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Gums of Eastern Ghats,Visakhapatnam : Potential for Pharmaceutical Applications: An Overview

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Abstract

Andhra Pradesh being found in the focal region of the Indian sub continent has brilliant Indian plant and creature life. Its changed geography extending from the slopes of Eastern Ghats and Nallamallas to the shores of Bay of Bengal supports differed ecotypes, which thusly bolster a rich assorted variety of vegetation and fauna. Visakhapatnam is one of the locale of Andhra Pradesh with thick woods on slopes, on slope inclines and in valleys secured by the Eastern Ghats. Because of recent innovations in drug delivery systems, right now, excipients are incorporated into novel dosage forms where they directly or indirectly can impact the degree of drug release and drug absorption. Ongoing patterns towards utilization of plant based products demand the swtiching of synthetic excipients with natural ones. Today, the entire world is progressively keen on natural drugs and excipients. These natural drugs have numerous focal points over synthetic ones as they are inert chemically, nontoxic, more affordable, biodegradable, and generally accessible. Gums are one such plant inferred polymeric exacerbates that can go about as flexible excipients. Visakhapatnam agency is a center point of numerous as of late explored plant gums and this review is an endeavor to show novel gums gathered by local tribal groups. It tends to be an incredible assistance to the aspiring researchers of Visakhapatnam district.

Introduction

Visakhapatnam district is one of the North Eastern Coastal area of Andhra Pradesh and it lies between 17º – 151 and 18º - 321 Northern scope and 18º - 541 and 83º - 301 in Eastern longitudes. It is bounded on the North partly by the Orissa State and partly by Vizianagaram District, on the South by East Godavari District, on the West by Orissa State and on the East by Bay of Bengal. The locale presents 2 Geographic divisions. The piece of the land along the coast and the inside called the plains division and sloping zone of the Eastern Ghats flanking it on the North and West called the Agency Division. The Agency Division comprises of the hilly regions secured by the Eastern Ghats with a height of around 900 meters dabbed by a few pinnacles surpassing 1200 meters. Sankaram Forest square fixing with 1615 meters grasps the mandals of paderu, G. Madugula, Hukumpeta Chintapalli, G.K. Veedhi, Koyyuru, Pedabayalu, Munchingiput, Dumbriguda, Arakuvalley and Ananthgiri[1]. Visakha patnam locale is wealthy in its woods assets. The complete region under woodland spread around there is 104811.91 Ha. against the all out degree of 3, 24,965 Ha. of the division. Among these, more than 100 plants are used for their gum. But very few gums are explored for their pharmacological and pharmaceutical properties. This review is an attempt to present the updated information on gums of Visakhapatnam agency that are recently investigated as pharmaceutical excipients.

Excipients are additives used to change active pharmaceutical ingredients into suitable dosage forms for adminstration to patients[2]. New and modified excipients keep on developing with better drug delivery. Excipients of natural source are quite compelling to us for reasons of reliability, sustainiability and staying away from dependence upon materials derived from fossil fuels[3]. Natural products are in this way appealing options in contrast to synthetic items in view of biocompatibility, low lethality, eco friendlieness, and low value compared to synthetic products. Excipients from natural origin are generally inexhaustible hotspots for the feasible stock of economic pharmaceutical products. Among these, natural gums acquired from plants have various applications in drug delivery as disintegrants [4], emulsifying[5], suspending agents [6]and as binders[7]. They have additionally been found helpful in formulating immediate and extended/ sustained release preparations[8, 9].

Gums are polysaccharide hydrocolloid by products acquired as a result of abnormal metabolic reactions of plants due to an injury or unfavourable conditions by breaking down cell walls[10]. Gums acquired from natural origin either absorb water to form thick solution or water soluble[11]. Gums are effectively accessible, more affordable and furthermore utilized as excipient in pharmaceutical preparations[12]. Unforturnately some disdvantages limit the use of gums industrially [13, 14]. Fortunately this can be overcome by chemical modifications of the gums without affecting their inherent characterstics and make them effective competitors of current synthetic excipients[15].

