

Survey Of Aspartame Studies: Correlation Of Outcome And Funding Sources

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ABSTRACT

Studies of aspartame in the peer reviewed medical literature were surveyed for funding source and study outcome. Of the 166 studies felt to have relevance for questions of human safety, 74 had Nutrasweet® industry related funding and 92 were independently funded. One hundred percent of the industry funded research attested to aspartame's safety, whereas 92% of the independently funded research identified a problem. A bibliography supplied by the Nutrasweet® Company included many studies of questionable validity and relevance, with multiple instances of the same study being cited up to 6 times. Questions are raised both about aspartame's safety and the broader issue of the appropriateness of industry sponsorship of medical research.

As the chart currently stands, it includes classic studies, case reports, literature reviews and letters to the editor. A meta-analysis, critically evaluating study protocols, pooling studies with data, evaluating case reports and letters separately, etc. is clearly needed. Even in its present form, however, the chart highlights findings which are noteworthy.

Of the industry-sponsored articles, 74/74 (100%) attested to aspartame's safety. Of the non-industry sponsored articles, 84/91 (92%) identified a problem. The seven non-industry studies attesting to aspartame's safety were six studies from the FDA and one literature review reflecting almost exclusively the industry sponsored research.

One could argue that the FDA studies should not be considered truly "independent". The role of the FDA in aspartame's approval has been quite controversial and is a matter of public record. In 1980, the FDA appointed a Board of Public Inquiry to address the question of aspartame's safety. The Board concluded that some of Searle's test results were "bizarre" and recommended additional long-term testing prior to approval. Commissioner Arthur Hull Hayes overruled the Board and granted approval for aspartame's use in dry foods in 1981 and in beverages in 1983. Within 3 months of the 1983 approval, Hayes resigned from the FDA and accepted a position as a paid consultant to Searle's public relations firm. If the FDA studies and the literature review

focusing only on the Nutrasweet® industry funded research are excluded, then 100% of the truly independently funded research demonstrated some type of adverse reaction to aspartame.

Whether 100% or 92%, the clear split in the literature, with outcome correlated so closely to funding source, is deeply troubling.

STUDY OUTCOME

| DATE | <u>INDUSTRY SPONSORED RESEARCH</u> | FUNDING SOURCE | ADVERSE REACTION IDENTIFIED | SAFETY OF ASPARTAME SUPPORTED |
|------|---|----------------|-----------------------------|-------------------------------|
| 1976 | Koch R, Schaeffler G, Shaw NF. Results of Loading Doses of Aspartame by two Phenylketonuric (PKU) Children Compared with two Normal Children. J Toxicol Environ Health 1976;2(2):459-469. | Searle | | X |
| 1976 | Stern SB, Bleicher SJ, Flores A, et al. Administration of Aspartame in Non-Insulin Dependent Diabetics, J Toxicol Environ Health 1976;2:429-439. | Searle | | X |
| 1976 | Knopp RH, Brandt K, Arky RA. Effects of Aspartame in Young Persons During Weight Reduction. J Toxicol Environ Health 1976;2:417-428. | Searle | | X |
| 1976 | Frey GH. Use of Aspartame By Apparently Healthy Children and Adolescents. J Toxicol Environ Health 1976;2:401-415. | Searle | | X |
| 1976 | Koch R, Shaw KN, Williamson M, Haber M. Use of Aspartame in Phenylketonuric Heterozygous Adults. J Toxicol Environ Health 1976;2(2):453-7. | Searle | | X |
| 1977 | Stegink LD, Filer LJ Jr, Baker GL. Effect of Aspartame and Aspartate Loading Upon Plasma and Erythrocyte Free Amino Acid Levels in Normal Adult Volunteers. J Nutr 1977;107:1837-1845. | Searle | | X |
| 1979 | Stegink LD, Filer LJ Jr, Baker GL. Plasma, Erythrocyte and Human Milk Levels of Free Amino Acids in Lactating Women Administered Aspartame or Lactose. J Nutr 1979;109:2173-2181. | Searle | | X |
| 1980 | Potts WJ, Bloss JL, Nutting EF. Biological Properties of Aspartame-Evaluation of Central Nervous System Effects. J Environ Pathol Toxicol 1980;3(5-6):341-353. | Searle | | X |
| 1980 | Saunders FJ, Pautsch WF, Nutting EF. The | Searle | | X |

