Food Science



Black Pepper Overview of Health Benefits

Keith Singletary, PhD

The black pepper (*Piper nigrum* L) vine and its extracts have been used as a folk medicine in a variety of cultures and are the source of the most commonly used spice worldwide. The chemical piperine is a major bioactive component present in black pepper (and white pepper as well) that has numerous reported physiological and drug-like actions. The scientific literature provides evidence that black pepper may have health benefits, particularly in enhancing digestive tract function. There is suggestive evidence that black pepper piperine may have nervous system benefits and may influence body energy usage in rats. Preliminary evidence in cell culture studies suggests that black pepper contains antioxidant constituents and possesses anti-inflammatory and antimicrobial properties. An overview of major uses for black pepper is presented here, and the strength of the evidence is graded. Nutr Today. 2010;45(1):43-47

lack pepper from the Piper nigrum L. vine (Figure 1) is the most commonly used spice worldwide, and its extracts have been used as a folk medicine in a variety of cultures. Piper nigrum is used for the production of both black pepper (from the unripened fruit) and white pepper (from the dehulled mature berry). In ancient Sanskrit literature, black pepper use for medicinal purposes was documented. In India, it was one of the most commonly used herbs in Ayurvedic medicine and has been considered for treatment of gastrointestinal disorders and, even more recently, of chronic malaria. Black pepper also was used for the treatment of epilepsy in traditional Chinese medicine. In the Middle Ages, black pepper was recorded as being used in seasoning and for concealing the flavor of salted, cured meat. This plant is indigenous to Southern India and also is cultivated on the islands of the Malay

archipelago, as well as Madagascar and other islands off the coast of Africa. Popular names for this spice depend on the source. For example, Malabar black pepper comes from the Malabar coast of southwest India, and Lampong black pepper is from Sumatra, Indonesia. Black pepper currently finds multiple uses in flavorings, in perfumes, and in insecticide formulations.^{1–3}

Overview

Black pepper constituents include fiber, essential oils, piperine, eugenol, the enzyme lipase, and minerals. Essential oil components include α - and β -pinene, limonene, and β -caryophyllene.^{2,4} Piperine and its isomers are the major factors responsible for the pungency and irritant action of black pepper. The chemical piperine, 1-piperoylpiperidine, is the major bioactive component present in both black and white peppers and individually has numerous reported physiological and drug-like actions similar to those reported for black pepper. The scientific literature provides evidence that black pepper may have health benefits, particularly in enhancing digestive tract



Figure 1. Black peppercorns.

function. It has been reported, for example, in rats and mice that black pepper and piperine can stimulate digestive enzymes, modify stomach secretions, alter gastrointestinal food transit time, and inhibit diarrhea.^{5–10} The acute effect of black pepper on the human stomach seems to be similar to that for aspirin, although the long-term effect of black pepper on the stomach is unknown.¹¹

Black pepper also has a substantial effect on enzyme systems that metabolize phytochemicals and drugs. Black pepper and piperine have been observed to inhibit cytochrome P450 enzymes, other phase I enzymes, the phase II detoxification enzyme uridine-5'-diphosphate (UDP)-glucuronyl transferase, and drug transporters in several tissues.^{9,12–18} This can lead to pronounced changes in the bioavailability of a natural compound or drug after ingestion. For example, coadministration of black pepper to rats along with curcumin, a phenolic constituent of turmeric, interferes with conjugation and metabolism of curcumin by UDP-glucuronyl transferase. Consequently, increased blood levels of curcumin have been noted in rats and humans.¹⁹ A similar increase in circulating levels of bioactive compounds associated with black pepper and piperine has been reported for other dietary factors such as the flavonoid (-)-epigallocathecin-3-gallate, beta carotene, and coenzyme Q_{10} .^{20–22} In healthy human volunteers, piperine administration increased blood levels of the antiepileptic drug phenytoin, the antihypertensive drug propranolol, and theophylline, a drug used to treat respiratory conditions.^{23–25} The clinical consequences of concomitant black pepper intake on dietary factors and drugs, particularly those with narrow therapeutic windows, will likely depend on multiple factors, including the dose of black pepper and drugs, the chemical characteristics of the agents, and the individual physiological responses to the specific agent.25

