

Selected MSG human safety studies demonstrating negative results

Study	Funding sources	Subjects recruited	Bias toward reducing reactions to monosodium glutamate test material**	Information given about placebos	Number of subjects	Focus on irrelevant variables
Altman <i>et al.</i> (1994)()	Allerx IGTC	With stipend	Selected reactions recorded no other information	Liquid vehicle		
Bazzano <i>et al.</i> (1970)	Public Health Service	Adult males	Selected reactions recorded no other information	Amino acid formula with glutamate as a basic diet	11	Neurologic function; Hepatic function; Serum cholesterol; Weight
Fernstrom <i>et al.</i> (1996)	IGTC NIH	Well subjects Giving informed consent		Beverage ¹	8	Plasma glutamate; Change in plasma glutamate; Pituitary hormone secretion.
Geha <i>et al.</i> (2000)	IGTC	Stipend Giving informed consent	Used capsules Selected reactions recorded Inadequate observation time	Part 1: "Citrus-flavored beverage." ² Part 2: Capsules containing sucrose		Reproducible response; ³ Pulse; Blood pressure; Respiratory rate; Relative risk
Germano <i>et al.</i> (1991)	no information given	Asthmatic and non-asthmatic adults	Limited reactions recorded Used capsules		13+30 1	

Germano <i>et al.</i> (1993)	no information given	Adults with a history of asthma	Selected reactions recorded Used capsules		21 10	.
Goldschmiedt <i>et al.</i> (1990)	Ajinomoto; NIH; ILSI; VA	Well subjects Giving informed consent		180 mL warm beef consommé soup supplied by Ajinomoto Co., Inc. Tokyo	17 15	variables were relevant to the study done, but irrelevant to adverse reactions to MSG
Kenney. (1979) Part 1.	IGTC (with thanks to NESTEC)	Well subjects Giving informed consent	Test material given with carbohydrates Selected reactions recorded Inadequate observation time	Tomato juice with common salt.	51 16	
Kenney (1979) Part 2.	IGTC	Giving informed consent	Inadequate observation time	Sucrose; citric acid; trisodium -citrate; lemon flavor; caramel color; naringin .	57 16	
Kenney. (1986)	IGTC		Selected reactions recorded	"...soft-drink solution...."	6	Objective parameters (routine chemical analyses)
Kerr <i>et al.</i> (1979)	Ajinomoto USA	Randomly drawn stratified random sample	Selected reactions recorded Inadequate observation time	(survey)		
Morselli <i>et al.</i> (1970)	COFAG (IGTC Europe)	Well subjects	Test material was given with carbohydrates Inadequate observation time	Beef broth (ingredients not specified)	24	Blood pressure; Pulse; Respiration rate

Prawirohardjo <i>et al.</i> (2000)	IGTC	Well subjects With stipend Giving informed consent	Small amounts of test material were given with carbohydrates Used capsules	Lactose in gelatin capsules	52	Blood pressure; Pulse; Respiratory rate
Rosenblum <i>et al.</i> (1971)	no information given	Males Giving informed consent	Selected reactions recorded Inadequate observation time	Diluted chicken stock or diluted chicken stock with sodium (ingredients not specified)	95	
Schwartzstein (1987)	IGTC	Asthmatics	Not all reactions were recorded Used capsules Medication not given for 12 hours prior to testing	Gelatin capsule containing sodium chloride	12	
Simon (2000)	IGTC	Patients with chronic urtic aria;	Subjects taking antihistamine; Used capsules; Dose was 2500 mg.			
Stegink <i>et al.</i> (1986)	IGTC	Giving informed consent	Test material was given with carbohydrates	Beef consommé supplied by Ajinomoto Co., Tokyo, Japan	8	Plasma glutamate; Plasma aspartate
Stevenson <i>et al.</i> (1997)	IGTC	CRS- asthmatics and non- CRS asthmatics Some subjects eliminated	Selected reactions recorded		10+30	
Tanphaichitr <i>et al.</i> (1983)	IGTC	Well subjects	Selected reactions recorded	Four full days' menus all different, without added	50	Plasma glutamate; Pleasantness or unpleasantness of food