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|------|---|--------------------|--|---|
| | Biological Properties of Aspartame. IV. Examination for Endocrine Like Activities. J Exper Pathol Toxicol 1980;3:363-373. | | | |
| 1980 | Lennon HD, Metcalf LE, Mares SE. The Biological Properties of Aspartame. IV. Effects on Reproduction and Lactation. J Environ Pathol Toxicol 1980;3:375-386. | Searle | | X |
| 1980 | Bianchi RG, Muir ET, Cook DL, Nutting EF et al. The Biological Properties of Aspartame. III. Actions Involving the Gastrointestinal System, J. Environ Pathol Toxicol 1980;3:355-362. | Searle | | X |
| 1980 | Aspinall RL, Saunders RN, Pautsch WF, Nutting SF. The Biological Properties of Aspartame: Effects on a Variety of Physiological Parameters Related to Inflammation and Metabolism. J Environ Pathol Toxicol 1980 Jun-Jul;3(5-6):387-95. | Searle | | X |
| 1981 | Stegink LD, Brummel MC, McMartin K, et al. Blood Methanol Concentrations in Normal Adult Subjects Administered Abuse Doses of Aspartame. J Toxicol Environ Health 1981;7:281-290. | Searle | | X |
| 1981 | Stegink LD, Filer LJ Jr, Baker GL. Plasma and Erythrocyte Concentrations of Free Amino Acids in Adult Humans Administered Abuse Doses of Aspartame. J Toxicol Environ Health 1981;7:291-305 | Searle | | X |
| 1981 | Stegink LD, Filer LJ Jr, Baker GL. Effect of Aspartame and Sucrose Loading in Glutamate-Susceptible Subjects. Am J Clin Nutr 1981;34(9):1899-1905. | Searle | | X |
| 1981 | Ishii H. Incidence of Brain Tumors in Rats Fed Aspartame. Toxicology Letters 1981;7:433-437. | Ajinomoto & Searle | | X |
| 1981 | Ishii H, Koshimizu T, Usami S, Fujimoto T. Toxicity of Aspartame and its Diketopiperazine for Wistar Rats by Dietary Administration for 104 weeks. Toxicology 1981;21:91-94. | Ajinomoto & Searle | | X |
| 1982 | Stegink LD, Filer LJ Jr, Baker GL. Effect of Aspartame Plus Monosodium L-Glutamate Ingestion on Plasma and Erythrocyte Amino Acid Levels in Normal Adult Subjects Fed a High Protein Meal. Am J Clin Nutr 1982;36:1145-1152. | Searle | | X |

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| 1983 | Stegink LD, Filer LJ Jr, Baker GL. Plasma Amino Acid Concentrations in Normal Adults Fed Meals with Added Monosodium L-Glutamate and Aspartame. <i>J Nutr</i> 1983;113:1851-1860. | Searle | | X |
| 1983 | Filer LJ Jr, Baker GL, Stegink LD. Effect of Aspartame Loading on Plasma and Erythrocyte Free Amino Acid Concentrations in One Year Old Infants. <i>J Nutr</i> 1983;113:1591-1599. | General Foods Corp. | | X |
| 1983 | Stegink LD, Brummel MC, Filer LJ Jr, Baker GL. Blood Methanol Concentrations in One-Year Old Infants Administered Graded Doses of Aspartame. <i>J Nutr</i> 1983;113:1600-1606. | General Foods Corp. | | X |
| 1984 | Roak-Foltz and Leveille. Projected Aspartame Intake: Daily Ingestion of Aspartic Acid, Phenylalanine, and Methanol. In: Stegink L, Filer L (eds). Aspartame: Physiology and Biochemistry, New York: Marcel Dekker Inc., 1984. | Searle | | X |
| 1985 | Sturtevant F. Does Aspartame Cause Methanol Toxicity. In: Wurtman and Ritter-Walker (eds). Dietary Phenylalanine and Brain Function. Boston: Birkhauser, 1988, pp. 163-168. | Searle | | X |
| 1985 | Nehrling JK, Kobe P, McLane MP, et al. Aspartame Use by Persons with Diabetes. <i>Diabetes Care</i> 1985;8:415-17. | Searle | | X |
| 1985 | Gaull GE. Aspartame and Seizures. <i>Lancet</i> 1985;2(8469-70):1431 | Nutra sweet | | X |
| 1986 | Torii K, Mimura T, Takasaki Y, Ichimura M. Dietary Aspartame with Protein on Plasma and Brain Amino Acids, Brain Monoamines and Behavior in Rats. <i>Physiol Behav</i> 1986;36(4):765-72. | Ajinomoto | | X |
| 1986 | Torii K, Mimura T, Takasaki Y, Ichimura M. Effect of Mealing on Plasma and Brain Amino Acid, and Brain Monoamine in Rats after Oral Aspartame. <i>Physiol Behav</i> 1986;36(4):759-64. | Ajinomoto | | X |
| 1986 | Szucs EF, Barrett KE, Metcalfe DD. The Effect of Aspartame on Mast Cells and Basophils. <i>Food Chem Toxic</i> 1986;24(2):171-174 | Intl. Life Sciences | | X |
| 1987 | Schiffman SS, Buckley CE 3 rd Sampson | Nutra | | X |

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|------|--|---------------------|--|---|
| | HA. Aspartame and Susceptibility to Headache. N Engl J Med 1987;317(19):1181-1185. | sweet | | |
| 1987 | Ryan-Harshman M, Leiter LA, Anderson GH. Phenylalanine and Aspartame Fail to Alter Feeding Behavior, Mood and Arousal in Men. Physiology and Behavior 1987;39:247-253. | Intl. Life Sciences | | X |
| 1987 | Stegink LD, Filer LJ Jr, Baker GL. Plasma Amino Acid Concentrations in Normal Adults Ingesting Aspartame and Monosodium L-Glutamate as Part of a Soup/Beverage Meal. Metabolism 1987;36(11):1073-1079. | Nutra sweet | | X |
| 1987 | Cho ES, Coon JD, Stegink LD. Plasma and Urine Diketopiperazine Concentrations in Normal Adults Ingesting Large Quantities of Aspartame. Food Chem Toxicol 1987;25(7):499-504. | Searle | | X |
| 1988 | Kanders BS, Lavin PT, Kowalchuck M, et al. An Evaluation of the Effect of Aspartame on Weight Loss. Appetite 1988;Volume II(Suppl 1):73-84. | Nutra sweet | | X |
| 1988 | Shaywitz, et. al. Effects of Aspartame on Seizures in Children. In: Wurtman, Ritter-Walker (eds.) Dietary Phenylalanine and Brain Function. Boston:Birkhauser, 1988, pp. 163-168. | Nutra sweet | | X |
| 1988 | Leiter, et. al., Effects of Phenylalanine and Aspartame on Mealtime Food Intake and Behavior in Adult Males. In: Wurtman, Ritter-Walker (eds.) Dietary Phenylalanine and Brain Function. Boston:Birkhauser, 1988, pp. 296-299. | Intl. Life Sciences | | X |
| 1988 | Keybach and Allen, Resources for Inferential Estimates of Aspartame Intake in the United States. In: Wurtman, Ritter-Walker (eds.) Dietary Phenylalanine and Brain Function. Boston:Birkhauser, 1988, pp. 365-372. | Nutra sweet | | X |
| 1988 | Jobe and Dailey. Role of Monoamines in Seizure Predisposition in the Genetically Epilepsy-Prone Rat. In: Wurtmann and Ritter-Walker (eds.). Dietary Phenylalanine and Brain Function. Boston:Birkhauser, 1988, pp. 127-130. | Nutra sweet | | X |

