Evaluation and characterization of carboxymethylated Gum odina : A novel approach towards newer drug delivery system

Thesis submitted in partial fulfillment for the requirement of the

Degree of Master of Pharmacy

By

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Class Roll No: 002211402028

Examination Roll No: M4PHL24002

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CERTIFICATE OF APPROVAL

This is to certify that the thesis entitled "**Evaluation and characterization of carboxymethylated Gum odina : A novel approach towards newer drug delivery system**" submitted to Jadavpur University, Kolkata for the partial fulfillment of the Master Degree in Pharmacy, is a faithful record of bona fide and original research work carried out by Mr. Ankit Tiwari bearing Class Roll no. 002211402028 and Registration no. 163670 of 2022-2024 under my supervision and guidance.

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Declaration of the Originality and Compliance of Academic Ethics

I, Ankit Tiwari, a student of M.Pharm, 2nd year, bearing Roll No: 002211402028, Registration no. of 2022-2024 studying in Department of Pharmaceutical Technology, Jadavpur University, Kolkata-32, hereby declare that my thesis work titled – "**Evaluation and characterization of carboxymethylated Gum odina : A novel approach towards newer drug delivery system**", is original and presented in accordance with academic rules and ethical conduct and no part of this project work has been submitted for any other degree of mine. All the information and works are true to the best of my sense and knowledge.

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ACKNOWLEDGEMENT

I deem it to be a privilege to work under the guidance of Prof. (Dr.) Amalesh Samanta, Division of Microbiology& Biotechnology, Jadavpur University on the very current and innovative topic "**Evaluation and characterization of carboxymethylated Gum odina : A novel approach towards newer drug delivery system**." I am blessed to work under his constructive and suggestive guidance throughout my work. His expert supervision with undue patience throughout my work at every stage helped me complete this work effortlessly.

I also express my sincere gratitude to our H.O.D., Department of Pharmaceutical Technology, Jadavpur University, Prof. (Dr.) Amalesh Samanta for providing me an opportunity to do my thesis work successfully.

I am grateful to All India Council for Technical Education (AICTE), Government of India for providing financial support and also thankful to University Potential for Excellency, Phase – II, and University Grant Commission for providing instrumental support.

I express my heartfelt gratitude to Ph.D. scholars – Abhishek Mohanta, Sohini Chatterjee, Mousumi Tudu, Ahana Hazra, Pankaj Paul; my classmate:- Khubaib Akhtar khan, kaushiki Priya, Ahsaan Ansari, and Riya Hazra.

I also thank my friends and all others who have extended their cooperation and helped me immensely during the entire project work.

I will remain forever grateful to The Almighty and my parents, whose dedication and untiring efforts towards me has brought me at this stage of life.

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LIST OF ABBREVIATION

Symbols	Abbreviations
MCA	Monochloroacetic acid
NaCl	Sodium Chloride
PBS	Phosphate Buffer Solution
FTIR	Fourier Transformed Infrared
DSC	Differential scanning calorimeter
XRD	X-Ray Diffraction
SEM	Scanning Electron Microscope
%	Percentage
gm	Gram
mg	Miligram
hrs	Hours
t	Time
CMGO	Carboxymethylated Gum Odina
DS	Degree of substitution
GO	Gum Odina
CMC	Carboxymethyl cellulose
PEEK	Poly-etheretherketone
PVC	Poly-vinyl chloride
PP	Poly-propylene
PE	Poly-ethylene

INTRODUCTION

1. INTRODUCTION: -

Carboxymethylation of the gum increases the lipophobicity and clarity of the solution, making it more soluble in aqueous systems (1) Modification of chemical structure of drug is possible with the help of carboxymethylation. Carboxymethyl gum has the advantage of higher intrinsic viscosity and water solubility (%) than natural gum. Carboxymethylation is of interest as a derivatization process that has already been successfully used in various polysaccharide gums. Carboxymethylation increases the aqueous solubility of polysaccharides and decrease viscosity and thereby increases the diffusion of monomer and free-radical initiator in the polysaccharide mass during grafting reaction and promotes the reactivity. But at the same time, carboxymethylation of natural gums suffers from premature erosion in gastro-intestinal fluid, which limits their application in sustained-release for longer period (2) The carboxymethylation of seed gum is an esterified gum. The hydroxyl group of the gum molecule is esterified with a carboxymethyl group. Gum reacts with sodium Monochloroacetate in the presence of sodium hydroxide. In the main reaction, sodium hydroxide first reacts with the hydroxyl group of the resin to form an alkoxide group (Equation 1). In the second step, the glucose units in the gum molecule are esterified with carboxymethyl groups (Equation 2). Side reactions occur both in the liquid mass and in the resin phase, forming sodium glycolate from monochloroacetic acid and sodium hydroxide (Eq. 3)

$$\text{Gum-OH} + \text{NaOH} \longrightarrow \text{Gum-ONa} + H_2O\ldots \quad (1)$$

$$\text{Gum-ONa} + ClCH_2COONa \longrightarrow \text{Gum-O}CH_2COONa + NaCl \quad (2)$$

$NaOH + ClCH_2COONa \longrightarrow OCH_2COONa + NaCl$ (3)

Carboxymethylated gum from plant seeds showed no cytotoxic activity at concentrations below 0.5 mg/mL (4)

Over the last two decades, the natural and modified polysaccharides have been extensively studied as pharmaceutical excipients as well as for their prospective applications in drug delivery and biomedical engineering. Biomimetic and intelligent drug delivery methods, tissue engineering scaffolds, and nanotheranostic materials have all received more attention. In nature, higher plants typically include polysaccharide hydrocolloids such as mucilage, gums, and glucans. Because of their structurally diversified class of biological macromolecules with a wide range of physicochemical properties, these polysaccharide hydrocolloids have found widespread use in pharmacy and medicine [1]. Diverse properties of "Natural Gums" have made them quite useful for various pharmaceutical applications. They are utilized as binding and disintegrating agents in solid dosage forms. They are also utilized as stabilizing, thickening and suspending agents in oral, liquid and topical formulations. Since natural gums are non-toxic, cheaper and easily available, they are more preferred over synthetic materials. In the form of per-oral drug delivery carriers food additives or per-oral drug delivery carriers, the consumption of most of the natural gums has been recognized as safe [2–5]. Natural gums also suffer from various disadvantages including uncontrolled rate of hydration, susceptible to enzymatic degradation, thickening, and drop in viscosity on storage, and microbial contamination, which limits their application in controlled drug delivery [6]. In order to make them suitable for designing specific drug delivery systems, these drawbacks need to be overcome. The polysaccharides possess a number of functional groups amenable for chemical modification or conjugation with other materials. Thus, the structural modifications open up the possibility of obtaining some desirable

physicochemical properties for the design of drug delivery carriers and tissue engineering scaffolds [7]. The non-ionic polysaccharides can be imparted ionic characteristics via suitable chemical modifications of their existing functional groups. Carboxymethylation represents such a process through which anionic O-carboxymethyl groups can be introduced into native polysaccharides under alkaline conditions with desirable physicochemical properties. The degree of carboxymethylation depends upon the molecular weight, procedures for chemical modification, availability and relative chemical reactivity of hydroxyl groups in the structure of native polysaccharides [8,9]. The physicochemical property, in particular gelling behavior of modified gums also differs with the variation in degree of substitution of carboxymethyl groups. Another important feature is that organic solvents are not required for the fabrication of drug delivery carriers. Thus, in the years to come there is going to be continued interest in the natural gums and their modifications [3,10]. The biological activity of various carboxymethylated polysaccharides has been reviewed by Chakka and Zhou [9]. However, till date no review is reported on the techniques of carboxymethylation of gums and their applications in drug delivery and other biomedical fields.

1.1 HISTORY OF POLYMER:-

The word “polymer” was introduced by the Swedish chemist J. J. Berzelius. He considered, for example, benzene (C_6H_6) to be a polymer of ethyne (C_2H_2). Later this definition underwent a subtle modification. Polymer science is a relatively new discipline which deals with plastics, natural and synthetic fibers, rubbers, coatings, adhesives, sealants, etc.; all of these materials nowadays have become very common. The concept of polymers is one of the great ideas of the 20^{th}

century. It emerged in the 1920s amid prolonged controversy and its acceptance is closely associated with the name of H. Staudinger who received the Nobel Prize in 1953(11). Many examples of synthetic polymers can be mentioned; some everyday, like polyesters or nylons, others less known, like the ones used for medical applications for organs, degradable sutures, etc (12)

On the basis of economic and application considerations plastic materials can be divided in commodity (characterized by high volume and low cost) and engineering plastics (higher cost and low volume). In the first group are considered polyethylene (PE), polypropylene (PP), poly(vinyl chloride) (PVC) and in the second polycarbonate (PC), poly(etheretherketone) (PEEK), polyimide (PI), etc. Fibers, natural, artificial (modified natural) and synthetic, are characterized by high aspect ratio, high strength and modulus and other properties depending on their applications. Elastomers exhibit the ability to stretch and retract rapidly (13)

1.2 POLYMER IN PHARMACEUTICAL APPLICATION :-

A. Water-Soluble Synthetic Polymers.

1) Poly (acrylic acid) Cosmetic, pharmaceuticals, immobilization of cationic drugs, base for Carbopol polymers
2) Poly (ethylene oxide) Coagulant, flocculent, very high molecular-weight up to a few millions, swelling agent.
3) Poly (ethylene glycol) Mw <10,000; liquid (Mw <1000) and wax (Mw > 1000), plasticizer, base for suppositories.

4) Poly (vinyl pyrrolidone) Used to make betadine (iodine complex of PVP) with less toxic.
5) Poly (vinly alcohol) water soluble packaging, tablet binder, tablet coating.

B. Cellulose base polymer.

1) Ethyl cellulose Insoluble but dispersible in water, aqueous coating system for sustained release applications.
2) Carboxymethyl cellulose Super disintegrate, emulsion stabilizer.
3) Hydroxyethyl and hydroxypropyl celluloses Soluble in water and in alco hol for tablet coating.
4) Hydroxypropyl methyl cellulose Binder for tablet matrix and tablet coati ng, gelatin alternative as capsule material.
5) Cellulose acetate phthalate enteric coating.

C. Hydrocolloids.

1) Alginic acid Oral and topical pharmaceutical products; thickening and su spending agent in a variety of pastes, creams, and gels, as well as a stabili zing agent for oil-in-water emulsions; binder and disintegrants.
2) Carrageenan Modified release, viscosifier.
3) Chitosan Cosmetics and controlled drug delivery applications, mucoadhe sive dosage forms, rapid release dosage forms.