			Test material was given with carbohydrates	monosodium glutamate		
Tanphaichitr <i>et al.</i> (1985)	IGTC	Well subjects	Selected reactions recorded Test material was given with carbohydrates	A full day's menu without added monosodium glutamate	12	
Tarasoff <i>et al.</i> (1993)	IGTC	Well subjects With stipend Giving informed consent	Used capsules Test material was given with carbohydrates Not all reaction were recorded Inadequate observation time	Both beverage and capsules: Beverage specified as containing aspartame; ⁴ prepared from powders supplied by the IGTC Placebos in gelatin capsules		After-taste; Intensity
Wilkin (1986)	VA	Well subjects	Selected reactions recorded	(No placebo)	6	
Woods <i>et al.</i> (1998)	The Asthma Foundation of Victoria	Asthmatics who perceived that MSG made their asthma worse	Subjects continued on medications 10 capsules rolled in lactose powder per treatment	5 gm lactose in 10 capsules rolled in lactose powder	12	
Woessner <i>et al.</i> (1999)	IGTC; Scripps Clinic, Green Hospital & Research Institute	Asthmatics with and without CRS Giving informed consent Some subjects eliminated	Selected reactions recorded Test material was given with carbohydrates Continued medications	5 gelatin capsules containing sucrose	30+70 30	

Yang <i>et al.</i> (1997)	IGTC	Well subjects (except subjects with symptoms of CRS were accepted) With stipend Giving informed consent	Selected reactions recorded Two or more reactions required to be counted as a reaction Inadequate observation time	Strongly citrus tasting beverage containing sucrose supplied by the IGTC	61 36	
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Legend

FUNDING SOURCES:

- COFAG: IGTC Europe
- IGTC: International Glutamate Technical Committee (includes manufacturers and users of monosodium glutamate)
- ILSI: International Life Sciences Institute (often under contract to the glutamate industry)
- IMC: International Minerals and Chemical Corporation
- NIH: National Institutes of Health
- VA: Veterans Administration

BIAS IN SELECTING SUBJECTS (Not all people are sensitive to monosodium glutamate at levels ordinarily found in food.)

- CRS: Chinese Restaurant Syndrome: a limited number of mild and transitory reactions reported in 1968 as being caused by ingestion of monosodium glutamate
- INFORMED CONSENT, while ethically appropriate, and required of all experiments using human subjects, biases these studies.
- MALES have been reputed to be less sensitive to MSG than females
- STIPENDS were given to those who claimed to be sensitive to MSG
- SUBJECTS were ELIMINATED prior to the study for responding to placebos that were going to be used in the study.
- WELL SUBJECTS would be persons who had never experienced any of the reactions alleged to be attributable to use of monosodium glutamate (irritable bowel, migraine headache, asthma, skin rash, heart irregularities, mood swings, and depression being possibilities, for example).

BIAS TOWARD REDUCING THE LIKELIHOOD THAT SUBJECTS WOULD REACT TO MONOSODIUM GLUTAMATE TEST MATERIAL

- CAPSULES guarantee slow release and, therefore, less effect of the material they contain
- TEST MATERIAL GIVEN WITH CARBOHYDRATES interferes with the uptake of the test material

PLACEBOS

It would appear that in most, if not all, glutamate-industry-sponsored studies, both test and placebo material were supplied by the IGTC. According to a 1991 letter from IGTC chairman Andrew G. Ebert to LSRO-FASEB and the FDA, a beverage mix designed to mask the taste of [monosodium glutamate], was modified in 1978 to replace the [former use of] sucrose with the low calorie sweetener Aspartame. Prior to the time that Northwestern University was alerted to the fact that aspartame was being used in placebo material being used in an IGTC-sponsored study being carried out by Geha et al. at Northwestern, Harvard, and UCLA, the use of aspartame in placebos was not acknowledged in research reports.

- BEVERAGE: Citric acid, trisodium citrate, lemon flavoring, caramel coloring, naringenin-7-rhamnosidio-glycoside (grapefruit bitter principle), sodium saccharin; prepared by Ajinomoto
- CITRUS-FLAVORED BEVERAGE: Sodium citrate, citric acid, saccharin, citrus flavor, and naringin were cited as ingredients. Aspartame was used (but not named) with the other ingredients prior to objections filed with Northwestern University by the Truth in Labeling Campaign.
- BEVERAGE: Sodium citrate dihydrate, citric acid monohydrate, potassium chloride, naringin, grapefruit flavour, caramel, and aspartame.

IRRELEVANT VARIABLES

- REPRODUCIBLE RESPONSE: Repetition of the same two or more responses to monosodium glutamate on two occasions, and no response to the “placebo” (which contained aspartame).

References

Altman DR, Fitzgerald T, Chiaramonte LT. Double-blind placebo-controlled challenge (DBPCC) of persons reporting adverse reactions to monosodium glutamate (MSG). *J Allergy Clin Immunol.* 1994;93:303 (Abstract 844).

Bazzano G, D’Elia JA, Olson RE. Monosodium glutamate: feeding of large amounts in man and gerbils. *Science.* 1970;169:1208-1209.

Fernstrom JD, Cameron JL, Fernstrom MH, McConaha C, Weltzin TE, Kaye WH. Short-term neuroendocrine effects of a large, oral dose of monosodium glutamate in fasting male subjects. *J Clin Endocrinol Metab.* 1996;81:184-191.