Classifcation of Gums

Based on natural origin Gums are classifed as[10]

Marine / seaweed (algal) derived gums: Agar, carrageenans, alginates, laminarin.

Plant Derived gums:

Exudates of stem/bark: Gum Arabic, gum karaya, gum ghatti, gum tragacanth, albizia gum and khaya gum

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Seed gums: Guar gum, Locust bean gum, Starch, amylase and cellulose
Extracted gums: Pectin, Larch gum
Tubers and Roots: Konjac gum
(c) Animal derived gums: chitin and chitosan, chondroitin sulfate, and hyaluronic acid;
(d) Microbe derived gums: Xanthan, dextran, curdian, pullulan, zanflo, emulsan, Baker's yeast glycan, schizophyllan, lentinan, krestin, scleroglucan
II. Based on charge gums are classfied as[15]
Non - Ionic : Guar gum, locust bean gum, tamarind gum, xanthan gum
Anionic : gum Arabic, gum karaya, gellan gum, carragennans
III. Based on gelation behaviour gums are classfied as [15]
Cold set gels: Gellan gum, flax seed gum, gelatin
Heat set gels: Konjac
Re-entrant gels: Xyloglucan
IV. Based on shape gums are classfied as
Short branch: Xanthan gum, guar gum
Branch on branch: Gum arabic, gum tragacanth
V. Based on chemical structure gums are classfied as
Galactomannans : Fenugreek gum, guar gum, locust bean gum, tara gum, diancha gum, cassia gum
Glucomannans : Konjac
Uronic acid containing gums : Xanthan gum
Tri heteroglycans : Gellan gum
Tetra heteroglycans: Gum arabic, Psyllium seed gum
Penta heteroglycans: Gum ghatti, tragacanth
VI. Based on Regulatory status gums are classifeid as [15]
GRAS[a], CNLAI[b] : acacia gum, guar gum, gum ghatti, carob bean gum
FDA inactive ingredients, excipients in non parenteral medicine: sodium alginate, acacia, guar gum, xanthan gum

[a]Generally recognized as safe

[b]Canadian list of acceptable non-medicinal ingredients

Characterization of Gums

The purified crude gums are subjected to preliminary confirmatory tests and characerterized as per the general protocol[10].
Gums are subjected to Molisch's test and Iodine test for the presence of carbohydrates and absence of starch.
Gums are characterized as follows.
Physicochemical properties: Colour, odour, taste,shape, texture, touch, solubility, p^H swelling index, loss on drying, hygroscopic nature, angle of repose, bulk and true densities, porosity and surface tension are determined., The microbial load and presence of microbial contaminants of specific interest are also determined. As gums form viscous solutions determination of rheological properties is an important criterion in deciding their commercial application[10].
Structural: Gums are mixtures of sugars and uronic acids. Hence, confirmation of various sugars can be done by chromatographic techniques and spectroscopic techniques (TLC/ HPLC, FT-IR/MASS/NMR) [10].
Purity: Absence of other phytochemicals viz., alkaloids, glycosides, tannins,steroids, aminoacids etc confirms the purity of gums. Impurity profiling by various analytical techniques dtermines impurities present[10].
Toxicity: The acute toxicity of gums can be determined by fixed dose method as per OECD guidelines no. 425 [16].

Draw backs of Synthetic Polymers.

Synthetic polymers have a few impediments, for example, toxic, poor tolerant consistence, and significant expense. Making of such polymers may influence environment. Skin and eye irritation have been accounted for in laborers managing synthesis of polymers, for example, methyl methacrylate (MMA) and poly (MMA). Development of subcutaneous granulomas at the site of infusion by povidone was observed. There is additionally a reality that povidone may accumulate in organs ensuing to intramuscular injections.Carbomer-934P demonstrated low oral toxicity during during toxicity studies at a dose upto to 8 g/kg. Residue of carbomer additionally causes eye and respiratory tract aggravation alongside irritation of mucous membrane[17].

