

## LETTER TO THE EDITOR

### DOES ASPARTAME CAUSE METHANOL TOXICITY?

Sir,—Digestion of the sweetener aspartame yields aspartic acid and phenylalanine, plus methanol. Because of the latter, an editorial (Monte, *J. appl. Nutr.* 1984, 36, 42) has questioned aspartame's safety, alleging (1) that methanol is a "cumulative poison", (2) that a toxicity syndrome is producible "only in humans", (3) that "formaldehyde is a known carcinogen", (4) that ethanol protects against methanol in food sources, (5) that the Environmental Protection Agency has set a limit for methanol, and (6) that anecdotal reports suggest the occurrence of methanol poisoning following aspartame ingestion. I should like to respond to these statements.

(1) Because of the very rapid metabolism of methanol, a bolus dose of 200 mg aspartame/kg in humans does not elevate blood formate, which is the toxic metabolite (Stegink, in *Aspartame Physiology and Biochemistry*, edited by L. Stegink & J. Filer, Chap. 26, Marcel Dekker, New York, 1984). This dose is over six times the estimated maximum daily consumption of aspartame; it is equivalent to a single ingestion of over fifty 12-oz cans of aspartame-sweetened soda and is the sweetening equivalent of over 5 lb sugar. Therefore, it is physically impossible for a human to develop methanol poisoning from aspartame ingestion.

(2) A model of methanol poisoning has in fact been produced in monkeys and has been re-created by formate administration (Martin-Amat *et al. Toxic. appl. Pharmac.* 1978, 45, 201). Toxicity was not observed in monkeys ingesting aspartame at 3 g/kg/day for 9 months (Reynolds *et al. in Aspartame Physiology and Biochemistry, op. cit.*).

(3) Formaldehyde is carcinogenic only by inhalation in rats, in which species it produces carcinomas of the nasal cavity (Kerns *et al. Cancer Res.* 1983, 43, 4382); it is not carcinogenic by ingestion in any species.

(4) Because ethanol is metabolized much more rapidly than methanol, any 'protective' effect in food sources will be pharmacokinetically evanescent. For example, the 'protective' effect of ethanol in 500 ml orange juice can be shown to persist for less than 1 min after a simultaneous aspartame dose of 200 mg/kg.

(5) The EPA has not set a limit for methanol ingestion. This allegation stems from a misunderstanding of the Agency's publications.

(6) Anecdotal reports from aspartame users are used by Monte (*loc. cit.*) to suggest that the symptoms are those of methanol poisoning. This is not confirmed by analyses of consumer complaints by the Centers for Disease Control (*Morbid. Mortal. Wkly Rep.* 1984, 33, 605). In particular, Monte (*loc. cit.*) associated aspartame with the death, from a heart condition, of a former employee in Searle's manufacturing plant in Arizona; in fact, the records reveal that (a) the employee was not exposed to aspartame during the 10 months before his death; (b) nothing in the autopsy report suggested methanol toxicity; (c) the subject was taking quinidine for ventricular ectopy and complained of known side effects of this drug; (d) Monte's statement that he was a non-drinker is false; (e) a heart problem had been noted at the decedent's pre-employment examination. "The clinical history has been reviewed by the FDA, and it was not felt that there was any indication that this death was associated with aspartame ingestion" (*Centers for Disease Control, loc. cit.*).

In summary, there is no responsible scientific evidence that aspartame ingestion can result in methanol toxicity. The allegations of Monte (*loc. cit.*) have been uniformly rejected by the Food and Drug Administration, by the Arizona Department of Health Services, and by state and federal courts; they have been given credence principally in the lay media.

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