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A spotlight on application of microwave-assisted modifications of plant derived polymers in designing novel drug delivery systems

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ABSTRACT

Polymers are a fundamental part of numerous industries and can be conjugated with many other materials and components to have a vast array of products. Biomaterials have been extensively studied for their application in pharmaceutical formulation development, tissue engineering, and biomedical areas. However, the native form of many polymers has limitations concerning microbial contamination, susceptibility, solubility, and stability. Chemical or physical modifications can overcome these limitations by tailoring the properties of polymers to meet several requirements. The polymer modifications are interdisciplinary, cutting across conventional materials, physics, biology, chemistry, medicine, and engineering limitations. Microwave irradiation has become a well-established technique for a few decades to drive and promote chemical modification reactions. This technique allows ease of temperature and power control to perform the synthesis protocols efficiently. Additionally, microwave irradiation contributes to green and sustainable chemistry. In this contribution, microwave-assisted polymer modifications were described with a special focus on their application in developing several novel dosage forms.

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1. Introduction

Polymer research has access to a wide and inexpensive supply of resources nature provides. Natural polymers are widely available in huge quantities. They serve as raw materials for developing different drug delivery systems, including but not limited to the packaging, paper, and textile industries. In many of the novel drug delivery systems, synthetic and natural polymers will plays a crucial role [1,2]. Natural polymers, alternatively, are more appealing for pharmaceutical applications owing to their biocompatibility, low cost, biodegradability, chemical modifiability, and necessary surface qualities. Furthermore, majority of the natural polysaccharide polymers are hydrophilic, enzymatically degradable, and capable of maintaining the stability and therapeutic efficiency of drug molecules contained in them [3]. The viscosity, microbial degradation, partial or low solubility, stability issues, antigenicity, and non-uniform features from batch to batch are some of the most significant drawbacks to using natural polymers as carriers.

On the other hand, natural precursors qualities must frequently be adjusted to make them acceptable for certain uses. This is when polymer modification processes come in handy. The reformation should be done so that the current polymers physical and biological properties are not compromised. Functional groups derivatization, grafting copolymerization, crosslinking, polymer blending and microwave modification are the common methods of modification [Figure 1]. Despite the applications of natural polymers, the conventional

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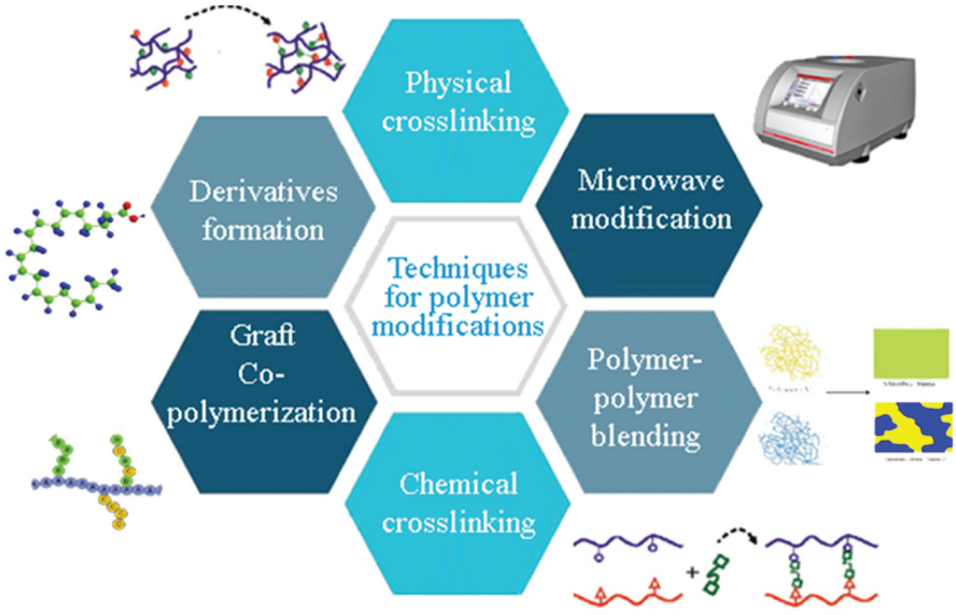

Figure 1. Various techniques for polymer modifications.

chemical techniques used are no longer environmentally friendly, owing to the energy-intensive nature of the process, the solvents and chemicals used in the process.

