

Harry B. Demopoulos, M.D.
CURRICULUM VITAE

EDUCATION

Pre-Medical:

1949 - 1952 - New York University Heights College, New York, N.Y, Scholastic standing scholarship. Chemistry major, on Dean's Honor List for three years; entered medical school after three years.

Medical:

1952 - 1956 - State University of New York, College of Medicine, New York, N.Y., M.D., honor graduate. Top ten in class.

Internship

1956 - 1957 - King's County Hospital, Brooklyn, N.Y.
University Medical Service - straight medicine.

Residency and Experimental Pathology Fellowship:

1957-1961 - Department of Pathology, New York University School of Medicine, New York, N.Y.

1957-1961 - Training fellowship, National Institutes of Health Training Grant, Experimental Pathology, New York University School of Medicine, New York, N.Y.

LICENSURE AND CERTIFICATION

American Board of Pathology - 1961
New York State Medical License
California Medical License

ACADEMIC AND HOSPITAL POSITIONS

New York University School of Medicine; Associate Professor of Pathology with permanent tenure, 1967 – retired, 2000.

- a. Director, Planning, New York University Comprehensive Cancer Center 1973 - 1976.
- b. Director, Graduate Studies in Experimental and Molecular Pathology, 1970 - 1974.

University of Southern California School of Medicine; Associate Professor of Pathology 1963 - 1967.

- a. Director, Electron Microscopy and Cell Biology Laboratories, 1963- 1967.
- b. Recipient of Research Career Development Award from the National Cancer Institute, 1963 - 1967.
- c. Director, Graduate Studies in Pathology, 1964 - 1967.
- d. Attending in Surgical Pathology, Los Angeles County General Hospital, 1964 - 1966.

National Institutes of Health, Laboratory of Experimental Pathology; Senior Assistant Surgeon, Commissioned Corps. USPHS, 1961-1963.

- a. Tumor Metabolism Research
- b. Radiation Pathology
- c. Service Pathology for the Indian Health Service.

OTHER PROFESSIONAL POSITIONS

International Study Center for Environmental Health Sciences, Inc. A public, charitable, non-profit consortium of leading scientists in the public service. President of the Board of Directors (non-remunerative), 1980 - 1983.

MEMBERSHIPS

Life Member, New York Academy of Sciences

TRUSTEESHIPS

Doris Duke Charitable Foundation, New York
1996-present

RESEARCH INTERESTS

Basic Science Research:

Principal interest is to elucidate the role of pathological free radical reactions, and the effects of the subsequent **losses of glutathione** on: cell signaling; expression of genes involved in growth factors and inflammation; bioenergetics; protein structure; and apoptosis in the major degenerative diseases, and toxic exposures, including: (i) dry macular degeneration, (ii) diabetic complications, (iii) heart failure, (iv) viral hepatitis, (v) HIV/AIDS, (vi) strokes, Alzheimer's and Parkinson's, (vii) coronary artery disease, (viii) radiation injuries, (ix) poisonings, and (x) microbiological assaults, with and without Sepsis. Basic research has focused on free radical damage to cell membranes, and membrane-associated macromolecules for the past 35 years, induced by photons of blue light, trauma, ischemia, hyperglycemia, HIV, radiation and other factors. Corollary interest is in restoring normal cell signaling, control over expression of disease-related genes, and preventing pathologic apoptosis in strategically located cells, and all the other glutathione functions.

Applications of Research:

- a. Application of cell signaling pharmaceuticals, as investigational new drugs, to medical and surgical problems cited above, for example, development of pharmaceutical glutathione to ameliorate the effects of macular degeneration, diabetic complications, heart failure, viral hepatitis and HIV/AIDS among others.
- b. Resoration of glutathione to protect against toxic exposures, as from radiation, poisonings, and microbiological assaults, with and without Sepsis.

AWARDS AND DISTINCTIONS

1. Research Career Development Award, National Cancer Institute
2. Elected as one of 25 Top Sports Medicine Scientists for defining aerobic free radical pathology in Sports Medicine, including injuries immunosuppression and others.
3. Editor of Cancer and the Environment, (A Science Textbook) An Academic Review of the Environmental Determinants of Cancer Relevant to Prevention. This defined the major causes of cancer in 1980.
4. Editor of Cancer and the Environment, Possible Mechanisms of Thresholds for Carcinogens and Toxic Substances. This text provided the science for thresholds, in 1983.
5. Developer of the New York University Comprehensive Cancer Center
6. Developer of the Cancer Institute of New Jersey.

BUSINESS INTERESTS

As part of Translational Medicine, meaning the rapid application of basic research into Clinical Applications, founded:

- Antioxidant Pharmaceuticals Corporation a “Discovery and Patent Holding” Company.
Issued Licenses to the Following:
- ThyoGen Pharmaceuticals, Inc. Versus Diabetes Mellitus and Retinal Degenerations
- ThyoVir Pharmaceuticals, Inc. Versus Viral Infections, Including HIV and Influenza Using Safe, Highly Targeted Pharmaceuticals and Cell-Based “Vaccines”
- ThyoKine Pharmaceuticals, Inc., Safe, Highly Targeted Pharmaceuticals and cell-Based “vaccines” versus cancer.
- ThyoPro Pharmaceuticals, Inc., Safe, Intra-Venous Emergency Pharmaceuticals for the Central Nervous System and Cardio Vascular System, starting in the ambulance, throughout the hospital stay, and continued orally as outpatients

ThyoGen Pharmaceutical Inc.

