CHAPTER 1

African Tropical Plant Gums: Grossly Unexploited Carriers or Adjuncts in Drug Delivery Systems

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Abstract: A volume of attention is currently being drawn to the potentials inherent in African tropical plants as sources of bioactive substances and drug carriers as well as adjuncts in the formulation of drug delivery systems. One group of such carriers or adjuvants consists of polymeric plant metabolites, which can hydrate into gels or mucilages. These are generally known as plant gums. Although gums obtained from African tropical plants have been known for a very long time, their extraction, purification and utilization in pharmaceutical formulations are still at rudimentary stages. There appears to be greater industrial preference for synthetic or semi-synthetic hydrogels as vehicles, carriers and excipients in pharmaceutical, cosmetic or food products. But because of the naturalness of biopolymers of plant origin, with associated inertness and safety, more interest has to be shown, particularly by the pharmaceutical industry, towards the employment of plant gums as drug carriers, or adjuncts, in drug dosage forms. This article seeks to draw attention to some African tropical plant gums, obtained from different plant species, which have been shown, via laboratory studies, to exhibit potential applicability in the development of drug delivery systems.

Introduction

Several tropical plants are sources of materials which possess properties that are of interest to the pharmaceutical, food and cosmetic scientists. The natural tendency, when considering the uses of natural (including plant-based) ingredients in food, drug or cosmetics formulations, is to compare their advantages and disadvantages with those of counterpart synthetic excipients. In this regard, raw materials of plant origin have proved to be relatively non-toxic, biocompatible, readily accessible, economical, and cost-effective, even for industrial scale production.

One group of excipients that are of significant interest in pharmaceutical formulations, are the hydrosoluble and swellable polymers of plant origin, otherwise called plant gums. These are predominantly polysaccharide in nature. Following their extraction and processing, frequently, they become amorphous, or crystalline, hydratable products. On hydration, they may form translucent gels or colloidal dispersions.

Chemically, plant gums are complex polysaccharides with some having molecular weights in the region of 9.5 million. Each gum has a unique combination of sugars, the monosaccharide units. The most widely distributed sugars in plant gums are mannose, galactose, rhamnose, glucose, fucose, xylose, arabinose and the sugar acids – galacturonic acid and glucuronic acid

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[1]. Some of the sugars are linked by 1, 4 linkages, while others are joined by 1, 6 bonds. Processed gums may contain residual amounts of fat, protein, plant metabolites, metal ions and crude fibre as contaminants [2]. Gelation concentration varies with different gums but, invariably, viscosity of fully hydrated gum dispersions is concentration-dependent. Similar to their synthetic counterparts, the viscosity of plant hydrogels is sensitive to environmental factors, such as electrolyte concentration, pH and temperature [3, 4].

Extraction of plant gums

Plant gums occur either as exudates or in extractive forms. It is believed that exudate gums are produced in response to injury to the plants. They may arise from the breakdown of compounds in injured cells. Their function is to seal off the wound and help prevent infection by fungi and bacteria through the open site of injury. To harvest exudate gums, the selected part(s) of the plant are punctured or slashed with a sharp object or knife. The exudates may be allowed to dry on the plant, and then collected as dried beads or strings. This method is preferable in order to minimize losses that can occur if the material is collected in the liquid form. Typical examples of exudate gum are acacia, tragacanth, karaya and ghatti gums.

Extractive gums come from the endosperms of seeds of some legume species, or are extracted from the wood or bark of other plants. The gum-rich part of the plant is pulverized, or otherwise reduced into particles, and macerated in water for several hours. During the period of maceration, the gum is hydrated and dissolved in the water, which finally becomes viscous. The resulting mucilage is screened through a fine sieve to remove insoluble plant materials. Gum is recovered by mixing the mucilage with a water-miscible counter solvent. Alternatively, the gum can be dehydrated out of the mucilage by lyophilization. One extractive gum that has been widely investigated for targeted drug delivery is guar gum. The gum and others will be discussed with some detail in this communication.

The extraction procedures described above will, at best, yield the gums in their rather crude forms. Purification of the crude extracts would involve properly constituted column chromatographic approaches.