D. Water-Insoluble Biodegradable Polymers.

1) (Lactide-co-glycolide) polymers nanoparticle for protein delivery.

E. Starch-Based Polymers.

1) Starch Glidant, a diluent in tablets and capsules, a disintegrant in tablets a nd capsules, a tablet binder.
2) Sodium starch glycolate super disintegrant for tablets and capsules in oral delivery.

F. Plastics and Rubbers.

1) Polyurethane Transdermal patch backing, blood pump, artificial heart, an d vascular grafts, foam in biomedical and industrial products.
2) Polyisobutylene Pressure sensitive adhesives for transdermal deliver.
3) Polycyanoacrylate Biodegradable tissue adhesives in surgery, a drug carri er in nano- and microparticles.
4) Poly (vinyl acetate) Binder for chewing gum.
5) Poly (vinyl chloride) Blood bag, and tubing.
6) Polyethylene Transdermal patch backing for drug in adhesive design, wra p, packaging, containers.
7) Poly (methyl methacrylate) Hard contact lenses.
8) Poly (hydroxyethyl methacrylate) Soft contact lenses. (14-16)

1.3 CLASSIFICATION OF POLYMER :-

A. Basis on interaction with water.

1. Non-biodegradable hydrophobic Polymers :- e.g. Polyvinyl chloride,
2. Soluble Polymers :- e.g. HPMC, PEG
3. Hydro gels :- e.g. Polyvinyl pyrrolidine

B. Based on polymerization method.

1. Addition Polymers :- e.g. Alkane Polymers
2. Condensation polymers :- e.g. Polysterene and Polyamide

C. Based on polymerization mechanism.

1. Chain Polymerization
2. Step growth Polymerization

D. Based on chemical structure.

1. Activated C-C Polymer
2. Inorganic polymers
3. Natural polymers

E. Based on occurrence.

1. Natural polymers:- e.g. 1. Proteins-
   collagen, keratin, albumin, cellulose
2. Synthetic polymers :- e.g. Polyesters, polyamides

F. Based on bio-stability.

1. Bio-degradable
2. Non Bio-degradable (17-20)

1.4 Characteristics of an ideal polymer :-

1. It should be versatile and possess a wide range of mechanical, physical, che mical properties.
2. It should be Non-toxic and have good mechanical strength and should be easily administered.
3. It should be inexpensive and easy to fabricate.
4. It should be inert to host tissue and compatible with environment (21-22)

1.5 Criteria followed in polymer selection :-

1. The polymer should be soluble and easy to synthesis.
2. It should have finite molecular weight.
3. It should be compatible with biological environment.
4. It should be biodegradable.
5. It should provide good drug polymer linkage. (23-24)

1.6 OVERVIEW OF GUM ODINA:-

Gum odina, also known as Odina gum or resins from the genus Odina, is an important natural product. This overview provides detailed information about its botanical characteristics, chemical composition, extraction methods, traditional and modern uses, as well as its economic significance (25)

1.6.1 Botanical Characteristics:-

- **Description and Distribution**

Odina belongs to the family *Anacardiaceae*, which includes several economically significant species. The most commonly known species for gum production is *Odina wodier*. This deciduous tree is native to tropical regions of South Asia, particularly India and Sri Lanka.

a. Formation of natural gum from Gum odina tree, **b.** Pictures of Gum odina tree, **c.** leaf of Gum odina tree.

- **Morphology**

The tree typically grows to a height of 10-15 meters with a trunk diameter of 30-60 cm. The bark is smooth and grayish-brown. The leaves are pinnate, with leaflets that are ovate to lanceolate. The tree produces small, yellowish-green flowers in panicles, which eventually give rise to small, drupaceous fruit (26)

1.6.2 Chemical Composition:-

- **Resin Composition**

The gum or resin extracted from Odina species is a complex mixture of various organic compounds. The primary constituents include:

- Polysaccharides: These are large carbohydrate molecules that form the backbone of the gum's structure.
- Tannins: Contributing to the astringency of the gum, tannins are polyphenolic compounds with antioxidant properties.
- Essential Oils: Volatile compounds that provide the characteristic aroma and therapeutic properties.
- Resin Acids: These contribute to the gum viscosity and adhesive properties (27)

- **Bioactive Compounds**

Research has identified several bioactive compounds in Odina gum, including flavonoids, triterpenoids, and saponins. These compounds are responsible for the

gum's medicinal properties, such as anti-inflammatory, antimicrobial, and antioxidant effects (28)

1.6.3 Extraction Methods:-

- **Traditional Techniques**

Traditionally, the gum is collected by making incisions in the bark of the tree. The exuded resin is then collected, cleaned, and dried. This method is labor-intensive and yields varying quantities of gum depending on the tree's age, health, and environmental conditions.

- **Modern Techniques**

Modern extraction methods involve the use of solvents or steam distillation to obtain a purer product. Solvent extraction is particularly effective in isolating specific bioactive compounds. Additionally, advances in biotechnology have enabled the use of cell cultures to produce gum in a controlled environment, enhancing yield and consistency (29)

1.6.4 Traditional and Modern Uses:-

- **Traditional Uses**

In traditional medicine, particularly in Ayurveda and Siddha practices, Odina gum has been used for centuries. Some of its applications include:

- Digestive Aid: The gum is used to treat dyspepsia and other digestive disorders.

- Wound Healing: Due to its antimicrobial properties, it is applied to wounds and cuts.
- Anti-inflammatory Agent: Used in the treatment of arthritis and other inflammatory conditions.
- Incense and Rituals: The aromatic properties of the gum make it a popular choice for use in religious ceremonies and as incense (30)

➢ **Modern Uses**

With growing interest in natural and organic products, Odina gum has found applications in various industries:

- Pharmaceuticals: Used as a natural excipient in drug formulations, enhancing the bioavailability of active compounds.
- Food Industry: As a natural thickener and stabilizer in food products, particularly in confectionery and beverages.
- Cosmetics: Incorporated into skincare and haircare products for its moisturizing and soothing properties.
- Adhesives: Employed in the production of natural adhesives for industrial and domestic use (31)

1.6.5 Economic Significance:-

➢ **Market Demand**

The demand for natural gums and resins has been steadily increasing due to the global shift towards organic and eco-friendly products. Odina gum is highly valued

in both domestic and international markets for its versatility and beneficial properties.

- **Cultivation and Sustainability**

Efforts are being made to cultivate Odina trees sustainably. Agroforestry practices, which integrate the cultivation of Odina trees with other crops, are being promoted to enhance biodiversity and provide additional income sources for farmers (32)

- **Trade and Commerce**

India is one of the leading producers and exporters of Odina gum. The gum is traded in various forms, including raw resin, processed powder, and as an ingredient in formulated products. The global market for natural gums and resins presents significant opportunities for rural economies in producing regions (33)

1.6.6 Challenges and Future Prospects:-

- **Challenges**

- Overharvesting: Unsustainable harvesting practices can lead to the depletion of natural populations of Odina trees.
- Quality Control: Variations in gum quality due to environmental factors and traditional extraction methods can affect marketability.
- Regulatory Issues: Ensuring compliance with international standards for natural products can be challenging for small-scale producers.

- **Future Prospects**

- Research and Development: Continued research into the bioactive compounds and potential new uses of Odina gum can open up new markets.

- Sustainable Practices: Promoting sustainable harvesting and cultivation practices will ensure the long-term availability of this valuable resource.
- Value Addition: Developing value-added products and improving processing techniques can enhance the economic viability of Odina gum (34)

1.7 Mono-chloroacetic acid : An overview –

1.7.1 Chemical properties :-

Monochloroacetic acid (MCA), also known as chloroacetic acid, is an organochlorine compound with the molecular formula $C_2H_3ClO_2$ It is a colorless or white crystalline solid that is highly soluble in water and various organic solvents. The chemical structure of monochloroacetic acid consists of a carboxyl group (-COOH) attached to a carbon atom, which is also bonded to a chlorine atom (Cl) and a hydrogen atom (H). The presence of the electronegative chlorine atom increases the acidity of the molecule, making MCA more reactive than acetic acid.

Molecular formula: $C_2H_3ClO_2$

Molecular weight: 94.50 g/mol

Melting point: 61-63°C

Boiling point: 189-190°C

Density: 1.58 g/cm³

Solubility: Highly soluble in water, alcohol, and ether (35)

1.7.2 Synthesis :-

Monochloroacetic acid can be synthesized through several methods, with the most common being the chlorination of acetic acid. This process involves the substitution

of one hydrogen atom in the acetic acid molecule with a chlorine atom. The reaction is typically carried out in the presence of a catalyst, such as acetic anhydride or sulfur trioxide, at elevated temperatures.

In this reaction, chlorine gas (Cl_2) reacts with acetic acid (CH_3COOH) to produce monochloroacetic acid ($CH_2ClCOOH$) and hydrochloric acid (HCl). The process can be controlled to minimize the formation of dichloroacetic acid and trichloroacetic acid, which are possible by-products (36-37)

1.7.3 Uses :-

Monochloroacetic acid is a versatile chemical intermediate used in the production of various chemicals and materials. Some of its major applications include:

I. **Herbicides and Pesticides:** MCA is a key intermediate in the synthesis of herbicides such as 2,4-D (2,4-dichlorophenoxyacetic acid) and MCPA (2-methyl-4-chlorophenoxyacetic acid). These herbicides are widely used in agriculture to control broadleaf weeds.

II. **Dyes and Pigments:** MCA is used in the production of indigo dye, which is used for coloring denim fabrics. It is also a precursor for other dyes and pigments used in the textile industry.

III. **Pharmaceuticals:** MCA is used in the synthesis of various pharmaceutical compounds, including local anesthetics like lidocaine and anti-inflammatory drugs.

IV. **Carboxymethylcellulose (CMC):** One of the most significant uses of MCA is in the production of carboxymethylcellulose, a water-soluble polymer used as a thickener, stabilizer, and binder in foods, cosmetics, and pharmaceuticals.

V. **Surfactants:** MCA is used to produce surfactants and detergents, which are essential components in cleaning products and personal care items.

