

Cumin

Potential Health Benefits

Keith W. Singletary, PhD

Cumin is an aromatic herb prepared from the dried seeds of the plant *Cuminum cyminum* L. (family Apiaceae). As a culinary ingredient, it is a major constituent of curry powder, and as a spice, its popularity is considered second only to pepper. Therapeutic uses of cumin in traditional medicines date back millennia and include treatment for gastrointestinal distress, diarrhea, and jaundice, as well as for hypertension, epilepsy, fever, childhood maladies, and gynecological and respiratory disorders. This narrative review summarizes recent human trials that assess its efficacy in relieving symptoms associated with diabetes and cardiovascular disease and considers suggestions for future studies. *Nutr Today*. 2021;56(3):144–151

The spice cumin is prepared from the dried seeds (Figure 1) of the plant *Cuminum cyminum* L. (family Apiaceae). Also called green cumin, comino, kummel, or, in South Asia, as zeera, it is not to be confused with sweet cumin (*Pimpinella anisum* or anise), wild cumin (*Bunium persicum*), and black cumin (*Nigella sativa*). It is an aromatic herb native to the eastern Mediterranean and South Asia, but now widely cultivated elsewhere such as in North Africa and East Asia.

Culinary Uses

As a spice, its popularity is considered second only to pepper, and as a culinary ingredient, it is a major constituent of curry powder. Cumin seed powder contributes to South Asian spice mixtures, such as 1 of the 10 spices in garam masala, and its whole seeds are included in panch phoron,

Keith W. Singletary, PhD, is professor emeritus of nutrition in the Department of Food Science and Human Nutrition at the University of Illinois. From 2001 to 2004, he was the director of the Functional Foods for Health Program, at the Chicago and Urbana-Champaign campuses of the University of Illinois. Dr Singletary received bachelor and master's degrees in microbiology from Michigan State University and his PhD in nutritional sciences from the University of Illinois. Dr Singletary's primary research interests include molecular carcinogenesis and the potential use of natural products in cancer chemoprevention. Dr Singletary currently resides in Florida.

The author has no conflicts of interest to disclose.

Correspondence: Keith W. Singletary, PhD, University of Illinois, Department of Food Science and Human Nutrition, 905 South Goodwin Ave, Urbana, IL 61801 (kws@illinois.edu).

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a blend of 6 spice seeds. In general, cumin flavors stews, soups, lamb and chicken dishes, sausages, breads, cheeses, pickles, and alcoholic beverages. Specifically, it can be found as an ingredient in a variety of regional foods such as chickpea falafel in the Middle East, the spiced cauliflower and potato dish, aloo gobi, in India, Moroccan carrot salad, pollo a la brasa in Peru, ropa vieja, and black beans and rice, to name a few. Depending on the recipe, cumin is often added in amounts varying from 1.4 to 5.7 g. Also, its oil is used as a fragrance in creams, lotions, and perfumes. The flavors attributed to the seeds are quite diverse, including such terms as warm, slightly bitter, peppery, metallic, astringent, pungent, burning, tingling, and nutty.^{1–5}

Composition

Cumin seeds contain 1% to 5% volatile oil, 18% to 19% protein, 56% to 60% carbohydrates, numerous phenolics, vitamins, and minerals.^{6,7} Cuminaldehyde (4-isopropylbenzaldehyde) is a prominent component of the essential oil (Figure 2) with *p*-cymene, γ -terpinene, β -pinene, and *p*-mentha-1,3-dien-7-al present as other main constituents in amounts varying considerably, depending on origin, cultivation harvesting, and extraction methods of the plant.^{1,7–11} Recently, the cumin proteome was comprehensively characterized.¹²

Intake

The intake of cumin seeds in different countries is not well documented, although it is estimated that 0.8 g/d is consumed per person in India.¹³ Limited information exists about the bioavailability of cumin constituents in humans after consumption. Such data are important because any potential uses of cumin to improve health are impacted by how much is consumed and the ultimate amount and form of its individual bioactive components in target tissues.¹⁴ This information also helps in discerning any negative effects of cumin constituents and their metabolites in various organs. Functional bioavailability of cumin in humans was demonstrated when human subjects ($n = 10$ –12) were given 2.8 g/d cumin and peripheral blood mononuclear cells subsequently isolated. In ex vivo analysis, those peripheral blood mononuclear cells isolated from subjects administered cumin showed evidence of protection from oxidative damage.¹⁵ The pharmacokinetics of cuminaldehyde were examined in rats orally administered a dose of 200 mg/kg.¹⁶ The peak drug concentration (C_{max}) in the blood was 4.63 μ g/mL, time to reach peak concentration (T_{max}) was 1.85 hours, and the

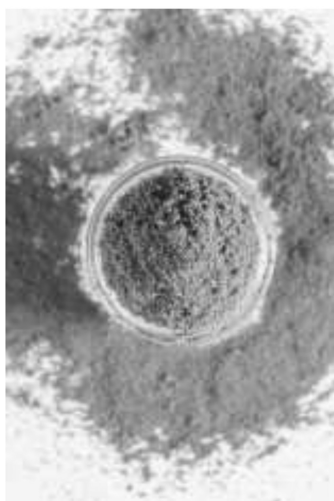
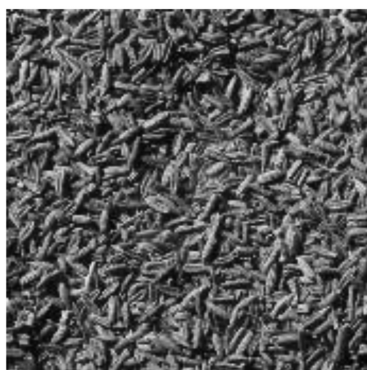


FIGURE 1. Cumin plant, seeds, and powder.

half-life was 1.45 hours. In rabbits, oral intake of a 2-g sample of cuminaldehyde resulted in the formation of the urinary metabolites cumyl alcohol and methyl esters of hydroxycuminic acids.^{17–19} For a small study in ewes (3 nonpregnant, 2 lactating), 250 g cumin seeds was fed within the daily grain rations.²⁰ Subsequently, the arrival of volatile essential oil constituents present in the seeds was measured in the plasma and milk. The maximum concentration of *p*-cymene in the blood was 194 parts per billion at 17 hours. No β -pinene, limonene, cineole, γ -terpinene, and cuminaldehyde were detected.

