

## Clinical effects of Gum Arabic (Acacia): A Mini Review

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### Abstract

Gum Arabic (GA) is a natural gummy exudate gained from the trees of Acacia species (*Acacia senegal* and *Acacia seyal*), Family: Fabaceae. GA is considered as a dietary fiber with a high percentage of carbohydrates and low protein content. Sugars arabinose and ribose were originally discovered and isolated from gum Arabic which represents the original source of these sugars. A gum emanation from trees occurs under stress conditions such as heat, poor soil fertility, drought, and injury. Mainly GA is produced in belt region of Africa mainly Sudan, Chad, and Nigeria. In the food industry, it is used in confectionery; in the pharmaceutical industry, it is used as emulsifier, film coating and others. Traditionally the gum used for chronic renal failure, digestive discomfort and others. Although gum Arabic considered as an inert substance, recent information revealed multiple pharmacological and medical effects, such as weight reduction, antihypertensive, antihyperlipidemic, anticoagulant, antibacterial, antidiabetic, anti-inflammatory, nephroprotective and other effects. The aim of present review was to demonstrate the clinical effects of gum Arabic.

**Key words:** Gum Arabic, Obesity, Diabetes, Renal failure.

### التأثيرات السريرية للصمغ العربي: مراجعة مصغرة

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### الخلاصة

الصمغ العربي هو إفراز طبيعي صمغي مكتسب من أشجار السنط (*Acacia senegal* and *Acacia seyal*)، العائلة البقولية. يعتبر الصمغ العربي بمثابة الألياف الغذائية المحتوية على نسبة عالية من الكربوهيدرات ونسبة منخفضة من البروتين. تم اكتشاف السكريات أرابينوز وربوز وعزلها من الصمغ العربي وهو يمثل المصدر الأصلي لهذه السكريات. يتم إفراز الصمغ من الأشجار في ظروف الإجهاد مثل الحرارة، ضعف خصوبة التربة، الجفاف و الإصابة أو الجروح والشقوق. يتم إنتاج الصمغ بشكل رئيسي في منطقة الحزام في أفريقيا، وخاصة السودان وتشاد ونيجيريا. في الصناعات الغذائية، يتم استخدامه في صناعة الحلويات. في صناعة المستحضرات الصيدلانية، يتم استخدامه كمستحلب، طلاء للأفلام وغيرها. تقليدياً يستخدم الصمغ في علاج الفشل الكلوي المزمن، سوء الهضم، وغيرها. على الرغم من أن الصمغ العربي يعتبر مادة غير فعالة، إلا أن المعلومات الحديثة أظهرت تأثيرات دوائية وطبية متعددة، مثل خفض الوزن، والضغط، خافض لدهون الدم، مضاد للتخثر، مضاد للجراثيم، مضاد السكري، مضاد للالتهابات وتأثيرات طبية أخرى.

الكلمات المفتاحية: الصمغ العربي، السمنة، داء السكري، الفشل الكلوي.

### Introduction

Gum Arabic (GA) is the air dried glutinous or gummy exudation obtained from branches and trunks of acacia species, mainly *Acacia senegal* (Hashab), and a nearly associated species *Acacia seyal* (Talha) <sup>(1-3)</sup>, which belong to Fabaceae family <sup>(2)</sup>.



Figure 1. Gum Arabic; raw material <sup>(4)</sup>

Both species naturally grown in belt region of Africa. Sudan, Chad and Nigeria are the main gum producing countries <sup>(3- 5)</sup>. Gum Arabic tree is a familiar medicinal plant in Arabian Peninsula, Pakistan and India <sup>(6)</sup>. Gum from *Acacia Senegal* is the highest quality, while from *Acacia seyal* is the least quality <sup>(7)</sup>.

The name gum Arabic was derived, while it was shipped from Arabian ports to Europe in 4,000 B.C <sup>(8)</sup>.

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Received: 8/4 /2019

Accepted: 3 /7 /2019

Stress conditions as heat, dryness, bad or poor nutrition, and sick trees induced gum production. Microbial infection (bacterial and fungal) in accidental or intentionally made incisions in GA trunks may provoke gum production<sup>(9)</sup>. This exudates or fluid that ooze out the crevices and wounding of Acacia trees, harden and solidify after a few weeks into glossy amber-colored teardrops. After harvesting, the teardrops are assorted into grades according to color and extraneous matter content.