To overcome these disadvantages, researchers have been studying environmentally friendly procedures in recent years, intending to achieve as many 'green chemistry' principles [4] as feasible. Radiation-induced procedures have grown in popularity over the previous few decades. Microwave-aided techniques have been used in organic chemistry for a few decades, but just lately for polymerization reactions [5]. In recent years, microwave (MW) irradiation as an energy source for polymer chemical processes has received much attention [6]. Since the initial findings were published 20 years ago, MW irradiation has evolved into a well-established method for fostering and boosting chemical processes. In the previous five years, there has been significant growth in the implementation of this strategy. As a result, an increasing number of articles discuss the use of MWs in chemical synthesis. The current review describes the application of MW-aided polymer modifications in designing and developing various novel dosage forms [7].

2. MW-assisted polymer modifications

MW irradiation as a flexible method for numerous chemical processes has increased in popularity. Recent decades have seen a significant increase in interest in MW-assisted reactions as a potential source for laboratory reactions. MW synthesizers are now part of almost every organic and pharmaceutical chemistry laboratory's basic equipment set. In contrast to conventional household MW ovens, MW synthesizers were created for specific scientific needs [8]. These primarily monomodal MW systems provide several benefits, including precise temperature and pressure control, which improves the reactions' safety and reproducibility [9]. Domestic MW ovens were often employed for high-temperature, short-reaction-time reactions of highly MW radiation-absorbing materials. A shielded cavity is used in modern MW synthesizers to prevent explosions and increase heat transfer. A robotic arm may move the vials in and out of the cavity, automating the execution of numerous reactions. Other MW synthesizers include a flexible platform that can be easily customized to meet specific requirements, such as a large batch application and continuous flow coil with an additional round-bottom flask with a reflux condenser. Special attention has been given to unattended automated MW synthesizers, which also prepare vials to be reacted from the samples vials following the reactions, which have recently been introduced apart from performing simple MW-assisted reactions.

MW radiation uses electromagnetic waves, which operate at a frequency of 2.45 GHz with wavelengths between 1 mm and 1 m (or the equivalent frequency range from 300 GHz to 300 MHz) to reduce interference with radio and radar frequencies [10]. In this region, electromagnetic radiation only affects molecular rotation, not molecular structure. Compared to Brownian motion, hydrogen contacts, and chemical activation interactions, the energy involved in material-MW interactions (calculated using Planck's equation) is substantially smaller. Because of this, no

reaction occurs in the MW field, but it is quicker and more focused. They are consistent in conventional reactions like thermal heating. MWs directly interact with the molecules in the reaction mixture, resulting in a quick and limited temperature increase. MW heating also makes it simple to control reactions because it is 'instant on-instant off.' Energy transmission results from polar molecules in MWs trying to line up with the MW's rapidly shifting electric field. The primary mechanism underlying the absorption of MW by materials is the electromagnetic interactions peculiar to polar or ionic molecules [10].

When compared to syntheses performed with conventional heating, the key advantages of MW-assisted chemistry include shorter reaction durations, higher yields, and fewer side reactions. Although most of these improvements are thermal effects, they can't always be accomplished or replicated with traditional heating. Such 'specific' MW effects are frequently caused by dielectric heating properties such as an inverted temperature profile [11], solvent superheating at ambient pressure [12,13], or selective heating of highly absorbing compounds in less polar reaction mediums [14]. There is still debate about whether non-thermal MW effects could explain specific synthetic pathways found in MW but not in conventional heating [15,16] [Table 1].

3. Polysaccharides

Polysaccharides are a natural and sustainable source of macromolecular materials with outstanding performance [17]. They are abundant in nature, and practically all living species contain them. They can be found in seed tissues, plant stems and leaves, animal body fluids, crab shells, and insect wings. Bacteria, yeast, and fungi have them in their cell walls and extracellular fluids. However, their structure prevents them from achieving all of the qualities required for specific applications, necessitating several modification methods.

The development of complex polysaccharides as a drug binder is currently generating a lot of attention in biochemistry and pharmacology due to their sustainability, biodegradability, and biosafety [18]. The modification of biopolymers is currently attracting a lot of attention. There have been a lot of published investigations on the functionalization of synthetic polymers using the generated monomer chitin [19] as formed monomers have been published. The literature has reported in vitro biocompatibility and cytotoxicity of polyurethane elastomers based on chitin/1,4-butanediol blends [20]. Several methods for grafting natural materials with synthetic polymers have been reported. MW irradiation, on the other hand, is a powerful approach for imbuing macromolecules with desirable characteristics.