There is suggestive evidence that black pepper and piperine may have nervous system benefits and may influence body energy usage in rats. Preliminary evidence in cell culture studies suggests that black pepper contains antioxidant constituents and possesses anti-inflammatory and antimicrobial properties. Likewise, anticancer actions have been observed.

Examples of these uses for black pepper are presented in the "Summary of Research" section, and an effort is made to give an overview of the variety of scientific research on this topic. Points of view for rating of evidence in each category are based on consideration of cell culture, animal, and human clinical data from the peer-reviewed scientific literature. A higher rating was given when there were both preclinical and clinical data and there was consistency of findings among well-controlled human studies.

Summary of Research

Scientific Findings for Select Uses	Rating
Alteration of digestive tract function: Black pepper (and its constituent piperine) is reported to act as a digestive tract stimulant in rats and mice, although the effect is not always consistent. ^{5–9} In small clinical studies, intake of black pepper extract stimulated stomach secretions and affected the rapidity of movement of food through the digestive tract. ¹⁰ Some of this effect of black pepper seems to be due to piperine activating specific drug receptors. ²⁶ Black pepper also may alter the bioavailability of certain food components and drugs, partly by altering the body's systems controlling the metabolism and absorption of dietary constituents and drugs. ^{20–25} This effect of black peppe has been reported to improve the bioavailability of some agents,	Emerging, suggestive
although the clinical consequences may not necessarily be beneficial. <i>Metabolism and obesity:</i> Piperine has been shown in animal studies to increase the body's expenditure of energy. Apparently, piperine does this by affecting the production of hormone-like chemicals that regulate energy balance. This may have important implications for human body weight regulation and obesity, although, to date, there is little evidence	Preliminary, inconclusive
to support such a benefit in humans. ²⁷ Nervous system benefits: In mice, an extract of black pepper exhibited activity in suppressing convulsions. ^{28–37} In one human study, inhalation of black pepper oil components improved the swallowing reflex in stroke patients, apparently by activating specific regions of the brain. ³² A novel effect o inhalation of black pepper extract was the stimulation of respiratory tract sensations that apparently alleviated	Preliminary, inconclusive

(continued)	
Scientific Findings for Select Uses	Rating
Animal studies suggest that piperine may have an antidepressant-like action, but the amounts that are beneficial are poorly defined. ^{34–36} <i>Treatment of skin disorders:</i> Several cell culture studies using pigment-producing cells from the skin showed that black pepper extracts stimulated cell multiplication and function. It has been suggested that piperine may be useful in treating the depigmentary skin disorder vitiligo. ^{37,38} Also, black pepper extract and piperine exhibited antiandrogenic activity and stimulation of hair regrowth in one animal study. ³⁹ However, there is a lack of evidence	Preliminary, inconclusive
for such benefit in human studies. Anti-inflammatory, antioxidant, and antibacterial effects: Black pepper has a high content of antioxidant chemicals. In cell culture studies and in a few animal studies, black pepper inhibited oxidative stress, protected against fat breakdown, and was able to scavenge and inactivate some, but not all, reactive oxygen species. Black pepper was reported in one study to slow the growth of a variety of types of bacteria isolated from human volunteers. One recent report suggests that piperine may be toxic to the parasite causing malaria. Black pepper may have anti-inflammatory and fever-suppressing actions, and there is preclinical evidence that it may have modest immune	Preliminary, inconclusive
system–enhancing properties. ^{40–47} Anticancer actions: Cell culture and animal studies indicate that black pepper may suppress the action of chemicals that cause mutations in the genetic material of cells. Administration of piperine or black pepper can inhibit the growth of tumors in mice and rats. ^{9,48–51} In contrast, there is one report that chronic painting of the skin of mice with a black pepper extract increased skin cancer, ⁵² a response likely due to a chronic irritant action.	Preliminary, inconclusive