Benchmark plant gums of pharmaceutical interest

Because of their desirable properties, a few selected African plant gums have been employed not only as adjuncts or carrier media in drug delivery systems, but also as important ingredients in other industrial products or processes. These gums hydrate readily to form stable gels. They are non-toxic and safe for human consumption. They include: tragacanth, acacia, karaya and guar

gums. The pharmaceutical uses of these gums will be discussed shortly, but it is important to highlight their other industrial applications as well.

In the paper and textile industries, these gums are used to fill pores and irregularities and, thus, make the paper or fabric stiff and smooth. Plant gums may be added to soil-water mixtures to serve as a drilling lubricant, in the petroleum industry. Moreover, they can be pumped into the ground to increase the density and pressure of water, thus helping to push oil and gas to the surface.

Acacia is the most important gum in the manufacture of ink. It is used as adhesive for postage stamps and envelopes. It may be added to candies with high sugar content to prevent crystallization of the sugar. It emulsifies oils and fats in foods, body lotions and liquid soaps.

Karaya gum is used as a dental adhesive. It is equally useful as emulsifier in salad dressings, ice cream and cheese spreads. It is an important ingredient in hair setting gels. In the tissue paper industry, it is a preferred adhesive when compared to gum arabic.

Guar gum is used mostly in the paper industry. Water that contains guar gum flows faster than regular water, and so it is mixed with water in fire-fighting hoses.

Let us now take a look at some possible uses of each of these model plant gums in drug carrier systems.

Acacia gum

This is a gummy exudate from the stem and branches of *Acacia Senegal*, Willdenow (Fam. Leguminoseae). The tree is indigenous to West and East Africa. Exudation of the gum is stimulated by making incisions or cuttings in the bark of the tree. Exuded gum congeals shortly after exposure to air. It is then collected and dried. Various quality grades of acacia gum are commercially available, but only the best qualities are suitable for pharmaceutical uses. Acacia gum for pharmaceutical uses should preferably be colourless but, at worst, it may be pale yellow. It should normally be opaque, brittle and inodorous. The gum is soluble in 2 parts of water, forming a mucilage, but insoluble in alcohol. This highly branched polysaccharide gum is a complex mixture of calcium, magnesium and potassium salts of arabic acid [5]. It has an approximate molecular weight of 250,000.

Traditionally, acacia gum (also known as gum arabic) is employed in pharmacy as a suspending or emulsifying agent. It can be incorporated into mixtures or syrups in the form of mucilage. In combination with gelatin, it can

form a base for pastilles. As an emulsifier, it can be mixed with twice its weight of water and four times its weight of a fixed oil to from a primary emulsion.

Acacia gum is also relevant in modern day drug delivery systems, especially for microencapsulation. In combination with whey protein, acacia gum forms a stable complex coacervate at pH of 4.0. A coacervate matrix so formed was successfully used to microencapsulate some vegetable oils [6]. Certain drugs can also be conjugated to acacia gum microspheres. Nishi and Jayakrishnan [7, 8] have found that periodate oxidation of acacia gum offers a convenient means of producing stable microspherical conjugates between the gum and certain types of drug. Thus, the investigators developed acacia gum microphores as carrier for sustained release of drugs such as primaquine and ampicillin.

Tragacanth gum

Tragacanth is an exudate gum from the stem of *Astragalus gummifer* Labill (Fam. Leguminoseae). The polysaccharide is said to be produced by the gummosis of the cell walls of the pith and medullary rays in the stem. It absorbs water, swells and thus exudes from the stem spontaneously through cracks. Incisions made on the stem would ease exudation. The exudates are collected when dry. The best grades of tragacanth appear as white or yellowish white, translucent ribbons. They are generally odourless and tasteless. Lower grades are obtained from different sub-species of the plant and are more visibly coloured than the higher grades. Tragacanth is not totally soluble in water, but swells to form a gel.

Its composition is not yet fully elucidated. On hydrolysis, the water-soluble part yields arabinose, galactose and geddic acid. The water-insoluble portion yields, by hydrolysis, tragacanthose, xylose and bassoric acid. Traces of starch and cellulose are also found in the gum.

The most important use of tragacanth in pharmacy is as a suspending agent. The mucilage is an efficient suspending agent, but the gum is not a good emulsifying agent. It can, at best, be used to stabilize a creaming emulsion by increasing the viscosity of the preparation. Apart from these traditional uses of tragacanth, a cross-linked form of it has been explored as a tablet disintegrant [9]. It was found that cross-linked tragacanth exhibited superior wicking and swelling actions. It could, therefore, be used as a superfunctional disintegrant, suitable for both soluble (e.g. lactose) and insoluble (e.g. dicalcium phosphate) diluents.