The gum tint ranges from dark brown to white based on tannin quantity, the lightest color being the best<sup>(7,8)</sup>. Chemically the Gum Arabic is a neutral or slightly acidic, complex mixture of polysaccharide and glycoproteins, characterized by a high percentage of carbohydrates (~97%), (D-galactose and L-arabinose) and a low percentage of protein (<3%)<sup>(10-12)</sup>. Sugars arabinose and ribose were originally discovered and isolated from gum Arabic which represent the original source of these sugars<sup>(13)</sup>. The sugars constituents of gum are identical, but the composition and molecular weight (Mwt) of the gum differs from one species to another in the range of 260,000-1,160,000 G.<sup>(14)</sup> GA is an extremely heterogeneous and naturally exists as a mixture of calcium, magnesium, potassium and sodium salts of a polysaccharic acid or Arabic acid<sup>(15)</sup>.

By hydrophobic affinity chromatography, three major fractions had been separated in GA these include arabinogalactan, arabinogalactan-protein complex and low molecular weight glycoprotein<sup>(2)</sup>. Flavonoids, chalcones, tannins, phenolic acid, alkaloids and terpenes like lutein were identified in GA<sup>(6,16)</sup>.

Varieties within the same species, environmental factors (climate, rainfall, and soil), period and method of harvesting or tapping and post-harvest treatment affect gum Arabic chemical composition or quality<sup>(17,18)</sup>. GA can be classified as a water-soluble dietary fiber or a non-digestible carbohydrate. It is not digested in the small intestine, but in the large intestine by the action of intestinal bacteria, it is fermented to short-chain fatty acids, predominantly propionic acid and butyric acid. GA is a prebiotic fiber supporting the growth of lactic acid bacteria and bifidobacteria which may be especially useful for certain groups of people like elderly who have reduced bifidobacteria populations. GA exerted a prebiotic effect at a dose 10gm/ day. This fiber (GA) may affect the physiological status of human through hindering glucose absorption, stool mass increment, bile acids trapping and other effects<sup>(19-22)</sup>.

About 80% of current gum production is utilized by the food in confectionery (due to its compatibility with high sugar concentration) and in pharmaceutical industries as an emulsifier, film coating and others<sup>(8,23)</sup>. Traditionally, GA

consumed by African and Indian peoples to ameliorate digestive comfort, inflammation and improve intestinal transit and as an oral hygiene agent<sup>(19,24)</sup>. In Arabic folk medicine, it was used in chronic renal failure patients for reducing the frequency of hemodialysis<sup>(25)</sup>, and for treatment of diabetes<sup>(26)</sup>. Egyptian people used gum in the embalmment process and in the development of several cosmetics and perfumes<sup>(4)</sup>. Despite the common assumption that the gum is an inert substance, new studies have shown that gum Arabic has some potential antioxidant, digestive nephroprotectant, antianemic, cardiovascular and other properties<sup>(27)</sup>.

Gum Arabic considered safe, a natural compound with no important toxic or side effects when ingested orally. Minor side effects as allergy and hypersensitivity have been reported in some cases<sup>(27-29)</sup>. The aim of the present review was to demonstrate the clinical effects of gum Arabic.

### **Gum Arabic clinical effects**

#### **Effect on hyperlipidemia**

Hyperlipidemia is a medical condition manifested by abnormal lipid profile (raising total cholesterol and/or triglycerides (TG), and/or reduced concentration of high-density lipoprotein cholesterol (HDL)).

It is considered as a risk factor for coronary heart disease<sup>(30)</sup>. Soluble dietary fibers have lipid lowering effects, including gum Arabic. Mohammad et al revealed improvement in lipid profile (cholesterol, TG) in hyperlipidemic patients without affecting the HDL level.

15 gm GA /day has no effect on the lipid profile as compared to placebo<sup>(31)</sup>. Rose *et al* (1983) and Sharma (1985) reported in studies that human ingestion of 25 and 30 gram of gum Arabic daily for 21-30 days decrease total cholesterol (LDL; low density lipoprotein and VLDL; very low density lipoprotein) but not TG and HDL<sup>(32,33)</sup>.

