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Guggul for hyperlipidemia: A review by the Natural Standard Research Collaboration

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KEYWORDS
Guggul;
Commifora mukul;
High-density lipoprotein

Summary
Objective: To evaluate the scientific evidence on guggul for hyperlipidemia including expert opinion, folkloric precedent, history, pharmacology, kinetics/dynamics, interactions, adverse effects, toxicology, and dosing.
Methods: Electronic searches were conducted in nine databases, 20 additional journals (not indexed in common databases), and bibliographies from 50 selected secondary references. No restrictions were placed on language or quality of publications. All literature collected pertained to efficacy in humans, dosing, precautions, adverse effects, use in pregnancy/lactation, interactions, alteration of laboratory assays, and mechanism of action. Standardized inclusion/exclusion criteria were utilized for selection.

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Results: Before 2003, most scientific evidence suggested that guggulipid elicits significant reductions in serum total cholesterol, low-density lipoprotein (LDL), and triglycerides, as well as elevations in high-density lipoprotein (HDL) [Kotiyal JP, Bisht DB, Singh DS. Double blind cross-over trial of gum guggulu (*Commiphora mukul*) Fraction A in hypercholesterolemia. *J Res Indian Med Yoga Hom* 1979;**14**(2):11—6; Kotiyal JP, Singh DS, Bisht DB. Gum guggulu (*Commiphora mukul*) fraction 'A' in obesity—a double-blind clinical trial. *J Res Ayur Siddha* 1985;**6**(1, 3, 4):20—35; Gaur SP, Garg RK, Kar AM, et al. Gugulipid, a new hypolipidaemic agent, in patients of acute ischaemic stroke: effect on clinical outcome, platelet function and serum lipids. *Asia Pacif J Pharm* 1997;**12**:65—9; Urizar NL, Liverman AB, Dodds DT, et al. A natural product that lowers cholesterol as an antagonist ligand for the FXR. *Science* 3 May 2002 [Science Express Reports]; Nityanand S, Srivastava JS, Asthana OP. Clinical trials with gugulipid. A new hypolipidaemic agent. *J Assoc Physicians India* 1989;**37**(5):323—8; Kuppurajan K, Rajagopalan SS, Rao TK, et al. Effect of guggulu (*Commiphora mukul*—Engl.) on serum lipids in obese, hypercholesterolemic and hyperlipemic cases. *J Assoc Physicians India* 1978;**26**(5):367—73; Gopal K, Saran RK, Nityanand S, et al. Clinical trial of ethyl acetate extract of gum gugulu (gugulipid) in primary hyperlipidemia. *J Assoc Physicians India* 1986;**34**(4):249—51; Agarwal RC, Singh SP, Saran RK, et al. Clinical trial of gugulipid—a new hypolipidemic agent of plant origin in primary hyperlipidemia. *Indian J Med Res* 1986;**84**:626—34; Verma SK, Bordia A. Effect of *Commiphora mukul* (gum guggulu) in patients of hyperlipidemia with special reference to HDL-cholesterol. *Indian J Med Res* 1988;**87**:356—60; Singh RB, Niaz MA, Ghosh S. Hypolipidemic and antioxidant effects of *Commiphora mukul* as an adjunct to dietary therapy in patients with hypercholesterolemia. *Cardiovasc Drugs Ther* 1994;**8**(4):659—64; Ghorai M, Mandal SC, Pal M, et al. A comparative study on hypocholesterolaemic effect of allicin, whole germinated seeds of bengal gram and guggulipid of gum gugglu. *Phytother Res* 2000;**14**(3):200—02]. However, most published studies were small and methodologically flawed. In August 2003, a well-designed trial reported small significant increases in serum LDL levels associated with the use of guggul compared to placebo [Szapary PO, Wolfe ML, Bloedon LT, et al. Guggulipid for the treatment of hypercholesterolemia: a randomized controlled trial. *JAMA* 2003;**290**(6):765—72]. No significant changes in total cholesterol, high-density lipoprotein (HDL), or triglycerides were measured. These results are consistent with two prior published case reports [Das Gupta R. Gugulipid: pro-lipaemic effect. *J Assoc Physicians India* 1990;**38**(12):346].

