live temperately, upon light and innocent Food; and abstain entirely from strong liquor. The Way to prevent this Calamity, is, to be very sparing in eating Pork, to forbear all salt, and high season'd Meats, and life chiefly upon the Garden, The Orchard, and the Hen-House (cancer cure in Virginia — 1734)."

The volatile oil contains *circa* 80% safrole, some anethole, apiole, asarone, camphor, caryophyllene, coniferaldehyde, copaene, elemicin, eugenol, l-menthone, 5-methoxyeugenol, myristicin, phellandrene, pinene, piperonylacrolein, sesquiterpenes, thujone. The alkaloids (*circa* 0.02%) include boldine, cinnamolaurine, isoboldine, norboldine, norcinnamolaurine, and reticuline. Two lignins, sesamin and desmethoxyaschantin, are reported along with sitosterol. Gum, mucilage, resin, tannin, and wax also occur.[27]

Toxicity — Safrole, having produced liver tumors in rats, has, like oil of sassafras, been banned because of its purported hepatotoxicity. Oil of sassafras is said to produce dermatitis in sensitive individuals. Morton[46] adds that the decoction makes pimples come out on arms and body if the root is used before it is aromatic. Heliotropin, a safrole derivative, used in cosmetics, has been reported to cause dermatitis.[6] Safrole (chemically like myristicin and asarone) is suspected of being hallucinogenic in large doses (carcinogenic and hepatotoxic).[11] A teaspoonful of oil produced vomiting, dilated pupils, stupor, and collapse in a young man. Its use has caused abortion.[2] Safrole-free sassafras extract (§ 172.580) and safrole-free sassafras leaves and extracts (§ 172.510) are approved for food use. Safrole, sassafras, and sassafras oil are prohibited from use in foods.[29] Safrole is also reported from basil, black pepper, mace, and nutmeg. After quoting a nice verse from the "Spring Ode" by Donald Robert Perry Marquis:

Fill me with sassafras, nurse,
And juniper juice!
Let me see if I'm still any use!

Tyler[37] gives some pessimistic data on sassafras. "As a result of research conducted in the early 1960s, safrole was recognized as a carcinogenic agent in rats and mice . . . No one really knows just how harmful it is to human beings, but it has been estimated that one cup of strong sassafras tea could contain as much as 200 mg of safrole, more than four times the minimal amount believed hazardous to man if consumed on a regular basis . . . Recent studies have shown that even safrole-free sassafras produced tumors in two-thirds of the animals treated with it. Apparently other constituents in addition to safrole are responsible for part of the root bark's carcinogenic acitivity."[39] Benedetti et al.,[286] however, detected no 1′-hydroxysafrole, the metabolite considered responsible for safrole's carcinogenicity, when small amounts of safrole were given by mouth to human volunteers, as opposed to rats. Tyler notes that the doses of safrole were very small (maximum 1.655 mg), perhaps resulting in the nonappearance of 1-hydroxy-safrole in the human's urine. Perhaps the high tannin content may be synergistic. Reviewing work on safrole, Buchanan[117] concluded that it is the most thoroughly investigated methylenedioxybenzene derivative. The major flavoring constituent in sassafras root bark, safrole, was identified as a "low grade hepatocarcinogen." It was banned in root beer, and the FDA in 1976 banned interstate marketing of sassafras for sassafras tea. The oral LD_{50} for safrole in rats is 1950 mg/kg body weight, with major symptoms including ataxis, depression, and diarrhea, death occurring in 4 to 5 days. Ingestion of relatively large amounts of sassafras oil produced psychoactive and hallucinogenic effects persisting several days in humans. With rats, dietary safrole at levels of 0.25, 0.5, and 1% produced growth retardation, stomach and testicular atrophy, liver necrosis, biliary proliferation, and primary hepatomas.[117]