VI. **Adhesives and Sealants:** MCA is a building block for various adhesive and sealant formulations used in construction and manufacturing industries (38-39)

1.7.4 Safety and Handling:-

Monochloroacetic acid is a hazardous substance that requires careful handling to prevent exposure and accidents. It is classified as a corrosive substance and can cause severe burns to the skin and eyes. Inhalation of MCA vapors can lead to respiratory irritation and damage, while ingestion can result in severe gastrointestinal distress.

- **Personal Protective Equipment (PPE):** When handling MCA, it is essential to wear appropriate PPE, including gloves, safety goggles, and protective clothing. Respiratory protection may also be necessary in environments with high vapor concentrations.
- **Storage:** MCA should be stored in a cool, dry place away from incompatible substances such as strong bases and oxidizing agents. It should be kept in tightly sealed containers to prevent moisture absorption and degradation.
- **Spill and Leak Procedures:** In case of a spill, the area should be evacuated and ventilated. Spilled material should be neutralized with a suitable neutralizing agent (e.g., sodium bicarbonate) and cleaned up using appropriate absorbent materials. Contaminated surfaces should be thoroughly washed (40-41)

1.7.5 Environmental Impact

Monochloroacetic acid poses environmental hazards due to its toxicity to aquatic organisms and potential for bioaccumulation. It can enter the environment through industrial discharges, spills, and improper disposal. Once released, MCA can contaminate soil and water bodies, affecting aquatic life and potentially entering the food chain.

- **Aquatic Toxicity:** MCA is highly toxic to fish and other aquatic organisms. Even low concentrations can cause significant harm to aquatic ecosystems.
- **Biodegradability:** MCA is relatively biodegradable under aerobic conditions. Microorganisms in the environment can break down MCA into less harmful substances, though the rate of degradation depends on various factors, including temperature, pH, and microbial activity.
- **Regulations:** Due to its hazardous nature, the use and disposal of MCA are regulated by environmental protection agencies in many countries. Industries that use MCA must adhere to strict guidelines to minimize environmental contamination and ensure safe handling practices (42-44)

1.8 The Role of Monochloroacetic Acid in the Carboxymethylation of Natural Gums

Carboxymethylation is a chemical modification process used to improve the properties of natural polymers, including natural gums. Monochloroacetic acid (MCA) plays a crucial role in this process by introducing carboxymethyl groups into the polymer structure. This modification enhances the solubility, viscosity, and functionality of natural gums, making them valuable in various industrial applications.

1.8.1 Natural Gums and Their Importance :-

Natural gums, such as guar gum, xanthan gum, and locust bean gum, are polysaccharides derived from plants and microorganisms. They have numerous applications due to their thickening, gelling, and stabilizing properties. However, their performance can be limited by factors like solubility and viscosity under different conditions. To overcome these limitations, natural gums are often chemically modified. Carboxymethylation, which involves introducing carboxymethyl groups (-CH_2-COOH) into the polymer backbone, is one of the most effective modification methods. This process improves the solubility, thermal stability, and overall functionality of the gums (45)

1.8.2 Mechanism of Carboxymethylation Using Monochloroacetic Acid:-

The carboxymethylation of natural gums involves a nucleophilic substitution reaction where the hydroxyl groups (-OH) in the gum react with monochloroacetic acid to form carboxymethyl groups. The process can be summarized in several steps:

- **Activation:** The natural gum is usually dispersed in an aqueous or aqueous-alcoholic solution, often in the presence of a base such as sodium hydroxide (NaOH). The base deprotonates the hydroxyl groups on the gum, forming alkoxide ions (-O^-), which are more nucleophilic.
- **Reaction with MCA:** Monochloroacetic acid is added to the solution, where it reacts with the alkoxide ions to form carboxymethyl groups. The reaction can be represented as:

  [R-OH + NaOH → R-O^- + Na^+ + H_2O]

[$R\text{-}O^- + Cl\text{-}CH_2\text{-}COOH \rightarrow R\text{-}O\text{-}CH_2\text{-}COOH + Cl^-$]

Here, (R-OH) represents the hydroxyl group in the natural gum, and ($R\text{-}O\text{-}CH_2\text{-}COOH$) represents the carboxymethylated gum.

- **Neutralization:** The reaction mixture is neutralized to stop the reaction and precipitate the modified gum. This is typically done by adding an acid such as acetic acid.
- **Purification:** The carboxymethylated gum is washed to remove any unreacted reagents and by-products, and then dried (46-48)

1.8.3 Factors Affecting Carboxymethylation :-

Several factors influence the efficiency and outcome of the carboxymethylation process, including:

- **Concentration of MCA:** Higher concentrations of monochloroacetic acid can increase the degree of substitution (DS), which refers to the average number of carboxymethyl groups introduced per anhydroglucose unit of the gum.
- **Reaction Time and Temperature:** The reaction time and temperature need to be optimized to achieve the desired degree of substitution without degrading the gum. Typically, higher temperatures and longer reaction times increase the DS.
- **pH and Base Concentration:** The pH of the reaction mixture, controlled by the concentration of the base (NaOH), affects the ionization of the hydroxyl groups and the efficiency of the nucleophilic substitution (49-51)

1.8.4 Benefits of Carboxymethylation:-

Carboxymethylation significantly enhances the properties of natural gums, making them more suitable for various applications:

- **Improved Solubility:** Carboxymethylation increases the hydrophilicity of the gum, making it more soluble in water. This is particularly beneficial for applications in food, pharmaceuticals, and cosmetics.
- **Enhanced Viscosity:** Carboxymethylated gums exhibit higher viscosity at lower concentrations compared to their unmodified counterparts. This property is useful in industries such as food processing and oil drilling, where thickening agents are required.
- **Thermal Stability:** The introduction of carboxymethyl groups can improve the thermal stability of the gum, allowing it to maintain its functionality at higher temperatures.
- **Gel-Forming Ability:** Carboxymethylated gums can form stronger and more stable gels, which are valuable in food products like jellies, sauces, and dressings (52-53)

LITERATURE REVIEW

2. Literature review :-

1. **H.R. Badwaik et al.(2022)** reported that carboxymethylation is a widely studied chemical procedure for modifying natural gums, offering potential for drug delivery, tissue engineering, and cell delivery in pharmaceutical applications.
2. **G. Dodi et al. (2011)** stated that the chemical modification of polysaccharides, specifically guar gum, for biomedical applications. The modifications include the introduction of carboxymethyl groups, optimizing conditions for carboxymethylation. The resulting products, characterized by NMR, FTIR spectroscopy, and TGA, may offer an efficient oral delivery method for hydrophilic macromolecules.
3. **Ahuja et al. (2017)** published a research work where he did carboxymethylation of natural seed gum, moringa gum and then used it as a nanocarrier for drug delivery containing ofloxacin drug. They extract the mucilage from the bark of the Moringa oleifer tree. They prepared ofloxacin loaded nanoparticle with carboxymethylated moringa gum and chitosan by modified coacervation technique. They saw after modification of moringa gum particles are polyhedral in shape. Further the micrographs show the presence of cracks and pores on the surface of moringa gum while the surface of CMG appears to be more granular and rougher than the MG, which is consistent with the results of XRD study. After carboxymethylation of natural gum viscosity of the gum is decreased. Carboxymethylation of natural gums imparts anionicity to the backbone of the polysaccharide, causing a Coulombic repulsion between the backbones, which lowers the viscosity. Because of the anionic properties imparted by the carboxymethyl group of Moringa gum, it exhibits ionic and cation interactions such as Ca2+, Mg2+,

Ba2+ and chitosan. We also used the response surface methodology to optimize the interaction between modified gum and chitosan to generate polyelectrolyte composite nanoparticles. Polyelectrolyte nanoparticle produce drug release in extend manner. However, further studies using drugs and interacting ions with different physicochemical properties are needed to fully explore the potential of modified moringa gum as nanometer carriers.

4. **Chakravorty et al., (2016)** published a research article in which they studied about the effect of carboxymethylation on the locust bean gum and its effect on the drug release from the tablet matrix and changes in rheological behaviour. Carboxymethylated gum have low viscosity and an almost Newtonian plateau was exhibited within of the lower shear rate range, above which shear thinning properties became evident. The highly entangled polymer chains were responsible for the high viscosity of and the shear reducing ability of LBG. Drug release from the tablet that is prepared from the carboxymethylated gum is higher than the native gum. A weak gel structure with the less viscosity characteristics of CMLBG in water and low viscosity due to its low molecular weight and intrinsic complex structure results in higher drug release. Conversely, which made due to the high molecular weight and entangled polymer chains of LBG, had a high viscosity and slowed drug release from the LBG tablets, mainly due to the elastic strong gel. ϖ Huanbutta and Sittikijyothin.,2017 in their work provide data about carboxymethylation of Cassia gum and tamarind gum. They have prepared tablet formulation. Carboxymethylated gum exhibit high intrinsic viscosity and its show high swelling profiles. Hardness of the modified gum tablet is more than the native gum tablet. The disintegration time of crude gums were faster that the carboxymethylated gums due to low swelling and solubility properties of the crude gum as presented in previous study. Swelling

behaviour of both crude and carboxymethylated gums for both seed types were observed. The obtained results from swelling test showed that the carboxymethylated gums could be better used than that crude gums for further pharmaceutical application as disintegrate, diluent and drug release controlling agent.

5. **Rana et al., (2011)** This article is aimed at discussing the modification of gums through derivatization of functional groups, grafting with polymers, cross-linking with ions etc. The factors influencing these processes in the pursuit of making them suitable for modifying the drug release properties of pharmaceutical dosage forms and for other purposes is discussed with respect to optimization of their performance.
6. **Verma and Ahuja et al., (2020)** in this research work they performed Carboxymethylation of Cassia obtusifolia galactomannan was carried out by Williamsons synthesis. Modification of galactomannan was confirmed by Fourier-transform infrared and 1 H Nuclear magnetic resonance spectroscopy. The degree of carboxymethyl substitution was found to be 1.69. Carboxymethylation was observed to increase the powder flow, solubility and swelling, while decrease the viscosity and alter the compression characteristics from elastic to plastic. The results of X-ray diffraction and scanning electron microscopy studies indicated increase in degree of crystallinity. The modified gum was used for preparing diclofenac sodium loaded, Ca2+-gelled beads which were coated with gastroresistant Eudragit-L100. The formulation of beads was optimized using central composite experimental design. The optimal formulation of beads contained carboxymethylated Cassia galactomannan-2.85%,w/v and calcium chloride −15%,w/v, which showed yield −185.4%, entrapment-95.41% and release of 93.32% of diclofenac over 24 h. The release of diclofenac followed first-order

kinetics by Super case-II transport. Thus, carboxymethyl Cassia galactomannan appears suitable for sustained drug delivery.