Only β -pinene and *p*-cymene were transferred into the milk in detectable quantities. Theoretical oral bioavailability as assessed by in silico analysis suggested cuminaldehyde is readily absorbed by the gastrointestinal tract and likely can cross the blood-brain barrier.²¹ Clearly, more information is needed about the bioavailability of cumin after human intake.

Uses in Traditional Medicine

Cumin and its essential oil have a long history of therapeutic uses in traditional medicines. Ancient Ayurvedic applications of cumin in India included treatment for gastrointestinal distress, diarrhea, and jaundice, whereas elsewhere it was used for hypertension, epilepsy, fever, childhood maladies, and gynecological and respiratory disorders.^{7,22,23} As determined more recently, cumin constituents might act in a variety of ways, including, for example, by reducing oxidative stress, suppressing inflammatory marker expression, modulating signaling pathways controlling cell death, and altering levels of circulating hormones.

METHODS

Studies providing evidence for potential health benefits of foods, ingredients, and plant constituents gather data from a variety of scientific methods, such as cell culture experiments, animal studies, and human clinical trials. Human studies are particularly important in determining public health recommendations, especially those randomized controlled trials (RCTs) testing well-characterized treatments and applying appropriate statistical analyses. With this in mind, a search of the PubMed and Science Direct databases was conducted using terms that included *C. cyminum*, cumin, zeera, and cuminaldehyde. Full reports of English-language publications and English-language abstracts of foreign-language articles from peer-reviewed journals were the primary sources of information. Although the quality of identified studies varied considerably, all relevant, published investigations were included in this overview so that the totality and diversity of information can be described, and issues for future research can be identified. Additional information was gleaned from bibliographies within these sources. Studies of cumin as a component within multi-ingredient preparations were not included in this overview.

POTENTIAL HEALTH BENEFITS

The human health issues for which clinical trials of cumin were most frequently conducted involved the dysregulation of blood glucose and lipid levels. The responses of subjects with signs and symptoms of type 2 diabetes mellitus (T2DM), cardiovascular disease, or the metabolic syndrome are summarized in Table 1. Most participants were recruited from populations in Iran and India. When subjects with hyperglycemia and hyperlipidemia are considered together, changes in fasting blood glucose (FBG),

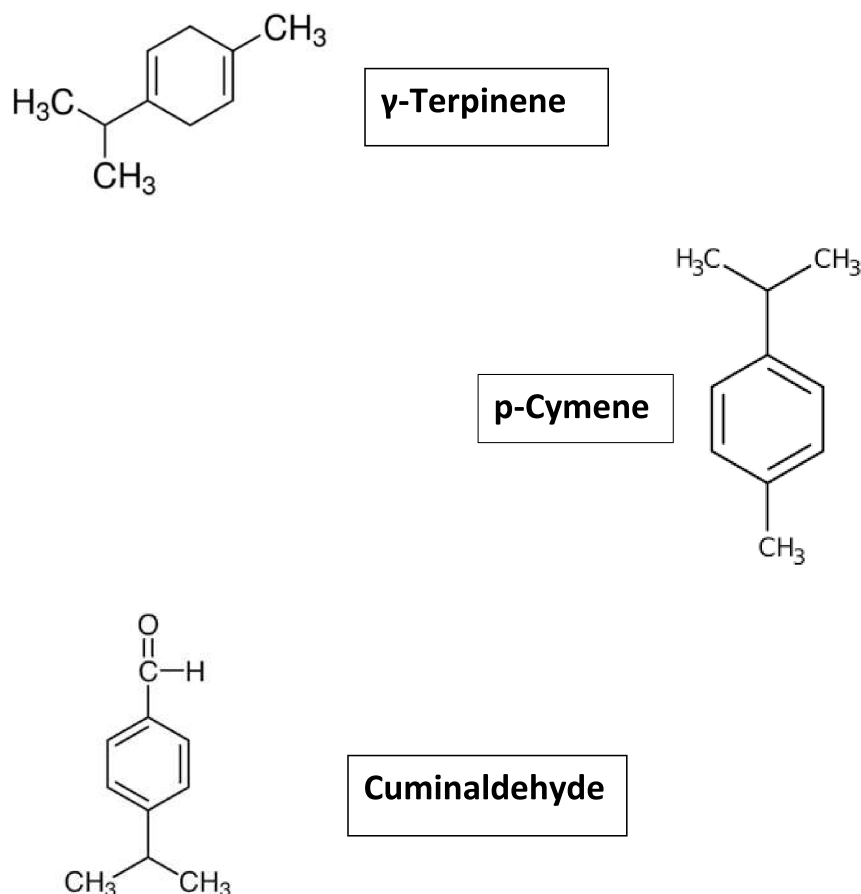


FIGURE 2. Structures of select cumin constituents.