Conclusion: The effects of guggulipid in patients with high cholesterol are not clear, with some studies finding cholesterol-lowering effects, and other research suggesting no benefits. At this time, there is not enough scientific evidence to support the use of guggul for any medical condition. Guggul may cause stomach discomfort or allergic rash as well as other serious side effects and interactions. It should be avoided in pregnant or breast-feeding women and in children. Safety of use beyond 4 months has not been well studied.

Contents

Introduction

Resin from the guggul (*Commifora mukul*) tree has been used in Ayurvedic medicine since at least 600 bc. This thorny tree has little foliage and is indigenous to Western India. In 1966, the hypolipidemic properties of soluble extracts from the resin were evaluated scientifically. In 1986, guggul oleoresin was approved in India for marketing as a lipid-lowering agent.[14,15] Guggul was introduced more recently to the Western medical literature in 1994.[10]

Guggul (gum guggul) is a resin produced by the mukul mirth tree.[j] Guggulipid is extracted from guggul, and contains plant sterols (guggulsterones E and Z), which are believed to be its bioactive compounds. Prior to 2003, the majority of scientific evidence suggested that guggulipid elicits significant reductions in serum total cholesterol, low-density lipoprotein (LDL), and triglycerides, as well as elevations in high-density lipoprotein (HDL).[1–11] However, most published studies were small and not well designed or reported. In August 2003, a well-designed trial reported small significant increases in serum LDL levels associated with the use of guggul compared to placebo.[12] No significant changes in total cholesterol, high-density lipoprotein, or triglycerides were measured. These results are consistent with two prior published case reports.[13] Although this evidence provides preliminary evidence against the efficacy of guggul for hypercholesterolemia, due to the precedent of prior research and historical use, further study is necessary before a definitive conclusion can be reached.

Initial research reports that guggulsterones are antagonists of the farsenoid X receptor (FXR) and the bile acid receptor (BAR), nuclear hormones which are involved with cholesterol metabolism and bile acid regulation.[15–17]

The scientific evidence of guggul was evaluated for hyperlipidemia, including expert opinion, folkloric precedent, history, pharmacology, kinetics/dynamics, interactions, adverse effects, toxicology, and dosing.

[j] *Guggul synonyms/common names/related substances*: African myrrh, Arabian myrrh, *Commiphora myrrha*, fraction A, guggal, guggulipid C+, guggulsterone, guggulsterone (4,17(20)-pregnadiene-3,16-dione), guggulu, guglip, gugulimax, gum guggal, gum gugglu, gum guggul, gum guggulu, gum myrrh, gum resin, Indian bdellium tree, Myrrha, Somali myrrh, Yemen myrhh.

Methods

To prepare each Natural Standard review, electronic searches are conducted in nine databases, including AMED, CANCERLIT, CINAHL, CISCOM, the Cochrane Library, EMBASE, HerbMed, International Pharmaceutical Abstracts, Medline, and NAPRALERT. Search terms include the common name(s), scientific name(s), and all listed synonyms for each topic. Hand searches are conducted of 20 additional journals (not indexed in common databases), and of bibliographies from 50 selected secondary references. No restrictions are placed on language or quality of publications. Researchers in the field of complementary and alternative medicine (CAM) are consulted for access to additional references or ongoing research. All literature is collected pertaining to efficacy in humans (regardless of study design, quality, or language), dosing, precautions, adverse effects, use in pregnancy/lactation, interactions, alteration of laboratory assays, and mechanism of action (in vitro, animal research, human data). Standardized inclusion/exclusion criteria are utilized for selection. Data extraction and analysis are performed by healthcare professional conducting clinical work and/or research at academic centers, using standardized instruments that pertain to each review section (defining inclusion/exclusion criteria and analytic techniques, including validated measures of study quality). Data are verified by a second reviewer. Blinded review of review is conducted by multidisciplinary research-clinical faculty at major academic centers with expertise in epidemiology and biostatistics, pharmacology, toxicology, complementary and alternative medicine (CAM) research, and clinical practice. In cases of editorial disagreement, a three-member panel of the Editorial Board addresses conflicts, and consults experts when applicable. Authors of studies are contacted when clarification is required.