Animal studies have evaluated the toxicity of black pepper or piperine and report mixed results. One study observed that black pepper caused acute toxicity in rats and mice,⁵³ whereas 2 studies reported no adverse effects of black pepper administration to rats.^{54,55} The reason for these disparate results is unknown, and it should be pointed out that the doses used were not representative of usual human intakes. Most reports suggest that black pepper and piperine are not genotoxic or immunotoxic. Black pepper is considered Generally Recognized as Safe (21 CFR 182.10) for use in foods as a flavoring agent. This Generally Recognized as Safe status of black pepper for use as a food flavoring agent reflects doses that are much lower than those used in animal and cell culture studies and is thus not meant to justify unrestricted use at these higher levels. In this regard, it has been estimated that consumption of black pepper in India is about 0.3 g/d, a value similar to that for Americans estimated from disappearance data published by the US Department of Agriculture.^{56,57} This amount is several-fold lower than those amounts of black pepper given in human studies (about 1.5 g/d). Interestingly, piperine has been administered in some human trials at levels of 5 to 20 mg,^{19,22,24} which, assuming piperine content is 6% of black pepper dry weight,⁵⁸ is approximately the amount consumed in 83 to 333 mg of black pepper.

Conclusions

Based on the current scientific evidence, more information is needed on the health benefits of black pepper, particularly in human subjects. There is suggestive evidence to support its benefit in improving the function of the digestive tract and increasing energy expenditure. More evidence from well-designed clinical trials is needed, particularly those that examine black pepper doses relevant to typical intakes.

There are numerous cell culture studies demonstrating the antioxidant effects of black pepper and its extracts and that it has anti-inflammatory properties. However, the bioavailability of these constituents of black pepper, once ingested by humans, and the subsequent improvement in appropriate biomarkers in humans are not well characterized.

There is very limited evidence that black pepper constituents may benefit symptoms of convulsions and stroke. Additional controlled human studies using several dietary doses of black pepper components are needed to confirm these purported and intriguing health benefits. Also, drug interactions after intakes of a wide range of black pepper and piperine doses need to be more carefully evaluated, so that interactions with medications can be better understood. Thus, black pepper will continue to be a popular spice for enhancing food flavor, but its use in improving human health must await more definitive scientific evidence.

Keith Singletary, PhD, is professor emeritus of nutrition at the Department of Food Science and Human Nutrition, University of Illinois, Urbana. He had a long-standing research interest in diet and cancer and on the role of functional foods in promoting health. Funding for this article was provided by the McCormick Science Institute. Correspondence: Keith Singletary, PhD, University of Illinois, 905 South Goodwin Ave, Urbana, IL 61801 (kws@illinois.edu).