Benefits of Natural Gums

Renewable biopolymers, independent of fossil sources
Non- toxic, safe for oral consumption as they are derived from edible sources.
Found abundantly in nature and biodegradable.
In expensive
Ease of patient compliance.

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As Excipients for Conventional Dosage forms

Albizia Gum (L.) Benth.

The genus *Albizia* comprises of around 150 species and a large portion of them are deciduous woody trees and bushes. *Albizia* trees are known to deliver gums and have been reported as alternatives for arabic gum as natural emulsifiers in food and pharmaceutical ventures like *Albizia lebbeck* (family : Mimosaceae)gums[18]. The wide conveyance of various *Albizia* species all through the world might lead *Albizia* gums as inexhaustible and less expensive industrial gums[19]. These gums were attempted as coating materials in compression coated tablets, which debased, by the colonic microflora, in this way releasing the drug [20].

Azadiractha Gum

Also called as Neem gum. It is obtained from the trunk of *Azadirachta indica* (family: *Meliaceae*). Mannose, glucosamine, arabinose, galactose, fucose, xylose and glucose are the constituents of neem gum[21]. Studies were performed to determine the physical, compressional and binding properties of neem gum. Results demonstrated that incorporation of neem gum improved the balance between binding and disintegration properties of paracetamol tablets produced than those containing acacia gum[22].

Lannea Gum

Commonly called as Gumpena gum (GG)/ Moi gum. It is acquired by injuring the epithelial cells of mature bark of *Lannea coromandelica* (Houtt.) Merr. Trees (family: Anacardiaceae). Investigations were undertaken to evaluate gumpena gum as binder in tablet formulation and compare its binding property with a standard binder (Povidone). Results showed that gumpena gum has better binding property and can possibly be utilized as a natural binder in tablet formulation.[23]

Tamarindus Gum

Tamarind gum also known as Tamarind seed polysaccharide (TSP) is obtained from extracting eed kernels of *Tamarindus indica* (family: Fabaceae). It is a neutral xyloglucan (XG) composed of –(1,4)- D-glucan back bone with –(1,6)- D- xylose branches that are partially substituted with –(1,2)- D-galactose [24]. TSP has the ability to form high viscous solution; hence researches are keen in using TSP as binder in diclofenac tablet formulation utilizing dry granulation method[25].

Konjac Gum

Konjac gum is derived from the tuberous roots of Elephant yam i.e, *Amorphophallus konjac* (Dennst.) Nicolson. (Family: Araceae). It is high molecular weight linear glucomannan consisting of D-glucose and D-mannose units in the ratio of (1:1.6). The high molecular weight of konjac gum is responsible for the gum's high viscosity in solution making it a good thickener[26]. Consequently it is obvious that it can possibly be used as versatile excipient in pharmaceutical preparations.

Mangifera Gum

Mango gum is derived from the exudates of barks of *Mangifera indica* (Family: Anacardiaceae). Studies were conducted to elucidate the properties of mango gum as binder and it was found that mango gum showed optimum drug release when compared with standard binder[27].

Cordia Gum

Cordia gum is acquired from raw fruits of *Cordia dichotoma* (family: *Boraginaceae*) using solvent precipitation method[28] or using 1% Hydrochloric acid solution. Physicohemical characterization of gum was conducted by researchers and found that the gum has all required properties to be utilized as an excipient in pharmaceutical dosage forms[29]. Research was carried to isolate, purify and characterize *Cordia dichotoma* gum and explore its disintegration property in oral tablets. Results revealed that *C. dichotoma* fruit polysaccharide is a potential contender for use as disintegrant in the formulation of orodispersible tablets. Since *C. dichotoma* polysaccharide is inexpensive, non-toxic, compatible and easy to manufacture, it can be used in place of commercially available synthetic superdisintegrants[30].