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|------|--|---------------------|--|---|
| 1988 | Horwitz DL, McLane M, Cobe P. Response to Single Dose of Aspartame or Saccharin by NIDDM Patients. <i>Diabetes Care</i> 1988;2:230-34. | Nutra sweet | | X |
| 1989 | McAnulty PA, Collier MJ, Enticott J, et al. Absence of Development Effects in CFI Mice Exposed to Aspartame in Utero. <i>Fundam Appl Toxicol</i> 1989 Aug;13(2):296-302. | Nutra sweet | | X |
| 1989 | Reilly MA, Debler EA, Fleischer A. Lack of Effect of Chronic Aspartame Ingestion on Aminergic Receptors in Rat Brain. <i>Biochem Pharmacol</i> 1989;38(23):433904361. | Nutra sweet | | X |
| 1989 | Stegink LD, Filer LJ Jr, Bell EF, Ziegler EE, Tephly TR. Effect of Repeated Ingestion of Aspartame-Sweetened Beverage on Plasma Amino Acid, Blood Methanol and Blood Formate Concentration in Normal Adults. <i>Metabolism</i> 1989;38(4):357-363. | Nutra sweet | | X |
| 1989 | Stegink LD, Filer LJ Jr, Bell EF, et al. Repeated Ingestion of Aspartame-Sweetened Beverage: Effect on Plasma Amino Acid Concentrations in Individuals Heterozygous for Phenylketonuria. <i>Metabolism</i> 1989;38(1):78-84. | Searle | | X |
| 1989 | Gupta V, Cochran C, Parker TF, et al. Effect of Aspartame on Plasma Amino Acid Profiles of Diabetic Patients with Chronic Renal Failure. <i>Am J Clin Nutr</i> 1989;49:1302-6. | Nutra sweet | | X |
| 1989 | Leon AS, Hunninghake DB, Bell C, et al. Safety of Long-term Large Doses of Aspartame. <i>Arch Intern Med</i> 1989;149(10):2318-24. | Searle | | X |
| 1989 | Dailey JW, Lasley SM, Mishra PK, et al. Aspartame Fails to Facilitate Pentylenetetrazol-Induced Convulsions in CD-1 Mice. <i>Toxicol Appl Pharmacol</i> 1989;98:475-486. | Nutra sweet | | X |
| 1989 | Anderson GH, Saravis S, Schacher R, Zlotstein S, Leiter LA et al. Aspartame: Effect on Lunch Time Food Intake Appetite and Hedonic Response in Children. <i>Appetite</i> 1989;13:93-103. | Intl. Life Sciences | | X |

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|------|---|---------------------|--|---|
| 1989 | Holder MD. Effects of Perinatal Exposure to Aspartame on Rat Pups. Neurotoxicology and Teratology 1989;11(1):1-6. | Nutra sweet | | X |
| 1989 | Cain DP, Boon F, Bevan M. Failure of Aspartame to Affect Seizure Susceptibility in Kindled Rats. Neuropharmacology 1989;28(4):433-435. | Nutra sweet | | X |
| 1989 | Carlson HE, Shaw JH. Aspartame and its Constituent Amino Acids: Effect on Prolactin, Cortisol, Growth Hormone, Insulin and Glucose in Normal Humans. Am J Clin Nutr 1989;49(3):427-432 | Nutra sweet | | X |
| 1990 | Saravis S, Schachar R, Zlotkin S, Leiter LA, Anderson GH. Aspartame: Effects on Learning Behavior and Mood. Pediatrics 1990;86(1):75-83. | Intl. Life Sciences | | X |
| 1990 | Stegink LD, Filer LJ Jr, Bell EF, et al. Repeated Ingestion of Aspartame-Sweetened Beverages: Further Observations in Individuals Heterozygous for Phenylketonuria. Metabolism 1990;39(10):1076-1081. | Searle | | X |
| 1990 | Lapierre KA, Greenblatt DJ, Goddard JE, Harmatz JS, Shader RI. The Neuropsychiatric Effects of Aspartame in Normal Volunteers. J Clin Pharmacol 1990;30(5):454-460. | Nutra sweet | | X |
| 1990 | Burns TS, Stargett WW, Hurwitz A. Bioavailability of Phenylalanine and Aspartame from Aspartame (20 mg/kg) in Capsules and Solution. Metabolism 1990;39(11):1200-3 | Nutra sweet | | X |
| 1991 | Koeppe RA, Shulkion BL, Rosenspire KC. Effect of Aspartame-Derived Phenylalanine on Neutral Amino Acid Uptake in Human Brain: A Positron Emission Tomography Study. J Neurochem 1991;1526-1535. | Nutra sweet | | X |
| 1991 | Garriga MM, Berkebile C, Metcalfe DD. A Combined Single - Blind, Double Blind, Placebo-Controlled Study to Determine the Reproducibility of Hypersensitivity Reactions to Aspartame. J Allergy Clin Immunol 1991 April;87(4):821-7. | Intl. Life Sciences | | X |
| 1991 | Mullenix PJ, Tassinari MS, Schunior A, | Nutra | | X |