We compiled a clinical evidence table organized by quality of study using the Jadad score calculation, listing main results followed by a discussion of each human study.

Quality of study

Jadad Score Calculation

Item	Score
Was the study described as randomized (this includes words such as randomly, random, and randomization)?	0/1
Was the method used to generate the sequence of randomization described and appropriate (table of random numbers, computer-generated, etc.)?	0/1
Was the study described as double blind?	0/1
Was the method of double blinding described and appropriate (identical placebo, active placebo, dummy, etc.)?	0/1
Was there a description of withdrawals and dropouts?	0/1
Deduct one point if the method used to generate the sequence of randomization was described and it was inappropriate (patients were allocated alternately, or according to date of birth, hospital number, etc.).	0/−1
Deduct one point if the study was described as double blind but the method of blinding was inappropriate (e.g., comparison of tablet vs. injection with no double dummy).	0/−1

Results

Pharmacology

- *Lipid-lowering effects*: Guggul (gum guggul) is a resin produced by the mukul mirth tree. Guggulipid is extracted from guggul using ethyl acetate. The preparation produced by extraction with petroleum ether is called a fraction A. Typical guggulipid preparations contain 2.5—5% of the plant sterols guggulsterones E and Z. These two components have been reported to exert effects on lipids.[16,17] Several hypotheses have been advanced to explain these effects on lipids. Guggulsterones, particularly guggulsterone (4,17(20)-pregnadiene-3,16-dione), have been reported to function as antagonists of the farsenoid X receptor and the bile acid receptor, nuclear hormones which are involved with cholesterol metabolism and bile acid regulation.[4,18,19] It has been reported that guggulsterone does not exert its lipid effects on mice lacking FXR. Other publications have proposed that guggul may inhibit lipogenic enzymes and HMG-Co A reductase in the liver[20,21]; increase uptake of cholesterol by the liver via stimulation of LDL receptor binding[17]; directly activate the thyroid gland[22—25]; and/or increase biliary and fecal excretion of cholesterol.[21]
- *Antioxidant effects*: Guggul extracts have been reported to possess antioxidant properties[26] possibly mediating protection against myocardial necrosis.[27,28]
- *Platelet effects*: Guggulipid has been found to inhibit platelet aggregation and increase fibrinolysis.[3,29—31]
- *Anti-inflammatory*: The results of several studies suggest possible anti-inflammatory and antiarthritic activities of guggul.[32—40] On a per-microgram basis, guggulipid appears to be significantly less potent than indomethacin or hydrocortisone.[35] Possible effects on high-sensitivity C-reactive protein (hs-CRP) have recently been observed in a clinical trial.[12]
- *Thyroid effects*: Data from animal models suggest that the guggul constituent guggulsterone Z may stimulate thyroid function.[23] However, results from a recent randomized controlled trial in 103 patients reports no difference in thyroid stimulating hormone (TSH) with the use of guggul.[12]

Clinical evidence

Author, year	Study type	*N*	Quality of study: 0—2 = poor; 3—4 = good; 5 = excellent	Main results	Discussion
Szapary, 2003	Randomized, placebo controlled, double-blind trial	103	5	1000 or 2000 mg guggulipid (standardized to 2.1—2.5% guggulsterones) three times daily in adults with hypercholesterolemia for 8 weeks elicited small elevation in LDL vs. placebo and no other significant effects on	The discrepancy from prior trials may be due to differences between American and Indian dietary habits, or other regional, environmental or genetic factors. Although this trial provides preliminary evidence against the