3.1. Guar gum

Guar gum is derived from the word 'guaran,' a polysaccharide that occurs naturally. This is extracted from the seeds of plant leguminous and Cyamopsis tetragonoloba. The extracted guar gum from these plants is obtained in crude form and is a neutral compound [21]. Like other gums, Guar gum is hydrophilic. It is available easily, possesses non-toxic nature, and is economical. Its peculiar property, so-called biodegradability, makes it a suitable compound for many pharmaceutical preparations. The polysaccharides present in the complex form are used as viscosifiers, flocculants, and matrices which are further used in the preparation of controlled drug release formulations for patients suffering from chronic diseases [22]. The derivatives obtained from the guar gum have great value and are used in the textile and food industries. Like other naturally-occurring gums, Guar gum also has some disadvantages upon storage. These include easy contamination by microorganisms, uncontrolled hydration, and reduced viscous nature upon storage for long days. Sometimes huge variations are observed in the physical and chemical properties of different batches of this compound when stored for longer durations [23]. Hence, purification and chemical modification of the compound are preferred before its use to improve its nature and applications.

In addition, grafting also plays a crucial role in enhancing the applications of guar gum. Previously radical initiators are used for graft copolymerization, but this method is not used recently due to their complexity during the processing of MW emissions. As an alternative to this, currently, on free radical mechanisms were applied for the synthesis of guar gum. This simple, globally accepted method possesses high reproducible nature and is considered a part of green chemistry.

The natural form of guar gum is rarely utilized in pharmaceutical applications due to a lack of stability. It's less stable owing to its biodegradable nature. Therefore, to rectify this disadvantage, surface modification is done through grafting. After the grafting is done, it is used as a medium to prepare drug formulations that requires the controlled release of therapeutic ingredient [24]. Currently, much-published evidence supports the use of MW-assisted modification methods to improve drug delivery [1,25–27]. Modifying the physicochemical properties of guar gum by utilizing the MW irradiation method at varying irradiation time was developed [18,23,28]. FTIR spectroscopic examination of the changed products

Table 1. Summary of MW assisted modifications of different polymers.

Corresponding section	Polymer	Grafting polymer	Method/Condition	Parameters	Initiator	Drug and Dosage form designed with modified polymer
3.1	Guar Gum	Acrylic Acid	MW irradiation	Time of exposure: 0 to 6 minutes Temperature: 60°C Reaction power : 800 W		Nanoclay Superabsorbent Composites
		2-hydroxyl ethyl methacrylate (PHEMA) as monomer	Graft copolymerization reaction	40 sec	CAN	5 - amino salicylic acid Matrix tablet
		acrylamide	Graft copolymerizatio	4 min, 700W		Triamcinolone tablets
3.2	Chitosan	Glutaraldehyde	MW irradiation	(1) **min, 50** °C **or** 190 seconds, 60 °C and 300W		Atenolol hydrogels
		Polyethylene glycol	MW irradiation	2450 MHz, 500 Watt and 120 s.		curcumin hydrogel membrane
3.3	Sodium alginate	PVP	MW-assisted polymerization technique.	70 °C, 2–120 min.		Ibuprofen hydrogel beads
3.4	Gum karaya-	G-poly (acrylamide):	MW-assisted grafting	2 min	CAN	
3.5	Moringa	N-vinyl-2-pyrrolidone (NVP)	assisted graft copolymerization technique	160W, 30 s,		
		N-vinyl imidazole	radiation-induced graft copolymerization technique			
4.1	Gum Colocasia	Acrylamide	MW assisted grafting	440W, 90 secs		
4.2	Gellan gum	Acrylamide		480W, 1 min heating and 1 min cooling,	Cerric ammonium nitrate	metformin HCl Controlled release tablets
4.3	Fenugreek seed mucilage	PVA, polyacrylamide	MW assietd grafting	40 sec		
4.4	Metallocene	Polyethylene (mPE)	MW-assisted surface modification of	2450 MHz, 1200 W		Enhanced blood compatibility
4.5	Aegle marmelos gum	Acrylamide	MW-assisted grafting of	<100C, 120 s		Diclofenac sodium matrix tablets
4.6	Cashew gum	Phthalic anhydride	MW-initiated rapid synthesis o	Phat-CG 1 (160 W, 3 min of reaction), Phat-CG 2 (250 W, 3 min of reaction), and Phat-CG 3 (250 W, 8 min of reaction)	Dimethyl formamide	Benznidazole nanoparticles
—	Poly (Acrylamide-co-2-hydroxyethyl methacrylate)/poly(vinyl alcohol) (P(AM-co-HEMA)/PVA	Glutaraldehyde	MW Assisted Synthesis	300 W, 10 min	Ammonium persulfate (APS) as an initiator.	Semi-IPN hydrogels

