CORRESPONDENCE

Rebuttal on Garlic Chemistry: Stability of *S*-(2-Propenyl) 2-Propene-1-sulfinothioate (Allicin) in Blood, Solvents, and Simulated Physiological Fluids

Sir: This letter is written in response to the comments made by Lawson and Block (L/B) in their letter that appeared in *J. Agric. Food Chem.* **1997**, *45*, 542, a letter which called into question certain aspects of our paper (*J. Agric. Food Chem.* **1995**, *43*, 2332−2339).

In contrast to the allegations of L/B, appropriate concentrations, correct premises, and valid tests were used in our study. We deeply regret that L/B's criticisms were written without respecting pharmacological, biochemical, pharmacokinetic, and toxicological standard practices. We demonstrated that allicin is not an active compound in the body, that allicin can be harmful, that garlic powder tablets contain no allicin, and that allicin-producing potential in the products varies with the test conditions. Since some manufacturers strongly promote allicin in their garlic preparations, we conducted our study to clarify their false claims. Other papers (Blania, 1991; Lawson, 1991, 1992) confirmed our results that allicin does not enter the blood circulation as L/B pointed out. For example, consumption of 25 g of raw garlic, which generates 90 000 μg of allicin in vitro, yielded no detectable amount of allicin in the blood (Lawson, 1992). In their letter L/B raised five major points of criticism which they mistakenly believe support their opinion that allicin is the active ingredient of garlic. However, since allicin is (a) not present in garlic or garlic preparations, (b) not generated in the stomach, (c) not bioavailable or detected in blood circulation (Lawson, 1992), (d) not effective in inhibiting cholesterol synthesis (Gebhaldt, 1991), and (e) not proven to exert an antibiotic effect in the intestinal tract or to be released in insignificant amounts from the enteric coated tablets to exert positive cardiovascular effects, it is obvious that allicin is not the active ingredient of garlic or any kind of garlic preparation. Thus, there is no mispresentation in the publication.

Since vegetable oil-macerated/suspended garlic products that have beneficial effects are also sold at the market, we conducted the allicin stability test in fatty oil and confirmed its instability. We have made clear that the effects of this kind of garlic preparation are not dependent upon allicin. Therefore, we concluded that "it is doubtful whether allicin is responsible for some of the pharmacological effects attributed to garlic".

L/B's criticism in comment 2 is irrelevant, and they substitute the issue from allicin itself to allicin metabolites. Such a criticism is unjustified and is contrary to pharmacological principles. It is standard practice in pharmacology (and in nutrition and physiology) to study the absorption, distribution to various organs/tissues, metabolism, and excretion of a compound that is considered an active principle (Osol, 1980). If a compound is not absorbed and cannot be distributed to the target organs where its pharmacological actions are needed, it cannot be considered an active principle, and, in this case, we have proven that allicin is not the active principle of garlic.

Our paper does not deny the likelihood that allicin metabolites might be pharmacologically active; however, there is no evidence indicating that the allicin metabolites from consumption of the enteric coated tablet can have any effect. It is well-known that many allicin-free preparations can provide health benefits. The fact that some garlic preparations are more potent than their allicin contents strongly argues against the belief that allicin and/or its metabolites are the active compounds of garlic (Kabelik, 1970; Gebhaldt, 1991; Small, 1947). Garlic and garlic preparations contain many pharmacologically active compounds that are not metabolites of allicin. Furthermore, there is no parallelism between allicin and other nutrients and antibiotics that L/B used as examples.

L/B allege in their comment 1 that "there is no evidence that normal consumption of garlic (1 clove/day), which releases allicin when crushed or chewed, leads to any harmful effects when eaten with a meal". It has been shown that large quantities of raw garlic can cause hemolysis and hemolytic anemia in humans (Miyamoto, 1935) and allergic contact dermatitis (Papgeogiou et al., 1983) and may be toxic to rats (Nakagawa et al., 1980) and mice (Cavalito and Bailey, 1944) when injected. Cavallito and Bailey (1944) reported the LD_{50} in mice for allicin in aqueous solutions to be on the order of 60 mg/kg intravenously and 120 mg/kg subcutaneously. Evidence is overwhelming that allicin can be toxic and injurious.

As L/B stated in their comment 4, "It has been known for several years that alliinase. . .is completely inhibited by the acidic conditions found in the stomach", which has been known for almost 50 years (Stall, 1951). Gastric acid-resistant enteric coated garlic tablets may prevent the degradation of alliinase and would provide allicin-releasing potential in the small intestine. The intention of enteric coating is to deliver allicin to the small intestines directly. However, since allicin is injurious and the small intestine is one of the most delicate and sensitive sections of the digestive tract, the safety of the enteric coated tablet is indeed a concern. The regular route of garlic consumption starts at biting/chewing in the mouth, followed by digestion in the stomach and then delivery to the intestine. Enteric coating delivers garlic directly to the intestine. Whenever the administration route is changed, it is the general toxicological rule to determine the safety of products. Prior to marketing enteric coating products and claiming allicin-producing potential in the intestine, manufacturers should conduct toxicological studies using their own products. Many of the research results and epidemiological data established as the activity of garlic are based upon non-enteric-coated preparations including fresh garlic.

