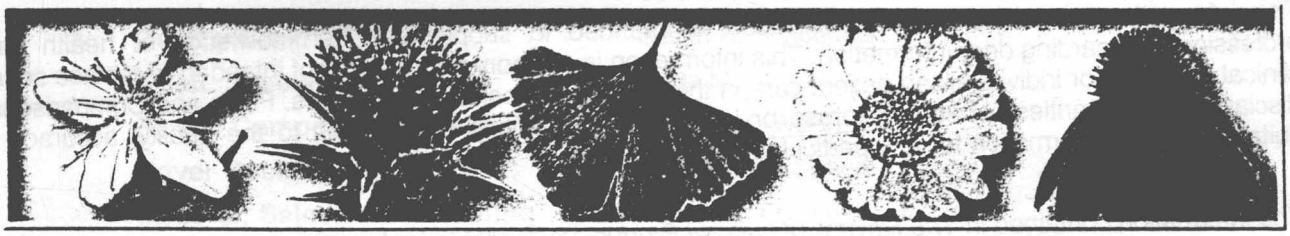
The Review of Natural Products 3rd Ed

THE REVIEW OF NATURAL PRODUCTS



the most complete source of natural product information

3rd Edition

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Preface

As the premier publisher of drug information, Facts and Comparisons® provides a broad range of print, electronic, and on-line resources to fulfill the day-to-day needs of practicing health care professionals. With the addition of dosing information to many of the monographs, the bound edition of *The Review of Natural Products (RNP)* continues our goal of fulfilling the various needs of our customers.

We acquired *The Lawrence Review of Natural Products* in 1989, and in 1996, we changed the name to *The Review of Natural Products,* established a reviewer panel, and added a patient information box to monographs. *RNP* provided objective information on herbal and other natural products at a time when the popularity of such products was just beginning to be noticed in the US. Since that time, the natural product industry has exploded, and Facts and Comparisons® continues to stay on top of this ever-changing market.

Although the annual bound edition of *RNP* is one manner in which to access the primary source of natural product information, we provide *RNP* in many formats. The original version of *RNP*, a monthly updated monograph system, is intended to keep subscribers constantly up-to-date. A pocket-size, abridged version, *Guide to Popular Natural Products,* is a quick-reference publication. Along with several of our drug reference tools, *RNP* is available electronically as part of the *Clinisphere* CD-ROM and *eFacts* internet, intranet, single-user, and LAN versions, which are updated monthly. It is available as an annually updated CD-ROM.

All monographs in *RNP* are consistent and easy to follow. Monographs list scientific and common names and include the following sections: Botany, History, Chemistry, Pharmacology, Interactions, Toxicology, and a Summary. A patient information section discusses uses, interactions, side effects, and where appropriate, dosing. An appendix contains many other interesting sections, including Herbal Diuretics; a Mushroom Poisoning Decision Chart; Mushroom Societies; the Poison Control Center hotline; Scientific and Trade Organizations that provide information on natural product research, evaluation, and education; and Herb/Drug Interaction tables. A useful primary index as well as an in-depth therapeutic index rounds out this premier source of natural product information.

As this edition goes to press, we continue to update our database daily for use in future editions and formats of *RNP*. We also continue to expand our extensive library of drug information resources to remain the full service drug information provider that our customers have come to expect. However, this can only be accomplished with feedback from the loyal health care professionals who use our information daily. Comments, criticisms and suggestions are always welcome and encouraged. Please call or visit us at www.factsandcomparisons.com or www.drugfacts.com.

Kenneth H. Killion
Publisher and CEO

Introduction

The *Review of Natural Products*, is intended to provide a referenced guide to the numerous plant and dietary supplements now widely used in medicine. It contains more than 300 monographs on natural products alphabetically arranged and categorized by scientific name(s), common name(s), botany, chemistry, history, pharmacology, interactions, toxicology, patient information (a synopsis of uses, interactions, side effects, and dosing), and pertinent medical and scientific references.