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|------|---|---------------------|--|---|
| | Kernan WJ. No Change in Spontaneous Behavior of Rats After Oral Doses of Aspartame, Phenylalanine and Tyrosine. Fundam Appl Toxicol 1991; 16(3):495-505. | sweet | | |
| 1991 | Moser RH. Aspartame. South Med J 1991;84(12):1509-10. | Nutra sweet | | X |
| 1991 | Daily JW, Lasley SM, Burger RL, et al. Amino Acids, Monoamines and Audiogenic Seizures in Genetically Epilepsy-Prone Rats: Effects of Aspartame. Epilepsy Res 1991;8:122-133. | Nutra sweet | | X |
| 1991 | Fernstrom JD, Fernstrom MH, Massoudi MS. In Vivo Tyrosine Hydroxylation in Rat Retina: Effect of Aspartame Ingestion in Rats Pretreated with P-Chlorophenylalanine. Am J Clin Nutr 1991;53(4):923-9. | Nutra sweet | | X |
| 1991 | Burns TS, Stargel WW, Tschanz C, Kotsonis PN, Hurwitz A, et al. Aspartame and Sucrose Produce a Similar Increase in the Plasma Phenylalanine to Large Neutral Amino Acid Ratio in Healthy Subjects. Pharmacology 1991;43:210-219. | Nutra sweet | | X |
| 1991 | Butchko HH, Kotsonis FN. Acceptable Daily Intake vs. Actual Intake: The Aspartame Example. J Am Coll Nutr 1991;10(3):258-266. | Nutra sweet | | X |
| 1992 | Hjelle JJ, Dudley RE, Marietta MP, et al. Plasma Concentrations and Pharmacokinetics of Phenylalanine in Rats and Mice Administered Aspartame. Pharmacology 1992;44(1):48-60. | Nutra sweet | | X |
| 1993 | Karstaedt PJ, Pincus JH. Aspartame Use in Parkinson's Disease. Neurology 1993;43(3 pt 1):611-613. | Intl. Life Sciences | | X |
| 1993 | Geha R, Buckley CE, Greenberger P, et al. Aspartame is no More Likely than Placebo to Cause Urticaria/Angioedema: Results of a Multicenter, Randomized, Double-Blind, Placebo-Controlled, Crossover Study. J Allergy Clin Immunol 1993;92:513-20. | Nutra sweet | | X |
| 1993 | Hertelendy ZI, Mendenhall CL, Rouster SD, Marshall L, Weesner R. Biochemical and Clinical Effects of Aspartame in Patients with Chronic, Stable Alcoholic | Nutra sweet | | X |

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|------|--|---------------------|--|---|
| | and Liver Disease. Am J Gastroenterol 1993;88(5):737-743. | | | |
| 1994 | Trefz F, deSonneville L, Matthis P, et al. Neuropsychological and Biochemical Investigations in Heterozygotes for Phenylketonuria During Ingestion of High Dose Aspartame. Human Genetics 1994;93:369-374. | Nutra sweet | | X |
| 1994 | Shaywitz BA., Anderson GM, Novotny EJ, et al. Aspartame has no Effect on Seizures or Epileptiform Discharges in Epileptic Children. Ann Neurol 1994;35:98-103. | Nutra sweet | | X |
| 1994 | Shaywitz BA, Sullivan CM, Anderson GM, et al. Aspartame, Behavior, and Cognitive Function in Children With Attention Deficit Disorder. Pediatrics 1994;93:70-75. | Nutra sweet | | X |
| 1994 | Wolraich ML, Lindgren SD, Stumbo PJ, et al. Effects of Diets High in Sucrose or Aspartame on the Behavior and Cognitive Performance of Children. N Engl J Med 1994;330(5):301-307. | Intl. Life Sciences | | X |
| 1994 | Drewnowski A, Massie C, Louis-Sylvestre J, et al. Comparing the Effects of Aspartame and Sucrose on Motivational Ratings, Taste Preferences, and Energy Intakes in Humans. Am J Clin Nutr 1994;59:338-65. | Nutra sweet | | X |
| 1994 | Moser RH. Aspartame and Memory Loss. JAMA 1994;272(19):1543. | Nutra sweet | | X |
| 1994 | Butchko HH, et al. Postmarketing Surveillance of Food Additives. In: Nutritional Toxicology. Kotsonig, Machky and Jhelle, (eds.) New York: Raven Press Ltd. 1994. | Nutra sweet | | X |
| 1994 | Drewnowski A, Massier C, Louis-Sylvestre J, et al. The Effects of Aspartame Versus Sucrose on Motivational Ratings, Taste Preferences, and Energy Intakes in Obese and Lean Women. International Journal of Obesity 1994;18:570-578. | Nutra sweet | | X |
| 1995 | Rowan AJ, Shaywitz BA, Tuchman L, et al. Aspartame and Seizure Susceptibility: Results of a Clinical Study in Reportedly Sensitive Individuals. Epilepsia 1995;36(3):270-5. | Nutra sweet | | X |