Geha R, Beiser A, Ren C, et al. Multicenter multiphase double blind placebo controlled study to evaluate alleged reactions to monosodium glutamate (MSG). *J Allergy Clin Immunol.* 2000;106:973-980.

Germano P, Cohen SG, Hahn B, Metcalfe DD. An evaluation of clinical reactions to monosodium glutamate (MSG) in asthmatics using a blinded, placebo-controlled challenge. *J Allergy Clin Immunol.* 1991;87:177 (Abstract 155).

Germano P, Cohen SG, Hibbard V, Metcalfe DD. Assessment of bronchial hyperactivity by methacholine challenge (MTC) in asthmatics before and after monosodium glutamate (MSG) administration. *J Allergy Clin Immunol.* 1993;91:340 (Abstract 798).

Goldschmiedt M, Redfern JS, Feldman M. Food coloring and monosodium glutamate: effects on the cephalic phase of gastric acid secretion and gastrin release in humans. *Am J Clin Nutr.* 1990;51:794-797.

Kenney RA. Placebo-controlled studies of human reaction to oral monosodium L-glutamate. In Filer LJ Jr, Garattini S, Kare MR, Reynolds WA, Wurtman RJ, eds. *Glutamic acid: advances in biochemistry and physiology.* New York: Raven; 1979:363-373.

Kenney RA. The Chinese restaurant syndrome: an anecdote revisited. *Food Chem Toxicol.* 1986;24:351-354.

Kerr GR, Wu-Lee M, El-Lozy M, McGandy R, Stare FJ. Prevalence of the "Chinese restaurant syndrome." *J Am Diet Assoc.* 1979;75:29-33.

Morselli P, Garattini S. Monosodium-glutamate and the Chinese restaurant syndrome. *Nature.* 1970;227:611-612.

Prawirohardjono W, Dwiprahasto I, Astuti I, et al. The administration to Indonesians of monosodium L-glutamate in Indonesian foods; an assessment of adverse reactions in a randomized double-blind, crossover, placebo-controlled study. *J Nutr.* 2000;130:1074S-1076S.

Rosenblum L, Bradley J, Coulston F. Single and double blind studies with oral monosodium glutamate in man. *Toxicol Appl Pharmacol* 1971;18:367-373.

Schwartzstein RM, Kelleher M, Weinberger WE, Weiss JW, Drazen JM. Airway effect of monosodium glutamate in subjects with chronic stable asthma. *J Asthma.* 1987;24:167-172

Simon RA. Additive-induced urticaria: experience with monosodium glutamate (MSG). *J Nutr.* 2000; Apr;130(4S Suppl):1063S-6S.

Stegink LD, Filer J, Baker GL, Bell EF. Plasma glutamate concentrations in 1-year-old infants and adults ingesting monosodium L-glutamate in consommé. *Pediatr Res*. 1986;20:53-58.

Stevenson DD, Simon RA, Woessner KM. The role of monosodium L-glutamate (MSG) in asthma: does it exist? *J Allergy Clin Immunol*. 1997;99:S411 (Abstract 1670).

Tanphaichitr V, Srianujata S, Pothisiri P, Sammasut R, Kulapongese S. Postprandial responses to Thai foods with and without added monosodium L-glutamate. *Nutr Rep Int*. 1983;28:783-792.

Tanphaichitr V, Srianujata S, Leelahabul P, Kulapongse S, Patchimasiri S, Pothisiri P. Effect of monosodium L-glutamate in take on protein-calorie status in healthy Thai adults. *Nutr Rep Int*. 1985;32:1073-1080.

Tarasoff L, Kelly MF. Monosodium L-glutamate: a double-blind study and review. *Food Chem Toxic*. 1993;31:1019-1035.

Wilkin JK. Does monosodium glutamate cause flushing (or merely "glutomania")? *J Am Acad Dermatol*. 1986;15:225-230.

Woessner KM, Simon RA, Stevenson DD. Monosodium glutamate sensitivity in asthma. *J Allergy Clin Immunol*. 1999;104:305-310.

Woods RK, Weiner JM, Thien F, Abramson M, Walters EH. The effects of monosodium glutamate in adults with asthma who perceive themselves to be monosodium glutamate-intolerant. *J Allergy Clin Immunol*. 1998;Jun;101(6 Pt 1):762-71.

Yang WH, Drouin MA, Herbert M, Mao Y. The monosodium glutamate symptom complex: assessment in a double-blind, placebo-controlled, randomized study. *J Allergy Clin Immunol*. 1997;99:757-762.

Zanda G, Franciosi P, Tognoin G, et al. A double blind study on the effects of monosodium glutamate in man. *Biomedicine*. 1973;19:202-204.