," *Journal of the American College of Cardiology, Abstracts—ACCIS2002 (Angiography & Interventional Cardiology)* Abstract No. 1005-6, p. 5A.
- Juven, B.J. et al. (1994). "Factors that Interact with the Antibacterial Action of Thyme Essential Oil and its Active Constituents," *J. Appl. Bacteriol.* 76(6):626-631.
- Klebanoff, S.J. et al. (Nov. 25, 1989). "Oxygen-based Free Radical Generation by Ferrous Ions and Deferoxamine," *J. Bio. Chem.* 264(33):19765-19771.
- Knibbe, C.A.J. et al. (1999). "Pharmacokinetics, Induction of Anaesthesia and Safety Characteristics of Propofol 6% SAZN vs

- Kolodgie, F. D. et al. (Sep. 3, 2002). "Sustained Reduction of In-Stent Neointimal Growth With the Use of a Novel Systemic Nanoparticle Paclitaxel," *Circulation* 106:1195-1198.
- Kovár, J. et al. (Mar. 2000). "Unexpected Effects of Albumin on Apoptosis Induction by Deferoxamine In Vitro," *In Vitro Cell Dev Biol. Anim.* 36(3):151-152.
- Kragh-Hansen, U. (1990). "Structure and Ligand Binding Properties of Human Serum Albumin," *Dan. Med. Bull.* 37(1):57-84.
- Kuenen, B.C. (Mar. 15, 2002). "Dose-Finding and Pharmacokinetic Study of Cisplatin, Gemcitabine, and SU5416 in Patients With Solid Tumors," *J. Clin. Oncol.* 20(6):1657-1667.
- Lanocita, R. et al. (2000). "A Novel Intra-Arterial Chemotherapeutic Approach of Squamous Cell Cancer of Head and Neck Using High Dose Cremaphore, Free Paclitaxel/Albumin Nanoparticles (ABI-007)," *Annals of Oncology, Second National Congress of Medical Oncology*, Oct. 28-31, 2000, Genova, Italy, vol. 11, Supplement 2, Poster Session A, Abstract No. A26, p. 7.
- Lanocita, R. et al. (Nov. 2000). "High Dose of Cremophore-Free Paclitaxel/Albumine Nanoparticles (ABI-007) for a Novel Intra-Arterial Approach to Squamous Cell Cancer of Head and Neck," *2000 Scientific Program, Radiological Society of North America, RSNA 2000, Explore, 86th Scientific Assembly and Annual Meeting*, Nov. 26-Dec. 1, 2000, McCormick Place, Chicago, Illinois, vol. 217, p. 288, Abstract No. 366.
- Lanocita, R. et al. (Nov. 2000). "Squamous Cancer of Anal Canal: Intra-Arterial Chemotherapeutic Approach Using High Dose of Cremaphore-Free Paclitaxel/Albumin Nanoparticles (ABI-007)," *2000 Scientific Program, Radiological Society of North America, RSNA 2000, Explore, 86th Scientific Assembly and Annual Meeting*, Nov. 26-Dec. 1, 2000, McCormick Place, Chicago, Illinois, vol. 217, p. 504, Abstract No. 1244.
- Larsen, B. et al. (Nov. 2001). "Less Pain on Injection by a New Formulation of Propofol?" *Der Anaesthetist*. 50(11):842-845.
- Lilley, E.M.M. et al. (Sep. 1996). "The Effect of the Addition of Lignocaine on Propofol Emulsion Stability," *Anaesthesia* 51:815-818.
- Mayer, M. et al. (1996). "Propofol and Etomidat-®Lipuro zur Einleitung einer Allgemeinanästhesie," *Der Anaesthetist* 45(11):1082-1084 and English translation of abstract only.
- Meijs, W. E. et al. (May 1996). "A Facile Method for the Labeling of Proteins With Zirconium Isotopes," *Nuclear Medicine & Biology* 23(4):439-448.