Karaya gum

Karaya gum, also known as sterculia gum or Indian tragacanth, is an exudate gum obtained from the stem and branches of *Sterculia ureus* Roxburg, or other species of *Sterculia* (*S. villosa* and *S. setigera*) (Fam. Sterculiaceae), *Cochlospermum gossypium* A.P. de Candolle, or other species of *Cochlospermum* (Fam. Bixaceae). It is a complex polysaccharide of high molecular weight. On hydrolysis, it yields galactose, rhamnose and galacturonic acid.

The gum does not dissolve in water but swells to give a colloidal sol. A 3 – 4 % sol in cold water gives a heavy gel with smooth texture. With high temperature boiling, a 20 – 25 % sol can be produced with the gum. It forms viscous sols in hydroalcoholic solutions containing up to 60 % alcohol. This distinguishes it from most other plant gums, which scarcely dissolve in alcoholic solvents. Karaya gum is acidic with acid number in the range of 13.4 – 22.7, depending on the source and age. It occurs as partially acetylated polysaccharide, and has a characteristic odour. A 1 % solution of the gum has a pH of 4.6. It also tends to have a buffering effect in the presence of small amounts of alkali. It is stable in environments of pH 8.0. The sols attain their maximum viscosity at pH 8.5. Above that pH, the sols tend to lose their consistency, and become stringy. Sols and gels produced with the gum are easily susceptible to bacterial attack. It is important, therefore, to incorporate appropriate antibacterial agents as preservatives. A mixture of 0.2 % methyl and 0.02 % propyl paraben is an adequate preservative for this purpose. Sodium benzoate at 0.1 % is an effective alternative preservative for karaya gum sols.

Karaya gum has a wide range of possible uses in food and pharmaceutical industries. Its excellent water-absorbing and water-holding capacities, as well as acid stability, make it suitable for a variety of uses. Of all the karaya gum produced, an estimated 10 per cent is used as food additive, with almost all of the remainder going into pharmaceutical production. It is also used to some extent in medicine, textile and paper making.

In the food industry, karaya gum functions principally as a stabilizer and emulsifier, especially in dairy products, ice creams, ice pops and salad dressings. It prevents the exudation of water (syneresis) from those products and improves spreadability of cheese. It is used as binder in low calorie bakery products, such as bread, pasta and doughnut. In the processing of mince-meat, karaya gum provides good water retention and binding properties; it emulsifies protein, fat and water, thus giving the finished product a smooth appearance. In paper or textile industries, karaya gum is used to bind cellulose fibres together. For printing on textile materials, the gum enhances the viscosity of dye solutions.

Medically, karaya gum is used in a number of ways, taking advantage of its various properties. By virtue of its enormous water-absorbing capacity, it can be used as an effective bulk laxative. For this reason, it is administered in a powdered form, at an appropriate dose. Its adhesive property has equally been exploited in medicine. It is used to hold in place the rings of colostomy bags when fixed. It can serve as a denture adhesive, but its use for this purpose has declined because of deleterious effects on existing natural teeth, arising from prolonged use of the acidic gum.

Of all plant gums, karaya is nearly the most widely evaluated for its suitability as a carrier for drug delivery, perhaps, second to guar gum. Its utility in this regard is based on the characteristic swelling and gelling properties of the gum. Its usefulness has been reported in the preparation of mini-matrix tablets [10, 11], hydrophilic matrices [12 – 16], microcapsules [17, 18] and mucoadhesive tablets for buccal drug delivery [19]. A thermally modified form of karaya gum has turned out to be a more efficient tablet disintegrant than the parent gum, and this was attributed to improved swelling capacity [20].

Guar gum

Guar is an extractive polysaccharide gum derived from the endosperm of the leguminous plant, *Cyamopsis tetragonolobus* (Fam. Leguminoseae). The chemistry of the gum is not complex, the major compound being galactomannan. It consists of a long chain of β-D-mannopyranosyl units connected by 1, 4 linkages. Alternate D-mannopyranosyl units in the chain are attached by 1, 6 linkages to single units of α-D-galactopyranose. Thus, the ratio of D-mannopyranosyl to D-galactopyranosyl units is 2:1 [21]. Guar gum hydrates rapidly in cold or hot water, and relatively low concentrations can give solutions of very high viscosity. The viscosity is, however, affected by temperature, pH and presence of electrolytes. The gum has an excellent gelling, water-retention, emulsifying and film forming properties. It is insoluble in alcohol or organic solvents.