Author, year	Study type	*N*	Quality of study: 0—2 = poor; 3—4 = good; 5 = excellent	Main results	Discussion
				lipids. Skin hypersensitivity in 33% of higher-dose patients.	efficacy of guggul for hypercholesterolemia, due to the precedent of multiple prior trials (of inferior design), further research is necessary before a definitive conclusion can be reached. Also of note, possible effects on high-sensitivity C-reactive protein (hs-CRP) were observed, which merit further evaluation.
Nityanand, 1989	Randomized, controlled, double-blind, crossover trial	125	5	500 mg guggulipid three times daily for 12 weeks no different from clofibrate (both reduced total cholesterol and triglycerides).	Although these results are promising, neither randomization nor blinding procedures were adequately described, no placebo group was utilized, and no power calculation was conducted prior to conducting the latter study (and the sample size may not have been adequate to detect differences between the guggulipid and clofibrate groups).
Gaur, 1997	Randomized, controlled, double-blind trial	68	4	500 mg guggulipid three times daily associated with significant reduction in LDL and increase in HDL vs. aspirin in patients following ischemic stroke.	Blinding and randomization were not clearly described. Notably, lipid levels can be affected by acute illnesses such as stroke, which potentially could confound results.
Verma, 1988	Before and after study	40	4	4.5 g purified gum guggulu daily for 16 weeks associated with reduced total cholesterol and triglycerides vs. baseline. Lesser reductions seen with placebo, but between-group differences were not compared statistically.	Although these results are compelling, direct comparisons were not made between the guggul and placebo groups.
Kotiyal, 1985	Before and after study	85	4	500 mg fraction A three times daily for 12 weeks associated with reduced total cholesterol vs. baseline. Lesser reductions seen with placebo, but between-group differences were not compared statistically.	Information on the method of statistical analysis or dropouts was not presented.

Author, year	Study type	*N*	Quality of study: 0—2 = poor; 3—4 = good; 5 = excellent	Main results	Discussion
Kuppurajan, 1978	Randomized, controlled, double-blind trial	120	4	2 g gum guggulu three times daily, vs. 500 mg fraction A twice daily, vs. 500 mg clofibrate three times daily, vs. placebo. After 21 days, reduced cholesterol in all guggul groups vs. placebo.	However, results were not adequately quantified.
Ghorai, 2000	Randomized, controlled, double-blind trial	30	3	Guggulipid (25 mg guggulsterone) twice daily for 8 weeks reduced cholesterol vs. allicin (from garlic). Unclear statistical analysis.	Although these results suggest superiority of guggul to this form of garlic therapy, there was no placebo arm, and statistical analysis and dropouts were not well described.
Singh, 1994	Randomized, controlled, single-blind trial	64	3	50 mg guggulipid twice daily associated with significant reduction in total cholesterol vs. baseline, but no significant difference vs. placebo. All subjects were placed on low-fat diets.	Although the changes in the guggulipid group were statistically significant compared to baseline values, they were not statistically significant compared to placebo. This may have been because of cholesterol-lowering that occurred in both groups due to pre-treatment with dietary restriction (suggesting that guggul therapy may not provide significant added benefit to dietary discretion). However, the lack of statistical significance between groups may also reflect a sample size too small to detect differences. This trial was not adequately investigator-blinded, and no information was given regarding compliance.
Tripathi, 1978	Randomized, controlled, double-blind trial	75	3	10—15 g gum guggulu daily for 3 months associated with reduced cholesterol vs. placebo.	Study methods, baseline patient characteristics, and statistical analysis were not adequately reported.