STUDY OUTCOME

| DATE | <u>NON-INDUSTRY SPONSORED RESEARCH</u> | FUNDING SOURCE | ADVERSE REACTION IDENTIFIED | SAFETY OF ASPARTAME SUPPORTED |
|-------------|---|---|--|--|
| 1970 | Olney, Brain Damage in Infant Mice Following Oral Intake of Glutamate, Aspartate or Cysteine. Nature 1970;227:609-610. | Washington University | X | |
| 1975 | Olney JW, Aspartame as a Sweetener. NEJM 1975;292(23):1244-1245. | Washington University | X | |
| 1977 | Mishiro Y and Keneko H, Effect of a Dipeptide, Aspartame, on Lactic Acid Production in Human Whole Saliva. J Dent Res 1977;56(11):1427. | Nippon Dental University, Tokyo | X | |
| 1979 | Brunner RL, Vorhees CV, Kinney L, Butcher RE, et al., Aspartame: Assessment of Developmental Psychotoxicity of a New Artificial Sweetener. Neurobehavioral Toxicology 1979;1:79-86. | USFDA | X | |
| 1980 | Olney, Brain Damage in Mice from Voluntary Ingestion of Glutamate and Aspartate. Neurobehavioral Toxicology and Teratology 1980;2:125-129. | Washington University | X | |
| 1982 | Uribe, Potential Toxicity of a New Sugar Substitute in Patients with Liver Disease. N Engl J Med 1982;173-174. | Institute National De La Nutrition Mexico | X | |
| 1983 | Wurtman, Effects of Aspartame and Glucose on Rat Brain Amino Acids and Serotonin. New England Journal of Medicine 1983;309(7):429-430. | M.I.T. | X | |
| 1983 | Wurtman RJ, Neurological Changes Following High Dose Aspartame with Dietary Carbohydrates. N Engl J Med 1983;309(7):429-430. | M.I.T. | X | |
| 1984 | Olney, Excitotoxic Food Additives Relevance of Animal Studies to Human Safety. Neurobehavioral Toxicology and Teratology 1984;6:455-562. | Research Scientist Award MH-38894 | X | |
| 1984 | Monte, Aspartame: Methanol and the Public Health. J Appl Nutr 36(1):42-54. | Arizona State University | X | |
| 1984 | Yokogoshi H,k Roberts CH, Canballero B, Wuetman RJ, Effects of Aspartame and | M.I.T. | X | |

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| | Glucose Administration on Brain and Plasma Levels of Large Neutral Amino Acids and Brain 5-Hydroxyindoles. Amer J Clin Nutr 1984;40:1-7. | | | |
| 1984 | Mahalik MP and Gautieri RF, Reflex Responsiveness of CF-1 Mouse Neonates Following Maternal Aspartame Exposure. Research Communications in Psychology, Psychiatry & Behavior 1984;9(4):385-403. | None Specified | X | |
| 1985 | Novick, Aspartame Induced Granulomatous Panniculitis. Ann Int Med 102(2):206-207. | Mt. Sinai Medical Center | X | |
| 1985 | Grobelny D and Galardy RE, A Metabolite of Aspartame Inhibits Angiotensin Converting Enzyme. Biochemical and Biophysical Research Communications, 1985; 128(2):960-964. | University of Kentucky | X | |
| 1985 | Wurtman, RJ, Aspartame: Possible Effects on Seizure Susceptibility. Lancet 1985;2(8463):1060. | M.I.T. | X | |
| 1985 | Ferguson JM, Interaction of Aspartame and Carbohydrates in an Eating Disordered Patient. Am J Psych 1985 Feb;142(2):271. | None | X | |
| 1986 | Kulczycki A Jr., Aspartame Induced Urticaria. Ann Intern Med 1986;104(2):207-208. | N.I.H. | X | |
| 1986 | Pardridge WM, The Safety of Aspartame [Letter]. JAMA 1986;256(19):2678. | UCLA School of Medicine | X | |
| 1986 | Koehler SM, A New Dietary Caution for Migraine Sufferers. Dir in Appl Nut 1986;1:1-7. | Center for Brain Sciences and Metabolism U of FL. | X | |
| 1986 | Kiritsky PJ and Maher TJ, Acute Effects of Aspartame on Systolic Blood Pressure in Spontaneously Hypertensive Rats. J Neural Transmission 1986;66(2):121-128. | National Institute of Neurological, Communicative Diseases and Stroke | X | |
| 1986 | Yokogoshi H and Wurtman RJ, Acute Effects of Oral or Parenteral Aspartame on Catecholamine Metabolism in Various Regions of Rat Brain. J Nutr 1986;116:356-364. | M.I.T. | X | |
| 1986 | Walton, Seizure and Mania After High Intake of Aspartame. Psychosomatics 27:218-220. | Chautauqua County Dept of Mental Health | X | |