blood glycosylated hemoglobin (HbA_{1c}), blood total cholesterol (TC), blood triglyceride (TG), LDL, serum low-density lipoprotein cholesterol (LDL), serum high-density lipoprotein cholesterol (HDL), serum insulin, and leptin are inconsistent. As for those trials specifically of T2DM,^{24–26} cumin treatment appeared to lower FBG and HbA_{1c}, but less consistently to improve blood lipid levels. In those with prediabetes,²⁷ treatment of women with cumin improved the aberrant blood lipid profile, compared with the lack of response to cumin in men. This is in contrast to women with hyperlipidemia,³² for whom administration of cumin resulted in a lesser effect on blood lipid levels. The findings of these 2 small studies suggest that gender differences in response to cumin deserve further examination in larger investigations. No consistent effect of cumin dosing on blood glucose and lipid parameters was observed in obese/overweight patients.^{29–31} Taken together, for trials in Table 1, measures of oxidative stress and anthropometric status were inconsistently affected by cumin. Only 1 trial³⁶ was initiated with healthy adults who were treated in a crossover design study with an aqueous extract of cumin either added to rice during cooking or given as a beverage along with a rice meal. Compared with a control meal of rice and water beverage, no significant effect of the

treatments on postprandial glucose and insulin levels was observed. No substantial adverse effects of these various cumin treatments were reported in the trials. From these human trials, the mechanisms for hyperglycemic or hyperlipidemic actions of cumin remain largely unidentified. When evaluated in trials, it was concluded that cumin's possible effects on serum leptin levels, oxidative stress, inflammation, and hormones controlling metabolic homeostasis were inconsistent.

Two meta-analyses^{37,38} examined these RCTs for significant, consistent outcomes of cumin treatment. These 2 analyses provided quality assessments of the trials, but used different cutoff values of the Jadad score for determining which were of high quality, resulting in disparities in quality ratings between the meta-analyses. In 1 review by Jafarnejad et al,³⁷ 7 trials of diabetic and overweight subjects were selected^{24,25,28–31,35} to evaluate the impact of cumin on anthropometric and metabolic outcomes. Three trials were classified as low quality. Significant decreases (mean changes) in body weight (–1.74 kg), body mass index (–0.67 kg/m²), FBG (–17.8 mg/dL), and TG (–21.23 mg/dL) and an increase in HDL levels (+4.16 mg/dL) were observed, compared with controls, whereas no significant effect of cumin was detected for HbA_{1c}, TC, and LDL. In comparison, the meta-analysis of Hadi et al³⁸ assessed blood lipid responses to cumin in 5

TABLE 1 Effect of Cumin on Blood Glucose and Lipid Regulation in Humans

Subjects	Treatment Dose and Duration	Outcomes of Cumin Treatment ^a	References
T2DM	CEO, 25 mg/d (n = 29); placebo (n = 24); 90 d	vs baseline: ↓FBG, ↓HbA _{1c} , ↓TG, ↓oxLDL, ↓leptin, ↑ApoA1, ↑PON1 NE: TC, LDL, ApoB	24
T2DM	CEO 50 mg/d (n = 30), CEO 100 mg/d (n = 30), placebo (n = 30); 8 wk	vs baseline: ↓FBG, ↓HbA _{1c} , ↓SI	25
T2DM	Cumin powder, 5 g/d (n = 10), glipizide, 5 mg/d (n = 10); 60 d	vs baseline: ↓FBG, ↓TC, ↓TG, ↓PL, ↓VLDL, ↓AI, ↑HDL NE: LDL No significant differences for glipizide vs baseline	26
Prediabetes	CEO, 7 mg/d (n = 25), controls (n = 29); 10 wk	vs controls: ♀: ↓TG, ↓LDL, ↑HDL, ↓BW, ↓BMI, ↓WC NE: FBG, SI, HbA _{1c} , leptin ♂: ↓SI, ↓HbA _{1c} NE: lipids, anthropometrics, leptin	27
Hypercholesterolemia	Dietary CEO, 9-15 drops/d (n = 39); 45d	vs baseline: ↓FBG (♀ only), ↓oxLDL, ↑PON1, ↑PON NE: TG, TC, LDL, HDL	28
Overweight/obese	Cumin powder, 3 g/d in yogurt (n = 44), controls in yogurt (n = 44); 3 mo	vs controls: ↓TG, ↓TC, ↓LDL, ↑HDL NE: FBG, BW, WC, BMI, fat mass	29
Overweight	CEO 100 mg/d (n = 26), placebo (n = 26); 8 wk	vs placebo: ↓BW, ↓BMI, ↓SI, ↑HOMA-B, ↑QUICKI NE: FBG, HOMA-IR, lipids, ox stress, TSH	30
Overweight/obese	CEO 50 mg/d (n = 24), CEO 150 mg/d (n = 24), placebo (n = 24)	150 mg/d vs placebo: ↓BW, ↓BMI, ↓FBG, ↓TG, ↓TC, ↓LDL, ↑QUICKI NE: HDL, SI, HOMA-IR, HOMA-B, HDL, ox stress 50 mg/d vs placebo: ↓BW, ↓BMI	31
Dyslipidemia (♀)	3 g/d cumin powder (n = 30), controls (n = 30); 8 wk	vs controls: ↓TC NE: BW, WC, BMI, LDL, HDL	32
MetS	CEO 225 mg/d (n = 22), placebo (n = 22); 8 wk	vs placebo: ↑SOD, ↑TAC, ↓MDA NE: CRP, TNF-α, CAT, GSH-Px	33
MetS	CEO 225 mg/d (n = 22), placebo (n = 22), 8 wk	vs placebo: ↓SBP NE: DBP, FBG, SI, HbA _{1c} , lipids, HOMA-IR, BMI, BW, WC	34
Nonalcoholic steatohepatitis	Cumin saponin 75 mg/d (n = 40), placebo (n = 41); 6 mo	vs placebo: NE: FBG, TG, TC, LDL, HDL, BMI, ALT, AST	35