Ahmed *et al* (2016) reported that normal fed mouse when taking 0.5% aqueous solution of GA for seven days, then 10% aqueous solution for an additional six weeks demonstrated a reduction in total cholesterol, LDL and also HDL reduction. This hypocholesteremic action due to reduced liver HMGCR mRNA gene (3-Hydroxy-3-Methylglutaryl-CoA Reductase mRNA) biosynthesis which ultimately reduced cholesterol levels<sup>(34)</sup>.

The lipid-lowering effect of gum Arabic attributed to the ability of GA to bind to bile acids and thus reduce bile acids absorption in the terminal ileum. The sequestered bile acids are released upon gum break down in the large intestine. The fermentation of GA generates acidic pH which renders the bile acids insoluble and aids their excretion in the stool therefore fat digestion and absorption are reduced. In liver new bile acids formation requires cholesterol. Thus, prolonged

digestion of gum Arabic may result in minimizing the plasma cholesterol level<sup>(31)</sup>. The increment in mitochondrial biogenesis and fatty acid oxidation by skeletal muscles is the more recent anticipated mechanism by which viscous dietary fibers can lessen adiposity<sup>(35)</sup>.

#### **Effect on obesity**

In developed countries, obesity and overweight are the most prevalent nutritional disorders affecting the vast number of adult. Obesity resulted when the consumed calories exceeded the used one<sup>(36)</sup>. Ingestion of GA seems to be an efficacious dietary strategy for overweight prevention or treatment affecting numerous biological mechanisms. Dietary fibers including GA affect fat and glucose metabolism. Babiker R and colleagues (2012) revealed in a study significant reduction in body mass index and body fat percent after six weeks of regular use of 30 gm of GA daily. GA consumption causes a considerable reduction in caloric intake along with an increased subjective feeling of satiety<sup>(37)</sup>.

Calame *et al* (2011) evaluated the satiating action induced by a mixture of two forms of gum Arabic (EmulGold [EG] and PreVitae [PV]). The energy consumption was examined three hours after ingestion of the GA aqueous solution. Both forms (EmulGold and previta), at forty-gram dose, produce a considerable decrease in energy intake of more than 100 and 200 kcal, successively. The decrease in energy intake equal to more than 100 kcal for both was observed at smaller doses (10 or 20 gram)<sup>(38)</sup>.

Ushida *et al* (2011) reported the probable anti-obesity action of GA as a dietary fiber. Authors reported that 1% of GA solution was given to three-month-old female mice for 180 days. This solution reduced age-dependent fat depositions; where, this effect was proposed to be due to  $\beta_3$ -adrenergic stimulation of adipocytes through tumor necrosis factor-  $\alpha$  (TNF- $\alpha$ ) down-regulation. This down-regulation might be attributed to large intestinal alteration of microflora, as proved by the modification in cecal short-chain fatty acid and 16S ribosomal deoxyribonucleic acid (16S rDNA)<sup>(39)</sup>.

A study of Ahmed *et al* (2015) revealed that administration of 10% aqueous solution of Arabic gum for nine weeks to mice minimized visceral adipose tissue accumulation. GA reduces 11 $\beta$ -HSD1 mRNA (11 beta-hydroxy steroid dehydrogenase type 1 mRNA) in mice liver and muscle. This may participate in the reduction of plasma lipid level and hence affect obesity. Inhibition of this enzyme is being pursued as a new medication for curing metabolic syndrome and obesity<sup>(40, 41)</sup>.

Arabic gum also down-regulate peroxisome proliferator-activated receptor gamma (PPAR- $\gamma$ ) and expression of the Stearoyl-CoA Desaturase (SCD gene) in mice receiving gum in

drinking water<sup>(41)</sup>. Omaima Nasir (2014) manifested in a study on mice that GA lessen weight through down-regulation of the membrane abundance of SGLT1 (sodium- glucose cotransporter 1) play an important role in intestinal glucose absorption, which will reduce glucose absorption recognized through reduction in plasma glucose level, and consequently insulin level and then body weight<sup>(42)</sup>. Eyibo *et al* (2018) revealed the decrease in albino rat body weight consuming GA which could be attributed to the probable ability of GA to displace available calories and nutrients besides that it increases the absorption efficacy in the small intestine and to appetite loss induced by GA consumption<sup>(43)</sup>.