REFERENCES

- 1. Majeed D, Prakash L. The medicinal uses of pepper. *Int Pepper News.* 2000;1:23–31.
- 2. Tainter D, Grenis A. *Spices and Seasonings, A Food Technology Handbook.* 2nd ed. Hoboken, NJ: Wiley-IEEE; 2001.
- Burdock G. Encyclopedia of Food Color Additives. Boca Raton, FL: CRC Press; 1997.
- Musenga A, Mandrioli R, Ferranti A, D'Orazio G, Fanali S, Raggi M. Analysis of aromatic and terpenic constituents of pepper extracts by capillary electrochromatography. *J Sep Sci.* 2007;30:612–619.
- 5. Capasso R, Isso A, Borrelli F, et al. Effect of piperine, the active ingredient of black pepper, on intestinal secretion in mice. *Life Sci.* 2002;71:2311–2317.
- 6. Platel K, Rao A, Saraswathi G, Srinivasan K. Digestive stimulant action of three Indian spice mixes in experimental rats. *Nahrung*. 2002;46:394–398.
- Bajad S, Bedi K, Singla A, Johri R. Piperine inhibits gastric emptying and gastrointestinal transit in rats and mice. *Plant Med.* 2001;67:176–179.
- Ganesh B, Chandrasekhara N. Effects of black pepper and piperine on bile secretion and composition in rats. *Nahrung*. 1987;31:913–916.
- 9. Srinivasan K. Black pepper and its pungent principle-piperine: a review of diverse physiological effects. *Crit Rev Food Sci Nutr.* 2007;47:735–748.
- Vazquez-Olivencia W, Shah P, Pitchumoni C. The effect of red and black pepper on orocecal transit time. J Am Coll Nutr. 1992;11:228–231.
- Myers B, Smith J, Graham D. Effect of red pepper and black pepper on the stomach. *Am J Gastroenterol*. 1987;82: 211–214.
- Sharma P, Varma M, Chawla H, Panchagnula R. In situ and in vivo efficacy of peroral absorption enhancers in rats and correlation to in vitro mechanistic studies. *Farmaco*. 2005;60:874–883.
- 13. Singh A, Rao A. Evaluation of the modulatory influence of black pepper (*Piper nigrum* L.) on the hepatic detoxification system. *Cancer Lett.* 1993;72:5–9.
- Piyachaturawat P, Kingkaeohol S, Toskulkao C. Potentiation of carbon tetrachloride hepatotoxicity by piperine. *Drug Chem Toxicol.* 1995;18:333–344.
- 15. Dalvi R, Dalvi P. Comparison of the effects of piperine administered intragastrically and intraperitoneally on the

liver and liver mixed function oxidases in rats. *Drug Metabol Drug Interact*. 1991;9:23–30.

- Reen R, Jamwal D, Taneja S, et al. Impairment of UDP-glucose dehydrogenase and glucuronidation activities in liver and small intestine of rat and guinea pig in vitro by piperine. *Biochem Pharmacol*. 1993;46:229–238.
- 17. Bhardwaj R, Glaeser H, Becquemont L, Klotz U, Gupta S, Fromm M. Piperine, a major constituent of black pepper inhibits human p-glycoprotein and CYP3A4. *J Pharmacol Exp Ther.* 2002;302:645–650.
- Atal C, Dubey R, Singh J. Biochemical basis of enhanced drug bioavailability by piperine: evidence that piperine is a potent inhibitor of drug metabolism. *J Pharmacol Exp Ther*. 1985;2323:258–262.
- Shoba G, Joy D, Joseph T, Majeed M, Rajendran R, Srinivas P. Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers. *Planta Med.* 1998;64:353–356.
- Lambert J, Hong J, Kim D, Mishin V, Yang C. Piperine enhances the bioavailability of the tea polyphenol (-)-epigallocatechin-3-gallate in mice. *J Nutr.* 2004;134:1948–1952.
- Badmaev V, Majeed M, Prakash L. Piperine derived from black pepper increases the plasma levels of coenzyme Q10 following oral supplementation. *J Nutr Biochem*. 2000;11:109–113.
- Badmaev V, Majeed M, Norkus E. Piperine, an alkaloid derived from black pepper increases serum response of beta-carotene during 14-days of oral beta-carotene supplementation. *Nutr Res.* 1999;19:381–388.
- Velpandian T, Jasuja R, Bhardwaj R, Jaiswal J, Gupta S. Piperine in food: interference in the pharmacokinetics of phenytoin. *Eur J Drug Metab Pharmacokinet*. 2001;26:241–247.
- 24. Pattanaik S, Hota D, Prabhakar S, Kharbanda P, Pandhi P. Effect of piperine on the steady-state pharmacokinetics of phenytoin in patients with epilepsy. *Phytother Res.* 2006;20:683–686.
- 25. Hu Z, Yang X, Ho P, et al. Herb-drug interactions: a literature review. *Drugs*. 2005;65:1239–1282.
- 26. Szallasi A. Piperine: researchers discover new flavor in an ancient spice. *Trends Pharmacol Sci.* 2005;26:437–439.
- Westerterp-Plantenga M, Diepvens K, Joosen A, Berube-Parent S, Tremblay A. Metabolic effects of spices, teas, and caffeine. *Physiol Behav.* 2006;89:85–91.
- Abila B, Richens A, Davies J. Anticonvulsant effects of extracts of the west African black pepper, *Piper guineense*. *J Ethnopharmacol.* 1993;39:113–117.
- 29. Mori A, Kabuto H, Pei Y. Effects of piperine on convulsions and on brain serotonin and catecholamine levels in E1 mice. *Neurochem Res.* 1985;10:1269–1275.
- D'Hooge R, Pei Y, Raes A, Lebrun P, van Bogaert P, de Deyn P. Anticonvulsant activity of piperine on seizures induced by excitatory amino acid receptor agonists. *Arzneimittelforschung*. 1996;46:557–560.
- 31. Pei Y. A review of pharmacology and clinical use of piperine and its derivatives. *Epilepsia*. 1983;24:177–182.
- Ebihara T, Ehihara S, Maruyama M, et al. A randomized trial of olfactory stimulation using black pepper oil in older people with swallowing dysfunction. *J Am Geriatr Soc.* 2006;54:1401–1406.