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| 1986 | Drake ME, Panic Attacks and Excessive Aspartame Ingestion [Letter]. Lancet 1986;2(8507):631. | None | X | |
| 1986 | Johns DR, Migrane Provoked by Aspartame. New Eng J Medicine 1986;315(7):456. | None | X | |
| 1986 | Blundell JE, Hill AJ, Paradoxical Effects of an Intense Sweetener Aspartame on Appetite. Lancet 1986;1(8489):1092-3. | None | X | |
| 1986 | Caballero B, Mahon BE, Rohr FJ, Levy HL, Wurtman RJ, et. al., Plasma Amino Acid Levels after Single Dose Aspartame Consumption in Phenylketonuria Mild Hyperphenylalaninemia and Heterozygous State for Phenylketonuria. Journal of Pediatrics 1986;109(4):668-671. | National Institute of Neurological, Communicate Diseases and Stroke | X | |
| 1986 | Bradstock MK, Serdula MK, Marks IS, et al., Evaluation of Reactions to Food Additives: The Aspartame Experience. AM J Clin Nutr 1986 Mar;43(3):464-9. | Federal Government | X | |
| 1986 | Coulombe RA Jr., Sharma RP, Neurobiochemical Alterations Induced by the Artificial Sweetener Aspartame. Toxicol Appl Pharmacol 1986;83(1):79-85. | Utah State University | X | |
| 1987 | Wurtman RJ, Aspartame Effects on Brain Serotonin. Am J Clin Nutr 1987 Apr;45(4):799-803. | M.I.T. | X | |
| 1987 | Maher TJ and Wurtman RJ, Possible Neurologic Effects of Aspartame, a Widely Used Food Additive. Environmental Health Perspectives 1987;75:53-57. | M.I.T. & Federal Government | X | |
| 1987 | Drogari E, Smith I, Beasley M, Lloyd JK, Timing of Strict Diet in Relation to Fetal Damage in Maternal Phenylketonuria: An International Collaborative Study by the MRC/DHSS Phenylketonuria Register. Lancet 1987;2(8565):927-30. | Institute of Child Health | X | |
| 1987 | Elsas, et al., Changes in Physiological Concentrations of Blood Phenylalanine Produce Changes in Human Brain Function. Dietary Phenylalanine and Brain Function Birkhauser Boston 1988;187-195. | Emory University | X | |
| 1988 | Roberts: Neurological, Psychiatric and Behavioral Reactions to Aspartame in 505 Aspartame Reactors. In: Wurtman and Ritter-Walker (eds.). Dietary Phenylalanine and Brain Function. Boston: Birkhauser, 1988, pp. | Palm Beach Institute for Medical Research | X | |

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| | 373-376. | | | |
| 1988 | Pinto and Maher, Aspartame, Phenylalanine and Seizures in Experimental Animals. In: Wurtman and Ritter-Walker (eds.). Dietary Phenylalanine and Brain Function. Boston: Birkhauser, 1988, pp. 95-103. | National Institute of Neurological and Communicative Diseases and Stroke | X | |
| 1988 | Roberts, Reactions Attributed to Aspartame Containing Products: 551 Cases. Journal of Applied Nutrition 1988;40:85-94. | Palm Beach Institute for Medical Research | X | |
| 1988 | Roberts, Neurological Psychiatric and Behavioral Reactions to Aspartame in 505 Aspartame Reactors. In: Wurtman and Ritter-Walker (eds.). Dietary Phenylalanine and Brain Function. Boston: Birkhauser, 1988, pp. 373-376. | None | X | |
| 1988 | Wurtman and Maher, Calculation of the Aspartame Dose for Rodents that Produces Neurochemical Effects Comparable to Those Occurring in People. In: Wurtman and Ritter-Walker (eds.). Dietary Phenylalanine and Brain Function. Boston: Birkhauser, 1988, pp. 144-148. | M.I.T. | X | |
| 1988 | Pinto JM, Mahea TJ, Administration of Aspartame Potentiates Pentylenetetrazole and Fluorothyl-Induced Seizures in Mice. Neuropharmacology 1988;27(1):51-55. | Massachusetts College of Pharmacy | X | |
| 1988 | Walton, The Possible Role of Aspartame in Seizure Induction. Proceedings of the first International Conference on Phenylalanine and the Brain. Wurtman RJ, Walker E (eds.), Center for Brain Sciences and Metabolism Charitable Trust, Cambridge, 1987. | Chautauqua County Dept of Mental Health | X | |
| 1988 | Tollefson L, Monitoring Adverse Reactions to Food Additives in the US Food and Drug Administration. Regulatory Toxicology and Pharmacology 1988;8(4):438-446. | FDA | | X |
| 1988 | Olney, Excitotoxic Food Additives Functional Teratological Aspects. In Progress in Brain Research, Vol 73 Biochemical Basis of Functional Neuroteratology: Permanent Effects of Chemical on the Developing Brain, edited by Boer, GJ, et al., Elsevier, New York 1988. | Washington University | X | |

| | | | | |
|------|--|--|---|---|
| 1988 | Tollefson L, Monitoring of Adverse Reactions to Aspartame Reported to the U.S. Food and Drug Administration. In: Wurtman and Ritter-Walker (eds.). Dietary Phenylalanine and Brain Function. Boston: Birkhauser, 1988, pp. 317-326. | FDA | | X |
| 1988 | Steinmetzer and Kunkel, Aspartame and Headache [letter]. N Engl J Med 1988;318(18):1201. | Cleveland Clinic | X | |
| 1988 | Spiers, et al., Aspartame and Human Behavior: Cognitive and Behavioral Observations. In: Wurtman and Ritter-Walker (eds.). Dietary Phenylalanine and Brain Function. Boston: Birkhauser, 1988, pp. 169-178. | Center for Brain Sciences and Metabolism Charitable Trust | X | |
| 1988 | Sardesai, et. al., Effect of Aspartame in Diabetic Rats. In: Wurtman and Ritter-Walker (eds.). Dietary Phenylalanine and Brain Function. Boston: Birkhauser, 1988, pp. 265-268. | Wayne State University | X | |
| 1988 | Matalon, et. al., Aspartame Consumption in Normal Individuals and Carriers for Phenylketonuria. In: Wurtman and Ritter-Walker (eds.). Dietary Phenylalanine and Brain Function. Boston: Birkhauser, 1988, pp. 41-52. | N.I.H. and The University of Illinois | X | |
| 1988 | Guiso G, Caccia S, Vezzani A, et. al., Effect of Aspartame on Seizures in Various Models of Experimental Epilepsy. Toxicology and Applied Pharmacology 1988;96:485-493. | Istituto di Ricerche Farmacologiche Mario Negri, Via Eritrea | X | |
| 1988 | Johns, Aspartame and Headache. In: Wurtman and Ritter-Walker (eds.). Dietary Phenylalanine and Brain Function. Boston: Birkhauser, 1988, pp. 303-312. | Johns Hopkins University | X | |
| 1988 | Fernstrom, Effects of Aspartame Ingestion on Large Neutral Amino Acids and Monoamine Neurotransmitters in the Central Nervous System. In: Wurtman and Ritter-Walker (eds.). Dietary Phenylalanine and Brain Function. Boston: Birkhauser, 1988, pp. 87-96. | N.I.M.H. | X | |
| 1988 | Maher and Kiritsy, Aspartame Administration Decreases the Entry of Alpha-Methyldopa into the Brain of Rats. In: Wurtman and Ritter-Walker (eds.). Dietary Phenylalanine and Brain Function. Boston: Birkhauser, 1988, pp. | Massachusetts College of Pharmacy | X | |