Abbreviations: AI, atherogenic index; ALT, alanine aminotransferase; ApoA1, apolipoprotein A1; ApoB, apolipoprotein B; AST, aspartate aminotransferase; BMI, body mass index; BW, body weight; CEO, cumin essential oil; DBP, diastolic blood pressure; FBG, fasting blood glucose; GSH-Px, plasma glutathione peroxidase; HbA_{1c}, glycosylated hemoglobin; HDL, serum high-density lipoprotein cholesterol; HOMA-B, homeostatic model assessment of β-cell function; HOMA-IR, homeostatic model assessment for insulin resistance; LDL, serum low-density lipoprotein cholesterol; MDA, malondialdehyde; MetS, metabolic syndrome; oxLDL, oxidized low-density lipoprotein cholesterol; PL, phospholipids; PON1, paraoxonase 1; QUICKI, quantitative insulin-sensitivity check index; SBP, systolic blood pressure; SI, serum insulin; SOD, superoxide dismutase; T2DM, type 2 diabetes mellitus; TAC, total antioxidant capacity; TC, blood total cholesterol; TG, blood triglycerides; TNF-α, tumor necrosis factor α; TSH, thyroid-stimulating hormone; VLDL, serum very low-density lipoprotein cholesterol; WC, waist circumference.

^aNote that the type of trial and quality varied considerably from trial to trial.

RCTs.^{24,25,29,30,35} Only 1 trial was classified as low quality. They detected a significant increase in HDL (+3.35 mg/dL) and a decrease in TC (−10.9 mg/dL) and LDL (−6.94 mg/dL)

levels, but observed no significant effect of cumin on TG level. Of interest, when their data were stratified according to primary level of TG (hypertriglyceridemia vs nonhypertriglyceridemia),

a significant decrease in TG concentration for the nonhypertriglyceridemia subjects was detected. Furthermore, a bigger increase in HDL level following cumin dosing was found for the subgroup of patients with hypertriglyceridemia, compared with the nonhypertriglyceridemics. In addition, supplementation with cumin decreased TC and LDL in those with nonhypertriglyceridemia more than in those subjects with hypertriglyceridemia. Jafarnejad et al³⁷ also conducted a subgroup analysis of diabetic subjects alone and found that cumin supplementation significantly decreased LDL levels, in contrast to the initial general analytic results when overweight individuals were included. These analyses suggest that susceptibility to cumin may have occurred among different stages of metabolic dysfunction and needs to be further clarified to better understand these different patterns of change.

When considered together, the variability in outcomes of the human trials reflects the poor quality of some of the studies. Inconsistencies in trial quality and results are likely due to several issues. Study methodologies differed in baseline health characteristics of subjects chosen for study. The source, dose, method of delivery, and duration of cumin samples administered varied among trials. For example, cumin essential oil was provided at doses ranging from 7 to 375 mg/d, whereas cumin powder was given at levels of 3 to 5 g/d. Duration of trials were from 45 days to 3 months. Other lifestyle behaviors impacting outcomes often were not assessed. Moreover, the relative amounts of bioactive chemicals in the oil and powder treatments were not consistently reported, and likely differed among study samples, because bioactive ingredients can vary based on geographical region of cultivation, the time of harvesting, and methods of processing.^{2,6,10,11,37}

Table 2 summarizes the diverse effects of cumin and its extracts in animal models on blood glucose and lipid dysregulation. In normal nonoverweight, nondiabetic animals, cumin generally lacked efficacy or showed inconsistent effects on blood glucose and lipid homeostasis. However, in obese or diabetic animals or those exhibiting aberrant blood lipid profiles, cumin, whether administered as essential oil, seed powder, or an extract, generally demonstrated some level of efficacy in correcting high blood cholesterol concentrations, hyperglycemia, and other metabolic characteristics of diabetes. In ovariectomized rats, cumin was more effective than estradiol in lowering elevated TC levels.⁵⁵ Of interest, the individual cumin constituents cuminaldehyde and cuminol demonstrated the capacity to normalize blood glucose and lipid dysregulation, which suggests that multiple phytochemicals in cumin ultimately may contribute to its beneficial actions. Mechanisms of action for these improvements hypothetically might include preventing damage to the kidneys and pancreas, stimulating antioxidant defenses, suppressing

expression of inflammatory pathways, and modulating signaling pathways and hormones that control insulin sensitivity, and lipid and glucose metabolism.

ADDITIONAL HUMAN BENEFITS

A small, randomized clinical trial⁵⁶ lacking placebo controls was conducted to evaluate the effect of cumin powder (3 g/d) on symptoms of dysmenorrhea over 3 menstrual cycles. Based on comparisons to baseline values, cumin provided to the subjects (n = 10) did not reduce pain, but was found to significantly reduce fatigue, cold sweats, cramps, and backache. The antimicrobial efficacy of cumin was examined in 2 human trials. Women with vulvovaginal candidiasis (n = 30) were instructed to change implanted cumin essential oil-containing vaginal suppositories daily for 6 consecutive days.⁵⁷ In comparison to baseline values, significantly lower rates of vaginal itching, discharge, and dyspareunia were reported following use of these suppositories. Moreover, in 70% of the patients, no *Candida* species were detected in discharges. In a different study,⁵⁸ a cumin essential oil-containing toothpaste was evaluated for efficacy in suppressing dental plaque following 4 weeks of twice per day brushing. The 2 main constituents in this essential oil were α -pinene and 1,8-cineole. Compared with controls, it inhibited dental plaque formation in volunteers in a manner similar to toothpastes containing the germicidal agent chlorhexidine. Lastly, for patients with irritable bowel syndrome (n = 57), compared with baseline values, orally administering 20 drops of 2% cumin essential oil per day for 4 weeks significantly decreased abdominal pain, bloating, incomplete defecation, and fecal urgency.⁵⁹

