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AN UPDATED PERSPECTIVE OF GHATTI GUM: PRIMARILY RELEASE RETARDANT POLYMER USES IN NOVEL DRUG DELIVERY SYSTEM

Suchitra Sharma*[1], Ritesh Kumar Tiwari[2], Nita Yadav[3]

[1,2,3]Shri Ram Murti Smarak College of Engineering & Technology (Pharmacy), Bareilly, India.

***Corresponding author:** Suchitra Sharma
*Shri Ram Murti Smarak College of Engineering & Technology (Pharmacy), Bareilly, India.
Email. Id.: suchitrsharma4@gmail.com

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ABSTRACT

Background: The *Anogeissus latifolia* (*Combretaceae*, *Myrtales*) bark is used to make Ghatti gum. It is an indigenous tree gum to India. Considering its toxicity, mutagenicity, and teratogenicity, the USA regularity status regarded gum ghatti as a safe ingredient in food additives due to their bioavailability, extended accessibility, non-toxicity, and affordable pricing, plant-based gums and mucilages are the main components in many pharmaceutical formulations.

Objective: The goal of the latest study was to create and describe a new drug delivery polymer that was used to create an innovative drug delivery system. These compete with numerous polymeric materials for use as various medications in the modern days and have made tremendous progress from being an excipient to creative drug carriers.

Method: In this article we have find all the information of ghatti gum in medicines and related fields have been found in literature, research publications, and patents**.**

Result: This paper includes a thorough examination of the grafting procedure as well as developments in the novel gum ghatti medication delivery system.

Conclusion: In this study article we will provide an overview of the Gum Ghatti and discuss how it may be viewed as a viable polystyrene for creating various novel drug delivery systems.

Key words: Ghatti gum, grafting technique, characterization, recent application, research & patent.

1. INTRODUCTION:

Natural polymers are frequently employed as means of transporting the denial and release of medicament [1, 2], Natural polymers outperform artificial polymers in three critical areas, including biocompatibility, biodegradability, and accessibility. Native natural polymers containing reactive groups can interact further with additional advantageous groups [3]. The compound is given new and/or improved physical and chemical properties through this transformation [4, 5]. Indian gum, also known as gum ghatti (GG), is an organic polymer that has gained a considerable lot of attention from the culinary industry, pharmaceutical, and other sectors owing to its outstanding thickening and emulsifying qualities [6, 7]. Gum ghatti has been hypothesized to be an amorphous, transparent secretion of the *Anogeissus latifolia* tree, a big, mature deciduous tree common in desert regions. D-mannose, D-galactose, L-arabinose, and D-glucuronic acid are combined to create this complex non-starch polymer [6]. *Latifolia* is a component in various Ayurvedic compositions. Ayaskrti, an Ayurvedic preparation, contains the stem bark of *Anogeissus latifolia* [8].A spray-dried powder is made from carefully chosen, top-quality Ghatti gum. Its colour is permanent and it is very soluble [9], due to their biodegradability, sustainability, and safety, polysaccharide gums are among the most frequently used raw materials in industry. They have also been the subject of much research when compared to analogous synthetic materials [10], due to its high accessibility and patient compliance, oral medication delivery is a favoured method of drug administration [11].Gum ghatti was invented circa 1900 as a replacement for gum Arabic. Several investigations, however, have revealed its poor quality due to variations in solubility and viscosity, and as a result, It has never been proven to be a substantial tree gum [12]. Additionally, there are a number of disadvantages to taking medications orally, such as the fact that many therapeutic medicines are substantially pre-systemically removed by gastrointestinal breakdown or first pass hepatic metabolism [13]. Reduced therapeutic effect and shorter therapeutic activity periods are the results and toxic or inactive metabolites are also produced [14, 15, 16]. In this study article we will provide all the information related to the Gum ghatti and discuss how it may be used for creating various novel drug delivery systems.