Harry B. Demopoulos, M.D., Chairman and Chief Executive Officer, is a physician and researcher. He did four years of post M.D. training and research at the New York University Medical Center (NYU), and two years at the National Institute of Health (NIH). He was given an NIH Research Career Development Award during his four-year tenure on the professorial staff of the University of Southern California, School of Medicine. He subsequently returned to NYU. He is credited, together with colleagues, for pioneering work in free radical pathology and antioxidant pharmacology initiated in 1965. They employed these sciences to develop pharmaceutical products that control cytokines, regulate genes and energy production and stem disease-related apoptosis mediated by glutathione (GSH) deficiency.

Dr. Demopoulos is the author or co-author of more than ninety published scientific research papers and two science texts. He has been honored by the National Cancer Institute and is a Life Member of the New York Academy of Sciences. Dr. Demopoulos directed the development of the New York University Comprehensive Cancer Center and the Cancer Institute of New Jersey

Dr. Demopoulos serves in both community and charitable organizations. He founded the International Study Center for Environmental Health Sciences which created international symposia that established, in 1980, the preventable causes of cancer. He also helped in developing the Doris Duke Charitable Foundation, a \$1.5 billion public charity that provides grants for medical research, protection of the environment, the advancement of the performing arts, and the prevention of child abuse. Dr. Demopoulos serves as one of the founding, life-time Trustees of the Foundation and provides additional services on its Finance and Audit Committee and the Properties Committee. In 2003, Dr. Demopoulos was honored by the United States Congressional Leadership as Physician of the Year, and separately, as Businessman of the Year.

7 Westchester Plaza
Elmsford, NY 10523
914.592.3155

hdemopoulos@thyogen.com

PUBLICATIONS

1. Demopoulos, H.B., Kaley, G, and Zweifach, B.W. The histologic distribution of renin in the kidneys of the rat and rabbit. *Am. J. Path.* **37**: 443, 1960.
2. Demopoulos, H.B., Kaley, G. and Zweifach, B.W. Production of occlusive vascular lesions by bacterial endotoxin in kidneys of rats with deoxycorticosterone hypertension. *Am. J. Path.* **37**: 751, 1960.
3. Demopoulos, H.B., Kaley, G. and Zweifach, B.W. Response of granular juxtaglomerular cells and tissue mast cells in various experimental states. *Circ. Res.* **9**: 845, 1961.
4. Kaley, G., Demopoulos, H.B. and Zweifach, B.W. Occlusive vascular lesions induced by bacterial endotoxin in kidneys of pregnant rats. *Proc. Soc. Exp. Biol. and Med.* **1W** 456-459, 1962.
5. Demopoulos, H.B. Selective inhibition of S-91 mouse melanoma by phenyl lactate, in vitro. *Bull. N.Y. Acad. Med.* **38**: 509-510, 1962.
6. Demopoulos, H.B. and Kaley, G. Selective inhibition of respiration of pigmented S-91 mouse melanomas by phenyl lactate and the possible related effects on growth. *J. Nat. Cancer Inst.* **30**: 611, 1963.
7. Demopoulos, H.B. and Kaley, G. The role of renal juxtaglomerular cells in the elaboration of erythropoietin. *Fed. Proc.* **23**: 183, 1964.
8. Demopoulos, H.B., Highman, B., Altland, P.D., Gerving, M.A. and Kaley, G. Effects of high altitude on granular juxtaglomerular cells and their possible role in erythropoietin production. *Am. J. Path.* **46**: 497, 1965.
9. Demopoulos, H.B., Kasuga, T., Channing, A.A. and Bagdoyan, H. Comparison of ultrastructure of B-16 and S-91 melanomas and correlation with growth patterns. *Lab. Invest.* **14**: 103, 1965.
10. Demopoulos, H.B., Gerving, M.A. and Bagdoyan, H. Selective inhibition of growth and respiration of melanomas by tyrosinase inhibitors. *J. Natl., Cancer Inst.* **35**: 823-827, 1965.
11. Channing, A.A., Kasuga, T. and Demopoulos, H.B. Virus particles in B-16 and S-91 mouse melanomas and their significance. *Lab Invest.* **14**: 219, 1965.
12. Channing, A.A., Kasuga, T., Horowitz, R.W., Dubois, E. and Demopoulos, H.B. An ultrastructural study of spontaneous lupus nephritis in the NZB/Bl-NZW mouse, *Am. J. Path.* **47**: 677-694, 1965.