It has wide application in food, cosmetic, paint and pharmaceutical industries. The functional value of guar gum can be tremendously improved by chemical modification of the polysaccharide. For example, by hydroxypropylation, hydroxypropyl guar was produced, which was found to be a better substitute for hydroxyethyl cellulose in water based paints [22]. Graft copolymerization of native guar gum, hydroxypropylated guar or carboxymethylated guar with other polymers, such as methacrylic acid, polyacrylamide, poly (acrylic acid) or polyacrylonitrile yielded products with improved properties for various industrial uses [22]. Guar gum or its derivatives can be used as a source of non-caloric soluble dietary fibre and slimming aid. When ingested with water, it swells in the stomach producing a feeling of fullness, thus reducing hunger.

Guar gum or its derivatives are used as viscosifiers, rheology control or water conditioners in hair and skin care products.

Guar gum, or any of the above-named products derived from it, can also be used as a pharmaceutical excipient. In the preparation of pharmaceutical dosage forms, guar gum can serve as suspending agent, emulsion stabilizer, viscosity control for suspensions and syrups, binder, tablet disintegrant or controlled delivery drug carrier. Abundance of information exists in pharmaceutical literature on the uses of guar gum as carrier in drug delivery systems; majority of these have revealed the excellent features of guar gum in colon-specific drug delivery [23 – 25].

Metronidazole loaded microcapsules prepared by calcium chloride cross-linking of sodium alginate were coated with guar gum, chitosan and cellulose acetate phthalate respectively to compare the effects of the coatings on colon-specific drug release. Among the coatings, guar gum gave the best controlled drug release rate and exhibited highest colon specificity [26]. On the basis of other pieces of empirical evidence, guar gum has been proposed as a feasible protective coating material for microspheres containing 5-fluorouracil [27, 28] or methotrexate [29] intended for use in the chemotherapy of colorectal cancer.

The distinctive features of guar gum as carrier for colon specific drug delivery are usually attributed to specific degradation of the gum by the microbial flora of the colon [30, 31]. The anaerobic bacteria that are responsible for degradation of guar gum in the colon are the *Bacteroides* species (*B. fragilis, B. ovatus, B. variabilis, B. uniformis, B. distasonis* and *B. thetaiotaomicron*) [32]. For degradative activities, these bacteria produce a number of enzymes such as, β-glucoamidase, β-xylosidase, β-galactosidase, α-arabinosidase, nitroreductase, deaminase and urea hydroxylase [33].

Several other studies have been reported in which guar gum was used to produce oral controlled release drug delivery systems. A water-soluble drug, diltiazem hydrochloride, was prepared as guar gum-based matrix tablets [34]. Drug release was comparable to commercial sustained release tablets of diltiazem hydrochloride. Similarly, guar gum was used as carrier in three-layer matrix tablet formulations of trimetazidine dihydrochloride [35] or metoprolol tartrate [36]. In these studies, guar gum consistently exhibited very good potentials as a carrier in the oral controlled delivery of water soluble drugs.

African tropical plant gums with potentials in drug delivery

In contrast to the benchmark plant gums discussed above, several African tropical plant gums have not been fully characterized. Their true chemical identities have not been properly elucidated, and products of their hydrolysis

are not clearly identified. Much of their potentialities have, therefore, been associated with the crude gummy extracts. Nonetheless, these gums, as can be seen from the plethora of literature reports, possess inherent capacities that make them potentially useful as adjuncts or carriers in drug delivery systems. They may function as suspending agents, emulsifiers, binders, disintegrants, bioadhesives, film formers or controlled release matrices.

Toxicity has been a major issue for concern regarding the use of synthetic excipients. From recent times, therefore, attention has been re-awakened in researchers towards plant-based excipients for foods, drugs and cosmetics. The main attraction for the plant polymers is in their relative safety and lack of serious toxicity. The plant gums presented in the following paragraphs have received much attention because of their ethno-history of use, in many African communities, as ingredients for foods and medicines. They are generally not associated with side effects; they are biocompatible, readily available, and can be obtained with minimal costs. They have economic value.