Anacardium Gum

Cashew/ *Anacardium* gum is an exudation procured from the stem bark of *Anacardium occidentale* (Family: Anacardiaceae) Work was attempted to study the extraction and purification of cashew gum by tests to characterize its physicochemical, thermal and structural properties and to establish its use as pharmaceutical excipient. Therefore, this gum can be a promising source of raw material based on these characterization tests [31].

Investigations were done to check the suitability of cashew gum powder as a direct compression excipient and assessed dependent on SeDeM Diagram Expert System. The IGC obtained for cashew gum in the current study was 5.173, indicating its appropriateness as a direct compression excipient[32].

As Release retardants in Novel Dosage forms

Albizia Gum(L.) Benth.

ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

Floating tablets of Cefuroxime Axetil were made utilizing *Albizia* gum as polymer for controlling the drug release. The formulation containing *albizia* gum with dicalcium phosphate shows the higher swelling[33]. Formulation of gum *Albizia stipulata* (AS) natural macromolecule based as a novel pharmaceutical excipient for the controlled-release of paracetamol (PC). Gum amazingly potentiated the anticancer impact of PC in formulation after 24 h treatment by actuating apoptosis. This is the principal report on *A. stipulata* gum as a promising biopolymer for drug delivery application in malignant growth therapeutics[34]. This can be a pathway for further investigating comparable characteristics of *Albizia lebbeck* gum.

Azadiractha Gum

Recently researchers' assesed the potential application of neem gum, as an aqueous film coating material, utilising ciprofloxacin hydrchloride (drug) as a model drug. Neem gum can be a promising environmentally safe and eco-accommodating film former which can be employed for aqueous film coating of tablets, containing bitter taste or moisture sensitive drug. Moreover neem gum is an effective film former in lower concentrations (10-15% w/w) and may be a cost-effective alternative over conventional film formers[35].

Investigation has been undertaken to isolate and characterize Azadirachta indica gum's potential as a drug release modifier. Neem gum showed good flow and swelling property and forms a thick gel and can control release of drug. Hence it is proved that neem gum is suitable to use as release retardant in controlled release tablet production[36].

Lannea Gum

Gumpena gum was liked wise examined for its suitability in controlled release matrix tablets of losartan potassium. The developed matrix tablets containing different concentrations of GG demonstrated better tabletting properties and controlled release over 12 hrs[37].

Research was taken to develop gastroretentive formuation of moxifloxacin using variable amounts of GG by wet granulation method.GG showed great swelling property that contribute to sustained release and gastroretention. Consequently lannea gum must be explored as a release retardant material on commercial scale[38].

Tamarindus Gum

Tamarind seed polysaccharide can be utilized as a gelling agent for controlled release of both water soluble and insoluble drug types in various pharmaceutical preparations. Partial Cross linking of the matrix can control the release of drug for water soluble drugs. The degree of cross linking of TSP Matrix can vary the extent of drug [39].

Mangifera Gum

Research was done using *Mangifera indica* gum (MIG) as sustained release polymer in glibenclaimide matrix tablets. his investigation give some insight about the assessment of MIG as a release retardant in the formulation of sustained release matrix tablets because of its good swelling, good flow and suitability for matrix formulations. The consequences of this investigation demonstrated that MIG sustained the drug release [40].

Sustained release tablets of diclofenac sodium were fabricated using *Mangifera indica* (mango) gum, Diclofenac sodium was used as model drug. The formulated matrix tablets of diclofenac sodium using natural polymer mango gum were capable of exhibiting sustained release properties[41].