AIMS AND OBJECTIVES

3. AIM AND OBJECTIVE OF THE RESEARCH WORK

3.1 Aims:-

Carboxymethylation of gum odina, a process where carboxymethyl groups are introduced into the gum molecular structure, aims to achieve several key objectives:

1. Improved Solubility: Carboxymethylation increases the solubility of gum odina in water, making it easier to use in various applications.

2. Enhanced Thickening Properties: The modified gum can provide better thickening and stabilizing properties, which is valuable in food, pharmaceutical, and cosmetic formulations.

3. Increased Stability: The process can improve the thermal and chemical stability of the gum, making it more resilient in different environmental conditions.

4. Better Compatibility: Carboxymethylated gum odina can be more compatible with other ingredients in formulations, enhancing its versatility and functionality.

5. Improved Bio adhesive Properties: In pharmaceuticals, enhanced bio adhesive properties can improve the performance of drug delivery systems.

6. Modification of Rheological Properties: The flow and deformation behavior of the gum can be tailored to specific needs, benefiting applications that require precise control over viscosity and texture.

7. Improved Functional Properties: This modification can enhance the emulsifying, film-forming, and binding properties of the gum, broadening its range of applications (54)

Overall, the carboxymethylation of gum odina aims to enhance its functional properties, making it more effective and versatile for industrial and commercial use.

3.2 Objective :-

Carboxymethylation of gum odina, like other polysaccharides, is typically aimed at modifying its physical and chemical properties to enhance its utility in various applications. Here are some specific objectives:

1. Solubility Enhancement: Improve the water solubility of gum odina to broaden its applications in aqueous systems.

2. Viscosity Modification: Adjust the viscosity of gum odina solutions to meet specific requirements for industrial applications, such as in food, pharmaceuticals, and cosmetics.

3. Stability Improvement: Enhance the thermal, chemical, and enzymatic stability of the gum to ensure it remains effective under various conditions.

4. Functional Group Introduction: Introduce carboxymethyl groups to create new functional properties, such as increased reactivity or the ability to form gels and films.

5. Biocompatibility and Biodegradability: Retain or improve the biocompatibility and biodegradability of gum odina for use in environmentally friendly and biomedical applications.

6. Thickening and Gelling Agent: Improve its capacity as a thickening and gelling agent for use in food and industrial applications.

7. Adsorption Capacity: Enhance its ability to adsorb ions or molecules, useful in wastewater treatment and drug delivery systems.

8. Rheological Properties: Modify the rheological properties to meet specific needs for products like coatings, adhesives, and encapsulation materials.

These objectives guide the chemical modification process to tailor gum odina for specific functional applications in various industries (55)

EXPERIMENTAL SECTION

4. Experimental section :-

4.1 Materials and methods:-

List of Materials used in the Research Work:-

Materials	**Source**
Gum odina	Tree of *Odina wodier Roxb*.
Mono-chloroacetic acid	Hi-media
Methanol	Rankem (A Avantar Brand)
Glacial Acetic Acid	Sigma-Aldrich
Sodium hydroxide (NaOH)	Sigma-Aldrich

List of instrument used in the Research work :-

Instrument	Source
Magnetic stirrer	Remi 1000
Weighing balance	Wesner
pH meter	Accumet (fisher scientific)
FTIR	Perkin Elmer RX1 FT-IR Spectrophotometer
XRD	Bruker D8 ADVANCE XRD

4.2 Collection, identification, purification of gum odina :

Tree of Odina wodier Roxb. Species

↓

Gum Collected for Unambiguous Identification

↓

Crude gum (100 g) was immersed in de-ionized water (1000 ml) and left for 24 h at room temperature (25 °C).

↓

After overnight swelling the gum was mixed thoroughly with the help of a laboratory stirrer for 8 h.

↓

The brown viscous solution obtained was passed through muslin cloth to remove fine extraneous materials and centrifuged at 1500 rpm for 15 min for clarification.

↓

Then the supernatant was slowly added to acidified (pH 4–5) ethanol, which resulted in the formation of a white precipitate that was collected and titrated with absolute ethanol and dry ether in a ratio of 1:1.

↓

The precipitated cake obtained was filtered. This process was repeated thrice and the obtained product was dried in vacuum at room temperature, (25 °C) pulverized by a mechanical blender and stored in air tight jars for future use (55-56)

4.3 Carboxymethylation of gum odina:-

Gum (2gm) +70ml of 35% w/v ice cold NaOH Vigorous stirring for 30 min

↓

Add Aqueous Solution of MCA/CA Stirring at 80ºC for 1hr

↓

80% v/v methanol added to it Neutralize with glacial acetic acid

↓

Washed thrice with Aqueous Methanol (90%w/v) Product dry at 80ºC.(58-59)

4.4 Scanning electron microscopy (SEM) :-

Morphological studies of PGO were carried out by scanning electron microscopy (SEM). The topography of PGO sample was studied by using a SEM(Model: ZEISS EVO-MA 10), at an extra high voltage of 15.00 kV under ambient condition. The dried sample was mounted on a metal stub and sputtered with Pt in order to make the sample conductive. The particles were observed under different magnifications (60)

4.5 Contact Angle: -

Wettability determination of CMGO was performed by contact angle measurements of samples using custom-made goniometer equipped with a camera monitor. A droplet of 10 μL CMGO dispersion in water (0.5 %, 1 %, 2 %) carefully deposited on the unpolished aluminium surface. The contact angle for each dispersion sample was measured three times. Images were analyzed using the snake fit method and compared to that of water (61)

4.6 FTIR :-

The FTIR spectra of Gum odina were carried out by an FTIR-8400S (Shimadzu, Japan) to confirm the formation of CMGO and the compatibility of different ingredients of the IPN formulation. A small amount of each material was mixed with KBr (1 wt. % sample content), taken into a sample holder, and scanned in the range 600−4000 cm^{-1}. (62)

4.7 Qualitative X-ray Diffractometry (XRD) :-

Ground samples of pristine gum, carboxymethylated gum, BH, and blank and drug loaded IPN microspheres were scanned from 10 to 60° 2θ, using an X-ray diffractometer (Bruker AXS D8 Advance, Germany; configuration vertical, θ/2θ geometry; X-ray Cu, wavelength 1.5406 Å, detector Si (Li) PSD). The diffractometer was run at a scanning speed of 2 deg/min and a chart speed of 2 deg/2 cm per 2θ, and the angular range fixed was from 10 to 60° (62)

4.8 THERMOGRAVIMETRIC ANALYSIS (TGA) :-

Differential thermogravimetric curves of the samples are presented in Figure 4. Thermogravimetric analysis of guar gum essentially reveals two distinct zones of weight loss. The initial weight loss occurred in the 25-115 °C range, due to the moisture traces present in the sample. The second step represents the degradation of the polymer backbone, having started at 230 °C and lasting until 350 °C. In addition to these zones of weight loss, the thermal degradation of carboxymethyl guar gum shows a third zone in the 408-478 °C range, due to the degradation of the carboxymethyl groups incorporated in the polymer moiety. This third step of weight loss, which was present only in CMG5, provided more proof on the insertion of carboxymethyl groups.

4.9 DIEFFERENTIAL SCANNING CALORIMETRY (DSC) :-

The thermal stability of the prepared CMG-Bt-St samples was obtained using the DSC technique (SDT Q600 V20.9 Build 20 instrument). A platinum tray was used to heat the sample at 10 °C/min from 20 to 600 °C under an N_2 atmosphere (100 mL/ min).(63)

RESULTS AND DISCUSSION

5 RESULTS AND DISCUSSION :-

5.1 FOURIER TRANSFORM INFRARED SPECTROSCOPY (FTIR) :-

FTIR Analysis of Carboxymethylated Gum Odina

The FTIR spectra of native Gum Odina and Carboxymethylated Gum Odina are presented in Figure X. The spectral analysis provides insight into the structural modifications that occur due to carboxymethylation.

1. **Native Gum Odina (Black Spectrum)**:
    - **Broad Peak at 3400-3200 cm^{-1}**: This broad band corresponds to the O-H stretching vibrations, indicating the presence of hydroxyl groups. This is typical for polysaccharides (64)
    - **Peak at 2920 cm^{-1}**: Assigned to C-H stretching vibrations from CH_2 groups.
    - **Peak at 1735 cm^{-1}**: This peak is attributed to the C=O stretching of ester groups, indicating the presence of uronic acid units in the gum.
    - **Peak at 1620 cm^{-1}**: Corresponds to the asymmetric stretching vibrations of COO- groups, which are indicative of carboxylate ions.
    - **Peak at 1420 cm^{-1}**: This is due to the symmetric stretching vibrations of COO- groups.
    - **Peak at 1050 cm^{-1}**: This is a characteristic peak of C-O-C stretching vibrations, indicating glycosidic linkages in the polysaccharide (65)

2. **Carboxymethylated Gum Odina (Red Spectrum)**:
    - **Broad Peak at 3400-3200 cm^{-1}**: Similar to the native gum, this broad band is due to O-H stretching vibrations. However, a slight decrease in intensity may be observed, suggesting partial substitution of hydroxyl groups by carboxymethyl groups (66)
    - **Peak at 2920 cm^{-1}**: The C-H stretching vibrations from CH_2 groups are still present.
    - **New Peak at 1600 cm^{-1}**: A significant increase in the intensity of the peak around 1600 cm^{-1} is observed, which corresponds to the newly formed COO- groups from carboxymethylation.
    - **Peak at 1420 cm^{-1}**: This peak becomes more pronounced, indicating an increase in carboxylate ions due to the carboxymethylation process.
    - **Peak at 1050 cm^{-1}**: The C-O-C stretching vibrations remain prominent, suggesting that the polysaccharide backbone is intact after modification.
    - **Additional Peak at 1370 cm^{-1}**: This peak can be attributed to the C-H bending of CH_2 groups in the carboxymethylated product, confirming the introduction of carboxymethyl groups (67)