This introduction provides an overview of historical and epidemiological data, the complimentary and alternative medicine (CAM) movement, the Dietary Supplement and Health Education Act (DSHEA) of 1994, and sufficient coverage of botany and pharmacology for the reader to appreciate and understand the details of proper use of natural products as medicinal agents.

Historical and epidemiological data: There is little doubt that herbal medicine or pharmacognosy is one of the oldest forms of health care. Almost every culture around the world has noted its individual contributions to pharmacognosy and use of foods as medicine. The oldest "prescriptions," found on Babylonian clay tablets and the hieratic writing of ancient Egyptians on papyrus, archive numerous ancient pharmaceutical and medical uses of hundreds of botanicals and foods (eg, olive oil, wine, turpentine, myrrh, opium, castor oil, garlic). This worldwide botanical cornucopia represents an eclectic collection of the most reliable early medicines that even today serve the ills of the world. The World Health Organization records the fact that 80% of the world's population still relies on botanical medicines. Several phytomedicines have advanced to widespread use in modern times and are familiar to all. These include morphine and related derivatives (from opium), colchicine (from Autumn crocus), cocaine (from Coca), digitoxin (from Foxglove), vincristine and vinblastine (from the Vinca plant), reserpine (from Indian Snakeroot), etoposide (from Mayapple), and taxol (from Yew). Many botanicals remain to be reevaluated as continued folkloric use around the world entices researchers to further scientific study.

History and science have shown repeatedly that almost all things are cyclical. Currently, we find ourselves in an era of resurgent interest in natural products as medicine. Ethnobotany, rain forest depletion of species, and certain limits in advancement using synthetic drugs continuously remind us that nature has and will always provide us with clues on how to develop new medicines. We have learned over and over the need to identify plants as to correct genus, species, variety, and even chemovar (chemical races) in order to obtain the same chemistry and medicinal properties desired for a particular botanical. Computers have helped us identify and categorize plants using the best of classical morphology and modern chemotaxonomy. Lessons from the complex phytochemistry of biologically active constituents have taught us that each plant is a unique chemical factory. We are trying to reach back to the old pharmacopoeias to update early attempts to standardize botanical medicines. Modern chemical procedures using chromatography, infrared spectroscopy, nuclear magnetic resonance spectroscopy, and mass spectrometry for molecular characterization of individual pharmacologically active principles have greatly facilitated the methodology. We now understand the complexity of standardization because of the innate biological variability of plant biochemistry. This allows us to fully appreciate all the complexities and variables that are introduced in plant collection, storage, transport, processing, and extraction to prepare uniform, stable dosage forms.

Natural product research has led to new physiological and pharmacological concepts, particularly when a new compound is found to have a specific biological effect. These have been referred to as "molecular keys" and include such examples as morphine (the chemical basis for natural and synthetic opioid analgesics), cocaine (the chemical basis for synthetic local anesthetics like procaine), and ephedra (the chemical basis for CNS stimulants like the amphetamines and the decongestants such as pseudoephedrine). Another recent resurrected plant drug is capsaicin from hot peppers. Previously used in topical analgesics as a "counterirritant," it is being reintroduced as a true analgesic because in low doses it depletes newly discovered substance P, which is involved in pain transmission.

Along similar lines, the ongoing competition with our new resistant pathogenic microbes has led us back into the race to find new antibiotics from soil microbes and fungi. New pandemic diseases like AIDS have taught us the importance of stimulating and protecting our immune system to fight such diseases. We are all living longer, and we need to help

conquer cancer as well. Many promising agents are being developed from plants. New uses of certain supplements and vitamins also have focused our attention on food as medicine (nutraceuticals) and phytochemicals (eg, flavonoids, betacarbolenes, phytosterols) that may help prevent diseases.