2. GUM GHATTI GRAFTING TECHNIQUES

Grafting is a kind of plant development in which one plant part (scion) is attached to other plant part (rootstock) so that another part can develop together and generate a new plant [17]. In the process of grafting, a parent polymer is used as a support structure to which branches of a second polymer are attached at various locations. The covalent bonding of monomers to the polymer chain is what is meant by the term "Polymer grafting." Sulfonation, phosphorylation, carboxymethylation, and acetylation are examples of polymer grafting processes that enhance the polymer functional characteristics [18, 19].

2.1. Making Thiolated Gum Ghatti

The 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (50 mm) and thioglycolic acid were added after the pure Ghatti gum (2 gm) had been dissolved in 50 ml of demonized H_2O (4 gm). Three hours were spent at a moderate temperature without touching the reaction mixture indicated before. Additionally, Dialysis was performed on the reaction solution for two hours over 5 mm of HCl that contained 1% sodium chloride, At room temperature, two hours were spent testing 1 mm HCl containing 1% NaCl, and 60 minutes were spent testing 5 mm Hydrochloric containing 1% sodium chloride. Following that, the reaction mixture was collected, stored at +4°C, and sealed at 30°C at 10.01 mbar pressure [20, 21].

S.no	Author name	Graft polymer	Application
1.	Alhakamy NA *et al.,* [22]	Xanthan gum	He has prepared mucoadhesive Tablets for Repaglinide
2.	Brar V*et al.,* [23]	Okra gum	He has work on preparation and optimisation as intranasal drug delivery agents

Table 1. Grafting of Thiolated Gum

2.2 Manufacturing of sodium Carboxymethyl ghatti

A specified amount of gum ghatti (500 mg) was completely blended with a little amount of water for the modification over the course of an hour using a magnetic stirrer. The solution of sodium hydroxide (55.59% w/v) was produced by break down 5.559 g of weighed NaOH in 10 millilitres of water. 5 ml of monochloroacetic acid were created by combining 2.259 g of monochloroacetic acid in 5 ml of water. The earlier created Ghatti gum solution was then combined with 2.72 ml of the freezing NaOH solution, and it was agitated for sixty minutes with a glass rod. 1.36 mL of monochloroacetic solution of acid was included and the resulting mixture was stirred in a glass for 60 minutes shown in Table 2 [24].

S.no	Author name	Graft Polymer	Application
1	Seeli DS *et al*., [25]	Guar gum	As a controlled medicine administration system for the colon, hydrogel is graft-polymethacrylic acid (methacrylic acid).
2.	P. More M *et al*., [26]	Gellan gum	Potential development of a novel mucoadhesive polymer is novel carboxymethyl-gellan gum.

Table 2. Grafting of sodium Carboxymethyl

2.3 Making grafted ghatti gum from poly (methyl methacrylate)

Ghatti gum was cooked for 30 minutes after being combined with 50 mm of double-distilled water. To initiate the polymerization process, which was carried out at 80^0C for one hour, MMA and CAN were added in exact amounts to the Ghatti gum aqueous solution. The resultant liquid was brought to room temperature, added to extra methanol, and let to sit for the night. The resultant copolymer was filtered; the methanol rinsed out of it, and it was then dried for 12 hours at 55 ºC in a hot air oven. Alkaline hydrolysis was performed on the prepared GG-g-PMMA copolymer using a 1 M NaOH solution while mixing for an hour at 75^0C. The hydrolyzed copolymer was continuously washed with methanol before drying in a warm air oven at 55^0C [27]. Some of gum grafted by this method is shown in Table 3.

S.no	Author name	Graft Polymer	Application
1.	Shahid M *et al*., [28]	Guar gum	Colonic drug administration via microwave-assisted graft deprotonation of guar gum and acryl amide.
2.	Maji B *et al*., [29]	Xanthan gum	Customized Features and Potential Uses for Drug Delivery and Wastewater Treatment.