- Micha, J. P. et al. (Feb. 2006, e-pub Oct. 14 2005). "Abraxane in the Treatment of Ovarian Cancer: the Absence of Hypersensitivity Reactions," *Gynecol Oncol* 100(2):437-438.
- Moreno-Aspitia, A. et al. (Oct. 2005). "North Central Cancer Treatment Group N0531: Phase II Trial of Weekly Albumin-bound Paclitaxel (ABI-007, Abraxane®) in Combination with Gemcitabine in Patients with Metastatic Breast Cancer," *Clinical Breast Cancer* 6(4):361-364.
- Müller, B. G. et al. (Jan. 1996). "Albumin Nanospheres as Carriers for Passive Drug Targeting: An Optimized Manufacturing Technique," *Pharm. Res.* 13(1):32-37.
- Nyman, D.W. et al. (Nov. 1, 2005). "Phase I and Pharmacokinetics Trial of ABI-007, a Novel Nanoparticle Formulation of Paclitaxel in Patients with Advanced Nonhematologic Malignancies," *J. Clin. Oncol.* 23(31):7785-7793.
- O'Shaughnessy, J. et al. (2003). "ABI-007 (Abraxane™), A Nanoparticle Albumin-Bound (*nab*) Paclitaxel Demonstrates Superior Efficacy vs Taxol in MBC: A Phase III Trial," *Breast Cancer Res. Treat, Proceedings of the 26th Annual San Antonio Breast Cancer Symposium (SABCS)*, San Antonio, Texas, Dec. 3-6, 2003, 82(Suppl. 1):3, Abstract No. 44, p. 182.
- Pál, K. et al. (2001). "High Affinity Binding of Paclitaxel to Human Serum Albumin," *Eur. J. Biochem.* 268(7):2187-2191.
- Patelli, G. et al. (2002). "Effectiveness of Intraarterial Chemotherapy by Taxane Charged Albumine Nanoparticles on Advanced Squamous Cell Cancer of Oral Cavity and Oropharynx," *International Journal of Cancer* 18th UICC International Cancer Congress, Jun. 30-Jul. 5, Purcell, M. et al. (2000). "Interaction of Taxol with Human Serum Albumin," *Biochim. Biophys. Acta* 1478:61-68.
- Ritov, V. B. et al. (Jun. 2001). "Hexokinase Isozyme Distribution in Human Skeletal Muscle," *Diabetes* 50:1253-1262.
- Rocha, J. L. L. et al. (Aug. 2002). "Uncommon Vancomycin-Induced Side Effects," *The Brazil. J. Infect. Diseases* 6(4):196-200.
- Shimoni, E. et al. (Jun. 1994). "Antioxidant Properties of Deferoxamine," *JAOCS* 71(6):641-644.
- Singh, N. P. et al. (Nov. 21, 2001). "Selective Toxicity of Dihydroartemisinin and Holotransferrin Toward Human Breast Cancer Cells," *Life Sci.* 70(1):49-56.
- Sparreboom, A. et al. (Feb. 17, 1995). "Determination of Paclitaxel and Metabolites in Mouse Plasma, Tissues, Urine and Faeces by Semi-Automated Reversed-Phase High-Performance Liquid Chromatography," *J. Chromatogr. B. Biomed. Appl.* 664(2):383-391.
- Sparreboom, A. et al. (Jun 1, 2005). "Comparative Preclinical and Clinical Pharmacokinetics of a Cremophor-Free, Nanoparticle Albumin-Bound Paclitaxel (ABI-007) and Paclitaxel Formulated in Cremophor (Taxol)," *Clin. Cancer Res.* 11(11):4136-4143.
- Sugio, S. et al. (1999). "Crystal Structure of Human Serum Albumin at 2.5 Å Resolution," *Protein Eng.* 12(6):439-446.
- Tan, C. H. et al. (May 1998). "Pain on Injection of Propofol," *Anaesthesia* 53(5):468-476.