Albizia gum

Albizia is an extractive gum from the stem of *Albizia zygia* (DC) Macbr. (Fam. Leguminoseae). The tree grows widely in Africa and Asia. The gummy exudate has been described as elongated tears that turn dark-brown on drying [37]. It consists largely of β-D-galactose units linked by 1, 3 or 1, 6 bonds [38]. In an early report, Ashton *et al.* [39] have described the physical properties of the gum. A pioneering assessment of the usefulness of albizia gum as a pharmaceutical excipient was done by Odeku and Fell [40]. These workers compared albizia with khaya gum in compression coating of tablets intended for drug targeting to the colon. The results showed that although both gums have potentials for drug targeting to the colon, albizia proved to be more colon-specific in their drug release patterns. The report indicates that both gums are susceptible to degradative actions of the colonic bacterial enzymes.

Albizia gum may also be used as a binding agent in tablets. Using paracetamol, a poorly compressible drug, Odeku [41] has demonstrated that albizia gum can bind poorly compressible powder mixes, resulting in tablets with good mechanical strength. The findings further indicate that albizia gum would be useful when tablets producing slow but controlled drug release are desired.

Brachystegia gum

This is a mucilaginous polysaccharide extracted from the cotyledons of the seed of *Brachystegia eurycoma* Harms (Fam. Leguminoseae). The plant is commonly found on river banks of the forest zones of southern Nigeria and Cameroon. It is low-branching, but can stand 35 metres tall with a large flat crown [42]. The seed yields a water-soluble gum which may have functional

values in food and pharmaceutical industries. Although the chemistry of the gum is not fully elucidated, data from rheological studies suggest that it may be a highly branched polysaccharide [43]. Used as a stabilizer in ice cream, the gum proved to be comparable to commercial polymers, such as sodium carboxymethyl cellulose, κ-carrageenan and sodium alginate [43]. The gum has also been matched against acacia and gelatin as binders in tablet formulations [44]. In concentrations up to 6 % w/w, the gum produced relatively softer tablets than gelatin or acacia, when the diametral crushing strength and friability were evaluated. Based on the results reported in the preliminary study, the tablet potentials of brachystegia gum need to be examined further.

Cissus gum

The plant source of this gum is *Cissus populnea* Guill & Perr. (Fam. Ampelidaceae). It is a climber, which is found most abundantly in the middle belt region of Nigeria. If the stem bark of the plant is cut or beaten into coarse pieces, and soaked in water, it quickly yields a densely viscid solution or gel, depending on the relative amounts of the solid portions used. The chemistry or biocompatibility of the polymeric material is not well documented. But the *Igala* and *Idoma* peoples of Nigeria incorporate the gel into their meals or use it to treat various diseases, with no associated adverse effects.

Physically, the gum has very high water-absorption and swelling capacities, becoming both pseudoplastic and thixotropic in an aqueous solution of at least 4 % w/v [45]. In order to assess its pharmaceutical importance, Balami and Bangudu [46] examined the gum as an emulsifying agent, in comparison with gum arabic. The results showed that cissus gum would perform better as an emulsion stabilizer than as emulsifying agent. More recently, Alfa *et al.* [47] have in a separate study confirmed this specific property of cissus gum. It can be stated that the gum, in appropriate concentrations, provides stabilizing effects for emulsions and suspensions. When evaluated as binder in tablets, cissus gum was found to have three times the binding efficiency of maize starch, but with much poorer disintegrant property [48].

Detarium gum

Detarium is a hydrophilic gum extracted from the cotyledon of the seed of *Detarium microcarpum* Guill & Perr. (Fam. Caesalpinioideae). The tree grows widely in tropical savannah Africa reaching a height of 10 metres. In Nigeria, the plant is commonly located in the forests of the southern zones. The *Igbo* people of the south-eastern zone traditionally use the powdered cotyledon as thickener in soup and sauce. The polysaccharide gum hydrates readily in hot water to give a stable, viscous, mucilaginous dispersion. Preliminary chromatographic analysis of acid hydrolysate of the gum suggests the presence of xylose and glucose units [49].