#### **Effect on hypertension**

The antihypertensive effect of GA had been proved in previous studies. Nasir *et al* (2016) evaluated the hypotensive effect of gum in healthy, prediabetes and diabetic individuals on regular GA intake of 10gm/ day for sixteen weeks<sup>(44)</sup>. Glover *et al* (2009) displayed the reduction effect of GA on systolic blood pressure when given in a dose of 25 gm/day in both healthy persons and patients with renal dysfunction secondary to diabetes mellitus<sup>(45)</sup>. Alkarib *et al* (2011) revealed the significant lowering effect of gum Arabic on systolic blood pressure with concomitant normalizing serum sodium level and raise in potassium level to the normal upper level. The gum causes insignificant alterations or changes in diastolic blood pressure in stage III renal failure patients<sup>(11)</sup>.

#### **Effect on fertility**

The prevalence of infertility among obese women is increased<sup>(46)</sup>. Abdominal or central obesity is the main sign of metabolic syndrome that results in female infertility. Ahmed AA *et al* (2016) demonstrated that administration of GA in drinking water of female mice fed with high fat diet to induce obesity, there was a reduction in lipid peroxidation and an elevation in ovarian antioxidant enzymes activity (superoxide dismutase, catalase and glutathione peroxidase) along with raised mRNA expression and reduced in ovary degenerative changes were observed which in turn may improve reproductive efficacy and manage sterility induced by obesity<sup>(47)</sup>.

Fedail JS *et al* (2016) reported that GA consumption resulted in improvement in degenerative testicular tissue of alloxan-induced diabetic rats, enhanced semen quality, and reduction in lipid peroxidation; furthermore, the activity of antioxidant enzymes together with their mRNA expression was reported to be increased; these effects might have roles in the management of reproductive dysfunction in diabetic men<sup>(48)</sup>.

**Anti-inflammatory effect**

Numerous chronic diseases such as arthritis, cancer, diabetes, cardiovascular (CV) and neurological diseases were reported to be instigated by chronic inflammation<sup>(49)</sup>. Rheumatoid arthritis (RA) is an autoimmune illness recognized by chronic synovial inflammation with higher female incidence<sup>(50)</sup>. Tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) is a main pro-inflammatory mediator involved in the development of RA<sup>(51)</sup>. Ebtihal *et al* (2018) demonstrated that the anti-inflammatory effect of GA through reduction TNF- $\alpha$ , erythrocyte sedimentation rate (ESR) level and improvement in clinical symptoms in RA patients when given (30 gm/day) of GA during the study period<sup>(52)</sup>.

Abdul Rahman *et al* study's (2016) shown the gastro protective effect of GA alone or in combination with other antiulcer drugs. GA possesses a good antiulcer effect and it potentiates or enhance the antiulcer effect of ranitidine in indomethacin-induced gastric ulcer rats<sup>(53)</sup>. Furthermore, Abd El-Mawla and colleges (2013) manifested the protective effect of GA (1gm/day) versus ulceration induced by meloxicam in rats<sup>(54)</sup>.

Moreover, a study of Khedr AA (2017) demonstrated a dose-dependent antiulcer effect of GA in ethanol-induced ulcer in the adult rat through the reduction in gastric juice, raise in pH and other cytoprotective effects; these effects were reported to be attributed to the polysaccharides which demonstrated antiulcer effects in their binding ability to the mucosal surface and to act as a protective coating by raising synthesis of mucus, or through scavenging radicals' activity<sup>(55)</sup>.

In ulcerative colitis, the beneficial effect of GA attributed to its trophic effects on the gut membrane and to its ability to reduce the incidence and duration of diarrhea<sup>(19)</sup>.

Cancer, is an uncontrolled cell growth or cell proliferation which may speared to new tissues<sup>(56)</sup>. Al Alawi *et al* (2018) study's revealed no cytotoxic effect for AG<sup>(6)</sup>, but it may have the ability for prevention or treatment of toxic aspects of some cytotoxic drugs as cyclophosphamide (CPA), doxorubicin, (DOX), and cisplatin beside other drugs and chemicals such as aspirin, acetaminophen, indomethacin, gentamycin, trichloroacetic acid and mercuric chloride<sup>(57,58)</sup>.