Table 3. Grafting from poly (methyl methacrylate)

3. PHYSICAL AND CHEMICAL CHARACTERIZATION

3.1. Preparation of Gum solution

The water-soluble gum was initially dissolved into 100 ml of water to produce the water-soluble lyophilized powder that would be utilised to create the gum solution (1% w/v) throughout the synthesis phases. After that, the solution was heated overnight at 40 °C while being regularly agitated [30].

3.2. Fractionation of the Gum Ghatti

Four fractions of Gum ghatti were produced using ethanol precipitation that happened gradually. In 200 ml of distilled water, 30 g of Gum ghatti was dissolved, and the resulting solution was spun down at 20^0C for 30 minutes at 11,000 rpm. The residual product was gathered for further fractionation. Alcohol was gradually append to the supernatant and kept below a continual stir ring at room temperature (25^0C) in order to reach the ethanol level of 50% (w/v). Centrifugation was used to remove the precipitate after keeping the solution at 4^0C to promote aggregation (11,000 rpm, 30 min multiply by 2, 22^0C). This fraction was air-dried in an air-tight chamber for five hours at 80°C after the sediment was combined with 100% isopropyl alcohol. By gradually increasing the ethanol concentration (F65: 65%, F80: 80%), a final alcoholic level of 80% was attained. Prior to being dried and labelled, the final supernatant underwent concentration [31].

3.3. Molecular characterisation of Gum Ghatti

By applying high performance size exclusion chromatography (HPSEC), the molecular mass and distribution of Gum ghatti and its four constituents were measured. The portable stage was used for the calculations and flowed at 0.6 ml/min with 0.03 percent (w/w) NaN3 at 50 mM NaNO3 (pH 5.8). The molecular weight and multiplication of standards such as were determined using a refractive index monitor. The polysaccharide pulullan, which has an Mw range. To ensure replication, each sample received two injections, and both columns were kept at 40 ^{o}C [31].

3.4. Analytical Techniques

3.4.1. Chemical and monosaccharides analyses of Gum ghatti

On a NA2100 Nitrogen and Protein Analyzer, the detected nitrogen was multiplied by 4 to get the protein concentration. The Association of Official Analytical Collaboration procedures were used to analyze the ash and moisture [32]. Using arabinose and galactose (1.6:1) and the interaction of sweeteners with alcohol in an acidic atmosphere served as a guide to assess the total sugar content of organic Ghatti gum [33]. Using the m-hydroxydiphenyl test method, the total amount of uronic acid was calorimetrically measured with galacturonic acid acting as the control [34].

3.4.2. FT-IR spectroscopic technique of Gum ghatti

Prior to the FT-IR analysis, the four fractions of the Ghatti gum sample were vacuum desiccated and dried. Five different compounds' Fourier transform infrared spectra were obtained using a FTS 7000 FT-IR spectrophotometer equipped with a DTGS detection system and a Golden Gate Diamonds single reflectance ATR. Spectra were created by doing 128 co-added scanning in the tMe absorption mode from 4000 to 800 cm1 at a resolution of 4 C. Two copies of each specimen spectra were made [31].

3.4.3. Methylation analysis of Gum ghatti

Deuterium oxide (D_2O) was used to dissolve and reproduce four 5 mg Gum ghatti samples (2 ml). The solution received 50 mg of 1-cyclohexyl-3- (2-morpholinoethyl)-carboiimidemethyl-p-toluenesulfonate while the pH was kept at 4.75 with 0.1 mol/L HCl in D2O. Add 5 ml of sodium borodeuteride (160 mg/ml) over the course of 0.5 hours, the solution was stirred for an hour. The pH of the opinion mixture was kept at 7.0 by including 2.0 mol/L of HCl in D_2O during the reduction process. After adding sodium borodeuteride, the reaction was continuously stirred at pH 7.0 for 0.5 hours. The solution pH was subsequently increased to 4.0. The decreased carbohydrate was lyophilized, and salts were removed before the decreased carbohydrate was recovered by hemodialysis over distilled water for a long duration at 25^0C (3500 Da molecular weight cutoff). 0.5 mL of 10% acetic acid-containing alcoholic was adding until the polysaccharide had been thoroughly redissolved. The combination was dried in a nitrogen airflow in order to get rid of the boric acid. The resulting solution was incorporated into 0.5 ml of 10% acetic acid in alcohol, which was then evaporated while nitrogen was being pumped through it [31].