- Taylor, C. et al. (Dec. 2002). "Preliminary Evidence of Antitumor Activity of ABI-007, Cremophor-Free Nanoparticle Paclitaxel, in Patients Previously Exposed to Taxanes," *Breast Cancer Research and Treatment, 25th Annual San Antonio Breast Cancer Symposium (SABCS)*, San Antonio, Texas 76(Suppl. 1) Abstract No. 525, p. S132.
- Tonner, P. H. et al. (Nov. 1992). "The General Anesthetic Potency of Propofol and Its Dependence on Hydrostatic Pressure," *Anesthesiology* 77(5):926-931.
- Tullis, J. L. (Jan. 24, 1977). "Albumin: 1. Background and Use," *JAMA* 237(4):355-360.
- Tullis, J. L. (Jan. 31, 1977). "Albumin: 2. Guidelines for Clinical Use," *JAMA* 237(5):460-463.
- Urien, S. et al. (May 1996). "Docetaxel Serum Protein Binding with High Affinity of Alpha₁-Acid Glycoprotein," *Invest. New Drugs* 14(2):147-151.
- Vallejo, C. et al. (Dec. 1996). "Ifosfamide and Vinorelbine as First-Line Chemotherapy for Advanced Non-Small Cell Lung Carcinoma," *Am. J. Clin. Oncol.* 19(6):584-588.
- Vorum, H. (Nov. 1999). "Reversible Ligand Binding to Human Serum Albumin," *Dan. Med. Bull.* 46(5):379-399.
- Waugh, W.N. et al. (Jul. 1991). "Stability, Compatibility, and Plasticizer Extraction of Taxol(NSC-125973) Injection Diluted in Infusion Solutions and Stored in Various Containers," *AJHP* 48(7):1520-1524.
- Yang, Y. Z. et al. (1993). "Alkylation of Human Albumin by the Antimalarial Artemisinin," *Biochem. Pharm.* 46(2):336-339.
- Yang, A. et al. (Jul. 2003). "Pulmonary Delivery of a Novel, Cremophor-Free, Protein Based Nanoparticle Preparation of Paclitaxel," *Proceedings of the American Association of Cancer Research (AACR) 94th Annual Meeting*, Jul. 11-14, 2003, Washington Convention Center, Washington D.C. 44(2nd edition), Abstract No. 3672, p. 731.
- U.S. Appl. No. 12/479,710, filed Jun. 5, 2009, for Desai et al.
- U.S. Appl. No. 12/818,099, filed Jun. 17, 2010 for De et al.
- U.S. Appl. No. 12/824,014, filed Jun. 25, 2010 for Desai et al.
- U.S. Appl. No. 12/874,965, filed Sep. 2, 2010, for De et al.
- U.S. Appl. No. 12/832,876, filed Jul. 8, 2010, for Desai et al.
- U.S. Appl. No. 12/910,693, filed Oct. 22, 2010, for Desai et al.
- Non-Final Office Action mailed on Jun. 12, 2008, for U.S. Appl. No. 11/520,546, filed Sep. 12, 2006, nine pages.
- Non-Final Office Action mailed on Dec. 2, 2008, for U.S. Appl. No. 11/520,546, filed Sep. 12, 2006, eight pages.
- Final Office Action mailed on Sep. 17, 2009, for U.S. Appl. No. 11/520,546, filed Sep. 12, 2006, 8 pages total.
- International Search Report mailed Nov. 30, 2004, PCT Application No. PCT/US03/38941 filed Dec. 9, 2003, published as WO 2004/052401 on Jun. 24, 2004, 8 pages.

(Abraxane) Compared to Taxol: Role of a Novel Albumin Transporter Mechanism," Poster presented at 26th Annual San Antonio Breast Cancer Symposium (SABCS) held on Dec. 3-6, 2003, San Antonio, Texas, one page (Poster).

Becher (1965). *Emulsions: Theory and Practice*, 2nd edition, American Chemical Society, Monograph Series, Reinhold Publishing Corporation, New York, USA, Table of Contents on p. xi, for a total of 3 pages.

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