SAFETY

No substantial adverse effects were recorded in RCTs when cumin powder was given at doses up to 5 g/d and when the essential oil was provided up to 375 mg/d.^{37,38} Cumin is generally recognized as safe for intended use in foods as a spice and flavoring by the US Food and Drug Administration, and cuminaldehyde was determined to be safe as a fragrance ingredient by the Expert Panel for Fragrance Safety.⁶⁰ There are concerns regarding allergic responses in those with sensitivities to cumin and related herbs,^{61,62} although some cases were attributed to contamination with other plant or food allergens such as peanut.⁶³ Toxicity evaluations in rodents are limited. The 50% lethal dose (LD₅₀) of the essential oil in mice is 0.78 mL/kg.⁶⁴ In contrast to feeding cumin powder to rats at 2% wt/wt in the diet, feeding cumin at a concentration of 10% resulted in hematological evidence of toxicity and intestinal, liver, and kidney damage.⁶⁵ Yet, in a multidose study, oral administration of the essential oil to rats for 45 days did not show evidence of adverse effects or aberrant clinical signs

TABLE 2 Summary of Effects of Cumin Samples on Blood Glucose and Lipid Regulation in Animal Models

Condition	Treatment			Outcomes	References
	Samples	Doses ^a	Duration		
Diabetes	Essential oil	50 mg/kg	6 wk	↓FBG, ↓IL-6, ↓TNF-α	39
	Powder	0.5%–5% wt/wt in diet	2–8 wk	↓FBG, ↓TC, ↓TG, ↓polyuria, ↓protein carbonyls, ↓urinary glucose + creatinine, ↓cataract progression	40,41
		0.26 mg/kg	6 wk	↓FBG, ↓HbA _{1c} , ↓TG, ↓TC, ↓PL, ↓FFA, ↓liver lipids	42
	Organic solvent extracts	0.6–600 mg/kg	2–6 wk	↓FBG, ↓HbA _{1c} , ↑SI, ↓TG, ↓TC, ↓LDL, ↑HDL, ↓HOMA-IR, ↓pancreatic damage, restore liver + muscle glycogen, improve kidney function	43–47
	Cuminaldehyde	5 mg/kg	Acute	↓PPBG	45
	Cuminol	5 mg/kg	Acute	↓PPBG	45
Hyperlipidemia, Obesity	Essential oil	3 mg/kg	5 wk	↓FBG, ↓TC, ↓TG, ↓LDL	48
	Powder	1.25% wt/wt in diet	8 wk	↓TG, ↓TC, ↓PL, ↓liver TG	49
	Organic solvent extracts	3–500 mg/kg	2–9 wk	↓TC, ↓TG, ↓LDL, ↓HDL NE: FBG	50
	Cuminaldehyde	12 mg/kg	4 wk	↓FBG, ↓TG, ↓LDL, ↑HDL, ↓SI, ↓BW, ↓visceral fat pad weight, ↓liver weight, ↓pancreatic lipase activity, ↓serum ALT, ↓hepatic necrosis NE: food intake, TC, serum leptin, AST	51
Normal	Essential oil	0.4–50 mg/kg	5–8 wk	↓TG, ↓TC, ↓LDL, ↓HDL NE: serum cytokines Inconsistent: FBG	39,44
		100 μL/d	30 d	↑TG, ↑TC, ↑HDL NE: FBG	52
	Powder	1.25%–5% wt/wt in diet	2–8 wk	NE: FBG, TC, TG, liver lipids, urinary creatinine	40,49,53
		0.25 mg/kg	6 wk	NE: FBG, HbA _{1c} , lipid profile	42
	Organic solvent extracts	200–600 mg/kg	4 wk	NE: FBG, SI, HbA _{1c} , liver + muscle glycogen ↓PPBG	43,44,47
	Water extract	528 mg/kg	Acute	↓PPBG	54

Abbreviations: BW, body weight; FBG, fasting blood glucose; FFA, blood free fatty acids; HbA_{1c}, blood glycosylated hemoglobin; HDL, serum high-density lipoprotein cholesterol; IL-6, serum interleukin 6; HOMA-IR, homeostatic model assessment for insulin resistance; LDL, serum low-density lipoprotein cholesterol; LPL, lipoprotein lipase; LCAT, lecithin-cholesterol acyltransferase; NE, no statistically significant effect; PL, phospholipids; PPBG, postprandial blood glucose; SI, serum insulin; TBARS, thiobarbituric acid reactive substances; TC, blood total cholesterol; TG, blood triglycerides; TNF-α, serum tumor necrosis factor α.

^aDoses are expressed per kg body weight; dietary amounts as weight/weight diet.

at doses up to 500 mg/kg per day.⁶⁶ Because it was reported that cumin constituents may increase the risk of bleeding, alter blood glucose levels, and enhance the bio-availability of a variety of medications, caution is needed

in using doses beyond those for flavoring of foods. Consultation with a physician about its possible interactions with patients' prescription medications is recommended. Caution also is recommended for use during pregnancy. Although it

has traditional medical uses as a galactagogue, consumption during lactation has not been well-studied.^{7,22,67–71}

CONCLUSION

There is preliminary evidence based on animal and human data of inconsistent quality that cumin in large doses may alleviate the dysregulation of blood glucose and lipid levels associated with diabetes and cardiovascular disease. However, the relative effectiveness of different forms of cumin, the identities of specific bioactive phytochemicals contributing to beneficial actions, and the disposition of cumin constituents after human consumption are not known. These findings point to the need for larger, well-designed trials of cumin's dose-dependent effects in diverse ethnic populations, with a greater emphasis on identifying those subgroups of individuals that may be more responsive to cumin's potential benefits while ensuring the safety of dose levels, as well as on characterizing potential mechanisms of action. These issues should be more fully addressed before general recommendations about cumin and health can be promoted.