3.5.4. NMR techniques

The spectrometer was used to record the 1H and 13C NMR spectra at 25^0C (35). Deuterium oxide was used to dissolve gum ghatti prior to NMR examination.

3.4. Rheological characteristics of Gum ghatti

Every rheological property was evaluated using a strain-controlled rheometer. The parallel plates were 50 mm in diameter and 1.0 mm apart. For two hours at room temperature, ghatti gum was immersed in purified water and vigorously stirred to examine how concentration affects rheological properties. Four 5% (w/v) fractions were made using the same method (F50, F65, F80, and FS). To avoid solvent evaporation during measurements, the sample received a little covering of a viscous mineral oil. The materials were placed into a rheometer at 25 ^{o}C [31].

3.5. Surface tension

The air-gum dispersal barrier friction coefficient was calculated using the Fisher Surface Tensiomat model 21 and the Du Nouy rings technique. In addition to measuring the force on the ring as it was elevated off an air-gum dispersion surface, 50 mL glass beakers were filled with sample liquids at concentrations (w/w) of 0.01%, 0.05%, 0.10%, 0.25%, 0.50%, 1.00%, and 1.50%. Throughout the course of two hours at 22 ^{0}C, variations in surface strain were observed at regular intervals. We conducted many runs of each test [31].

4. ADVANCEMENT IN NEW DRUGS DELIVERY

According to a survey of the literature on Ghatti gum uses, the following classes of dosage forms have made substantial use of it.

4.1. Hepatoprotective and antioxidant action

Anogeissus latifolia plant extracts were found to have moderate to good antioxidant properties [36]. The hydro-alcoholic extract of Ghatti gum was tested for its hepatoprotective activities in vitro and in animals. Its antioxidant capabilities are determined by the content of flavonoids and polyphenols [37]. Gallic acid is also contained in the medicine. The considerable levels of quercetin, rutin, and gallic acid contained support the abstraction's significant antioxidant activity and associated hepatoprotective potential, due to their capacity to prevent the production of free radicals, the

oxidation of lipids, and oxidation DNA damage, rutin and quercetin are viewed as prospective therapeutic agents [38].

4. 2. Antimicrobial and antiulcer activity

It has been studied for potential use as an ulcer treatment. *Anogeissus latifolia* hydroalcoholic extract has shown promise for gastroprotective effectiveness; the mechanism is thought to be created by a decrease in LPO and SOD with a concurrent rise in catalase activity [39]. Because gallic acid, ellagic acid, and its derivative are present in sufficient amounts in leaf extracts and volatile oils, they have a mild antibacterial and antifungal action.

4.3. Wound healing process

It looked at how well *Anogeissus latifolia* extracts could heal wounds and discovered that there was a shortening of the epithelization period as well as a noticeable reduction in scar area, which promotes the use of ghatti gum for a variety of skin diseases like ulcers, boils, and itching in Indian conventional healthcare systems [40].

4. 4. Antineoplastic action

A model earthworm was used to evaluate several barks and leaf extracts of *Anogeissus latifolia* for their anthelmintiic properties. Each extract has varying degrees of moderate to significant anthelmintiic action. Both the bark extract in chloroform and the leaf extract in pet ether showed substantial anthelmintiic action [41].