Current epidemiological data and the current complimentary and alternative medicine movement: There are several factors that may be cited for the resurgence of interest in complementary and alternative medicine including the use of botanical medicines. These include consumer interest in perceived "natural" medicines, increased interest in fitness, health, and prevention directed toward longer and healthier lives, the general interest in improving the environment, and the increase in chronic diseases related to aging. Coupled with these factors has been the rise in cost of conventional medicines, an increased fear of potential adverse reactions to modern powerful drugs, and a desire to self-medicate to circumvent these difficulties. This has led to the movement toward CAM (eg, acupuncture, biofeedback, chiropractic, diet, homeopathy, hypnosis, massage), particularly herbal medicine. A brief overview of the prevalence, costs, and patterns of use of CAM therapies in the US compiled by Dr. David Eisenberg at Peter Bent Brigham Hospital in Boston is quite revealing. The prevalence of CAM use increased from 33.8% in 1990 to 42.1% in 1997. The total number of visits to CAM providers increased by 47%, from 427 million in 1990 to 629 million in 1997. The total visits to CAM providers (629 million) exceeded total visits to all primary care physicians (386 million) in 1997. The estimated expenditures for alternative medicine professional services increased by 45% exclusive of inflation and in 1997 were estimated at $21.2 billion. An estimated 15 million adults in 1997 took prescription medications concurrently with herbal remedies or high-dose vitamins. It is obvious that there is a high risk for potential adverse drug-herb or drug-supplement interactions. The monographs provided herewith are intended to provide information that can preclude some of these difficulties. There is little doubt that even the current use of CAM services is underrepresented and that insurance coverage for holistic therapies will increase in the future. Health professionals and laity need reliable data to base decisions about which botanical supplements are possibly useful for various medical conditions.

The Dietary Supplement Health and Education Act (DSHEA): While several phytomedicinal agents have been used for a long time and thoroughly evaluated for safety and efficacy (eg, cascara, psyllium, digitalis, ipecac, belladonna), the majority of herbs have not been fully evaluated. For the most part, this rests with the problem of not being able to patent natural products in the US and the enormous costs (several hundred million dollars) and time (8 to 12 years) required to fully evaluate them. These reasons, coupled with the strong consumer movement to maintain the freedom of choice in self-medication, led to the DSHEA Act of 1994. For the first time, this law defined herbal products, vitamins, minerals, and amino acids as "dietary supplements." It also prohibited dietary supplements from being regulated as food additives, which normally require premarket approval. Further, it states that the burden of proof for safety and adulteration falls on the FDA. However, if a supplement poses an imminent health hazard, DSHEA allows the Secretary of Health and Human Services emergency powers to remove it from the market. The act permits general health claims regarding the activity of herbals but does not permit therapeutic claims. The herbal product manufacturer must be able to substantiate any health claim as being truthful and not misleading. The label also must include the following statement: "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease." Finally, the label must include the designation "dietary supplement" and list each ingredient by name and quantity. Another provision allows for the distribution of information at the time of sale, giving a balanced view from scientific and related literature on the herbal products. The literature must not be misleading or false, cannot promote any specific brand, and should be displayed in an area physically separate from the product. It is up to the FDA to prove that any such information is misleading or false. Before this time, such literature was viewed as an extension of the label and any implied therapeutic claims could be considered in judging a product "misbranded."

On January 6, 2000 the FDA issued final regulations regarding types of structure/function claims that are allowed to be made under DSHEA. In general, claims that a product affects the normal structure/function of the human body are allowed. Any claim that explicitly or implicitly claims that the product can be used to "prevent, treat, cure, mitigate, or diagnose disease" are considered "disease claims" and would subject the product to the drug requirements under the Act. The rule clarifies that such prohibited express or implied claims are made through the name of a product, through a statement about the formulation of a product (contains aspirin) or through the use of pictures, vignettes, or symbols (EKG tracings). The rule allows for claims that do not relate to disease, including health maintenance claims ("maintains a healthy circulatory system"), other nondisease claims ("for muscle enhancement," "helps you relax"), and claims for common, minor symptoms often associated with life stages ("for common symptoms of PMS," "for hot flashes").