REFERENCES

- Sowbhagya HB. Chemistry, technology, and nutraceutical functions of cumin (*Cuminum cyminum* L): an overview. *Crit Rev Food Sci Nutr*. 2013;53:1–10.
- Bettaieb I, Bourgou S, Wannes WA, et al. Essential oils, phenolics, and antioxidant activities of different parts of cumin (*Cuminum cyminum* L.). *J Agric Food Chem*. 2010;58:10410–10418.
- Tahir H, Sarfraz R, Ashraf A, Adil S. Chemical composition and antidiabetic activity of essential oils from two spices (*Syzgium aromaticum* and *Cuminum cyminum*). *Inter J Food Proper*. 2016;19:2156–2164.
- Swahn J. *Caraway and Cumin, in The Lore of Spices*. Accokeek, MD: Stoeger Publishing Co; 2001:154–155.
- Legrand C, Merlini JM, de Senarclens-Bezencon C, Michlig S. New natural agonists of the transient receptor potential ankyrin 1 (TRPA1) channel. *Sci Rep*. 2020;10:11238. <https://doi.org/10.1038/s41598-020-68013-2>.
- Rebey IB, Kefi S, Bourgou S, et al. Ripening stage and extraction method effects on physical properties, polyphenol composition and antioxidant activities of cumin (*Cuminum cyminum* L.) seeds. *Plant Foods Hum Nutr*. 2014;69:358–364.
- Mnif S, Aifa S. Cumin (*Cuminum cyminum* L.) from traditional uses to potential biomedical applications. *Chem Biodivers*. 2015;12:733–742.
- Wanner J, Bail S, Jirovetz L, et al. Chemical composition and antimicrobial activity of cumin oil (*Cuminum cyminum*, Apiaceae). *Nat Prod Commun*. 2010;5:1355–1358.
- Mutlu-Ingok A, Karbancioglu-Guler F. Cardamom, cumin, and dill weed essential oils: chemical compositions, antimicrobial activities, and mechanisms of action against *Campylobacter* spp. *Molecules*. 2017;22:1191.
- Vallverdu-Queralt A, Regueiro J, Martinez-Huelamo M, et al. A comprehensive study on the phenolic profile of widely used culinary herbs and spices: rosemary, thyme, oregano, cinnamon, cumin and bay. *Food Chem*. 2014;154:299–307.
- Merah O, Sayed-Ahmad B, Talou T, et al. Biochemical composition of cumin seeds, and biorefining study. *Biomolecules*. 2020;10:1054.
- Zaman U, Urlaub H, Abbasi A. Protein profiling of non-model plant *Cuminum cyminum* by gel-based proteomic approach. *Phytochem Anal*. 2018;29:242–249.
- Uma Pradeep K, Geervani P, Eggum BO. Common Indian spices: nutrient composition, consumption and contribution to dietary value. *Plant Foods Hum Nutr*. 1993;44:137–148.
- Bi X, Lim J, Henry CJ. Spices in the management of diabetes mellitus. *Food Chem*. 2017;217:281–293.
- Percival SS, Vanden Heuvel JP, Nieves CJ, et al. Bioavailability of herbs and spices in humans as determined by ex vivo inflammatory suppression and DNA strand breaks. *J Am Coll Nutr*. 2012;31:288–294.
- Adu-frimpong M, Qiuyu W, Firempong C, et al. Novel cuminaldehyde self-emulsified nanoemulsion for enhanced antihepatotoxicity in carbon tetrachloride-treated mice. *J Pharm Pharmacol*. 2019;71:1324–1338.
- Ishida T, Toyota M, Asakawa Y. Terpenoid biotransformation in mammals. V. Metabolism of (+)-citronellal, (+)-7-hydroxycitronellal, citral, (–)-perillaldehyde, (–)-myrtenal, cuminaldehyde, thujone, and (+)-carvone in rabbits. *Xenobiotica*. 1989;19:843–855.
- Ishida T. Biotransformation of terpenoids by mammals, microorganisms, and plant-cultured cells. *Chem Biodivers*. 2005;2:569–590.
- Watanabe K, Narimatsu S, Yamamoto I, Yoshimura H. Hepatic microsomal oxygenation of aldehydes to carboxylic acids. *Biochem Biophys Res Commun*. 1990;166:1308–1312.
- Désage M, Schaal B, Soubeyrand J, Orgeur P, Brazier J. Gas chromatographic–mass spectrometric method to characterise the transfer of dietary odorous compounds into plasma and milk. *J Chromatogr B Biomed Appl*. 1996;678:205–210.
- Monteiro-Neto V, DeSouza C, Gonzaga L, et al. Cuminaldehyde potentiates the antimicrobial activity of ciprofloxacin against *Staphylococcus aureus* and *Escherichia coli*. *PLoS One*. 2020. doi.org/10.1371/journal.pone.0232987.
- Johri R. *Cuminum cyminum* and *Carum carvi*: an update. *Pharmacogn Rev*. 2011;5:63–72.
- Gürol A, Şener Taplak A, Polat S. Herbal supplement products used by mothers to cope with the common health problems in childhood. *Complement Ther Med*. 2019;47:102214. doi.org/10.1016/j.ctim.2019.102214.
- Samani Keihan G, Gharib MH, Momeni A, et al. A comparison between the effect of *Cuminum cyminum* and vitamin E on the level of leptin, paraoxonase 1, HbA_{1c} and oxidized LDL in diabetic patients. *Int J Mol Cell Med*. 2016;5:229–235.
- Jafari S, Sattari R, Ghavamzadeh S. Evaluation the effect of 50 and 100 mg doses of *Cuminum cyminum* essential oil on glycemic indices, insulin resistance and serum inflammatory factors on patients with diabetes type II: a double-blind randomized placebo-controlled clinical trial. *J Tradit Complement Med*. 2017;7:332–338.
- Andallu B, Ramya V. Anti-hyperglycemic, cholesterol-lowering and HDL-raising effects of cumin (*Cuminum cyminum*) seeds in type 2 diabetes. *J Nat Remedies*. 2007;7:142–149.
- Jafari T, Mahmoodnia L, Tahmasebi P, et al. Effect of cumin (*Cuminum cyminum*) essential oil supplementation on metabolic profile and serum leptin in pre-diabetic subjects: a randomized double-blind placebo-controlled clinical trial. *J Funct Foods*. 2018;47:416–422.
- Samani KG, Farrokhi E. Effects of cumin extract on oxLDL, paraoxonase 1 activity, FBS, total cholesterol, triglycerides, HDL-C, LDL-C, Apo A1, and Apo B in the patients with hypercholesterolemia. *Int J Health Sci (Qassim)*. 2014;8:39–43.
- Zare R, Heshmati F, Fallahzadeh H, Nadjarzadeh A. Effect of cumin powder on body composition and lipid profile in overweight and obese women. *Complement Ther Clin Pract*. 2014;20:297–301.
- Taghizadeh M, Memarzadeh MR, Asemi Z, Esmailzadeh A. Effect of the cumin cyminum L. intake on weight loss, metabolic profiles and biomarkers of oxidative stress in overweight subjects: a randomized double-blind placebo-controlled clinical trial. *Ann Nutr Metab*. 2015;66:117–124.
- Taghizadeh M, Memarzadeh MR, Abedi F, et al. The effect of cumin cyminum L. plus lime administration on weight loss and metabolic status in overweight subjects: a randomized double-blind