Cordia Gum

Cordia dichotoma fruit mucilage was found to have a film filming property and was employed in the formulation of transdermal film loaded with alfuzosin hydrochloride.The *in vitro* drug release study showed that a greater release of alfuzosin hydrochloride was observed with the increase of concentration of *Cordia dichotoma* mucilage in the formulation[42, 43]

Boswellia Gum

Also called as Olibanum gum, is a dried, gummy exudation obtained from *Boswellia serrate* (family: *Burseraceae*). Investigations carried out to develop colon targeted drug delivery system using gum of *Boswellia serrata* for slow and controlled release of Diclofenac sodium over a period of 24 hours was successful in retarding the drug release [44].

Current anti ulcer medications available in the market pose some adverse drug reactions which not only limite their use but also prompted the need to search for newer alteratives. Boswellia gum resin (BR) emerged as a safe, efficient, natural, and economic potential cytoprotective agent [45].

Olibanum resin was evaluated as microencapsulating agent and to prepare resin-coated microcapsules. Drug release from the resin-coated microcapsules was determined by non-fickian diffusion mechanism.

Good linear relationships were observed between wall thickness of microcapsules, release rate (K0) and T50 values. Thus, olibanum resin was found suitable as microencapsulating agent [46]

ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

Anacardium Gum

Study was conducted to formulate and evaluate sustained release tablets using cashew gum and cross-linked cashew gum as controlled release polymer. The outcomes have demonstrated an indication of the usage of natural gums as a viable option in contrast to synthetic polymers[47].

The suitability and usefulness of cashew gum (CG) as pharmaceutical excipient in dental pastes containing aceclofenac (AC) for management of pain in the periodontitis was investigated. The formulated dental pastes showed *in vitro* sustained release of AC over 6 h and also revealed good oro mucosal adhesion[48].

Limitations of Natural Gums

In spite of the advantages, the use of polysaccharides as industrially useful raw material at a enormous scale is hindered by certain downsides associated with gums like uncontrolled rate of hydration, microbial contamination, reduced viscosity on storage, pH-dependent solubility, and batch-to-batch variation [13]. In this way, researchers are presently provoked to chip away at the chemical modification of natural gums to overcome these limitations without the loss of their inherent characteristics. Modification of natural polysaccharides gives tailor-made materials fitting the many needs of drug delivery systems and in this manner can compete with the currently available synthetic excipients [15].

As Modified Gums

Tamarindus Gum

Substitution of Functional groups: It is been found that the carboxymethylation process could add carboxymethyl group in the chemical structure of crude gum. Melting point, solubility properties and viscosity of the polymer solution increased after the chemical structure modification[25]

Konjac Gum.

Chemical Cross linking: Diclofenac sodium's release rate was retarded using chitosan- oxidized konjac glucomannan polymer film. Konjac glucomannan was oxidized by sodium periodate first and later cross linked to chitosan via imine bonds to form a new co polymer. The new copolymer offered high encapsulation efficiency and helped in minimal release of diclofenac[49].

In a broad pursuit to discover novel composite material for the controlled release of drugs, modifications of konjac glucomannan like konjac glucomanan/sodium alginate (KGM/SA), KGM/SA/grapheme oxide (KGM/SA/GO) were prepared as pH sensitive hydrogels. Results indicated that KGM/SA/GO) hydrogels could be suitable polymer carrier for site specific drug delivery in the intestine[50].

Researchers additionally endeavored the formulation of oxidized konjac glucomannan (OKGM) for targeted delivery of sensitive antioxidant anthocyanins into intestine. Results revealed that the OKGM microspheres can be powerful carriers for targeted delivery of bioactive components in the intestine [51]. This encouraged researchers to evaluate the use of KGM in colon targeted drug delivery systems. Hydrogels were prepared by cross linking KGM with tri sodium trimetaphosphate. Postivie results obtained indicated the potential of phosphated KGM as potent carrier for poorly water soluble, oral colon specific drugs[52].

Mangifera Gum

Chemical Cross linking: Work was carried out to check the feasibility of mango gum polymeric nanoparticles (NPs) as a carrier for central nervous system (CNS) delivery using model drug donepezil (DZP). The NPs were prepared by modified ionic gelation method and emulsion cross-linking method. This work set up anionic mango gum as an appropriate alternative carrier of other anionic polymers for brain delivery[53].