Author, year	Study type	*N*	Quality of study: 0—2 = poor; 3—4 = good; 5 = excellent	Main results	Discussion
Malhotra, 1977	Randomized, controlled, double-blind comparison study	51	3	1.5 g fraction A daily or 2 g clofibrate daily for 75 weeks associated with reduced cholesterol levels. No placebo group.	The results for each group were not compared statistically. There was no placebo arm, and therefore it is not clear that these reported changes in cholesterol levels were not due to confounding factors.
Malhotra, 1971	Randomized, controlled, double-blind trial	44	3	Guggul fraction A 500 mg three times daily no different from ethyl-*p*-chloro-phenoxy-isobutyrate or ''Ciba-13437 Su.'' No power calculation performed.	It is not clear if this trial was too small to detect between-group differences, or if there was true equivalence between these therapies. Without a placebo arm, it is not clear if changes in cholesterol levels might have been due to confounding factors.
Kotiyal, 1979	Before and after study	48	3	500 mg gum guggulu fraction A three times daily for 4 weeks associated with reduced cholesterol and triglycerides.	Results were reported in comparison to baseline values, rather than between-groups. Blinding procedures were not described.
Sharma, 1976	Randomized, controlled, double-blind, crossover trial	60	2	4 g guggul daily for 4 weeks associated with reduced cholesterol and triglycerides vs. placebo. Large dropout.	Descriptions of blinding and randomization were not presented, and there was a 40% dropout in the placebo group.
Upadhyaya, 1976	Unclear study design	25	2	12—16 g guggul daily for 3 months associated with reduced cholesterol and triglyceride levels.	Statistical analysis was not adequately reported.
Kuppurajan, 1973	Before and after study	120	2	Guggul 2 g daily or fraction A 300 mg three times daily for 21 days not associated with changes in cholesterol vs. baseline.	All values were compared to baseline, not to the placebo arm.
Beg, 1996	Unclear study design	50	1	Guggulsterone 25 mg three times daily for 8 weeks associated with reduced LDL and total cholesterol.	Confidence intervals were large for these results, and statistical analysis was not clearly described.
Singh, 1993	Unclear study design	200	1	6—8 g of combination guggul plus pushkarmool daily for 6 months associated with significantly reduced cholesterol and triglycerides.	Limited information regarding study design or statistical analysis was provided.
Jain, 1980	Case series (published abstract)	93	NA	2 g guggul three times daily for 1 month associated with significantly reduced cholesterol (not quantified). Large dropout.	This study was not well described, and results were not adequately quantified.

Author, year	Study type	*N*	Quality of study: 0—2 = poor; 3—4 = good; 5 = excellent	Main results	Discussion
Gopal, 1986	Unclear study design	22	NA	500 mg guggulipid three times daily for 6 weeks associated with reduced cholesterol.	Although a placebo group was noted in the study's description, no details of number of placebo subjects or outcomes were included in the results.
Agarwal, 1986	Phase I/II trial (safety, efficacy)	21	NA	400—500 mg guggulipid three times daily for 4—12 weeks associated with no adverse effects and reduced cholesterol and triglycerides.	By these criteria, 78.9% of subjects were reported as ''responders''. It is not clear if there were baseline differences between subjects that were or were not ''responders''.

Dosing/toxicology

Recommended doses are based on those most commonly used in available trials, or on historical practice like regimens recommend by the German Commission E. However, with natural products it is often not clear what the optimal doses are to balance efficacy and safety. Preparation of products may vary from manufacturer to manufacturer, and from batch to batch within one manufacturer. Because it is often not clear what the active components of a product are, standardization may not be possible, and the clinical effects of different brands may not be comparable.

Guggulipid preparations are often standardized to contain 2.5—5% of guggulsterones. In July 2003, www.consumerlab.com evaluated five guggulsterone supplements. They report that Vitamin World® Select Herbals Standardized Extract Guggul Plex 340 mg, Standardized to contain 2.5% Guggulsterones (8.5 mg per capsule, 3 per day), manufactured by Vitamin World, Inc. was ''approved'' based on its claimed constituents. The remaining four brands contained from as little as 4—74% of the expected ingredient. None of the products was contaminated with lead or arsenic. A recent human trial used guggulipid provided by Sabinsa Corporation (Piscataway, NJ), standardized to contain at least 2.5% of the guggulsterones E and Z, and found the tablets to contain 2.1% guggulsterones (85% of the claimed ingredients). This was felt to be satisfactory for research and clinical use (12). There are other third party testers such as Consumer Reports, USP.org and NSF.org, but results for guggule could not be found. There is also a potential for bias as third party testers are often reimbursed by manufacturers to test their products.

Adult dosing (18 years and older)

Oral

- *Hyperlipidemia*: 500—1000 mg of guggulipid (standardized to 2.5% guggulsterones) taken twice or three times daily has been used clinically and in research. An equivalent dose of commercially prepared guggulsterone is 25 mg three times daily or 50 mg twice daily by mouth.[3,5,10] A higher dose has been studied (2000 mg three times daily, standardized to 2.5% guggulsterones), although this dose may be associated with a greater risk of hypersensitivity skin reactions.[12]
- *Nodulocystic acne*: A dose of guggulipid equivalent to 25 mg guggulsterone per day has been used.[41]

Pediatric dosing (younger than 18 years)

- Insufficient evidence to recommend.

