## Special Communication

# Sassafras and Herb Tea

## Potential Health Hazards

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HOT WATER infusions (tea) prepared from the root bark of the sassafras tree (*Sassafras albidum* [Nuttall] Nees [family Lauraceae]) have long been employed by the public as tonics as well as for a variety of unsubstantiated therapeutic purposes.

Extensive studies conducted by the Food and Drug Administration (FDA) in 1960 showed that safrole (4-allyl-1,2-methylenedioxybenzene), the major chemical constituent (eg, up to 80% by weight) of the aromatic oil present in sassafras root bark, was a hepatocarcinogen in rats. As a result, an order published in the *Federal Register* of Dec 3, 1960, prohibited the use of safrole in foods.[1] Prior to this regulation, safrole (up to 20 ppm) and safrole-containing sassafras extracts found wide use as flavoring agents especially in beverages such as root beer. Since that time, the hepatotoxic effects of safrole in animals have been reported and confirmed by numerous investigators.[2]

To be considered unsafe and hence prohibited for human use, any particular food additive need only be found to induce cancer in man or animal as shown by appropriate tests.[3,4] Therefore, safrole carcinogenicity-testing in animals may be pertinent to human experience. For example, it was found that a small total dose of 0.66 mg of safrole (approximately 66 mg/kg) administered subcutaneously in divided doses over a period of 21 days to infant male mice (an acceptable model for testing carcinogens) produced hepatomas as well as lymphomas, pulmonary adenomas, and adenocarcinomas in animals surviving one year.[5] If a commonly used margin-of-safety factor of 100 to extrapolate animal doses to humans is applied,[6] it follows that a safrole dose of approximately 0.66 mg/kg may prove hazardous in man. Yet man may be exposed to safrole doses on the order of 3.0 mg/kg when using, for example, one manufacturer's product containing 2.5 gm of sassafras bark per tea bag, which may afford up to 200 mg of safrole. Of course, the actual amount of ingested safrole depends on the safrole content of the sassafras, the duration of the infusing process, and the total amount of tea consumed.

Recognizing the confirmed toxic potential of safrole, the FDA has recently clarified the 1960 ruling in terms that clearly state that safrole and safrole-containing products cannot be recognized as being safe for human use.[7] In spite of the foregoing evidence and legal restrictions, sassafras continues to be freely available in health food shops and similar outlets in the United States. Indeed, it appears that the use of not only sassafras but herb tea in general has increased in accord with the current public interest in natural products.

Our laboratory is presently characterizing several alkaloids that we have isolated from sassafras root bark. In conjunction with this work, we have also isolated in significant yield (170 ppm) and identified a safrole derivative, (+)-3-(3,4-methylenedioxyphenyl)-propane-1,2-diol.[8] It is noteworthy that this compound has recently been detected by other investigators[9] as a major urinary metabolite in rats and guinea pigs dosed with safrole, and its carcinogenic potential is now under investigation.

Moreover, we have shown in preliminary pharmacological experiments that certain aqueous and alcoholic extracts prepared from sassafras root bark are capable of eliciting a variety of pharmacological responses in mice, including ataxia, ptosis, hypersensitivity to touch, central nervous system depression, and hypothermia. Safrole is also a potent inhibitor of certain liver microsomal hydroxylating systems,[10] a property that could lead to toxicity problems if drugs metabolized by these enzymes are administered together with sassafras tea.

In addition to the known and potential toxic properties of a number of commonly employed herbs used in making tea,[11] one should also recognize that the consumption of herb tea generally may result in changes in the bioavailability characteristics of concomitantly administered drugs.[12,13] We plan to publish evidence showing that herb tea is rich in tannins which can complex with, inactivate, or prolong the absorption of certain drugs.

Consequently, to ensure safe and effective drug therapy, it would seem appropriate for physicians to evaluate their patients in terms of extemporaneous herb tea usage and to discourage these practices whenever feasible.

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