According to the above evidence, L/B's criticism of our paper is biased and misleading. Most of the studies on allicin cited by L/B in their letter refer to their own studies and have not been verified by independent researchers. We believe that both our paper and the above comments are sufficient to prove our findings.

We also take issue with what they presented as

S0021-8561(97)00340-3 CCC: $14.00

additional comments. We will mention allicin concentration in the blood only for the sake of discussion.

In their comment 1, L/B are mistaken when they say that the allicin used in Figure 8 is 53 mg/mL. As stated in our paper, "One milliliter of an allicin solution (53 mg/mL in EtOH) was pipetted into a 50 mL volumetric flask, and saline was added to volume. Heparinized blood (1 mL) was pipetted into a 50 mL volumetric flask, and saline was added to volume. Five milliliters of this solution were transferred to a 25 mL volumetric flask, 5 mL of the diluted allicin solution was added, and saline was added to volume. The visible spectrum . . .was obtained...".

Thus, the allicin concentration was 0.212 mg/mL, not 53 mg/mL. As a result of this error, L/B's allegation that "the dose (sic) used. . .(53 mg/mL blood) is 25 000 times the maximum possible dose (sic) achievable by consumption of a typical clove" is erroneous. The 0.2 mg/mL concentration used by us is appropriate and below the commonly used concentrations for this type of study. For example, the in vitro activity of allicin against certain bacteria is about 100 times less than that of penicillin (Cavallito and Bailey, 1944), suggesting the proper allicin concentration for the study to be 0.5−1 mg/mL or higher.

Contrary to L/B's comment 5, we never intentionally used any old lots of commercially available garlic preparations for our study. We purchased all products at a local health food store in 1991. All experiments were completed in early 1992, and we submitted the manuscript to *J. Agric. Food Chem*. on June 10, 1993. It was revised in conformance with the comments of the reviewers and returned to the Editor on September 23, 1993.

In summary, we would like to cite a passage by Lin (1994) which states in part that "For more than a decade allicin has been heavily promoted to be the active principle of garlic and garlic supplements by most garlic supplement vendors; each of them has been forceful in claiming that its garlic supplements contain the highest amount of allicin. The truth is that there is no truth in these allicin promotions and claims".

LITERATURE CITED

Blania, G.; Spangenberg, B. Formation of allicin from dried garlic (*Allium sativum*). A simple HPTLC method for simultaneous determination of allicin and ajoene in dried garlic and garlic preparations. *Planta Med*. **1991**, *57*, 371−375.

Cavallito, C. J.; Bailey, J. H. Allicin, the antibacterial; principle of *Allium sativum*, I isolation, physical properties and antibacterial actions. *J. Am. Chem. Soc.* **1944**, *16*, 1950−1951.

Gebhaldt, R. Inhibition of cholesterol biosynthesis by a water-soluble garlic extract in primary cultures of rat hepatocytes. *Arzneim.-Forsch*. **1991**, *41*, 800−804.

Kabelik, J. Antimicrobielle Eigenschaften des Knoblauchs. *Pharmazie* **1970**, *25*, 266.

Lawson, L. D.; Hughes, B. G. Characterization of the formation of allicin and other thiosulfinates from garlic. *Planta Med*. **1991**, *58*, 345−350.

Lawson, L. D.; Ransom, D. K.; Hughes, B. G. Inhibition of whole blood platelet-aggregation by compounds in garlic clove extracts and commercial garlic products. *Thromb. Res*. **1992**, *65*, 141−156.

Lin, R. I. S. Phytochemicals and Antioxidants. In *Functional Foods*; Goldberg, I., Ed.; Chapman and Hall: New York, 1994; pp 393−449.

Miyamoto, T. Effects of garlic components upon hemograms. *Manchurian Med. J.* **1935**, *22*, 369−386.

Nakagawa, S.; Masamoto, K.; Sumiyoshi, H.; Kunihiro, K.; Fuwa, T. Effect of raw and aged garlic extract garlic on growth of young rats and their organs after peroral administration. *J. Toxicol. Res*.**1980**, *5*, 91−112.

Osol, A. Ed. *Remington's Pharmaceutical Science*; Mack Publishing: Easton, PA, 1980; pp 656−715.

Papgeogiou, J. P.; Corbet, F.; Menezes-Brandao, M.; Pecegueiro, M; Benezra, C. Allergic contact dermatitis to garlic (*Allium sativum* L.). Identification of the allergens; the role of mono-, di-, and trisulfides present in garlic. *Arch. Dermatol. Res*. **1983**, *275*, 229−234.

Small, L. D.; Bailey, J. H.; Cavallito, C. J. Alkyl Thiosulfinates. *J. Am. Chem. Soc.* **1947**, *69*, 1710−1713.

Stall, A.; Seebeck, E. Chemical investigation on alliin, the specific principle of garlic. *Adv. Enzymol*. **1951**, *11*, 377−400.

Received for review January 27, 1997.

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JF970340C