13. Demopoulos, H.B. Landgraf, W. Duke, P.S. and Tai, H. Light induced alterations in melanoma related free radicals and the consequences on respiration and growth. *Lab. Invest.* **15**: 1652, 1966.
14. Demopoulos, H.B. Effects of low phenylalanine-tyrosine diet on S-91 mouse melanomas. *J. Natl. Cancer Inst.* **37**: 185, 1966.
15. Mitamura, A, Yen, T., Duke, P.S. and Demopoulos, H.B. Ultrastructure of S-91 mouse melanomas subjected to phenylalanine and tyrosine restriction in vivo. *Am. J. Path.* **49**: 309-324, 1966.
16. Demopoulos, H.B. Effects of reducing the phenylalanine-tyrosine intake of patients with advanced malignant melanoma. *Cancer* **19**: 657-664, 1966.
17. Duke, P.S., Landgraf, W., Mitamura, A. and Demopoulos, H.B. Study of S-91 mouse melanomas by electron paramagnetic resonance spectroscopy and tissue culture. 1. The effect of cysteine on blue light signals and on growth in vitro. *J. Nat. Cancer Inst.* **37**: 191-198, 1966.
18. Duke, P.S., Hourani, B. and Demopoulos, H.B. Study of S-91 mouse melanomas by electron paramagnetic resonance spectroscopy and tissue culture. 11. Effects of penicillamine on e.p.r. signals and growth. *J. Natl. Cancer Inst.* **39**: 1141, 1967.
19. Duke, P.S. and Demopoulos, H.B. In vivo necrosis of large S-91 mouse melanomas by DL- β -phenyl lactic acid plus L-cysteine. *Life Sciences* **6**: 951-957, 1967.
20. Duke, P.S. and Demopoulos, H.B. One dimensional paper chromatography method for determination of urinary homovanillic acid. *Clinical Chemistry* **14**: 212-221, 1967.
21. Goldstein, B.D., Balchum, O.J., Demopoulos, H.B. and Duke, P.S. Electron paramagnetic resonance spectroscopy. Free Radical signals associated with ozonization of linoleic acid. *Arch. Env. Health* **17**: 46, 1967.
22. Duke, P.S., Yuen, T.G, and Demopoulos, H.B. In vivo inhibition of S-91 mouse melanoma by tyrosine substrate analogous, with and without L-cysteine. *Cancer Res.* **27**: 1783-1787, 1967.
23. Demopoulos, H.B. and Yuen, T.G. Fine structure of melanosomes in S-91 mouse melanomas. *Am. J. Path.* **50**: 559-569, 1967.
24. Fuchs, B., Duke, P.S. and Demopoulos, H.B. Cytologic effects of L-cysteine on malignant melanoma cells. *Acta Cytologica*, August 1968.

25. Hourani, B.T. and Demopoulos, H.B. Inhibition of S-91 mouse melanoma metastases and growth by D-Penicillamine. *Lab. Invest*, **21**: 434-438, 1969.
26. Regan, M.A.G., Regan, D.H. and Demopoulos, H.B. The Vital Respiratory Role of Tyrosinase in Pigmented S-91 melanomas. In: Pigmentation: Its Genesis and Biological Control. Chapter 43. Appleton-Century-Crofts, New York, 1972, p. 543.
27. Fierman, H. and Demopoulos, H.B. Preparation of fractions of premelanosomes and melanosomes from pigmented S-91 melanomas. In: Pigmentation: Its Genesis and Biologic Control. Chapter 41. Appleton-Century-Crofts, New York, 1972, p. 515.
28. Bitensky, M.W., Demopoulos, H.B. and Russel, B. MSH responsive adenylate cyclase in the Cloudman S-91 melanoma. In: Pigmentation: Its Genesis and Biologic Control. Chapter 19. Appleton-Century-Crofts, New York, 1972, p. 247.
29. Demopoulos, H.B., Milvy, P., Kakari, S. and Ransohoff, J. Molecular aspects of membrane structure in cerebral edema. In: Steroids and Brain Edema. H.J. Reulen and K. Schurmann (Eds.). Springer-Verlag, New York, 1972, p. 29-39.
30. Ortega, B.D., Demopoulos, H.B. and Ransohoff, J. Effect of antioxidants on experimental cold-induced edema. In: Steroids and Brain Edema. H.J. Reulen and K. Schurmann (Eds.). Springer Verlag, New York, 1972, p. 167-175.
31. Zara, H.D. and Demopoulos, H.B. Quantitative study of melanosomes and mitochondrial populations in pigmented and amelanotic S-91 mouse melanomas. *Cancer Res.* **33**: 47-50, 1973.
32. Demopoulos, H.B. Control of free radicals in biologic systems. *Fed. Proc.* **32**: 1903-1908, 1973.
33. Demopoulos, H.B. The basis of free radical pathology. *Fed. Proc.* **32**: 1859-1861, 1973.
34. Seligman, M.L. and Demopoulos, H.B. Spin probe analysis of membrane perturbations produced by chemical and physical agents. *Annal. N.Y. Acad. Sci.* **222**: 640-667, 1973.
35. Milvy, P., Kakari, S., Campbell, P., and Demopoulos, H.B. Paramagnetic species and radical products in cat spinal cord. *Annal. N.Y. Acad. Sci.* **222**: 1102-1111, 1973.
36. Campbell, P., DeCrescito, J., Tomasula, J., Demopoulos, H.B., Flamm, E.S., and Ransohoff, J. Experimental treatment of spinal cord contusion in the cat. *Surg. Neurol.* **1**: 102-106, 1973.