The FTIR spectra provide clear evidence of the carboxymethylation of Gum Odina shown in **figure 1**. The characteristic peaks of the carboxymethyl groups at 1600 cm^{-1} and 1420 cm^{-1} confirm the successful introduction of carboxymethyl groups into the gum structure. The decrease in the intensity of the O-H stretching vibration band indicates partial substitution of hydroxyl groups by carboxymethyl groups.The preservation of the C-O-C stretching vibrations suggests that the polysaccharide backbone of Gum Odina remains largely intact during the carboxymethylation process. This structural integrity

is crucial for maintaining the desired properties of the gum. the FTIR analysis confirms that carboxymethylation has been successfully achieved in Gum Odina, introducing carboxymethyl groups while preserving the polysaccharide structure. This modification is expected to enhance the solubility and functional properties of the gum, making it suitable for various industrial applications (68)

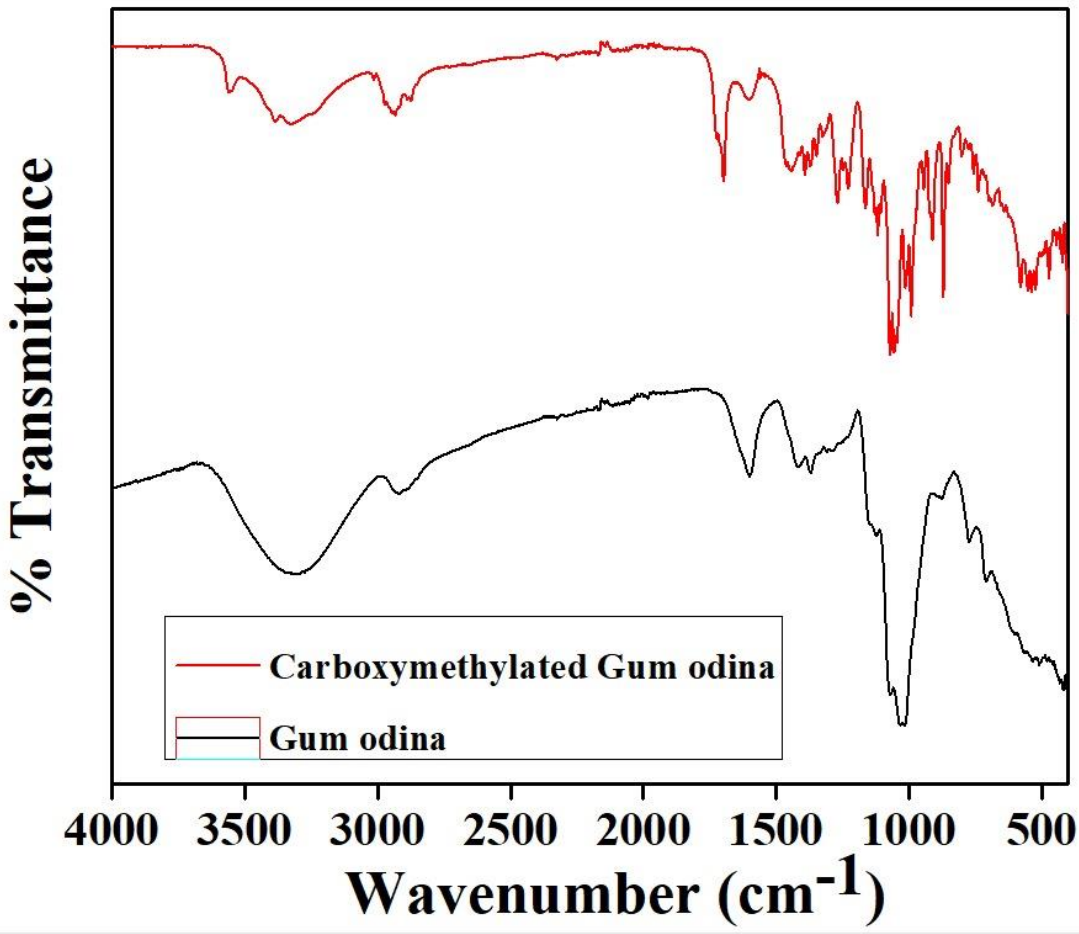

Figure: 1

5.2**X-RAY DIFFRACTION ANALYSIS (XRD)** :- The XRD patterns of both native and carboxymethylated gum odina are presented in Figure 1. The diffraction pattern of native gum odina shows broad peaks, indicating its amorphous nature. In contrast, the XRD pattern of carboxymethylated gum odina displays more defined peaks, suggesting the presence of crystalline regions introduced by carboxymethylation.

Figure 2: XRD Patterns of Native Gum Odina.

Figure 3: XRD patterns of Carboxymethylated Gum Odina.

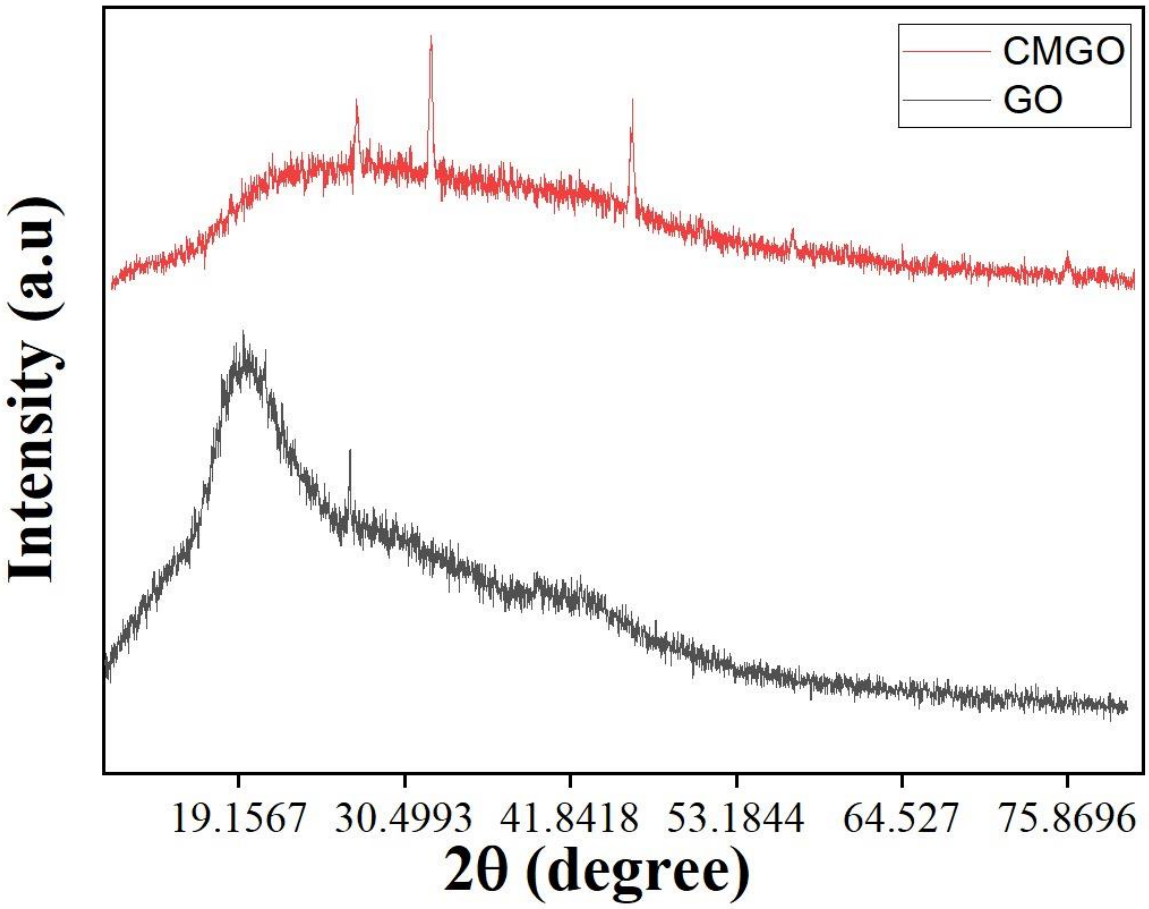

Figure 2

The CI for native gum odina was found to be approximately 20%, whereas for carboxymethylated gum odina, the CI increased to around 45%. This significant increase in CI indicates that carboxymethylation induces a higher degree of crystalline order within the polymer matrix. Peak Analysis The XRD pattern of native gum odina exhibited a broad peak centered at approximately 2θ = 20°, characteristic of amorphous materials. Upon carboxymethylation, additional peaks emerged at 2θ values of 15°, 22°, and 25°, indicative of crystalline structures. These peaks correspond to the ordered arrangement of carboxymethyl groups within the polymer matrix (69)

5.3 DIFFERENTIAL SCANNING CALORIMETRY (DSC) :-

Initial Weight: 27.207 mg

Temperature Range: 30°C to 600°C

Heating Rate: 5°C/min

Key observations from the DSC data include:

Endothermic Peaks: Presence of endothermic peaks indicates the thermal transitions such as glass transition (Tg), melting (Tm), and decomposition temperatures (Td).

Exothermic Peaks: Exothermic peaks may indicate crystallization or other exothermic reactions within the sample.

The DSC curve of carboxymethylated gum odina shows multiple thermal events Shown in figure 4. The endothermic peak may correspond to the glass transition temperature (Tg), indicating the temperature at which the polymer transitions from a hard, glassy material to a soft, rubbery state. The melting peak (Tm) observed suggests the melting of crystalline regions within the gum. Finally, the decomposition temperature (Td) is observed, indicating the

temperature at which the thermal degradation of the sample begins. The DSC data provide insight into the thermal properties and stability of carboxymethylated gum odina, which are crucial for understanding its potential applications in various industries (70)

5.4 THERMOGRAVIMETRIC ANALYSIS (TGA) :-

Initial Weight: 27.207 mg

Temperature Range: 30°C to 600°C

Heating Rate: 5°C/min

Key observations from the TGA data include: Weight Loss: The percentage of weight loss at various temperatures indicates the decomposition stages of the sample. Thermal Stability: The temperature at which significant weight loss occurs gives an indication of the thermal stability of the sample. The TGA curve shows a multi-stage decomposition pattern in figure 4. The initial weight loss observed can be attributed to the loss of moisture and volatile components. The subsequent weight loss stages at higher temperatures indicate the breakdown of the polymer structure. The temperature at which the maximum rate of weight loss occurs (Td) is crucial for determining the thermal stability of the material. The TGA data indicate that carboxymethylated gum odina undergoes significant thermal degradation, highlighting its stability range and decomposition behavior. This information is essential for processing and application considerations, especially in environments with elevated temperatures (71)

5.5 CONTACT ANGLE :-

The contact angle of carboxymethylated gum odina was measured to be 41 degrees Shown in figure 5. This measurement indicates the degree of wettability and surface energy of the modified gum. The contact angle provides insights into the hydrophilic or hydrophobic nature of the material.