Abd-El-Hafez *et al* (2017) and Abd-Allah *et al* (2002) reported that GA has strong antioxidant action<sup>(59,60)</sup> may be attributed to its amino acids content<sup>(61)</sup>. GA considered as a rich source of amino acids, aspartic acid and serine were the main amino acids, lysine, histidine, glycine, tyrosine and other amino acids were also detected in *Acacia senegal* and *Acacia seyal* acids<sup>(62)</sup>. Experimental evidence displayed that there is a relation between the antioxidant effect and the protein fraction, predominantly the amino acid residues such as histidine, tyrosine, and lysine, which are generally

regarded as antioxidant molecules<sup>(61)</sup>. GA increasing the concentration of the antioxidant enzymes and minimizing the oxidizing molecules in various organs<sup>(28)</sup>.

Kaddam *et al* at (2017) demonstrated the beneficial effect of GA in the management of sickle cell anemia at a dose 30 gm/ day for twelve weeks. GA ingestion produce a reduction in the oxidative stress markers as hydrogen peroxide and hydroxyl radicals level, meanwhile increase in antioxidant activity. The markers (hydrogen peroxide and hydroxyl radicals) increase in sickle cell anemia twice as much as in healthy individuals<sup>(63)</sup>.

**Effect on diabetes**

Diabetes mellitus (DM) is a chronic illness with steadily increasing frequencies in all countries<sup>(64)</sup>, microvascular and macrovascular complications of diabetes that may result in mortality and morbidity<sup>(44)</sup>. GA among the dietary fibers reported to have antidiabetic effect in the human and animals. Food supplemented with GA (10 gm/day for sixteen weeks) in prediabetes and diabetic subjects showed a significant reduction in fasting blood sugar (FBS) and glycated hemoglobin (HbA<sub>1c</sub>)<sup>(44)</sup>. Babiker *et al* (2017) observed the beneficial effect of GA in poor glycemic control diabetic patients' receiving 30gm of gum for 4 months<sup>(65)</sup>. GA has an intrinsic glycaemic index is proximate zero snice it is not absorbed in small intestine<sup>(21)</sup>. While Ibrahim *et al* at (2017) observed that in type II diabetic patients' ingestion of 60gm/day of GA produced no significant or appreciable effect on blood glucose concentration and body mass index<sup>(66)</sup>.

Al-Nagar and Faid (2017) reported the hypoglycemic effect of GA in alloxan-induced diabetic rats; where, GA caused beta cell activation or proliferation and/or antagonizing the blocking of the immune receptors of Beta-cell of islets of Langerhans which result in stimulation of insulin release. Also, it minimizes histopathological alterations in damaged islets, plus antioxidant and anti- apoptotic activities<sup>(67,68)</sup>. Omaima Nasir (2014) and El Tobgy (2019) observed in studies on diabetic mice, the antihyperglycemic effect of GA mediated via a reduction in intestinal glucose absorption, which will reduce plasma glucose level, and consequently the insulin level. Also, gum consumption reduces glucose urea and urinary volume<sup>(36,69)</sup>.

Concerning diabetic complications, the protective and or preventive effect of GA was reported. GA ameliorated neuropathy<sup>(70)</sup> and albuminuria, it is effective for delaying the progression to renal failure. Nasir *et al* displayed in a study the protective effect of gum on renal function in diabetic rats since it decreases the blood pressure, additionally GA significantly decrease proteinuria, serum phosphate concentration and enhanced

glomerular filtration rate which ultimately improve renal functions<sup>(69,71)</sup>.