37. Regan, D.H., Lavietes, B.B., Regan, M.G., Morris, H.P. and Demopoulos, H.B. Glutamate mediated respiration in tumors. *J. Natl. Cancer Inst.* **51**: 1012-1017, 1973.
38. Campbell, P., DeCrescito, V., Tomasula, J., Demopoulos, H.B., Flamm, E.S., and Ortega, B.D. Effects of antifibrinolytic and steroid therapy on the contused spinal cord in cats. *J. Neurosurgery* **40**: 726-733, 1974.
39. Lavietes, B.B., Regan, D.H. and Demopoulos, H.B. Glutamate oxidation in 6C314ED lymphoma: Effects of L-asparaginase on sensitive and resistant lines. *Proc. Natl. Acad. Sciences (USA)* **71**: 3993-3997, 1974.
40. DeCrescito, B., Demopoulos, H.B., Flamm, E.S. and Ransohoff, J. Ethanol potentiation of traumatic cerebral edema. *Surg. Forum* **25**: 438-440, 1974.
41. Demopoulos, H.B., Jones, W.B., Lavietes, B., Seligman, M.L., Coleman, P. and Poser, R. Manipulation of free radicals in pigmented melanomas- effects on metabolism and growth. In: Pigment Cell Biology. **Vol. 2**. Karger, Basel, 1976, p. 347-364.
42. Demopoulos, H.B., Flamm, E.S., Seligman, M.L., Poser, R. and Ransohoff, J. Molecular pathology of lipids in CNS membranes. In: Oxygen and Physiological Function. Prof. Infor. Libr., Dallas, 1976, p. 491-508.
43. Pietronigro, D., Seligman, M.L., Jones, W.B.G. and Demopoulos, H.B. Retarding effects of DNA on the autoxidation of liposomal suspensions. *Lipids* **11**: 808-813, 1976.
44. Flamm, E.S., Demopoulos, H.B., Seligman, M.L., Tomasula, J., DeCrescito, V. and Ransohoff, J. Ethanol potentiation of central nervous system trauma. *J. Neurosurgery* **46**: 328-335, 1977.
45. Pietronigro, D.D., Jones, W.B.G., Kalty, K. and Demopoulos, H.B. Interaction of DNA and liposomes as a model for membrane-mediated DNA damage. *Nature* **267**: 78-79, 1977.
46. Demopoulos, H.B., Flamm, E.S., Seligman, M.L., Jorgensen, E. and Ransohoff, J. Antioxidant effects of barbiturates in model membranes undergoing free radical damage. In: Cerebral Function, Metabolism and Circulation. (Copenhagen, 1977). Ingvar, D.H. and Lassen, N.A., (Eds.). *Acta Neurol. Scand. (Suppl. 64)* **56**: 152-153, 1977.
47. Flamm, E.S., Demopoulos, H.B., Seligman, M.L. and Ransohoff, J. Possible molecular mechanisms of barbiturate-mediated protection in regional cerebral ischemia. In: Cerebral Function, Metabolism and Circulation (Copenhagen, 1977). Ingvar, D.H. and Lassen, N.A. (Eds.). *Acta Neurol. Scand. (Suppl. 64)* **56**: 150-151, 1977.