- placebo-controlled clinical trial. *Iran Red Crescent Med J.* 2016;18: e34212. 10.5812/ircmj.34212.
32. Pishdad S, Nadjarzadeh A, Abargouei A, et al. Effect of cumin and cinnamon on lipid profile in middle-aged women with dyslipidemia: a double-blind, randomized controlled clinical trial. *Prog Nutr.* 2018;20(suppl 2):232–237.
 33. Morovati A, Pourghassem Gargari B, Sarbakhsh P, et al. The effect of cumin supplementation on metabolic profiles in patients with metabolic syndrome: a randomized, triple blind, placebo-controlled clinical trial. *Phytother Res.* 2019;33:1182–1190.
 34. Morovati A, Pourghassem Gargari B, Sarbakhsh P. Effects of cumin (*Cuminum cyminum* L.) essential oil supplementation on metabolic syndrome components: a randomized, triple-blind, placebo-controlled clinical trial. *Phytother Res.* 2019;33:3261–3269.
 35. Shavakhi A, Torki M, Khodadoostan M, Shavakhi S. Effects of cumin on nonalcoholic steatohepatitis: a double blind, randomised, controlled trial. *Adv Biomed Res.* 2015;4:212. 10.4103/2277-9175.166149.
 36. Haldar S, Gan L, Tay S, et al. Postprandial glycemic and insulinemic effects of the addition of aqueous extracts of dried corn silk, cumin seed powder or tamarind pulp, in two forms, consumed with high glycemic index rice. *Foods.* 2019;8. 10.3390/foods8100437.
 37. Jafamejad S, Tsang C, Taghizadeh M, et al. A meta-analysis of cumin (*Cuminum cyminum* L.) consumption on metabolic and anthropometric indices in overweight and type 2 diabetes. *J Funct Foods.* 2018;44:313–321.
 38. Hadi A, Mohammadi H, Hadi Z, et al. Cumin (*Cuminum cyminum* L.) is a safe approach for management of lipid parameters: a systematic review and meta-analysis of randomized controlled trials. *Phytother Res.* 2018;32:2146–2154.
 39. Moulbarz G, Embaby M, Doleib N, Taha M. Effect of dietary antioxidant supplementation (*Cuminum cyminum*) on bacterial susceptibility of diabetes-induced rats. *Cent Eur J Immunol.* 2016;41:132–137.
 40. Willatgamuwa S, Platel K, Saraswathi G, et al. Antidiabetic influence of dietary cumin seeds (*Cuminum cyminum*) in streptozotocin induced diabetic rats. *Nutr Res.* 1998;18:131–142.
 41. Kumar PA, Reddy PY, Srinivas PN, Reddy GB. Delay of diabetic cataract in rats by the antiglycating potential of cumin through modulation of alpha-crystallin chaperone activity. *J Nutr Biochem.* 2009;20:553–562.
 42. Dhandapani S, Subramanian VR, Rajagopal S, Namasivayam N. Hypolipidemic effect of *Cuminum cyminum* L. on alloxan-induced diabetic rats. *Pharmacol Res.* 2002;46:251–255.
 43. Jagtap AG, Patil PB. Antihyperglycemic activity and inhibition of advanced glycation end product formation by *Cuminum cyminum* in streptozotocin induced diabetic rats. *Food Chem Toxicol.* 2010;48: 2030–2036.
 44. Srivastava R, Srivastava S, Jaiswal N, et al. Antidiabetic and antidyplipidemic activities of *Cuminum cyminum* L. in validated animal models. *Med Chem Res.* 2011;20:1656–1666.
 45. Patil SB, Takalikar SS, Joglekar MM, et al. Insulinotropic and β -cell protective action of cuminaldehyde, cuminol and an inhibitor isolated from *Cuminum cyminum* in streptozotocin-induced diabetic rats. *Br J Nutr.* 2013;110:1434–1443.
 46. Mohamed D, Hamed I, Fouda K. Antioxidant and anti-diabetic effects of cumin seeds crude ethanol extract. *Aust J Biol Sci.* 2018;18:251–259.
 47. Kaur G, Upadhyay N, Tharappel LJP, Invally M. Pharmacodynamic interaction of cumin seeds (*Cuminum cyminum* L.) with glyburide in diabetes. *J Complement Integr Med.* 2019;16. 10.1515/jcim-2018-0080.
 48. Mohiti-Ardekani J, Akbarian Z, Piri-Ardekani M, Mohiti-Ardekani A. Comparison of the effects of *Cuminum cyminum* L and sibutramine on weight, serum leptin, glucose and lipids in rat. *Iran J Diabetes Obes.* 2012;4:74–78.
 49. Sambaiah K, Srinivasan K. Effect of cumin, cinnamon, ginger, mustard and tamarind in induced hypercholesterolemic rats. *Nahrung.* 1991;35:47–51.