Hydrophilicity and Surface Energy

A contact angle of 41 degrees suggests that carboxymethylated gum odina exhibits hydrophilic properties. Typically, a contact angle less than 90 degrees indicates that the material is hydrophilic, meaning it has a good affinity for water. This can be attributed to the carboxymethylation process, which introduces carboxymethyl groups into the gum structure, increasing its polarity and thereby its affinity for water (72)

Impact of Carboxymethylation

Carboxymethylation is a chemical modification process aimed at enhancing the water solubility and functional properties of natural gums. For gum odina, the introduction of carboxymethyl groups has likely resulted in an increased number of hydrophilic sites, thus reducing the contact angle. This modification enhances the gum's potential applications in areas where water interaction is crucial, such as in drug delivery systems, food industry as a stabilizer, and in coatings.

Comparison with Native Gum Odina

The contact angle of the native (unmodified) gum odina is expected to be higher than that of the carboxymethylated version, indicating a more hydrophobic nature. The significant reduction in the contact angle upon carboxymethylation demonstrates the effectiveness of the modification process in enhancing the hydrophilicity of the gum.

The increased hydrophilicity of carboxymethylated gum odina, as evidenced by the lower contact angle, makes it more suitable for applications requiring good water interaction. For instance, in pharmaceutical formulations, the modified gum can improve the dissolution rate of active ingredients. In food applications, it can enhance the texture and stability of water-based products. Additionally, in the field of coatings, the modified gum can improve the adhesion properties due to its enhanced wettability (73)

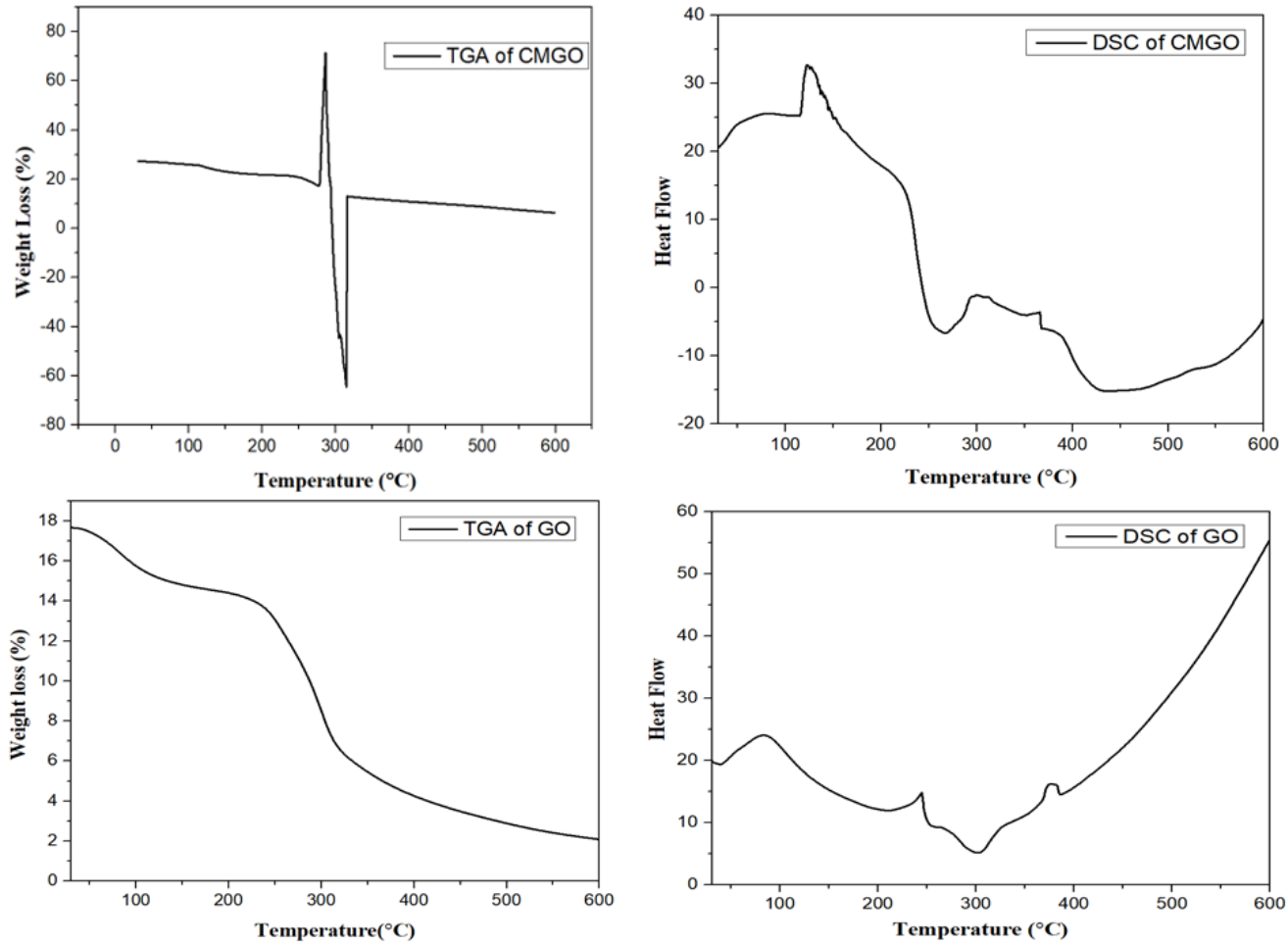

Figure: 3 DSC and TGA graph of GO and CMGO

Figure: 4 contact angle of CMGO

5.6 Scanning Electron Microscopy (SEM):-

Descriptive Analysis of Image 1 (CMGO)

The SEM image titled "Image 5 (CMGO) " shows a detailed view of the sample's microstructure. The image has an average pixel intensity of 110.91, indicating the overall brightness of the image. The standard deviation of pixel intensity is 60.01, which reflects the contrast within the image. The image has a balanced contrast, indicating a mix of dense and porous regions within the sample. There is significant variation in the texture and morphology of the sample, with both smooth and rough areas observable.

Descriptive Analysis of Image 2 (GO)

The SEM image titled "Image 6 (GO)" shows a detailed view of the sample's microstructure. The image has an average pixel intensity of 127.11, indicating the overall brightness of the image. The standard deviation of pixel intensity is 55.24,

which reflects the contrast within the image. The image has a balanced contrast, indicating a mix of dense and porous regions within the sample. There is significant variation in the texture and morphology of the sample, with both smooth and rough areas observable.

Particle Size Distribution Analysis of Image 1 (CMGO) Number of particles detected: 161 Mean particle size: 20.19 pixels Standard deviation of particle size: 35.14 pixels Minimum particle size: 7.98 pixels Maximum particle size: 401.81 pixels

Particle Size Distribution Analysis of Image 2 (GO)

Number of particles detected: 100 Mean particle size: 25.24 pixels Standard deviation of particle size: 50.73 pixels Minimum particle size: 8.06 pixels Maximum particle size: 495.58 pixels These results summarize the particle size distribution within each SEM image. The number of particles detected, along with their mean size and distribution, gives insight into the microstructural characteristics of the samples.