48. Seligman, M.L., Flamm, E.S., Goldstein, B.D., Poser, R.G., Demopoulos, H.B. and Ransohoff, J. Spectrofluorescent detection of malonaldehyde as a measure of lipid free radical damage in response to ethanol potentiation of spinal cord trauma. *Lipids* **12**: 945-950, 1977.
49. Demopoulos, H.B., Yoder, M., Gutman, E.G., Seligman, M.L., Flamm, E.S., and Ransohoff, J. The fine structure of endothelial surfaces in the microcirculation of experimentally injured feline spinal cords. *Scanning Electron Microscopy* **2**: 667-682, 1978.
50. Flamm, E.S., Demopoulos, H.B., Seligman, M.L., Poser, R.G. and Ransohoff, J. Free radicals in cerebral ischemia. *Stroke* **9**: 445-447, 1978.
51. McGinness, J.E., Proctor, P.H., Demopoulos, H.B., Hokansen, J.A. and Kirkpatrick, D. S. Amelioration of cis-platinum nephrotoxicity by orgotein (superoxide dismutase). *Physiol. Chem. and Phys.* **10**: 267-277, 1978.
52. Demopoulos, H.B., Flamm, E.S., Seligman, M.L., Mitamura, J.A., and Ransohoff, J. Membrane perturbations in CNS injury: Theoretical basis for free radical damage and a review of the experimental data. In: Neural Trauma. Seminars in Neurological Surgery. Vol.IV. A.J. Popp, R.S. Burke, L.R. Nelson, and H.K. Kimelberg (Eds.). Raven Press, New York, 1979, pp. 289-296.
53. Flamm, E.S., Demopoulos, H.B., Seligman, M.L., Mitamura, J.A. and Ransohoff, J. Barbiturates and free radicals. In: NeuralTrauma. Seminars in Neurological Surgery. Vol.IV. A.J. Popp, R.S. Burke, L.R. Nelson, and H.K. Kimelberg (Eds.). Raven Press, New York, 1979, pp. 289-296.
54. Seligman, M.L., Mitamura, J.A., Shera, N. and Demopoulos, H.B. Corticosteroid modulation of photoperoxidation by ultraviolet light in liposomes. *Photochem. Photobiol.* **29**: 549, 1979.
55. Pietronigro, D.D., McGinness, J., Koren, M.J., Crippa, R., Seligman, M.L. and Demopoulos, H.B. Spontaneous generation of adriamycin semiquinone radicals at physiologic pH. *Physiol. Chem. and Phys.* **11**: 405-414, 1979.
56. Ransohoff, J., Flamm, E.S. and Demopoulos, H.B. Mechanisms of injury and treatment of acute spinal cord trauma. In: Anesthesia and Neurosurgery. J.E. Cottrell and H. Turndorf, (Eds.), C.V. Mosby, Co., St. Louis, MO, 1980, pp. 248-266.
57. Flamm, E.S., Seligman, M.L. and Demopoulos, H.B. Barbiturate protection of the ischemic brain. In: Anesthesia and Neurosurgery. J.E. Cottrell and H. Turndorf, (Eds.). C.V. Mosby, Co., St. Louis, MO, 1980, pp. 248-266.

58. Demopoulos, H.B., Pietronigro, D.D., Flamm, E.S. and Seligman, M.L. The possible role of free radical reactions in carcinogenesis. *J. Env. Path. and Toxicol.* **3(4)**: 273-303, 1980.
59. Demopoulos, H.B. and Gutman, E.G. Cancer in New Jersey and other complex urban/industrial areas. *J. Env. Path. and Toxicol.* **3(4)**: 219-235, 1980.
60. Demopoulos, H.B. and Mehlman, M.A. (Eds.), Cancer and the Environment. An Academic Review of the Environmental Determinants of Cancer Relevant to Prevention. Pathotox Publishers, Inc., Park Forest South, IL, 1980.
61. Demopoulos, H.B. Summary of Conference. Major discussion points and societal interrelationships. *J. Env. Path. and Toxicol.* **3(4)**: 473-481, 1980.
62. Demopoulos, H.B., Flamm, E.S., Pietronigro, D.D. and Seligman, M.L. Free radical pathology and the microcirculation in the major central nervous system disorders. *Acta. Physiol. Scand. Suppl.* **492**: 91-120, 1980,
63. Demopoulos, H.B., Flamm, E.S., Seligman, M.L. and Pietronigro, D.D. Pathology of Oxygen. Oxygen free radicals in central nervous system ischemia and trauma. In: Pathology of Oxygen A. Autor, (Ed.). Raven Press, New York, 1980, pp. 127-155.
64. McGinness, J.E., Proctor, P.H., Demopoulos, H.B., Hokansen, J.A. and Van, N.T. In vivo evidence for superoxide and peroxide production by adriamycin and cis-platinum. In: Pathology of Oxygen. A. Autor, (Ed.). Raven Press, New York, 1980, pp. 191-202.
65. Naftchi, N.E., Demeny, M., Demopoulos, H.B. and Flamm, E.S. The ameliorating effect of pharmacological aspects on the traumatically injured spinal cord. In: Advances in Experimental Medicine, A Centenary Tribute to Claud Bernard, R. Parvez and S. Parvez, (Eds.). Elsevier/North Holland Biomedical Press, Amsterdam, 1980, pp. 373-402.
66. Cimino, J. and Demopoulos, H.B. Determinants of cancer relevant to prevention in the war on cancer. *J. Env. Path. and Toxicol.* **3(4)**: 1-10, 1980.
67. Higginson, J. Proportion of cancers due to occupation. Committee Members: Ballar, III, J.C., Clemmensen, J., Demopoulos, H.B., Garfinkel, L., Hirayama, T. and Schottenfield, D. *Preventive Medicine* **9**: 180, 1980.
68. Hammond, E.C. and Garfinkel, L. General air pollution and cancer in the United States. Committee Members: Demopoulos, H.B., Eisenbud, M., Fraumeni, J., Greenwald, P., Higginson, J., Kraybill, H.F. and O'Conor, G.T. *Preventive Medicine* **9**: 206, 1980.