 50. Chouhan H, Purohit A. Protective effect of cumin (*Cuminum cyminum* L.) seed extract on cardiovascular system, toxicity and hematology in hyperlipidemic rabbits: an experimental study. *Asian J Pharm Clin Res.* 2018;11: <http://dx.doi.org/10.22159/ajpcr.2018.v11i10.27400>.
 51. Haque MR, Ansari HS. Anti-obesity effect of arq zeera and its main components thymol and cuminaldehyde in high fat diet induced obese rats. *Drug Res (Stuttg).* 2018;68:637–647.
 52. Allahghadri T, Rasooli I, Owlia P, et al. Antimicrobial property, antioxidant capacity, and cytotoxicity of essential oil from cumin produced in Iran. *J Food Sci.* 2010;75:H54–H61. 10.1111/j.1750-3841.2009.01467.x.
 53. Ahmed S, Faraj R, Al-Shaikh M. Study effects of cumin and DNA profile in diabetic rats. *IOSR J Pharm Biol Sci.* 2013;5:14–16.
 54. Roman-Ramos R, Flores-Saenz JL, Alarcon-Aguilar FJ. Anti-hyperglycemic effect of some edible plants. *J Ethnopharmacol.* 1995;48:25–32.
 55. Shirke SS, Jagtap AG. Effects of methanolic extract of *Cuminum cyminum* on total serum cholesterol in ovariectomized rats. *Indian J Pharmacol.* 2009;41:92–93.
 56. Omidvar S, Nasiri-Amiri F, Bakhtiari A, Begum K. Clinical trial for the management dysmenorrhea using selected spices. *Complement Ther Clin Pract.* 2019;36:34–38.
 57. Abd Ellah NH, Shaltout AS, Abd El Aziz SMM, et al. Vaginal suppositories of cumin seeds essential oil for treatment of vaginal candidiasis: formulation, in vitro, in vivo and clinical evaluation. *Eur J Pharm Sci.* 2021;157:105602. <https://doi.org/10.1016/j.ejps.2020.105602>.
 58. Shayegh S, Rasooli I, Taghizadeh M, Astaneh SD. Phytotherapeutic inhibition of supragingival dental plaque. *Nat Prod Res.* 2008;22:428–439.
 59. Agah S, Taleb AM, Moeini R, et al. Cumin extract for symptom control in patients with irritable bowel syndrome: a case series. *Middle East J Dig Dis.* 2013;5:217–222.
 60. Api AM, Belsito D, Biserta S, et al. RIFM fragrance ingredient safety assessment, cuminic aldehyde, CAS registry number 122-03-2. *Food Chem Toxicol.* 2020;144. <https://doi.org/10.1016/j.fct.2020.111498>.
 61. Boxer M, Roberts M, Grammer L. Cumin anaphylaxis: a case report. *J Allergy Clin Immunol.* 1997;99:722–723.
 62. Jensen-Jarolim E, Leitner A, Hirschehr R, et al. Characterization of allergens in Apiaceae spices: anise, fennel, coriander and cumin. *Clin Exp Allergy.* 1997;27:1299–1306.
 63. Garber EA, Parker CH, Handy SM, et al. Presence of undeclared food allergens in cumin: the need for multiplex methods. *J Agric Food Chem.* 2016;64:1202–1211.
 64. Ozbek H, Ozturk A, Ceylan E, Yener Z. Determination of lethal doses of volatile and fixed oils of several plants. *East J Med.* 2009;9:4–6.
 65. Haroun E, Mahmoud O, Adam S. Effect of feeding *Cuminum cyminum* fruits, *Thymus vulgaris* leaves or their mixture to rats. *Vet Hum Toxicol.* 2002;44:67–69.
 66. Taghizadeh M, Ostad SN, Asemi Z, et al. Sub-chronic oral toxicity of *Cuminum cyminum* L.'s essential oil in female Wistar rats. *Regul Toxicol Pharmacol.* 2017;88:138–143.
 67. Singh R, Gangadharappa H, Mruthunjaya K. *Cuminum cyminum*—a popular spice: an updated review. *Pharm J.* 2017;9:292–301.
 68. Al-Snafi A. The pharmacological activities of *Cuminum cyminum*—a review. *IOSR J Pharm.* 2016;6:46–65.
 69. NLM Citation. *Cumin. Drugs and Lactation Database (LactMed)*. Bethesda, MD: National Library of Medicine (US); 2006: (Updated 2018).
 70. Qazi G, Bedi K, Johri R, et al. Bioavailability/bioefficacy enhancing activity of *Cuminum cyminum* and extracts and fractions thereof. US patent no. 7,070,814 B2, 2006.
 71. Bartoňková I, Dvořák Z. Essential oils of culinary herbs and spices display agonist and antagonist activities at human aryl hydrocarbon receptor AhR. *Food Chem Toxicol.* 2018;111:374–384.