Safety

Allergy

- Known allergy/hypersensitivity to guggul or any of its constituents.

- Hypersensitivity skin reactions were noted in a clinical trial, occurring in 5 of 34 patients (15%) receiving 50 mg of guggulsterones three times daily, and in 1 of 33 patients (3%) receiving 25 mg of guggulsterones three times daily.[12] In most cases, reactions occurred within 48 h of starting therapy, and resolved spontaneously within 1 week of therapy discontinuation, although one patient required oral steroids. The guggulipid formulation used was prepared by the Sabinsa Corporation (Piscataway, NJ).

Adverse effects/post market surveillance

- *General*: Standardized guggulipid is generally regarded as being safe in healthy adults at recommended doses for up to 6 months. Gastrointestinal upset is the predominant adverse effect that has been described in humans, most commonly involving loose stools or diarrhea.
- *Neurologic/CNS*: Headache was reported in 22 of 31 patients (71%) in one study.[32] Restlessness and apprehension were noted in one of 44 patients in a different study.[42]
- *Gastrointestinal*: In clinical studies and historically, guggul and guggulipid have been associated with diarrhea, loose stools, nausea, vomiting, eructation (belching), and hiccough. Frequency has varied between 10—30%; these symptoms have been observed both with guggul[42—44] and with guggulipid.[5,10,12] Most symptoms have been well controlled with supportive care or treatments such as antacids, although discontinuation is occasionally necessary.
- *Endocrine*: Stimulation of thyroid function has been noted in animal studies,[22—24] although a recent human trial reports no effects of guggulipid in thyroid stimulating hormone (TSH) levels after 8 weeks of therapy.[12] Multiple small trials in India and traditional accounts reported to lower serum lipid levels with regular use of guggulipid (decreasing cholesterol, triglycerides, and low-density lipoproteins; increasing high-density lipoproteins),[1—11] although subsequent evidence from a well-designed U.S. trial reports small increases in LDL and no significant changes in total cholesterol, HDL, or triglycerides.[12] Initial research reports that guggulsterones are antagonists of the farsenoid X receptor (FXR) and the bile acid receptor (BAR), nuclear hormones which are involved with cholesterol metabolism and bile acid regulation.[4,18,19]
- *Hematologic*: Guggulipid administration has been associated with inhibition of platelet aggregation and increased fibrinolysis.[3,29—31] In theory, the risk of bleeding may increase, although there are no reports of bleeding in the available literature.
- *Genitourinary*: Weight reduction and chemical changes in reproductive organs have been observed in female rats.[45]
- *Dermatologic*: Hypersensitivity skin reactions were noted in a clinical trial, occurring in 5 of 34 patients (15%) receiving 50 mg of guggulsterones three times daily, and in 1 of 33 (3%) of patients receiving 25 mg of guggulsterones three times daily. In most cases, reactions occurred within 48 hours of starting therapy, and resolved spontaneously within 1 week of therapy discontinuation, although one patient required oral steroids.[12] The guggulipid formulation used was prepared by the Sabinsa Corporation (Piscataway, NJ).
- *Musculoskeletal*: A case report exists of a 55 year-old man was taking an extract of *Commifora mukul* 300 mg three times daily to lower his cholesterol level.[46] He developed rhabdomyolysis with hemoglobinuria after 2 weeks of treatment. Laboratory tests showed creatine kinase 144600 IU/L (reference range 24—195), myoglobin >3000 ng/mL (28—72), lactate dehydrogenase 7157 IU/L (230—460), aspartate aminotransferase 1115 IU/L (10—35), and alanine aminotransferase 205 IU/L (10—35). Analysis of a urine sample was 2+ positive for hemoglobin. All parameters returned to normal after the herbal preparation was discontinued. The Naranjo probability scale indicates *C. mukul* as the possible cause of rhabdomyolysis in this patient.
- *Renal*: A case of rhabdomyolyis has been reported.[46] Rhabdomyolis may lead to renal failure.