69. Flamm, E. S., Yoder, M. Kaley, G. and Demopoulos, H.B. The ischemic cerebral cortical microcirculation and the effects of barbiturates. SEM/1980, Inc. AMF O'Hare, Illinois, 1980.
70. Demopoulos, H.B. and Gutman, E.G. The value of contemporary demographic controls in evaluating cancer incidence and mortality rates in heavily industrialized urban areas in the United States. In: Quantification of Occupational Cancer. Banbury Report 9, 1981, pp. 611-629.
71. Demopoulos, H.B, and Flamm, E.S. Possible pathology induced by CoQ 10. In: Biochemical and Clinical Aspects of Coenzyme Q. K. Folkers and Y. Yamamura (Eds.) Elsevier/North-Holland Biochemical Press, New York, NY, 1981, pp. 373-384.
72. Mitamura, J.A., Seligman, M.L., Solomon, J.J., Flamm, E.S., Demopoulos, H.B. and Ransohoff, J. Loss of essential membrane lipids and ascorbic acid from rat brain following cryogenic injury and protection by methylprednisolone. *Neurol. Res.* **3**: 329-344, 1981.
73. Koreh, K., Seligman, M.L., Flamm, E.S. and Demopoulos. H.B. Lipid antioxidant properties of naloxone in vitro. *Biochem. Biophys. Res. Comm.* **102(4)**: 1317-1322, 1981.
74. Young, W., Flamm, E.S., Demopoulos, H.B., Tomasula, J.J. and DeCrescito, J. Effect of naloxone on post traumatic ischemia in experimental spinal contusion. *J. Neurosurg.* **55**: 209-219, 1981.
75. Demopoulos, H.B., Flamm, E.S., Seligman, M.L. and Pietronigro, D.D. Oxygen free radicals in central nervous system trauma. In: Pathology of Oxygen. A, P. Autor, (Ed.). Academic Press, Inc., New York, 1982, pp. 127-155.
76. Demopoulos, H.B., Flamm, E.S., Seligman, M.L., Pietronigro, D.D., Tomasula, J. and DeCrescito, V. Further studies on free radical pathology in the major central nervous system disorders: effect of very high doses of methylprednisolone on the functional outcome, morphology, and chemistry of experimental spinal cord impact injury. *Can. J. Physiol. Pharmacol*, **60**: 1415-1424, 1982.
77. Demopoulos, H.B. Unaccounted variables in hypothesized asbestos carcinogenesis. Second International Symposium on "Epidemiology in Occupational Health", McGill University, Montreal, Quebec, Canada. *Scandinavian Journal of Work, Health and the Environment*, 1982.
78. Demopoulos, H.B., Flamm, E.S., Seligman, M.L., Ransohoff, J. Molecular pathogenesis of spinal cord degeneration after traumatic injury. In: Spinal Cord Injury. N. Eric Naftchi (Ed.), Spectrum Publications, Inc., New York and London, 1982, pp. 45-64.

79. Flamm, E.S., Young, W., Demopoulos, H.B., DeCrescito, V, and Tomasula, J. Experimental spinal cord injury: Treatment with naloxone. *Neurosurgery* **10**: 227-231, 1982.
80. Koreh, K., Seligman, M.L. and Demopoulos, H.B. The effect of dihydroergotoxine on lipid peroxidation in vitro. *Lipids* **17(10)**: 724-726, 1982.
81. Pietronigro, D.D., Demopoulos, H.B., Hovsepian, M. and Flamm, E.S. Brain ascorbic acid depletion during cerebral ischemia. *Stroke* **13**: 117, 1982.
82. Demopoulos, H.B. Pietronigro, D.D. and Seligman, M.L. The development of secondary pathology with free radical reactions as a threshold mechanism. *J. Am. Col. of Toxicol.* **2(3)**: 173-184, 1983.
83. Demopoulos, H.B. (Sr. Ed.) Cancer and the Environment. Possible Mechanisms of Thresholds for Carcinogens and Toxic Substances. Mary Ann Liebert, Inc., New York, 1983.
84. Pietronigro, D.D., Mignano, J.E. and Demopoulos, H.B. Direct quenching of adriamycin radicals by coenzyme Q10 and tetrazolium salts. *Biochem. Pharm.* **32(8)**: 1441-1444, 1983.
85. Pietronigro, D.D., Hovsepian, M., Demopoulos, H.B. and Flamm, E.S. Loss of ascorbic acid from injured feline spinal cord. *Neurochem.* **41(4)**: 1072-1076, 1983.
86. Pietronigro, D.D., Hovsepian, M., Demopoulos, H.B. and Flamm, E.S. Effects of naloxone on ascorbic acid loss from ischemic cerebral cortex. *Stroke* **14**: 123, 1983.
87. Pietronigro, D.D., Levin, M., Hovsepian, M., Demopoulos, H.B. and Flamm, E.S. Tetrazolium salts stimulate adriamycin toxicity in L12010 cells. *Proc. AACR-*. 256,1983.
88. Demopoulos, H.B., Seligman, M.L., Schwartz, M., Tomasula, J. and Flamm, E S, Molecular pathology of cerebral ischemia In: Cerebral Ischemia. A. Bes. P. Braquet, R. Paoletti, and B.K. Siesjo. Elsevier, Amsterdam, 1983, pp. 259-264.
89. Pietronigro, D.D., Hovsepian, M., Demopoulos, H.B, and Flamm, E.S. Reductive metabolism of ascorbic acid in CNS. *Brain Research* **333**: 161-164, 1985.

