

puerperium, and rheumatism. White pepper suggested for cholera, malaria, and stomachache; black for abdominal fullness, adenitis, cancer, cholera, cold, colic, diarrhea, dysentery, dysmenorrhea, dysuria, furuncles, headache, gravel, nausea, poisoning due to fish, mushrooms, or shellfish. Heavy dose of pepper with wild bamboo shoots said to produce abortion.⁴¹

Per 100 g, the fruit is reported to contain 255 calories, 10.5% H₂O, 11.0 g protein, 3.3 g fat, 64.8 g total carbohydrate, 13.1 g fiber, 4.3 g ash, 437 mg Ca, 173 mg P, 28.9 mg Fe, 44 mg Na, 1259 mg K, 114 µg β-carotene equivalent, 0.11 mg thiamine, 0.24 mg riboflavin, and 1.14 mg niacin. Pepper contains 2 to 4% volatile oil; and 5 to 9% piperine, piperidine, piperettine, and other minor alkaloids (piperyline, piperolein A, piperolein B, piperanine, etc.).²⁹ White pepper contains little volatile oil but has the same pungent principles and alkaloids as black pepper. Pepper oil contains a complex mixture of monoterpenes (70 to 80%), sesquiterpenes (20 to 30%). Major monoterpenes include alpha-thujene, alpha-pinene, camphene, sabinene, beta-pinene, myrcene, 3-carene, limonene, and beta-phellandrene. Sesquiterpenes include, mostly, beta-caryophyllene, some beta-bisabolene, beta-farnesene, ar-curcumene, humulene, beta-selinene, alpha-selinene, beta-elemene, alpha-cubebene, alpha-copaene, and sesquisabinene. Oxygenated components include linalool, 1-terpinen-4-ol, myristicin, nerolidol, safrol, beta-pinone, *N*-formalpipidine, etc.²⁹ Purselglove et al. devote a 2¹/₂-page table to the constituents of black pepper.⁶⁴ One pungent principle of pepper is piperine, present at levels of 2 to 6%. Piperine may be useful as an analeptic in barbiturate poisoning. It has a central stimulant action in frogs, mice, rats, and dogs. Piperine, at 1 mg/ml, decreased the contraction of isolated guinea pig ileum. When injected i.v. into dogs at 1 mg/kg, it decreased blood pressure and respiration rate. When given orally to rats at 100 mg/100 g, it showed slight febrifugal activity. Piperine interacts with nitrite in vitro under slightly acidic conditions at 37° to form carcinogenic nitrosamines. Piperine is a stimulant. It is mutagenic with *Leptospira*; with large doses a bactericidal effect is produced. Isolated piperine has an inhibiting effect on *Lactobacillus plantarum*, *Micrococcus specialis*, and two fecal microorganisms (*Escherichia coli* and *Streptococcus faecalis*.)⁴¹

Toxicity — Reviewing work on piperine, Buchanan¹¹⁷ notes that black pepper is probably the most abundantly employed of the various methylenedioxybenzene-containing spices in the U.S. While containing some myristicin and safrole, pepper's main pungent flavoring compound is the piperine (trans, *trans*-5-[3,4-methylenedioxyphenyl]-2,4-pentadienoic peridide]). Since piperine and other pepper alkaloids have chemical structures similar to that of the mutagenic urinary safrole metabolite, 3-piperidyl-1-(3',4'-methylenedioxyphenyl)-1 propanone, pungent components of black pepper are sometimes suspected to be mutagenic and/or carcinogenic. Russians have suggested that the consumption of tea flavored with black pepper may have contributed to the unusually high incidence of esophageal cancer in the Aktibinsk region of the U.S.S.R. Like safrole, piperine stimulates hepatic regeneration in partially hepatocomized rats. Topical application of pepper extract to mice skin has increased the incidence of total malignant tumors. Reviewing the work on safrole, Buchanan concluded that it is the most thoroughly investigated methylenedioxybenzene derivative. Safrole also occurs in black pepper, basil,¹⁰ as well as cinnamon leaf oil, cocoa, mace, nutmeg, parsley, and star anise oil. Safrole was banned in root beer. The oral LD₅₀ for safrole in rats is 1950 mg/kg body weight, with major symptoms including ataxia, depression, and diarrhea, death occurring in 4 to 5 days. Ingestion of relatively large amounts of sassafras oil produces 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, and biliary proliferation and primary hepatomas. Also, reviewing research on myristicin, which occurs in nutmeg, mace, black pepper, carrot seed, celery seed, and parsley, Buchanan hypothesized that myristicin and elemicin can be readily modified in the body to amphetamines.