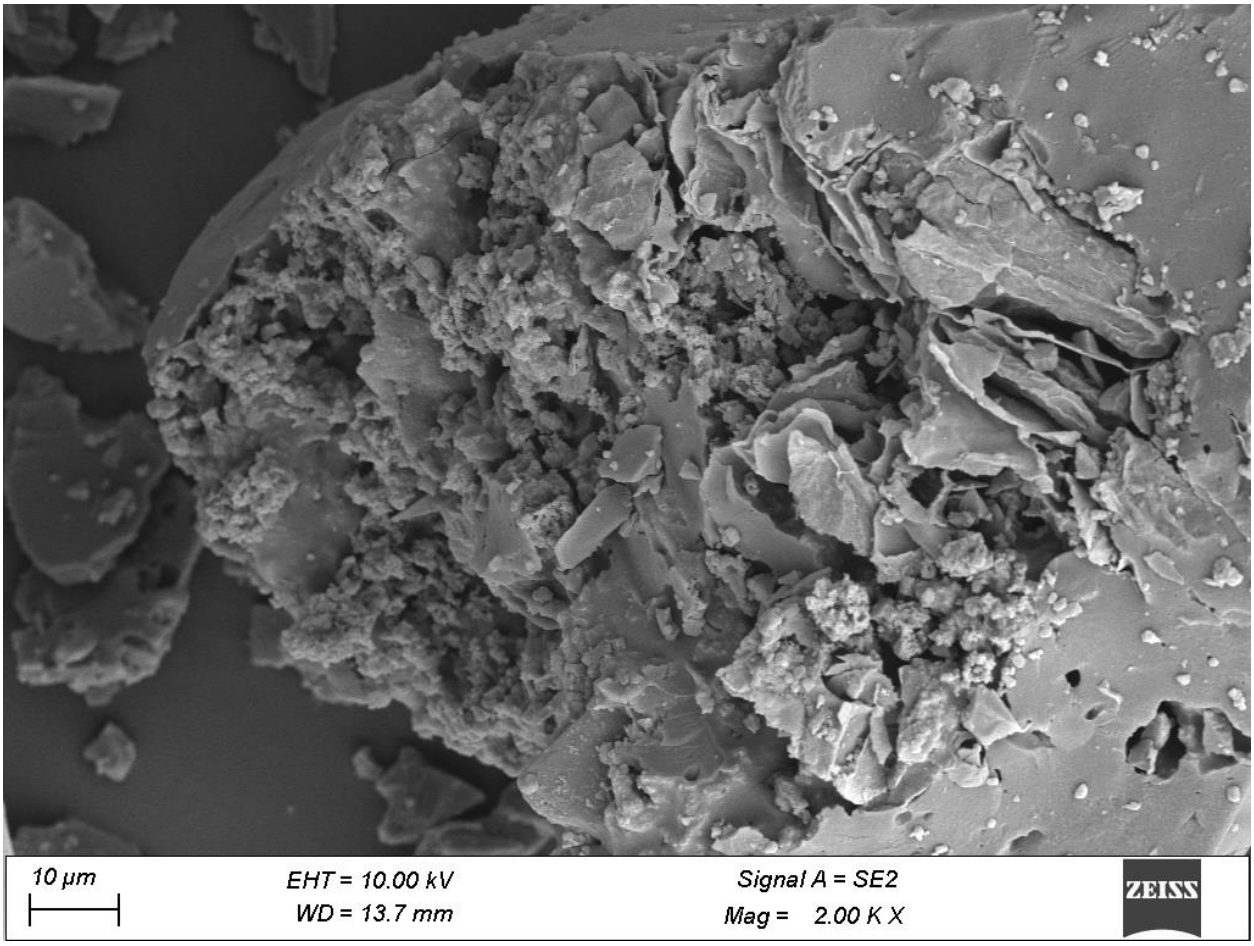

Figure 5 :- SEM image of CMGO

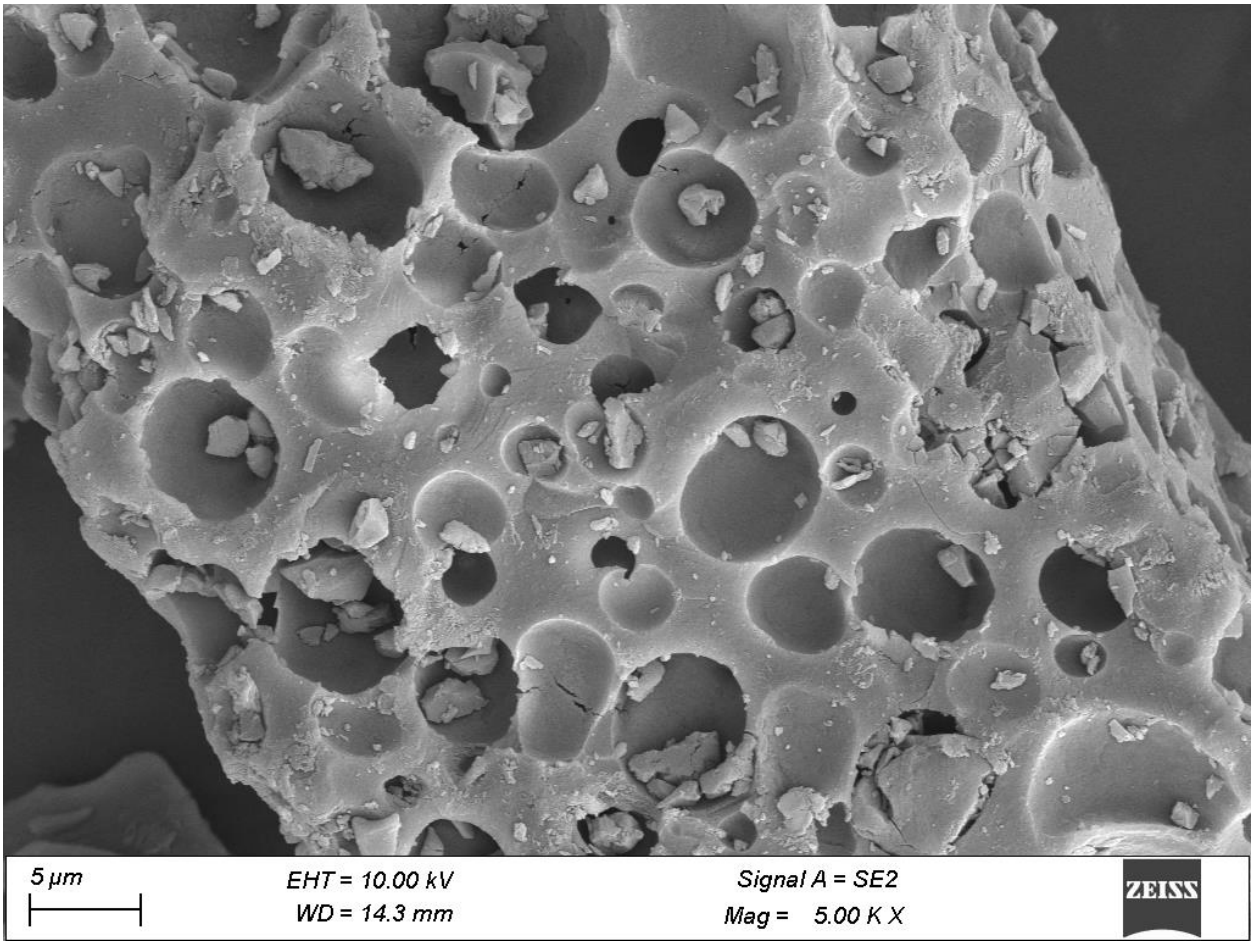

Figure 6 :- SEM image of GO

CONCLUSION

6 Future perspectives :-

The evaluation and characterization of carboxymethylated gum odina present a promising avenue in the development of novel drug delivery systems. By modifying gum odina, a natural polysaccharide, through carboxymethylation, researchers aim to enhance its solubility, stability, and bioavailability. This novel approach could lead to more efficient drug encapsulation and controlled release, improving therapeutic outcomes. Additionally, carboxymethylated gum odina's biocompatibility and non-toxic nature make it a favorable candidate for pharmaceutical applications. Future studies could further explore its potential in targeted drug delivery, potentially revolutionizing current drug delivery methodologies.

7 Conclusion :-

Carboxymethylated gum has shown promising potential in various industrial and biomedical applications due to its enhanced properties compared to the native gum. The carboxymethylation process significantly improves the solubility, viscosity, and functional attributes of gum Odina, making it a versatile material for use in pharmaceuticals, food industries, and as a biopolymer in various formulations. Its biodegradability and non-toxic nature further underscore its suitability for environmentally friendly applications. Future research could focus on optimizing the carboxymethylation process and exploring its full range of potential uses, ensuring that this modified natural gum can be effectively and efficiently utilized in different formulation.

8 References :-

1. R. J. Chudzikowski, Journal of the Society of Cosmetic Chemists, 22, 43 (1971).
2. J. Tripathya, D. K. Mishraa, A. Srivastavaa, M. M. Mishraa and K. Behari, Carbohydr. Polym., 72, 462 (2008).
3. D. Risica, A. Barbetta, L. Vischetti, C. Cametti and M. Dentini, Polymer, 51, 1972 (2010).
4. D. Risica, M. Dentini and V. Crescenzi, Polymer, 46, 12247 (2005).
5. R. T. Thimma and S. Tammishetti, J. Appl. Polym. Sci., 82, 3084 (2001).
6. L. R. Pablyana Cunha, C. M. Regina de Paula and J. P. A. Feitosa, Int. J. Biol. Macromol., 41, 324 (2007).
7. V.D. Prajapati, G.K. Jani, N.G. Moradiya, N.P. Randeria, Pharmaceutical applications of various natural gums, mucilages and their modified forms, Carbohydr. Polym. 92 (2013) 1685–1699.
8. A.M. Avachat, R.R. Dash, S.N. Shrotriya, Recent investigations of plant based natural gums, mucilages and resins in novel drug delivery systems, Indian J. Pharm. Educ. Res. 45 (2011) 86–99.
9. P.D. Choudhary, H.A. Pawar, Recently investigated natural gums and mucilages as pharmaceutical excipients: an overview, J. Pharm. 2014 (2014) 1–9.
10. A.J. Rajamma, H.N. Yogesha, S.B. Sateesha, Natural gums as sustained release carriers: development of gastroretentive drug delivery system of ziprasidone HCl, DARU J. Pharm. Sci. 20 (2012) 1–9.

11. A. Saha, S. Tyagi, R.K. Gupta, Y.K. Tyagi, Natural gums of plant origin as edible coatings for food industry applications, Crit. Rev. Biotechnol. 37 (2017) 959–973.
12. Feldman D. Polymer history. Designed monomers and polymers. 2008 Jan 1;11(1):1-5.
13. Taylor and Francis, Polymers in Drug Delivery System, 2006, 1-236.
14. Hoffman, A.S., Hydrogels for biomedical applications, Adv. Drug Delivery Rev.54, 2002, 3
15. Park, J.H., Ye, M.L., and Park, K., Biodegradable polymers for microencaps ulation of drugs, Molecules, 10, 146–161, 2005.
16. Almeida, Biomedical application of polymer based pharmaceuticals, Biomed ical Engineering – Group XII,2008.
17. Park, K. and Robinson, J.R., Bioadhesive polymers as platforms for oral-controlled drug delivery: method to study bioadhesion, Int. J. Pharm., 19, 19 84, 107.
18. Chang, H.S., Bioadhesive polymers as platforms for oral controlled drug deli very II: synthesis and evaluation of some swelling, water-insoluble bioadhesive polymers, J. Pharm. Sci., 74(4), 1985, 399.
19. Harris, D., Fell, J.T., Sharma, H.L., and Taylor, D.C., Gastrointestinal transit of potential bioadhesive formulations in man: a scintigraphic study, J. Contr olled Release, 12, 1990, 45.
20. Leung, S.H.S. and Robinson, J.R., Polymer structure features contributing to Mucoadhesion II., J. Controlled Release, 12, 1990, 187.
21. Elisangela C, Antonio J, Antonio A, Jose A, Luiz H, Preparation and charact erization of thermoplastic starch/zein blends, Mat. Res., 10, 3, 2007, 1516- 1 439.

22. Carien E. Beneke, Polymeric Plantderived Excipients in Drug Delivery, Mol ecules 14,2009, 2602-2620
23. Jones D. Pharmaceutical applications of polymers for drug delivery.
24. Lu H, Zhang S, Wang J, Chen Q. A review on polymer and lipid-based nanocarriers and its application to nano-pharmaceutical and food-based systems. Frontiers in nutrition. 2021 Dec 1;8:783831.
25. Dinda SC, Mukherjee B, Samanta A. Gum odina: a novel matrix forming material for sustained drug delivery. Oriental pharmacy and experimental medicine. 2011 Aug;11:131-6.
26. Samanta A, De A, Hasnain MS, Bera H, Nayak AK. Gum odina as pharmaceutical excipient. InNatural Polysaccharides in Drug Delivery and Biomedical Applications 2019 Jan 1 (pp. 327-337). Academic Press.
27. De A, Malpani D, Das B, Mitra D, Samanta A. Characterization of an arabinogalactan isolated from gum exudate of Odina wodier Roxb.: Rheology, AFM, Raman and CD spectroscopy. Carbohydrate polymers. 2020 Dec 15;250:116950.
28. De A, Das B, Mitra D, Sen AK, Samanta A. Exploration of an arabinogalactan isolated from Odina wodier Roxb.: Physicochemical, compositional characterisations and functional attributes. Polymers for Advanced Technologies. 2020 Aug;31(8):1814-26.
29. Samanta A, Ojha D, Mukherjee B. Stability analysis of primary emulsion using a new emulsifying agent gum odina. Natural Science. 2010 Jun 1;2(05):494.
30. Mitra D, Basu A, Das B, Jena AK, De A, Das M, Bhattacharya S, Samanta A. Gum odina: an emerging gut modulating approach in colorectal cancer prevention. RSC advances. 2017;7(46):29129-42.