Anacardium Gum

Graft Modification: A flocculant based on cashew gum (CG) grafted with polyacrylamide (PAM) was synthesized using potassium persulfate as the chemical initiator and ultrasound energy. The grafted copolymer CG-g-PAM-15285 obtained with 0.285 mmol of initiator showed higher hydrodynamic radius, with flocculation efficacy of 96% comparable with the flocculant Flonex-9045[54].

Azadiractha Gum

Graft Modification: The examination was started with the aim to combine acrylamide grafted neem gum polymer (AAm-g-NG), and screen its drug release retardation capacity both *in vitro* and *in vivo*. The pharmacokinetic parameters got during *in vivo* study utilizing rabbits for the prepared SR tablets were higher aside from elimination rate constant shows the similar capacity of the grafted polymer polymer to extend the drug release with the marketed formulation[55].

A part from the afore discussed gums Visakhapatnam Agency is also a rich source of other gums whose applications are very well known as pharmaceutical excipients since ages viz., *Anogeissus latifolia* (Gum Ghatti), *Sterculia urens* (Gum Karaya), *Acacia Arabica* (Gum Arabica). This review highlights recently investigated gums only. Tribes of Visakhapatnam Agency also utilize many plants gums for their pharmacological actions. These therapeutic gums can also be potent pharmaceutical excipients if they are made chemically inert.

ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

Gums as Therapeutic Agents

***Buchanania* Gum**

It is obtained from *Buchanania lanzan* Spreng. (Family: Anacardiaceae). This gum is used in the treatment of post delivery backache by the locals of Visakhapatnam agency and other medicinal purposes. Study was conducted to evaluate the phytochemicals, physic chemical properties and anti oxidant activity of *Buchanania lanzan* gum. Results revealed that the magnitude of the antioxidant activity of the gum is attribute to the presence and levels of tannins[56].

***Boswellia* Gum**

The oleo gum resin of *Boswellia serrata* is used in various traditional systems of medicine. It is useful in the treatment of various respiratory problems and gastro intestinal problems. The gum is also used in the treatment of jaundice and an astringent in the treatment of diarrhea, dysentery and hemorrhoids[57].

***Pterocarpus* Gum**

The gum is bitter with a bad
taste. However, it is antipyretic, anthelmintic and
tonic to liver, useful in all diseases of body and
styptic vulnerant and good for griping and
biliousness, opthalmiya, boils and urinary
discharges

The Kino gum is obtained from the bark of *Pterocarpus marsupium* Roxb (Family: Fabaceae). The gum is used for its antipyretic and anthelmintic properties. It is used as a liver tonic, styptic vulnerant and for biliousness and urinary discharges[58].

Conclusion

Forests of Visakhapatnam Agency are a huge fortune of plants, a significant number of which are restoratively significant and different other constitutes non timber forest products (NTFPs). Gums are one amongst NTFPs. This review is an endeavor to abridge a few gums that are as of late explored for their excipient potential in pharmaceuticals in Visakhapatnam Agency. Because of the benefits, natural gums are of prime choice for many pharmaceutical applications. Gums are initially used as excipients in various pharmaceutical preparations to improve their physicochemical characters and stability. The use of gum in novel drug delivery systems has changed the whole impression of gums and earned them a way of life as potential carrier material for sustained/ controlled drug release. The modifications of gums produced another sort of polymeric materials investigated for pharmaceutical applications, and these enlarged the extent of gums in formulation development. The feasibility of gums in the formation of polymeric nanoparticles sets up new avenues for further examinations and utilizations of natural gums in the design and development of advanced systems of drug delivery. This review can be an insight to little explored gums of Visakhapatnam agency and help the aspiring institutional researchers to further investigate the gums that are abundantly available in their locale of Visakhapatnam.

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