The probable pharmaceutical uses of the gum have been subjects of several laboratory investigations. Ozumba and Bangudu [49] have demonstrated that detarium gum compares favorably with maize starch or gelatin as binding agent in tablets. It can also produce sustained drug release from capsules [50] and tablets [51]. In concentrations as low as 2 % by weight, detarium gum has proved to be an efficient suspension stabilizer [52]. It has also exhibited excellent film properties, with potentials for film coating of tablets [53]. The gum can act as gel carrier of pharmacologically active agents intended for mucoadhesive drug delivery [54, 55].

Irvingia gum

This is a hydrocolloid extracted from defatted cotyledons of *Irvingia gabonensis* (Aubry-Lecomte ex O'Rorke) Baill (Fam. Irvingiaceae). The plant source of the gum is a deciduous tree that grows to a height of 30 metres. Known variously as "wild mango", "African mango" or "bush mango", it produces yellow edible fruits that resemble mango. It is found in most parts of tropical Africa, and is valued for its wax-rich seeds. In Nigeria, the cotyledon is known as "ogbono". In the powdered form, the cotyledon is used as thickening agent for dishes, such as *ogbono soup*. It is rich in mucilaginous contents, extracted as the gum. Admittedly, not much work has been reported on the chemistry of the gum or its pharmaceutical potentials. Isimi *et al.* [56] have evaluated the gum as a possible emulsifying or suspending agent. The irvingia mucilage compared well with tragacanth in concentrations up to 2 % w/v. Above 2 % w/v, irvingia gum produced stable emulsions, comparable to those of acacia.

When used as binding agent in metronidazole tablet formulations, the irvingia seed mucilage produced granules showing plastic deformation under compression pressure [57]. The tensile strength of the resulting tablets increased with the concentration of the binder, whereas brittle fracture index and friability decreased. The results of the study indicate that, used as binder in appropriate concentrations, irvingia gum can yield tablets having acceptable mechanical and drug release properties.

Grewia gum

Although its chemistry has not been clearly elucidated, the mucilaginous polymer from leaves and stem bark of *Grewia mollis* Juss (Fam. Tiliaceae) is believed to be a polysaccharide [58]. The shrub grows well in the savannah regions of Africa reaching a height of about 7 metres. It is valued by the indigenous people of northern Nigeria who cultivate the plant. Mucilage from the stem bark forms part of some of their meals. The mucilage is extracted by maceration of pieces of the bark or leaf in hot or cold water.

Okafor [59] has studied the rheological properties of grewia mucilage, and found out that the polymer could be of benefit in some pharmaceutical formulations. This researcher and his associates have, therefore, evaluated the gum as either a bioadhesive agent [60, 61] or material for producing polymer matrix-based tablets [62]. These studies indicate that grewia gum may find application as suitable polymer for producing sustained drug release tablets. In a related study, Emeje *et al.* [63] examined grewia gum as binder in paracetamol tablets. The plant polymer was comparable to a synthetic polymer, polyvinylpyrollidone, in their effects on densification and flow properties of granulations as well as mechanical strength of tablets, thus reaffirming the pharmaceutical potentials of the gum.

Khaya gum

Khaya gum can be obtained from any of two species of khaya plant – *Khaya senegalensis* and *Khaya grandifoliola* (Fam. Meliaceae). In a number of reported studies [64 – 67], the usefulness of the gum as binder in paracetamol tablets has been demonstrated. Odeku and Fell [68, 69] have shown that khaya gum can also be used in matrix-type tablets for sustained drug release.

Mucuna gum

This is a biodegradable polymer extracted from the cotyledon of the tropical plant, *Mucuna flagillepes* (Fam. Papilionaceae). The gum is hydrophilic and hydrates quickly in water to give a viscous mucilage. In many parts of southern Nigeria, the powdered cotyledon is added in making soup, to produce a thickening effect. No adverse effects are associated with it. The polymer consists mainly of D-galactose as well as D-glucose and D-mannose units [70].

There are features that make the gum attractive as a potential pharmaceutical polymer. It has, therefore, been severally evaluated for application in various types of drug delivery system. Udeala and Uwaga [71] and, later, Onunkwo and Adikwu [72] and Attama *et al.* [73] have independently demonstrated that mucuna gum could be a good stabilizer for emulsions and suspensions. Other studies have revealed that it could be used as binder in tablets [74, 75], a gel matrix for bioadhesive drug delivery [76, 77], alternative oral formulation of glibenclamide in microspheres [78] and film former for tablet coating [79]. There is sufficient evidence that mucuna gum, although susceptible to oxidative reactions and discoloration, can be applied in a variety of drug delivery systems.