Copyright © 2010 Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

- 33. Rose J, Behm F. Inhalation of vapor from black pepper extract reduces smoking withdrawal symptoms. Drug Alcohol Depend. 1994;34:225-229.
- 34. Lee S, Hong S, Han X, et al. Piperine from the fruit of Piper longum with inhibitory effect on monamine oxidase and antidepressant-like activity. Chem Pharm Bull. 2005;53:832-835.
- 35. Li S, Wang C, Wang M, Li W, Matsumoto K, Tang Y. Antidepressant like effects of piperine on chronic mild stress treated mice and its possible mechanisms. Life Sci. 2007;80:1373-1381.
- 36. Li S, Wang C, Koike K, Nikaido T, Wang M. Antidepressant-like effects of piperine and its derivative antiepilepsirine. J Asian Nat Prod Res. 2007;9:435-444.
- 37. Lin Z, Hoult J, Bennett D, Raman A. Stimulation of mouse melanocyte proliferation by Piper nigrum fruit and its main alkaloid piperine. Plant Med. 1999;65:600-603.
- 38. Lin Z, Liao Y, Venkatasamy R, Hider R, Soumyanath A. Amides from Piper nigrum L. with dissimilar effects on melanocyte proliferation in vitro. J Pharm Pharmacol. 2007;59:529-536.
- 39. Hirata N, Tokunaga M, Naruto S, Linuma M, Matsuda A. Testosterone 5 alpha-reductase active constituents of Piper nigrum leaf. Biol Pharm Bull. 2007;30:2402-2405.
- 40. Vijayakumar R, Surya D, Nalini N. Antioxidant efficacy of black pepper (Piper nigrum L) and piperine in rats with high fat diet induced oxidative stress. Redox Rep. 2004;9:105-110.
- 41. Vijayakumar R, Nalini N. Efficacy of piperine, an alkaloid constituent from Piper nigrum on erythrocyte antioxidant status in high fat diet and antithyroid drug induced by hyperlipidemic rats. Cell Biochem Funct. 2006;24:491-498.
- 42. Chaudhry N, Tariq P. Bactericidal activity of black pepper, bay leaf, aniseed and coriander against oral isolates. Pak J Pharm Sci. 2006;19:214-218.
- 43. Kumar S, Arya P, Mukherjee C, et al. Novel aromatic ester from Piper longum and its analogues inhibit expression of cell adhesion molecules on endothelial cells. Biochemistry. 2005;44:15944-15952.
- 44. Kumar S, Singhal V, Roshan R, Sharma A, Rembhotkar G, Ghosh B. Piperine inhibits TNF-alpha induced adhesion of neutrophils to endothelial monolayer through suppression of NF-kappaB and IkappaB kinase activation. Eur J Pharmacol. 2007;575:177-186.
- 45. Mujamdar A, Dhuley J, Deshmukh V, Raman P, Naik S. Anti-inflammatory activity of piperine. Jpn J Med Sci Biol. 1990;43:95-100.