31. Subha V, Kirubanandan S, Arulmozhi M, Renganathan S. Green Synthesis of Copper Nanoparticles Using Odina Woider Gum Extract and their Effect on Photocatalytic Dye Degradation. Chemist. 2018 May 1;91(1).
32. Sarraf A, Verton E, Addoun N, Boual Z, Ould El Hadj MD, El Alaoui-Talibi Z, El Modafar C, Abdelkafi S, Fendri I, Delattre C, Dubessay P. Polysaccharides and derivatives from Africa to address and advance sustainable development and economic growth in the next decade. Applied Sciences. 2021 Jun 4;11(11):5243.
33. Dalziel JM. Notes on the Botanical Resources of Yola Province, Northern Nigeria. Bulletin of Miscellaneous Information (Royal Botanic Gardens, Kew). 1910 Jan 1;1910(5):133-42
34. Mate CJ, Mishra S. Exploring the potential of moi gum for diverse applications: A Review. Journal of Polymers and the Environment. 2020 Jun;28:1579-91.
35. Gupta R, Kumar P, Narasimhan B. Synthesis, antimicrobial evaluation and QSAR studies of monochloroacetic acid derivatives. Arabian Journal of Chemistry. 2017 Feb 1;10:S909-20.
36. Yakovenko EA, Baimurzina YL, Raskil'dina GZ, Zlotskii SS. Synthesis and herbicidal and antioxidant activity of a series of hetero-and carbocyclic derivatives of monochloroacetic acid. Russian Journal of Applied Chemistry. 2020 May;93:712-20.
37. Ostwald R. Synthesis of chloroacetic acid and glycine labeled with radioactive carbon in the carboxyl group. Journal of Biological Chemistry. 1948 Mar 1;173(1):207-9.
38. Unni NG, Shah BH, Patel NM. Simulation Study of Reactive Distillation for Monochloroacetic Acid using CHEMCAD. Simulation. 2014;1:02.

39. Ozawa H, Tsukioka T. Gas chromatographic separation and determination of chloroacetic acids in water by a difluoroanilide derivatisation method. Analyst. 1990 Jan 1;115(10):1343-7.
40. Chang LW, Daniel FB, Deangelo AB. Analysis of DNA strand breaks induced in rodent liver in vivo, hepatocytes in primary culture, and a human cell line by chlorinated acetic acids and chlorinated acetaldehydes. Environmental and molecular mutagenesis. 1992;20(4):277-88.
41. Ellis DA, Hanson ML, Sibley PK, Shahid T, Fineberg NA, Solomon KR, Muir DC, Mabury SA. The fate and persistence of trifluoroacetic and chloroacetic acids in pond waters. Chemosphere. 2001 Feb 1;42(3):309-18.
42. Lewis TE, Wolfinger TF, Barta ML. The ecological effects of trichloroacetic acid in the environment. Environment international. 2004 Oct 1;30(8):1119-50.
43. Li X, Ma J, Liu G, Fang J, Yue S, Guan Y, Chen L, Liu X. Efficient reductive dechlorination of monochloroacetic acid by sulfite/UV process. Environmental science & technology. 2012 Jul 3;46(13):7342-9.
44. McCulloch A. Trichloroacetic acid in the environment. Chemosphere. 2002 May 1;47(7):667-86.
45. Santos MB, Dos Santos CH, de Carvalho MG, de Carvalho CW, Garcia-Rojas EE. Physicochemical, thermal and rheological properties of synthesized carboxymethyl tara gum (Caesalpinia spinosa). International journal of biological macromolecules. 2019 Aug 1;134:595-603.
46. Plapp BV. Mechanisms of carboxymethylation of bovine pancreatic nucleases by haloacetates and tosylglycolate. Journal of Biological Chemistry. 1973 Jul 1;248(14):4896-900.

47. Bisht SS, Pandey KK, Joshi G, Naithani S. New route for carboxymethylation of cellulose: synthesis, structural analysis and properties. Cellul. Chem. Technol. 2017 Jul 1;51(7-8):609-19.
48. Salmi T, Valtakari D, Paatero E, Holmbom B, Sjoholm R. Kinetic study of the carboxymethylation of cellulose. Industrial & engineering chemistry research. 1994 Jun;33(6):1454-9.
49. Hebeish A, Khalil MI. Chemical factors affecting preparation of carboxymethyl starch. Starch-Stärke. 1988;40(4):147-50.
50. Beghello L. The influence of carboxymethylation on the fiber flocculation process. Nordic Pulp & Paper Research Journal. 1998 Dec 1;13(4):269-73.
51. Chien SN. Exploring major factors affecting the fractionation of wood polymers by carboxymethylation. State University of New York College of Environmental Science and Forestry; 2011.
52. Sun T, Zhan B, Zhang W, Qin D, Xia G, Zhang H, Peng M, Li SA, Zhang Y, Gao Y, Lee WH. Carboxymethyl chitosan nanoparticles loaded with bioactive peptide OH-CATH30 benefit nonscar wound healing. International journal of nanomedicine. 2018 Sep 25:5771-86.
53. Wang ZJ, Xie JH, Shen MY, Tang W, Wang H, Nie SP, Xie MY. Carboxymethylation of polysaccharide from Cyclocarya paliurus and their characterization and antioxidant properties evaluation. Carbohydrate polymers. 2016 Jan 20;136:988-94.
54. Bartakova V, Kollarova R, Kuricova K, Sebekova K, Belobradkova J, Kankova K. Serum carboxymethyl-lysine, a dominant advanced glycation end product, is increased in women with gestational diabetes mellitus. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2016 Mar 30;160(1):70-5.

55. Upadhyaya L, Singh J, Agarwal V, Tewari RP. Biomedical applications of carboxymethyl chitosans. Carbohydrate polymers. 2013 Jan 2;91(1):452-66.
56. De A, Das B, Mitra D, Sen AK, Samanta A. Exploration of an arabinogalactan isolated from Odina wodier Roxb.: Physicochemical, compositional characterisations and functional attributes. Polymers for Advanced Technologies. 2020 Aug;31(8):1814-26.
57. Mitra D, Jena AK, De A, Das M, Das B, Samanta A. Prebiotic potential of gum odina and its impact on gut ecology: in vitro and in vivo assessments. Food & function. 2016;7(7):3064-72.
58. Badwaik HR, Kumari L, Maiti S, Sakure K, Nakhate KT, Tiwari V, Giri TK. A review on challenges and issues with carboxymethylation of natural gums: The widely used excipients for conventional and novel dosage forms. International Journal of Biological Macromolecules. 2022 Jun 1;209:2197-212.
59. Dodi G, Hritcu D, Popa MI. Carboxymethylation of guar gum: synthesis and characterization. Cellulose chemistry and Technology. 2011 Mar 1;45(3):171.
60. De A, Das B, Mitra D, Sen AK, Samanta A. Exploration of an arabinogalactan isolated from Odina wodier Roxb.: Physicochemical, compositional characterisations and functional attributes. Polymers for Advanced Technologies. 2020 Aug;31(8):1814-26.
61. Wang X, Liu B, Ren J, Liu C, Wang X, Wu J, Sun R. Preparation and characterization of new quaternized carboxymethyl chitosan/rectorite nanocomposite. Composites Science and Technology. 2010 Jul 1;70(7):1161-7.
62. Kaity S, Ghosh A. Carboxymethylation of locust bean gum: application in interpenetrating polymer network microspheres for controlled drug delivery. Industrial & engineering chemistry research. 2013 Jul 31;52(30):10033-45.

63. Bachra Y, Grouli A, Damiri F, Zhu XX, Talbi M, Berrada M. Synthesis, characterization, and swelling properties of a new highly absorbent hydrogel based on carboxymethyl guar gum reinforced with bentonite and silica particles for disposable hygiene products. ACS omega. 2022 Oct 19;7(43):39002-18.
64. De A, Das B, Mitra D, Sen AK, Samanta A. Exploration of an arabinogalactan isolated from Odina wodier Roxb.: Physicochemical, compositional characterisations and functional attributes. Polymers for Advanced Technologies. 2020 Aug;31(8):1814-26.
65. Jena AK, Das M, De A, Mitra D, Samanta A. Determination of efficacy of a natural tablet binder: characterization and in-vitro release study. Asian J Pharm Clin Res. 2014;7(3):184-68.
66. Dodi G, Hritcu D, Popa MI. Carboxymethylation of guar gum: synthesis and characterization. Cellulose chemistry and Technology. 2011 Mar 1;45(3):171.
67. Chakravorty A, Barman G, Mukherjee S, Sa B. Effect of carboxymethylation on rheological and drug release characteristics of locust bean gum matrix tablets. Carbohydrate polymers. 2016 Jun 25;144:50-8.
68. Adhikary P, Krishnamoorthi S, Singh RP. Synthesis and characterization of grafted carboxymethyl guar gum. Journal of applied polymer science. 2011 Jun 5;120(5):2621-6.
69. Ahuja M. Evaluation of carboxymethyl moringa gum as nanometric carrier. Carbohydrate polymers. 2017 Oct 15;174:896-903.
70. Santos MB, Dos Santos CH, de Carvalho MG, de Carvalho CW, Garcia-Rojas EE. Physicochemical, thermal and rheological properties of synthesized carboxymethyl tara gum (Caesalpinia spinosa). International journal of biological macromolecules. 2019 Aug 1;134:595-603.

71. Sharma R, Rana V. Effect of carboxymethylation on rheological and drug release characteristics of Terminalia catappa gum. Carbohydrate polymers. 2017 Nov 1;175:728-38.
72. Huang Y, Yu H, Xiao C. Effects of Ca2+ crosslinking on structure and properties of waterborne polyurethane-carboxymethylated guar gum films. Carbohydrate Polymers. 2006 Nov 23;66(4):500-13.
73. Sharma R, Rana V. Effect of carboxymethylation on rheological and drug release characteristics of Terminalia catappa gum. Carbohydrate polymers. 2017 Nov 1;175:728-38.