Okra gum

Okra gum is obtained from the fruits of *Hisbiscus esculentus* Linn (Fam. Malvaceae). The plant is an annual tropical shrub, valued for its pods which

are edible when fresh or hydrated. In the hydrated state, the gum turns mucilaginous, a property that imparts viscosity. The gum is a polysaccharide consisting of D-galactose, L-rhamnose and L-galacturonic acid units [80].

Okra gum has been reported as a polymer with potential pharmaceutical uses [81]. Ganji *et al.* [82] and Nasipuri *et al.* [83] have studied the usefulness of the gum a suspending agent. In concentrations of 1 – 2 %, the gum was found to be as effective as sodium carboxymethyl cellulose, and better than both acacia and tragacanth. When evaluated as an emulsifying agent [84], only 0.4 or 0.5 % w/v of okra mucilage was required to produce stable oil-in-water emulsions of olive oil or liquid paraffin, indicating high levels of efficiency of the gum as an emulgent. Dispersions containing okra gum mucilage produced pseudoplastic flow, showing that such emulsions would pour easily on agitation. When used as granulating/binding agent in conventional tablets [85, 86], the gum induced a slow release of the drugs, signaling that okra gum could be a polymer with sustained release effects. The sustained release potential was confirmed by Kalu *et al.* [87] who produced monolithic matrix compacts of the gum. The result was that okra gum compared favorably with sodium carboxymethyl cellulose, and a combination of the two polymers resulted in a near zero-order release of paracetamol from the matrix tablets. It was concluded that okra gum could be used as a matrix material for producing tablets that would sustain drug release for more than 6 hours. Okra gum has also proved to have bioadhesive potentials when formulated as matrix tablets [88, 89].

Prosopis gum

Prosopis gum is a xylogalactan extracted from hydrated tegmina of seeds of a tropical plant, *Prosopis africana* (Fam. Mimosaceae). The major monosaccharide components are xylose and galactose [90]. It also contains fructose and glucose to a lesser degree. The seed source of the gum is normally fermented and used as taste enhancer in some Nigerian diets.

The gum has particularly interesting properties, exhibiting great versatility as a potential pharmaceutical excipient. Adikwu and his research collaborators have extensively studied this plant polymer, and reported on the variety of possible applications of the gum. Thus, they have revealed its potentials as binding agent in tablets [91], tablet disintegrant [92], suspending agent [93], emulsifying agent [94], gel-former for sustained drug release [95], bioadhesive [96, 97] and film-forming polymer [98].

Sesamum gum

This is mucilage that forms from hydrated leaves of *Sesamum radiatum* (Fam. Pedalaceae). The plant grows in many parts of tropical Africa, particularly

Nigeria. It grows wildly as weed, but in some communities, it is cultivated for its culinary and medicinal uses.

The extracted leaf mucilage has not been a subject of much research. Ajakaiye [99] has reported that the leaf contains nitrates and proteins. Allagh *et al.* [100] have evaluated the leaf gum as binder in sulphamethoxazole tablets. They reported that granules and tablets produced with sesamum gum exhibited similar physical properties as those made with maize starch or gelatin in the same concentrations. However, sesamum gum produced longer disintegration times and slower release rates than the standard binders. Nonetheless, it was concluded that sesamum gum could be used to produce tablets of pharmaceutical qualities.

Zanthoxylum gum

Zanthoxylum is a generic group consisting of several species in the botanical family, Rutaceae. These species were formerly classified under the genus, *Fagara*, but due to some "chemosystematic considerations", the name, *Fagara*, has been replaced with *Zanthoxylum* [101]. It appears that out of about twelve species of Nigerian *Zanthoxylum*, gums obtained from only two species (*Z. tesmanii* and *Z. macrophylla*) have been examined for pharmaceutical uses.

Z. tesmanii (Engl.) Waterm grows in the forest vegetation of southern Nigeria, Cameroon, Democratic Republic of Congo, and Zimbabwe [102]. The gum oozes out from wounds inflicted on the trunk of the tree. The tears of gum are collected when dry and may be purified by precipitation from an aqueous mucilage.

Orafidiya *et al.* have studied some physicochemical [103] as well as rheological [104] properties of the gum. They have also examined the emulsifying properties, arriving at a conclusion that the gum could produce emulsions of similar stability to those prepared with acacia gum.