- 46. Pathak N, Khandelwal S. Cytoprotective and immunomodulating of piperine on murine splenocytes: an in vitro study. Eur J Pharmacol. 2007;576:160-170.
- 47. Freire-de-Lima L, Ribeiro T, Rocha G, et al. The toxic effects of piperine against Trypanosoma cruzi: ultrastructural alterations and reversible blockage of cytokinesis in epimastigote forms. Parasitol Res. 2008;102:1059-1067.
- 48. Sunila E, Kuttan G. Immunomodulatory and antitumor activity of Piper longum Linn. and piperine. J Ethnopharmacol. 2004;90:339-346.
- 49. Nalini N, Manju V, Menon V. Effect of spices on lipid metabolism in 1,2-dimethylhydrazine-induced rat colon carcinogenesis. J Med Food. 2006;9:237-245.
- 50. Selvendiran K, Banu M, Sakthisekaran D. Oral supplementation of piperine leads to altered phase II enzymes and reduced DNA damage and DNA-protein crosslinks in benzo(a)pyrene induced experimental lung carcinogenesis. Mol Cell Biochem. 2005;268:141-147.
- 51. Nalini N, Sanitha K, Viswanathan P, Menon V. Influence of spices on bacterial (enzyme) activity in experimental colon cancer. J Ethnopharmacol. 1998;62:15-24.
- 52. Schwaireb M, Wrba H, El-Mofty M, Dutter A. Carcinogenesis induced by black pepper (Piper nigrum) and modulated by vitamin A. Exp Pathol. 1990;40:233-238.
- 53. Piyachaturawat P, Glimsukon T, Toskulkao C. Acute and subacute toxicity of piperine in mice, rats and hamsters. Toxicol Lett. 1983;16:331-339.
- 54. Srinivasan M, Satyanarayana M. Effect of black pepper (Piper nigrum Linn.) and piperine on growth, blood constituents, and organ weights in rats. Nutr Rep Int. 1981:23:871-876.
- 55. Bhat B, Chandrasekhara N. Studies on the metabolism of piperine: absorption, tissue distribution and excretion of urinary conjugates in rats. Toxicology. 1986;40:83-92.
- 56. UmaPradeep K, Geervani P, Eggum B. Common Indian spices: nutrient composition, consumption and contribution to dietary value. Plant Foods Hum Nutr. 1993;44:137-148.
- 57. USDA, ERS. Spice Supply and Disappearance, 1966–2005. http://www.ers.usda.gov/Data/FoodConsumption. Accessed December 20, 2009.
- 58. US Department of Agriculture, Agricultural Research Service. Nutrient data laboratory. http://www.nal.usda.gov/ fnic/foodcomp/search. Accessed December 20, 2009.

Books Received

Preventive Nutrition: The Comprehensive Guide For Health Professionals. Adrienne Bendich and Richard Deckelbaum, editors. New York: Humana Press; 2009. ISBN 9781603275415. \$345.00.

Nutrition Today, Volume 45 • Number 1 • January/February, 2010

McBride, W.D., and C. Greene. Characteristics, Costs, andIssues for Organic Dairy Farming, ERR-82, U.S. Department of Agriculture, Economic Research Service, 2009.