DSHEA allowed for the establishment of a commission to conduct a 2-year study of the regulation of label claims and literature used in the sale of supplements. Finally, the bill also established the Office of Dietary Supplements (ODS) at the National Institutes of Health to coordinate research on dietary supplements. In order to keep up with the continuously evolving status, legal, and regulatory issues relating to the botanicals covered by ODS, refer to its Web site: http://odp.od.nih.gov/ods

Another important Web site for information on complementary and alternative medicine in general is http://nccam.nih.gov

Basic botany, pharmacognosy, and pharmacology: As it relates to herbals, basic botany, pharmacognosy, and pharmacology require the understanding that all plants have Latin binomial names (usually accurate and understood around the world) and numerous common names and synonyms. Therefore, botanical products should be identified with the proper Latin name and the most common synonym. Secondly, the active principles in a given plant may be found in one or more parts of the plant (eg, seeds, flowers, leaves). This is the reason that the plant part used should be indicated on the label of a commercial herbal product. For example, in ginkgo biloba, the active components are found in the leaves; in ginseng (*Panax* species), the roots contain the active constituents. Because the species or variety used may have differing concentrations of active principles, it is important to note this as well as geographic source, local environmental conditions of growth, and the processing procedures. All of these factors may influence the final product. Whichever plant part has shown the most active level of therapeutic effect and accompanying clinical evidence should be standardized and used. The proper extract or solvent should be specified by the manufacturer. Some require water soluble extraction while others may need a more nonpolar or lipid extraction. Many of the commercial extracts do not follow official procedures, so it may be necessary to contact the manufacturer to determine how they produced the product. This may be difficult for proprietary reasons, and this is why particular extracts by particular manufacturers that have been clinically evaluated must be used for further studies verifying effects.

All solvents used to yield tinctures, extracts, etc. need to be fully defined for comparison studies and proper dosage determination. When advanced, concentrated, or standardized to active ingredients, the herb or dietary supplement comes closer to the definition of a drug. Yet many manufacturers do not bother to carry the quality control of their products to as high a level as traditional medicine dictates. It must be noted that pharmacologically active compounds in crude herbs are often present in lower concentrations than in conventional advanced, concentrated, or extracted products (eg, tablets, capsules, tinctures). This usually means that the toxicological risks associated with crude botanicals are minimal with moderate use. This may be true, particularly if there is data indicating safe use in many countries for centuries. Unfortunately, the US has always promoted the idea of "more is better," and this is where adverse reaction potential increases.

Another important factor about herbal products is that they often contain a wide variety of compounds from various classes. Often, therapeutic action is due to the combined action of several constituents. Some, like the primary metabolites (cellulose, starches, sugars, and fixed oils), are not particularly active pharmacologically. Others, like the secondary metabolites (alkaloids, cardiac glycosides, and steroids), are quite active pharmacologically. Content varies depending on genetics, environment (sunlight and rainfall), and fertilization. In fact, it is possible to see mixed activity depending on which compounds predominate. Selection at different times of the year also affects herb quality and clinical efficacy.

Potential toxicity, carcinogenicity, or liver toxicity: One must keep in mind dose levels and duration of use. In addition, there are growing concerns about plants such as comfrey *(Symphytum officinale)* that contain the externally useful drug allantoin (which promotes tissue regeneration) and rosmarinic acid (which acts as an anti-inflammatory). When taken internally, the content of pyrrolizidine alkaloids from comfrey is potentially hepatotoxic, mutagenic, and carcinogenic as seen in test animals. Many countries have banned or restricted its use. Unfortunately, because comfrey is regulated in the US as a dietary supplement and not a drug, it has remained on the market. The same story is seen with borage *(Borago officinalis)* and coltsfoot *(Tussilago farfara)* that also contain pyrrolizidine alkaloids. Fortunately, many products such as these have been withdrawn by reputable manufacturers and suppliers.