Z. macrophylla (Engl.) Waterm can also be found in Nigeria and other West African countries, such as Ghana, Sierra Leone, Ivory Coast, Togo and Cameroon [105]. The wounded stem and branches of the plant exude the gum in large quantities. Nasipuri [106] has evaluated the gum for physicochemical properties as well as suitability as an emulsifying agent. The researcher found out that the polymer may contain arabinose, galactose, glucuronic acid and galacturonic acid as the building units. He also concluded that the emulsions produced with zanthoxylum gum had similar appearance and "eye appeal" as acacia emulsions.

Challenges in the uses of plant gums for pharmaceutical formulations

There is already an abundance of empirical evidence of numerous plant gums with potentials for use as carriers for drug delivery or adjuncts in drug delivery systems. But the levels of research on these plant hydrogels are still at the foundational stages, and much refining of the gums is yet to be done for them to be officially incorporated into drug delivery systems design and implementation. A number of challenges, therefore, still stand on the way of full exploitation of the natural gums.

Physical and chemical purity is a fundamental requirement for any pharmaceutical raw material. Plant gums at the point of harvesting are normally heavily contaminated by polymeric and inorganic impurities. These may be plant metabolites, volatile oils and metal ions. In most of the reported investigations cited in this review, the best degree of purification involved, simply, the hydration of the gum in water, followed by precipitation with a non-solvent, such as acetone or ethanol. In as much as the non-solvent could dissolve some organic contaminants, there was no guarantee of the precipitating gums being totally freed of contaminants. Usually, there were no attempts to free the gums of possible co-precipitates. Any efforts to develop plant gums to an officially acceptable level must address this fundamental challenge.

A common experience in handling crude gum extracts is the problem of discoloration. Most plant gums undergo oxidative reactions that produce a darkening effect. In order to checkmate this phenomenon, many investigators have used solutions of an antioxidant, such as sodium metabisulphite, as the processing liquor [44, 75, 77, 78]. This has, however, produced varying levels of success, and so the method needs to be examined further.

Studies of the physicochemical properties of plant gums have revealed the polymers as containing peroxidase enzymes [82, 103, 106]. Peroxidases, if not inactivated, can cause a discoloration of the gum. While heating in an autoclave at 121^{o}C and 15 psi for 15 minutes was employed to inactivate the enzyme in mucuna gum [78], heating at 110^{o}C for 60 minutes and 120 minutes was required to achieve enzyme inactivation in acacia and zanthoxylum gums respectively [106]. Use of heat for this purpose must be done with caution in order not to denature the desired polymer.

Although the plant hydrogels are expected to be hydrosoluble, after they have been precipitated by means of a non-solvent, and dried, their rates of hydration are greatly reduced. Many of the plant gums do not get fully hydrated or dissolved, but will rather swell in water to produce a colloidal translucent dispersion. In such situations, the usefulness of the polymer as emulgent, viscosity enhancer, film former or bioadhesive medium becomes highly compromised.

Yield, however, is not generally a major setback in the production of plant gums. In this regard, many gum-producing plants can be said to generous, offering copious quantities of the extractive or exudative polymer.

Future of African plant gums in the development of drug carrier systems

The beauty of African plant gums resides in their good yield, relative inertness, cost-effectiveness and non-toxicity. The challenges identified above, though significant enough, are not severe deterrents to the development and industrial applications of the plant gums. They are also not insurmountable! This review seeks to draw the attention of indigenous pharmaceutical, food and chemical industries to one reality**:** local industries do not have to cross the seas and oceans for sources of some industrial polymers. Researchers have demonstrated that needed raw materials are all around us, in our immediate biodiversity. They need only to be explored, refined and exploited. Several African plant gums have been shown to be comparable to imported synthetic or semi-synthetic polymers in their functionality as pharmaceutical excipients and drug carrier systems. Therefore, they may serve as cheap alternatives to their more expensive imported counterparts.

The future of the African plant gums lies in a healthy alliance between the industries and the researchers. Industries are the major consumers of research outputs. Industries will have to demonstrate their interest in the researches going on daily in the laboratories of universities and research institutes. Industries will desire to convert research-based findings into realities. Only then will the future of African plant gums, and their immense potentials, be actualized.

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