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- (54) **COMPOSITIONS AND METHODS OF DELIVERY OF PHARMACOLOGICAL AGENTS**
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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	Spelchauer 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	Hendler
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.

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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.

(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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(57) **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

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-2004/052401 A2 6/2004
 WO WO-2004/052401 A3 6/2004

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 Disopropofol (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 Polyoxyethylated 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 Society for Biomaterials*, New Orleans, LA, Apr. 30-May 4, 1997, 20:172.

- 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-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.
- Egging, 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.
- Erllich, 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. Esp. Anestesiología. Reanim.* 41(6):308-312, with English abstract (one page).
- 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). "Streptozotocin-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 Ill 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):viii-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 Propofol 1% SAZN and Diprivan®-10 after Bolus Injection," *Br. J. Clin. Pharmacol.* 47(6):653-660.

- 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.
- Kuonen, 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 Cremophore, 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/Albumin 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 Cremophore-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 Anaesthesist*, 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 Anaesthesist* 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.
- Paál, 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 Albumin Nanoparticles on Advanced Squamous Cell Cancer of Oral Cavity and Oropharynx." *International Journal of Cancer* 18th UICC International Cancer Congress, Jun. 30-Jul. 5, 2002, Oslo, Norway, Abstract Book, Supplement 13, Abstract No. p. 371, p. 258.
- 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.
- Desai, N. et al. (Dec. 2003). "Evidence of Greater Antitumor Activity of Cremophor®-Free Nanoparticle Albumin-Bound (nab) Paclitaxel

(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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