#### Effect on renal failure

In Sudan, GA frequently prescribed for renal dysfunction patients, as it decrease uremia, dialysis frequency and thus improving life quality<sup>(72)</sup>. Ebtihal Y. Khojah observed in study that orally used GA in pomegranate juice (1ml/day/Kg body weight) in rats having chronic kidney disease (KCD) for four weeks along with low protein, phosphorus and potassium diet, result in a considerable improvement in kidney functions (lower serum creatinine, urea), nutritional status and serum minerals (calcium, potassium, and phosphorus)<sup>(73)</sup>. Al Mosawi (2007) observed the salutary effect of GA. 1gm/kg/day with a low protein diet was given to eleven years old girl with ESRF (end stage renal failure) who was managed with dialysis. While using this regime there was a decrease in blood urea, creatinine, no sign of acidosis or uremia and the most important thing was the dialysis-free period (four years)<sup>(74)</sup>. Elamin and colleges (2017) noticed a significant decrease in C-reactive protein level in CKD patients when diet supplemented with 10–40 g/day of gum Arabic, with no noticeable effect on blood urea nitrogen and indoxyl sulfate<sup>(75)</sup>.

Al Za'abi *et al* (2018) proved the valuable GA effect in rats with adenine- induced CKD, since improvement in biochemical markers and histopathological features of affected kidneys had been observed<sup>(76)</sup>.

#### Effect on blood coagulation

GA may be considered as a natural anticoagulant. Muhanad E.Abdalla *et al* (2014) observed in a study on healthy females that ingestion GA (30 gm/day) rise the prothrombin time within the common physiological range, promoting GA safety (no bleeding tendency). GA fermentation products as acetate that formed in large intestine affecting the coagulation cascade<sup>(77)</sup>.

Hadi and colleges (2010) demonstrated that different concentrations of GA (6gm/100ml and 10gm/100ml) were given to albino rats for four weeks, the bleeding time, and prothrombin time were considerably prolonged, while no remarkable effect on activated Partial Thromboplastin Time (APTT). Thus GA modulate its effect through suppression of the intrinsic coagulation cascade without causing extrinsic pathway suppression<sup>(78)</sup>.

#### Antibacterial effect

GA exhibited an antibacterial effect<sup>(79)</sup>. Al-Alawi *et al* (2018) study's show the significant antibacterial activity of n.hexane extract of Sudanese and Omani GA against one Gram positive bacterium: *Staphylococcus aureus* and three Gram negative bacteria: two strain of *E. coli* and *Klebsiella pneumonia*. The antibacterial effect attributed to high concentration of non-polar constituents<sup>(6)</sup>.

Bnuyan *et al* (2015) study's revealed that GA aqueous extract is effective in inhibiting the growth of the tested gram-positive bacteria (*Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae*) and gram-negative bacteria (*Salmonella typhi*, *Proteus mirabilis*, *Klebsiella pneumonia*, *Enterobacter* species, *Acinetobacter*, *E. coli*, and *Serratia* species). Also effective against fungus *Candida albicans*. GA antimicrobial effect's attributed to the high terpene content<sup>(80)</sup>.

Moreover, Lawrence R *et al* (2015) study's evaluated the antibacterial effect of acetone and methanol extract of GA against *Listeria monocytogenes*, *Bacillus cereus*, *Bacillus subtilis*, *Clostridium perfringens*, *Staphylococcus aureus*, *Streptococcus pyogenes*, *Escherichia coli*. Secondary metabolites as tannins, flavonoids and others that have been detected in these fractions were responsible for antibacterial effect<sup>(81)</sup>.

#### Effect on oral hygiene

GA considered as a dental caries protective agent. 0.5%- 1% of GA when added to culture medium suppress the growth of *Porphyromonas gingivalis* and *Prevotella intermedia* (periodontic bacteria) and inhibit early plaque formation. The antimicrobial effect attributed to the presence of cyanogenic glycosides and various enzymes as oxidases, peroxidases, and others<sup>(29,82)</sup>. GA, repress acid-dependent demineralization and uphold remineralization even under fluoride-free settings<sup>(83)</sup>.

## Conclusion

GA has several advantages and it is widely consumed as one of the important ingredients in dietary, pharmaceutical and other industrial products. According to the previous data and outcomes, GA demonstrated proven pharmacological effects and have therapeutic usefulness. More studies are required to clarify the exact mechanism(s), constituent(s) and the proper dose responsible for the specific medical or pharmacological effects.

## Acknowledgment

The author grateful to lecturer Iman S Jaafar / Department of Pharmaceutics/ College of Pharmacy, University of Almustansiriyah for her valuable assistance in this work.

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