4. 5. Emulsifying substance

Gum ghatti is considered to be superior to gum Arabic because of its different molecular components, which seem to be effective emulsifiers and attach to oil [42]. A US patent illustrated how it may be used to create an oil-in-water emulsion. Natural gums with molecular weights equivalent to or greater than that of gum ghatti, for example, may be used to emulsify oil-in-water emulsions and acid-stable wax emulsions at a cheaper cost. However, due to the gum's high solution viscosity, In stabilizing thick pharmaceutical formulations, it performs well., such as those used to create oil-soluble, stable vitamins that are then ground into powder [43]. Gum ghatti is used as an intermediate agent in the formulation of aquatic resole dispersions, according to another US patent. The innovation expands the usage of these dispersions in their ultimate applications as coatings and adhesives. It illustrates the use and efficacies of gum ghatti in the manufacturing of highly evenly tiny phenolics resole particles. In addition, gum ghatti is said to have served specialised purposes as an emulsifier, stabiliser, and flavour fixative in beverages, oil, table sweeteners, petrochemical waxes, and non-petroleum waxes [43].

4. 6. Excipient in solid dosage form

Researchers have long been intrigued by natural gums and polysaccharides due to their capacity to produce solid dosage forms such as tablets. Because of its GRAS accreditation, Gum ghatti is no exception. After researching several gums and their derivatives for their pharmacological uses (tablet binder), it was revealed that gum ghatti might be employed as an efficient excipient. In a different experiment, the possibility of gum ghatti as an innovative release modifier for the zero-order distribution of diltiazem hydrochloride in 3-layered matrix formulation was explored [44].

4. 7. Hydrogels

Ghatti gum having the reaction of the network elongating behaviour, network makeup, permeation, or stiffness to various stimuli, both internally and externally, superabsorbent, intelligent, and wise hydrogels are utilised to build sensitive drug delivery systems. Free radical initiators fell in the synthetic polymer-based hydrogel as cationic charges and ionic strength increased in one of these hydrogel systems, which was made by copolymerizing acrylamide and acrylonitrile with gum ghatti [44].

4. 8. Miscellaneous

The lack of usage of plant polysaccharides like gum Arabic, gum karaya, gum ghatti, or fucoidan by any of the examined strains suggests that the bacteroids under investigation had varying levels of proficiency. Additionally, it was investigated how 21 distinct complex polysaccharides might be fermented by 154 *Bifidobacterium, Peptostreptococcus, Lactobacillus*, *Ruminococcus*, *Coprococcus*, and *Fusobacterium* strains from 22 different species [45]. Studies using Rear III and EcoRI showed that acidified glycan have a significant inhibitory impact on DNA restrictions, such as gum ghatti, carageenan, and pectins, were strongly inhibitory, even at modest fixations. The bacteria in the human colon that digest mucus and plant polysaccharides (dietary fibres) [46] strains was thoroughly explored [45]. Ghatti gum-immunized mice produced antibodies that were only reactive with 1,6-linked d-galactoses [(46)]. Ghatti gum has also been demonstrated to be beneficial in powdered explosives to increase water resistance, as a penetrating mud conditioner, as an acidifying specialist for oil wells, and as a fastener in long fibered, thin papers [43].

5. APPLICATIONS AND FUNCTIONS OF GUM GHATTI IN THE INDUSTRY [47] some important application of Ghatti gum shown in table 4.

S. No.	Applications	Functions
1.	Emulsifier for carbonate drinks	Stabilizers water and oil emulsion
2.	Flavours (Powdered)	Encapsulation of oil entrapment
3.	Beverages (Powdered)	Encapsulation of flavour
4.	Chewing gum	Flavour and water retention softening
5.	Gum drops	Independent gelling of sugar
6.	Sweets	Source of fibre
7.	Coated sweets	Coating film forming and glazing
8.	Caramels	Improves chewability
9.	Printing	Film forming
10.	Hair fixers	Binding agent
11.	Wine	Colloidal stabilization and tannin suspension
12.	Powdered medicines	Encapsulation and oil entrapment
13.	Cigarette industry	Adhesive for sticking paper

Table 4. Pharmaceutical application of Ghatti gum

6. RECENT STUDIES AND PATENTS SHOW THAT GHATTI GUM HAS A VARIETY OF USES

Numerous uses of Ghatti gum in medicines and related fields have been documented in literature, research publications, and patents shown in Table 5 and Table 6-