Precautions/warnings/contraindications

- Use cautiously in patients with thyroid disorders due to potential thyroid stimulating properties.
- Use cautiously in patients at risk for bleeding.

Pregnancy and lactation

- Not recommended due to lack of sufficient data.

Interactions

- *Beta-blockers*: Co-administration of guggulipid to humans has been reported to decrease the bioavailability of the beta-blocker propranolol.[47] Effects on other beta-blockers have not been evaluated.

- *Diltiazem* (*Cardizem®*, *Dilacor®*, *Tiazac®*): Co-administration of guggulipid to humans has been found to decrease the bioavailability of the calcium channel blocker diltiazem.[47] The chemical structures of other calcium channel blockers are sufficiently distinct that guggul may not affect other members of this class. Patients on diltiazem should be monitored for changes in blood pressure and heart rate if guggulipid therapy is initiated.
- *Thyroid agents*: Data from animal models suggest that the guggul constituent guggulsterone Z may stimulate thyroid function.[23] However, results from a recent randomized controlled trial in 103 patients reports no difference in thyroid stimulating hormone (TSH) with the use of guggul.[12] Nonetheless, guggulipid should be used with caution in patients taking thyroid drugs.
- *Lipid-lowering agents*: Initial research reports that guggulsterones are antagonists of the farsenoid X receptor and the bile acid receptor, nuclear hormones which are involved with cholesterol metabolism and bile acid regulation.[4,18,19] Multiple small trials in India and traditional accounts reported to lower serum lipid levels with regular use of guggulipid (decreasing cholesterol, triglycerides, and low-density lipoproteins; increasing high-density lipoproteins),[1–11] although subsequent evidence from a well-designed U.S. trial reports small increases in LDL and no significant changes in total cholesterol, HDL, or triglycerides.[12] It is not clear if guggulipid affects the action of other agents used for cholesterol reduction. Initial research reports that guggulsterones are antagonists of the farsenoid X receptor and the bile acid receptor, nuclear hormones which are involved with cholesterol metabolism and bile acid regulation.[4,18,19] Multiple small trials in India and traditional accounts reported lower serum lipid levels with regular use of guggulipid (decreasing cholesterol, triglycerides, and low-density lipoproteins; increasing high-density lipoproteins),[1–11] although subsequent evidence from a well-designed U.S. trial reported small increases in LDL and no significant changes in total cholesterol, HDL, or triglycerides.[12] It is not clear if guggulipid affects the action of other agents used for cholesterol reduction.
- *Anti-coagulants*, *anti-platelet agents*: Guggulipid administration has been associated with inhibition of platelet aggregation and increased fibrinolysis.[3,29–31] In theory, the risk of bleeding may increase, although there are no reports of bleeding in humans in the available literature, including multiple controlled trials. Guggulipid administration has been associated with inhibition of platelet aggregation and increased fibrinolysis.[3,29–31] In theory, the risk of bleeding may increase, although there are no reports of bleeding in humans in the available literature, including multiple controlled trials.

Conclusion

Prior to 2003, the majority of scientific evidence suggested that guggulipid elicits significant reductions in serum total cholesterol, low-density lipoprotein, and triglycerides, as well as elevations in high-density lipoprotein.[1–11] However, most published studies were small and methodologically flawed. In August 2003, a well-designed trial reported small significant *increases* in serum LDL levels associated with the use of guggul compared to placebo.[12] No significant changes in total cholesterol, high-density lipoprotein, or triglycerides were measured. These results are consistent with two prior published case reports.[13] Although this evidence provides preliminary evidence against the efficacy of guggul for hypercholesterolemia, due to the precedent of prior research and historical use, further study is necessary before a definitive conclusion can be reached. There is no reliable research comparing guggul preparations with HMG-CoA reductase inhibitors (''statins''), or evaluating long-term effects of guggul on cardiac morbidity or mortality outcomes. Safety concerns exist as outlined above.

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