| | | | | |
|------|---|---|---|---|
| | 122-126. | | | |
| 1988 | Elsas, Aspartame and Migraine. N Engl J Med 1988;318(18):1201. | Emory University | X | |
| 1988 | Kim, et al., The Effect of Aspartame on 50% Convulsion Doses of Lidocaine. In: Wurtman and Ritter-Walker (eds.). Dietary Phenylalanine and Brain Function. Boston: Birkhauser, 1988, pp. 127-130. | Indiana University and Ball State University | X | |
| 1988 | Blundell, Effects of Aspartame on Appetite and Food Intake. In Dietary Phenylalanine and Brain Function, Wurtman and Ritter-Walker, Editors, 1988;Birkhauser, Boston, 275-295. | University of Leeds | X | |
| 1988 | Lipton RB, Newman LC, Cohen JS, Solomon S, Aspartame and Headache. The New England Journal of Medicine 1988 May 5;1200. | Albert Einstein College of Medicine | X | |
| 1988 | Lipton, et al., Aspartame as a Dietary Factor in Headache. Neurology 1988;38:356. | National Headache Foundation | X | |
| 1988 | Lipton, et al., Aspartame as a Dietary Trigger of Headache. Headache 1989;29(2):90-2. | National Headache Foundation | X | |
| 1988 | Koehler SM, Glaros A, The Effect of Aspartame on Migraine Headache. Headache 1988;28:10-13. | Center for Brain Sciences and Metabolism Charitable Trust & The University of Florida | X | |
| 1989 | Potenza DD and el-Mallakh RS, Aspartame: Clinical Update. Conn Med 1989;53(7):395-400. | None | X | |
| 1989 | Holder MD and Yirmiya R, Behavioral Assessment of the Toxicity of Aspartame. Pharmacology Biochemistry and Behavior 1989;32:17-26. | N.I.H. | X | |
| 1989 | Yost DA, Clinical Safety of Aspartame [Review].* AFP 1989 Feb;39(2):201-206. | University of Arizona | | X |
| 1989 | Dow-Edwards DL, Scribani LA, Riley EP, et al., Impaired Performance on Odor-Aversion Testing Following Prenatal Aspartame Exposure in the Guinea Pig. Neurotoxicology and Teratology. 1989 Jul-Aug;11(4):413-416. | Laboratory of Cerebral Metabolism, State University of New York. | X | |

| | | | | |
|------|---|---|---|---|
| 1989 | Dow-Edwards DL, Scribani LA, Riley EP, Impaired Performance on Odor-Aversion Testing Following Prenatal Aspartame Exposure in the Guinea Pig. <i>Neurotoxicol Teratol</i> 1989;11(4):413-6. | State University of N.Y. | X | |
| 1989 | Bresnick, Excitotoxins: A Possible New Mechanism for the Pathogenesis of Ischemic Retinal Damage. <i>Arch Ophthalmol</i> 1989 Mar;107(3):339-41. | N.I.H. | X | |
| 1990 | Turdooff MG, and Alleva AM, Oral Stimulation with Aspartame Increases Hunger. <i>Physiology Behavior</i> 1990;47(3):555-9. | None Specified | X | |
| 1990 | Pan-Hou H, et. al., Effect of Aspartame on N-Methyl-D-Aspartate Sensitive L-[3H] Glutamate Binding Sites in Rat Brain Synaptic Membranes. <i>Brain Res</i> 1990;520(1-2):351-353. | Setsunan University | X | |
| 1991 | Strathman, Recurrent Vulvovaginitis Resulting From the Heavy Dietary Use of Aspartame. <i>J Reprod Med</i> 1991 Aug;36(8):572. | No Funding | X | |
| 1991 | Roberts, Does Aspartame Cause Human Brain Cancer. <i>Journal of Advancement in Medicine</i> 4(4):231-241. | None | X | |
| 1991 | Watts RS, Aspartame, Headaches and Beta Blockers. <i>Headache</i> 1991;31(3):181-2. | None | X | |
| 1991 | Tilson HA, Hong JS, Sobotka TS, et. al., High Doses of Aspartame have no Effect on Sensorimotor Function or Learning and Memory in Rats. <i>Neurotoxicology & Teratology</i> 1991;13(1):27-35. | FDA | | X |
| 1991 | McCaulliffe DP, Poitras K, et. al., Aspartame-Induced Lobular Panniculitis. <i>J Am Acad Dermatol</i> 1991;24(2 Pt 1):298-300. | U.S. Air Force | X | |
| 1991 | Moller SE, Effect of Aspartame and Protein, Administered in Phenylalanine-Equivalent Doses on Plasma Neutral Amino Acids, Aspartate, Insulin and Glucose in Man. <i>Pharmacol Toxicol</i> 1991;68(5):408-12. | St. Hans Hospital, Denmark | X | |
| 1991 | Diomed L, Romano M, Guiso G, et. al., Interspecies and Interstrain Studies on the Increased Susceptibility to Metrazol-Induced Convulsions in Animals given Aspartame. <i>Food & Chem Toxicol</i> 1991;29(2):101-106. | Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy | X | |
| 1991 | Guiso, et. al., Effect of Tyrosine on the Potentiation by Aspartame and Phenylalanine | Instituto di Ricerche | X | |