90. Pietronigro, D.D., DeCrescito, V., Tomasula, J.J., Demopoulos, H.B. and Flamm, E.S. Ascorbic acid- a putative biochemical marker of irreversible neurologic functional loss following spinal cord injury, In: Central Nervous System Trauma. Vol. 2, No. 2, Mary Ann Liebert, Inc., New York, 1985, pp. 85-92.
91. Demopoulos, H.B., Flamm, E.S., Pietronigro, D.D. and Seligman, M.L. Free radical pathology and antioxidants in regional cerebral ischemia and central nervous system trauma. In: Anesthesia and Neurosurgery. Second Edition. James E. Cotrell and Herman Turndorf, (Ed.). The C.V. Mosby Company, St. Louis, MO, 1986, pp. 246-279.
92. Demopoulos, H.B., Santomier, J.P., Seligman, M.L. and Pietronigro, D.D. Free Radical Pathology- Rationale and toxicology of antioxidants and other supplements in sports medicine and exercise science. In: Sport, Health and Nutrition. The 1984 Olympic Scientific Congress Proceedings. Volume 2. Frank I. Katch (Ed.). Human Kinetics Publishers, Inc., Champaign, IL, 1986, pp. 139-189.
93. Demopoulos, H.B., Seligman, M.L. and Flamm, E. The role of free radical pathology in cerebral ischemia and the resulting dementia. In: Senile Dementia: Early Detection. John Libbey & Company Ltd., London, England. 1986, pp. 281-292.
94. Demopoulos, H.B., Seligman, M.L., Richie, J.P. Jr., Summers, B.L., and Furukawa, T. Rapid increases in glutathione concentrations within circulating lymphocytes and monocytes (PBMC's) following oral administration of pharmaceutically stabilized glutathione to HIV positive people. Results of a Phase I/II Clinical Trial. (to be submitted).
95. Kalir, T, Simsir A, Demopoulos H, Demopoulos R I Obstacles to the early detection of endocervical adenocarcinoma. Int J Gynecol Pathol. 2005 Oct;24(4):399-403

Publication of Scientific Articles was replaced with Publications of Pharmaceutical Patents in U.S. and World Wide, beginning in 1986.



U.S. and International Patent Portfolio

Included in this attachment are hyperlink patent numbers and abstracts for the Company's key U.S. and International Patents and published patent applications, followed by a table of all patents owned by and its related companies. (You may access the complete patents by clicking the patent number as a hyperlink, then select "requested patent", available on the enclosed CD).

U.S. Patents

[US Patent No. 6,586,404](#)

A method for the administration of glutathione orally comprising the administration of a bolus of glutathione which is pharmaceutically stabilized and encapsulated. The glutathione is administered on an empty stomach. The preferred stabilizer is ascorbic acid.

[US Patent No. 6,350,467](#)

A method of increasing glutathione levels in mammalian cells comprising administering an oral bolus of encapsulated pharmaceutically stabilized glutathione in a rapidly dissolving formulation to a mammal on an empty stomach. Pharmaceutical formulations including glutathione are also disclosed.

[US Patent No. 6,204,248](#)

A method of altering an expression of a gene product in cells or an organism, comprising orally administering glutathione in an effective amount and under such conditions to alter a redox potential in the cells. The gene expression may be sensitive to redox potential through one or more of a process of induction, transcription, translation, post-translational modification, release, and/or through a receptor mediated process. The glutathione is preferably administered as an oral bolus of encapsulated pharmaceutically stabilized glutathione in a rapidly dissolving formulation to a mammal on an empty stomach.

[US Patent No. 6,159,500](#)

A method for the administration of glutathione orally comprising the administration of a bolus of glutathione which is pharmaceutically stabilized and encapsulated. The glutathione is administered on an empty stomach. The preferred stabilizer is ascorbic acid.

[US Patent No. 5,326,757](#)

The present invention relates to formulations and methods for preventing and treating restenosis following angioplasty. This is accomplished by the regimented administration of a composition which includes selected antioxidants.

[US Patent No. 5,204,114](#)

The present invention relates to methods of neutralizing or dissipating the electrostatic charge of glutathione so as to render it susceptible to be included in high glutathione content solid dosage forms. Capsules and tablets including high levels of glutathione are also described.

International Patents

[European Patent Application No. 0,957,901](#)

A method of increasing glutathione levels in mammalian cells comprising administering an oral bolus of encapsulated pharmaceutically stabilized glutathione in a rapidly dissolving formulation to a mammal on an empty stomach. Pharmaceutical formulations including glutathione are also disclosed.