S. no.	Author name	Methods name	Drug / polymer	Result
1.	Sharma K *et al*., [48]	Free radical polymerization process	Amoxicillin trihydrate, paracetamol/Gum ghatti, Ammonium peroxydisulfate, N,N0-methylene-bisacrylamide, aniline, hydrochloric acid	The research has shown that crosslinker hydrogels may offer a promising alternative for colon-specific pH when initial quick release of the medication is desired, followed by prolonged absorption.
2.	Verma A Moin A. *et al*., [49]	Ionotropic gelation process	Diclofenac sodium/Deacetylated Gellan Gum, Chitosan, Gum karaya, Gum ghatti	This clearly shows how Chitosan-Gellan Gum ghatti and Gum Karaya PEC globules could be used as multi-unit polymers transporter frameworks for the delayed administration of medications that irritate the gastrointestinal tract.
3.	Moin A , *et al*., [50]	Microwave-assisted copolymerization method	Diclofenac sodium / Ghatti gum, Ceric ammonium nitrate, Polyacrylamide, Acetone	When the pH of the solvent medium was raised, the discharge of Diclofenac sodium from the microbeads enhanced instead of decreased in an acidic medium. It was shown that the majority of the medication, or around 90%, is released in the colon's pH range.
4.	Ray S *et al*., [51]	Ionotropic gelation method	Ropinirole Hydrochloride/ Gum ghatti, Ethanol, Sodium hydroxide, Monochloro acetic acid	The findings gave strong evidence that NaCMGG is as effective as, if not more successful than, known biopolymers at drug retardation.
5.	Gurpreetarora null *et al*., [52]	Direct compression technology	Domperidone / HPMC K 15M, Vivapur-102, Ghatti gum, Talc and magnesium stearate	The mucoadhesive polymers gum ghatti and HPMC K 15M work better together than alone to provide the optimal stomach retention and medicine release profile. Ghatti, a natural polymer gum, may be utilised as a binder, release retardant, and mucoadhesive in medicine.
6.	Bhosale RR *et a*l., [24]	Free radical polymerization technique	Metformin hydrochloride/ Ghatti gum, Ceric ammonium nitrate, Methyl methacrylate, Chitosan, Hypromellose, MCC, Talc.	GG-g-PMMA pellets were used in in vitro drug release tests, which revealed a pH-sensitive long-lasting release of the medication. Histological analyses and acute oral toxicity tests further demonstrated the biocompatibility and safety of the grafted gum.

Table 5. Latest research article shown uses of ghatti gum in novel drug delivery

PATENTS:

S. No.	Application no.	Title	Year
1.	US8680161B2	Designs comprising gum ghatti and fat-soluble active components	2014
2.	EP3521320A1	Low molecular gum ghatti	2017
3.	US3362833A	Table syrup emulsion containing gum ghatti Classifications	1968

Table 6. Recent patents are published related to ghatti gum.

CONCLUSION:

The Ghatti gum is a natural polymer which can be use in novel drug delivery system. It is nontoxic, biodegradable and also economical. The ghatti gum shows the compatibility with various synthetic polymers, it shows that it can be use in a wide variety of delivery system and polymeric matrix systems also the ghatti gum is having some medicinal properties due to this it will give the synergistic effect with the drug and also increase its potency, after reading this review, it is clear that plant-based polymer gum ghatti can be employed as a mucoadhesive, releasing retardant, and binding agents for medicinal applications. This conclusion is supported by recent research and patents.

ABBREVIATIONS

NMR: Nuclear magnetic Resonance, ATR: Attenuated Total Reflection, HCl: Hydrochloric acid, ^{O}C: Degree Celsius, GRAS: Generally Recognized as Safe, DTGS: Deuterated triglycine sulfate, pH: potential of Hydrogen, AOAC: Association of Official Analytical Collaboration.

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