| | | | | |
|------|--|---|---|---|
| | of Metrazol-Induced Convulsions in Rats. Food Chem Toxicol 1991 Dec;29(12):855-7. | Farmacologiche Mario Negri, Italy, Via Eritrea | | |
| 1992 | Tollefson L and Barnard RJ, An Analysis of FDA Passive Surveillance Reports of Seizures Associated with Consumption of Aspartame. Journal of the American Dietetic Association 1992;92(5):598-601. | FDA | | X |
| 1992 | Camfield PR, Camfield CS, Dooley JM, et. al., Aspartame Exacerbates EEG Spike Wave Discharge in Children With Generalized Absence Epilepsy: A Double-Blind Controlled Study. Neurology 1992;42:1000-1003. | Ontario Ministry of Health | X | |
| 1992 | Gulya AJ, Sessions RB, Troost TR, et. al., Aspartame and Dizziness: Preliminary Results of a Prospective, Nonblinded, Prevalence and Attempted Cross-over Study. American J of Otology 1992 Sept;13(5):438-42. | Georgetown University | X | |
| 1993 | Shephard SE, Wakabayashi K, Nagao M, et. al., Mutagenic Activity of Peptides and the Artificial Sweetener Aspartame After Nitrosation. Food & Chemical Toxicol 1993;31(5):323-9. | National Cancer Center Research Institute Japan | X | |
| 1993 | Walton RG, Hudak R, Greenwaite RJ, Adverse Reaction to Aspartame: Double-Blind Challenge in Patients from a Vulnerable Population. Biological Psychiatry 1993;34(1-2):13-17. | Western Reserve Care System | X | |
| 1993 | Tollefson L, Multiple Chemical Sensitivity: Controlled Scientific Studies as Proof of Causation. * Regulatory Toxicology and Pharmacology 1993;18:32-43. | FDA | | X |
| 1993 | Eshel Y and Sarova-Pincus I, Aspartame and Seizures. Neurology 1993;43(10):2154-2155. | None Specified | X | |
| 1993 | Kasamaki A, Uresawa S, et. al., The Effect of Food Chemicals on Cell Aging of Human Diploid Cells in Vitro Culture. J Toxicol Sci 1993;18(3):143-53. | Sapporo Medical College Japan | X | |
| 1993 | Meldrum, Amino Acids as Dietary Excitotoxins: A Contribution to Understanding Neurodegenerative Disorders. Brain Res Rev 1993 Sept-Dec;18(3):293-314. | Institute of Psychiatry London | X | |
| 1994 | Van Den Eeden SK, Koepsell TD, Langstreth WT Jr, et a., Aspartame Ingestion and Headaches: A randomized Crossover Trial. | University of Washington | X | |

| | | | | |
|------|---|---|---|---|
| | Neurology 1994;44(10):1787-93. | | | |
| 1994 | Stokes AF, Belger A, Banich MT, Bernadine E, et. al., Effects of Alcohol and Chronic Aspartame Ingestion Upon Performance in Aviation Relevant Cognitive Tasks. Aviation, Space, and Environmental Medicine 1994;65:7-15. | FDA | | X |
| 1994 | Olney, Excitotoxins in Foods. Neurotoxicology 1996;15(3):535-544. | Washington University | X | |
| 1994 | Gerrard JW, Richardson JS, Donat J, et. al., Neuropharmacological Evaluation of Movement Disorders that are Adverse Reactions to Specific Foods. Int J Neurosci 1994 May;76(1-2):61-9. | University of Saskatchewan, Saskatoon, Canada | X | |
| 1994 | Barua J, Bal A, A Health Alert: Emerging Facts about Aspartame. Jour Diab Assoc India 1995;35(4):92-107. | S. L. Raheja Hospital Bombay | X | |
| 1995 | Sonnewald U, Muller T, Unsgaro G, Peterson SB, et. al., Effect of Aspartame on 45 CA Influx and LDH Leakage from Nerve Cells in Culture. Neuroreport 1995 45 CA;6(2):318-320. | Research Council of Norway | X | |
| 1995 | Kulczychi A Jr., Aspartame Induced Hives. Journal of Allergy and Clinical Immunology 1995;95(2):639-40. | Washington University | X | |
| 1996 | Roberts HJ, Aspartame as a Cause of Allergic Reactions, Including Anaphylaxis. Arch Intern Med 1996;156(9):1027-8. | Palm Beach Institute for Medical Research | X | |
| 1996 | Olney JW, Farber NB, Spitznagel E, Robins L, Increasing Brain Tumor Rates: Is There a Link to Aspartame? Journal of Neuropathology and Experimental Neurology 1996;55(11):1115-1123. | N.I.M.H. | X | |
| 1998 | Trocho C, Pardo R, Rafecas I, Virgili J, Remesar X, Fernandez-Lopez JA, Alemany M, Formaldehyde Derived From Dietary Aspartame Binds to Tissue Components In Vivo. Life Sciences 1998;63(5):337-349. | Universitat de Barcelona | X | |