On occasion, there have been some unusual toxicities reported with commercial herbal products because of contamination with poisonous plants (eg, belladonna) or arsenic or mercury (imported products) and purposeful adulteration with synthetic drugs such as analgesics, anti-inflammatory agents, corticosteroids, and tranquilizers. These problems can be precluded by using products from reliable sources where rigorous good manufacturing practices (GMPs) are observed. Be aware that many imported products from underdeveloped countries may not adhere to good manufacturing practices.

While documented and published reports on herb-drug interactions are still minimal, there is the possibility that these can occur. The relatively few reports of herb-drug interactions probably is due to safety and a lack of professional surveillance. Because herbs have been classified as dietary supplements, there are no requirements for reporting acute or chronic toxicity. This is why the health professional should carefully monitor the use of herbal products by patients. There is a voluntary system for reporting suspected adverse effects (USP at 800-4USP-PRN and Medwatch at 800-FDA-1088).

Basic factors for the patient: The following general guidelines should be considered before advising patients about natural products: All products should be purchased from reliable sources. Even though GMPs are implicit in DSHEA guidelines for identity, cleanliness, and good quality control in manufacturing, there are significant differences in the purity, quality, and potency of products on the market. Further, many structure or function claims have not been evaluated by the FDA or by other independent and objective agencies. Generally, the more ambitious the claims, the more one should be suspicious of the quality of the product. One way to determine reliability of a manufacturer is to request professional health information from the company about the products, the nature of the company, testing, quality control standards, and the like. As with all legitimate and reliable pharmaceutical firms, such requests should elicit data on which decisions can be made about quality, return policies, and guarantees of structure and function claims in research and literature.

Most botanical products (particularly crude herbals) should be dry, appear fresh, and have appropriate colors (eg, bright yellows or reds for flowers, green for leaves, tan for roots). Moldy appearance or off odors are cause for return. Crude herbs, their extracts, or capsule forms should be stored in a cool, dry environment away from direct sunlight and out of the reach of children. Anyone handling crude botanicals should wear plastic gloves. Botanical dust should be kept at a minimum because of contamination concerns and potential allergy problems (eg, to molds, spores, pollen). All surfaces where herbs are handled should be wiped clean immediately. Botanicals should be dated; discard them after 1 year.

Excessive dosages of phytomedicines should be avoided. Because many herbs are considered mild, the tendency is to use them for prolonged periods of time or to use too much at one time. Patients can delude themselves into thinking that they can avoid more potent and effective drugs by using "natural" herbs. All patients should be advised of risk/benefit ratios on all medical treatments and that serious illnesses can develop by assuming an herb will solve the problem over time. Also, patients should be counseled about abuses seen with "diet teas" containing herbal laxatives that may lead to colonic impairments and excessive loss of potassium. Generally, natural products should not be used for serious health conditions without the advice and supervision of a qualified health practitioner. Most natural products are intended to treat mild, short-term disorders (eg, headaches, insomnia, dyspepsia, constipation). Any natural products causing undesirable side effects should be discontinued or the mode of administration changed. For example, while feverfew may be useful in preventing migraine headaches, aphthous mouth ulcers can result from chewing the leaves. Thus, capsules should be taken to avoid such local effects. Like many prescription and OTC drugs, most natural products should be discontinued during pregnancy or lactation and not used in young children. Qualified health professionals should be consulted in these situations. Generally, avoid excessive combination products. Most research with prescription and OTC medications has shown that more than 2 or 3 ingredients in 1 product is not always justifiable. Fixed combinations of active principles often result in excessive doses of 1 ingredient or use of an ingredient that may not be needed.

There is a good rationale for well-conceived combination products when appropriate, standardized dosages of a few synergistic herbals are coupled with vitamins and minerals. Herbal supplement users often start their nutritional regimen coupled with multivitamins. There is a growing market in higher quality, recognized brand-name products that feature concentrated, standardized botanical extracts in combination with appropriate dosages of vitamins and minerals. These

offer convenience and simple once-daily dosing for patients. Examples of recent commercial products of this type have combined echinacea, vitamin C, and zinc for colds; echinacea polysaccharides and vitamin C may stimulate and improve the immune system, and zinc is an essential nutrient for immune system function. While not a cure, this combination may decrease the incidence and severity of the cold. Similar ideas have spawned combinations of B-vitamins, chromium, and ginseng for energy support, and combinations of St. John's wort and kava-kava for tension and mood control. Further research is needed to substantiate the efficacy of such combinations, but many companies have started to document the usefulness of such products. However, excessive use of more than a few botanicals in combination can be a potential problem because each botanical contains numerous active principles.