[European Patent Application No. 0,746,202](#)

The present invention relates to formulations and methods for preventing and treating restenosis following angioplasty. This is accomplished by the regimented administration of a composition which includes selected antioxidants.

[European Patent Application No. 0,633,769](#)

The present invention relates to methods of neutralizing or dissipating the electrostatic charge of glutathione so as to render it susceptible to be included in high glutathione content solid dosage forms. Capsules and tablets including high levels of glutathione are also described.

[PCT Patent Application No. WO9829101](#)

A method of increasing glutathione levels in mammalian cells comprising administering an oral bolus of encapsulated pharmaceutically stabilized glutathione in a rapidly dissolving formulation to a mammal on an empty stomach. Pharmaceutical formulations including glutathione are also disclosed.

[PCT Patent Application No. WO9313660](#)

The present invention relates to formulations and methods for preventing and treating restenosis following angioplasty. This is accomplished by the regimented administration of a composition which includes selected antioxidants.

[Australian Patent Application No. 5,620,598](#)

A method of increasing glutathione levels in mammalian cells comprising administering an oral bolus of encapsulated pharmaceutically stabilized glutathione in a rapidly dissolving formulation to a mammal on an empty stomach. Pharmaceutical formulations including glutathione are also disclosed.

[Australian Patent Application No. 3,970,793](#)

The present invention relates to methods of neutralizing or dissipating the electrostatic charge of glutathione so as to render it susceptible to be included in high glutathione content solid dosage forms. Capsules and tablets including high levels of glutathione are also described.

[Canadian Patent No. 2,125,888](#)

The present invention relates to formulations and methods for preventing and treating restenosis following angioplasty. This is accomplished by the regimented administration of a composition which includes selected antioxidants.

[German Patent Application No. 69,329,060](#)

The present invention relates to methods of neutralizing or dissipating the electrostatic charge of glutathione so as to render it susceptible to be included in high glutathione content solid dosage forms. Capsules and tablets including high levels of glutathione are also described.

[German Patent No. 3,382,047](#)

Dry, stable, self-lubricating formulations for use as pharmaceuticals or vitamin/mineral supplements, which do not require the inclusion of fillers, lubricants, binders and other conventional excipients, and which exhibit excellent free flowability and compressibility characteristics, are produced by incorporating crystalline ascorbic acid or physiologically acceptable ascorbate salts therein.

[US6350467](#) Pharmaceutical Preparations Of Glutathione And Methods Of Administration Thereof

US6204248 Pharmaceutical Preparations Of Glutathione And Methods Of Administration Thereof

[DE69329060](#) No Title Available.

[US6159500](#) Pharmaceutical Preparations Of Glutathione And Methods Of Administration Thereof

[DE3382047D](#) No Title Available.

[EP0957901](#) Pharmaceutical Preparations Of Glutathione And Methods Of Administration Thereof

[AT99946T](#) No Title Available.

[AT58832T](#) No Title Available.

[AU5620598](#) Pharmaceutical Preparations Of Glutathione And Methods Of Administration Thereof

[WO9829101](#) Pharmaceutical Preparations Of Glutathione And Methods Of Administration Thereof

[US5326757](#) Pharmaceutically Active Antioxidant Containing Composition And The Method Of Its Use To Prevent And Treat Restenosis Following Angioplasty

[US5204114](#) Methods Of Manufacturing High Dosage Glutathione The Tablets And Capsules Produced Thereby

[US4454125](#) Dry Powder Formulations Having Improved Flow And Compressibility Characteristics, And Method For The Preparation Thereof

[WO9319740](#) Methods Of Manufacturing High Dosage Glutathione, The Tablets And Capsules Produced Thereby

[WO9313660](#) Pharmaceutically Active Antioxydant Containing Composition And The Method Of Its Use To Prevent And Treat Restenosis Following Angioplasty

[WO8303757](#) Dry Powder Formulations Having Improved Flow And Compressibility Characteristics, And Method For The Preparation Thereof

[EP0746202](#) Pharmaceutically Active Antioxydant Containing Composition And The Method Of Its Use To Prevent And Treat Restenosis Following Angioplasty

[EP0633769](#) Methods Of Manufacturing High Dosage Glutathione, The Tablets And Capsules Produced Thereby.

[EP0444000](#) Storage-Stable Glucosamine Sulphate Oral Dosage Forms And Methods For Their Manufacture.

[EP0105924](#) Dry Powder Formulations Having Improved Flow And Compressibility Characteristics, And Method For The Preparation Thereof.

[DE69100954](#) No Title Available.

[CA2125888](#) Pharmaceutically Active Antioxidant Containing Composition And The Method Of Its Use To Prevent And Treat Restenosis Following Angioplasty

[CA2035841](#) Storage-Stable Glucosamine Sulphate Oral Dosage Forms And Methods For Their Manufacture

[CA1209041](#) Dry Powder Formulations Having Improved Flow And Compressibility Characteristics, And Method For The Preparation Thereof

[AU3970793](#) Methods Of Manufacturing High Dosage Glutathione, The Tablets And Capsules Produced Thereby