There is no doubt that efficacy becomes very difficult, if not impossible, to prove with excessive mixtures. Polypharmacy, an older pharmacy practice where small amounts of 10 to 15 ingredients were used in 1 combination product, is shunned today. Unfortunately, the practice of using many botanicals (often each in minute dosages) is still common in Asian and even in some American botanical products. It is highly unlikely that any of these are effective because there are often too many ingredients in ineffective amounts. Some patients feel that all of these botanicals work together, and therefore, such combinations are better, or that if one ingredient doesn't work another will. In reality, there is virtually no reliable clinical data on the efficacy of such complex mixtures.

Caution is advised not only in using combination herbal products but also in using single botanical products. *The Review of Natural Products* is intended to provide the reader with scientific data on the benefits and the risks of various products.

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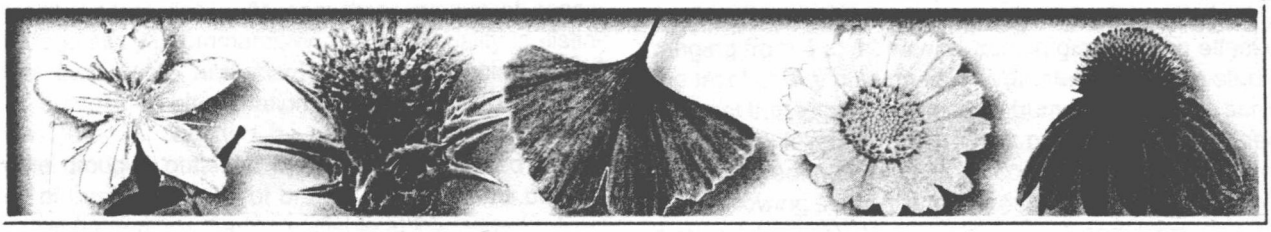
MONOGRAPHS



Acacia Gum

SCIENTIFIC NAME(S): *Acacia senegal* (L.) Willd. (syn. with *A. verek* Guill et Perr.). Other species of Acacia have been used in commerce. Family: Leguminosae or Fabaceae

COMMON NAME(S): Acacia gum, acacia vera,[1] Egyptian thorn,[1] gummi africanum,[2] gum Senegal, gummae mimosae, kher, Sudan gum arabic, Somali gum, yellow thorn

BOTANY: The acacia tree (*A. senegal*) is a thorny, scraggly tree that grows to heights of about 15 feet. It grows most prolifically in regions of Africa, in particular in the Republic of Sudan. During times of drought, the bark of the tree splits, exuding a sap that dries in small droplets or "tears."[3] In the past, these hardened sap tears served as the major source of acacia gum, but today commercial acacia gum is derived by tapping trees periodically and collecting the resin semi-mechanically. At least three grades of acacia gum are available commercially and their quality is distinguished by the color and character in the collected tears.[4] There is considerable variation in gum quality depending on whether it is obtained by natural flow secondary to extreme drought, obtained by tapping or induced by the boring of beetles at sites of branch injury.[5] Gums derived from *Combretum* are readily available at low prices in East and West Africa and are often offered for sale as "gum arabic." Because there is no toxicologic data supporting the safety of these gums, they are not recognized as food additives by most countries.[14] Similarly, trees of the genus *Albizia* are often confused with *Acacia* and should not be used as acacia substitutes.[15]

HISTORY: Acacia gum has long been used in traditional medicine and in everyday applications. The Egyptians used the material as a glue and as a pain-reliever base. Arabic physicians treated a wide variety of ailments with the gum, resulting in its current name.[3] Today, it is used widely in the pharmaceutical industry as a demulcent and in the cooking industry to give body and texture to processed food products. It also is used to stabilize emulsions. The fibers of the bark are used to make cordage.[6]

CHEMISTRY: Acacia gum is a brittle, odorless and generally tasteless material that contains a number of neutral sugars, acids, calcium and other electrolytes.[7] The main component of the gum is arabin, the calcium salt of arabic acid.[4] The structure of the gum is complex and has not yet been fully explained. A comprehensive analysis, including NMR spectra for 35 samples of gum arabic, has been published to serve as the basis for international standardization of acacia gum.[11] The gum is built upon a backbone of D-galactose units with side chains of D-glucuronic acid with L-rhamnose or L-arabinose terminal units. The molecular weight of the gum is large and estimates suggest the weight lies in the range of 200,000 to 600,000 daltons.[7] It is very soluble in water, but does not dissolve in alcohol.

PHARMACOLOGY: Acacia gum has no significant systemic effects when ingested. Although related gums have been shown to be hypocholesterolemic when ingested, there is no evidence for this effect with acacia. When administered to hypercholesterolemic patients for periods ranging from 4 to 12 weeks, acacia gum had no effect on the level of any plasma lipid evaluated.[9,12] Some studies suggest that ingestion of acacia gum may increase serum cholesterol levels in rats.[7] In the past, the gum has been administered intravenously to counteract low blood pressure following surgery and to treat edema associated with nephrosis, but this administration caused renal and liver damage and allergic reactions, and its use was abandoned.[5]

Acacia gum is a demulcent, and soothes irritated mucous membranes. Consequently, it is used widely in topical preparations to promote wound healing and as a component of cough and some gastrointestinal preparations. Whole gum mixtures of acacia have been shown to inhibit the growth of periodontic bacteria, including *Porphyromonas gingivalis* and *Prevotella intermedia* in vitro when added to culture medium in concentrations ranging from 0.5% to 1.0%.[8] At a concentration of 0.5%, acacia whole gum mixture also inhibited bacterial protease enzymes, suggesting acacia may be useful in limiting the development of periodontal disease. In addition, chewing an acacia-based gum for 7 days has been shown to reduce mean gingival and plaque scores compared to a sugar-free gum; the total differences in these scores was significant ($P < 0.05$) between groups suggesting that acacia gum primarily inhibits the early deposition of plaque.[13]

TOXICOLOGY: Acacia is essentially nontoxic when ingested. Allergic reactions to the gum and powdered forms of acacia have been reported and include respiratory problems and skin lesions.[7]

Acacia contains a peroxidase enzyme, which is typically destroyed by brief exposure to heat. If not inactivated, this enzyme forms colored complexes with certain amines and

phenols and enhances the destruction of many pharmaceutical products including alkaloids and readily oxidizable compounds such as some vitamins.[5,7] Acacia gum reduces the antibacterial effectiveness of the preservative methyl-p-hydroxybenzoate against *Pseudomonas aeruginosa*, presumably by offering physical barrier protection to the microbial cells from the action of the preservative.[10] A trypsin inhibitor also has been identified, but the clinical significance of the presence of this enzyme is not known.[6]

SUMMARY: Gum acacia has been used in commerce for millennia. Because of its soothing properties, it is included in cough and cold remedies and it is used topically in wound healing preparations. It is used as a stabilizer for foods. Although generally considered safe for internal use, some persons have developed severe allergic reactions following exposure to the gum.

PATIENT INFORMATION – Acacia Gum

Uses: Acacia gum has been used in food as a stabilizer and in pharmaceuticals as a demulcent. It is used topically for healing wounds and has been shown to inhibit the growth of periodontic bacteria and the early deposition of plaque.

Side Effects: Ingestion may raise serum cholesterol. Intravenous administration causes renal and liver damage. Various forms of acacia gum can cause allergic reactions, including respiratory problems and skin lesions.

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