produced by MW irradiation revealed a broad peak at 3298 cm^{-1}, whereas the grafted guar gum revealed a second peak at 1541 cm^{-1}. The grafting with polyacrylamide resulted in improved crystallinity, which was demonstrated by an X-ray diffraction (XRD) examination. Scanning electron microscope (SEM) images confirmed the change in the physical appearance of guar gum after grafting. It has a granular appearance in the crude form, but the modified product obtained through MW irradiation revealed fibrillar structures. The key character of guar gum as a matrix form for the controlled release of triamcinolone drug is also assessed. The guargum-acrylamide grafted samples conferred an association linking drug release and MW exposure time. This concluded that grafted products obtained from this method have wide applications in the colonic delivery of drug products.

Differently, graft copolymerization of guargum was carried out utilizing the MW irradiation method, 2-hydroxyethyl methacrylate as the monomer, and ceric ammonium nitrate (CAN) as the free radical initiator [29]. Different grades of grafted copolymers were produced using various monomer and initiator concentrations. With the most grafting, a higher quality of copolymers was achieved. These generated grades were used as pH-sensitive drug delivery carrier systems, simulating gastrointestinal tract settings with pH variations. In pH 1.2, the swelling research showed a lower value, whereas a high value was observed at a basic pH 7.4 condition. This unusual behavior influences the development of various medication delivery methods by acting as a carrier [20]. Various mathematical models are used to study the kinetics involved in the drug release mechanism of 5 - aminosalicylic acid.

Yet, another interesting approach was carried out by Shruthi *et al* [30]. Acrylic acid grafted guar gum and silane-modified nano clays of different quantities are used in the preparation of superabsorbent nanocomposite particles by the method of MW irradiation. The optimization of reaction parameters for grafting was done. The addition of modified nano clay increases the swelling nature of the compound in different pH mediums ranging. The carboxylic and hydroxyl groups of grafted guar gum can effectively interface with the Silane groups found on nano clay. As confirmed from the XRD diffractograms, this tends to exfoliate nano clay. Thus, the recently created superabsorbent nanocomposites can be used to remove harmful dyes that pollute water sources. Additionally, this improves water storage and the efficient use of stored water for agricultural purposes. Though, this methodology not directly related with the development of novel drug delivery systems, but the method can be applied to the formulation several nanocomposite systems.

3.2. Chitosan (CS)

One of the well-known natural polymers with distinctive chemical, physical, and biological characteristics is CS. The C-2 hydroxyl groups in cellulose are substituted with acetamide in the structure of CS, which is structurally identical to cellulose; nevertheless, the presence of additional nitrogen (6.89%) makes CS more advantageous for usage in commercial applications. Biologically it is a highly intrinsic compound, so its properties do not alter with the amount of substance; more alkaline; hence this can be used in various applications when compared to naturally occurring acidic polysaccharides. CS and its products produced from enzymatic reactions can interact with human cells safely without adverse drug effects. As an antibacterial and antimicrobial agent having oxidative capabilities that can damage the bacterial cell membrane, CS is utilized therapeutically.

CS is a product of chitin-derived N-deacetylation. Depending on the number of amino acid groups in its chemical structure, chitosan is sold in various deacetylation grades and molecular weights [31]. Because of its alkaline nature, CS is insoluble in various aqueous solutions. Hence, this is considered to be a limiting factor. CS is insoluble at conditions like neutral and high pH values due to chemical groups like acetyl, hydroxyl, and amine groups. To increase the application areas of CS, its structural and chemical properties are modified, which ultimately enhances the solubility and porosity of the chitosan compound. Techniques such as physical modifications, chemical modifications, and molecular imprinting are used to improve their properties

Using MW technology, curcumin-containing CS and polyethylene glycol hydrogel membranes were created at specified frequencies, powers, and times of 2450 MHz, 500 Watt, and 120 s [31] [Figure 2a]. Distinctive polymers were solubilized, then they were mixed with the drug in two different ratios. Hydrogel formulations were fabricated by using untreated and MW- treated polymer and evaluated for various in vitro parameters such as the degree of swelling, degree of degradation, tensile strength, surface morphology, vibrational and thermal analyses, and in vitro drug release. Results showed that the MW- treated polymer contained formulation showed non-Fickian diffusion, slow erosion release mechanism with high swelling (96.49%) and low degradation (9.88%). The hydrophilic domains of the polymers were found to become rigid by the formation of hydrogen bonds between chitosan and polyethylene glycol moieties (OH/NH), while the hydrophobic domains were found to be elastic (asymmetric and symmetric CH moieties and/or C=O moieties). This significantly increased

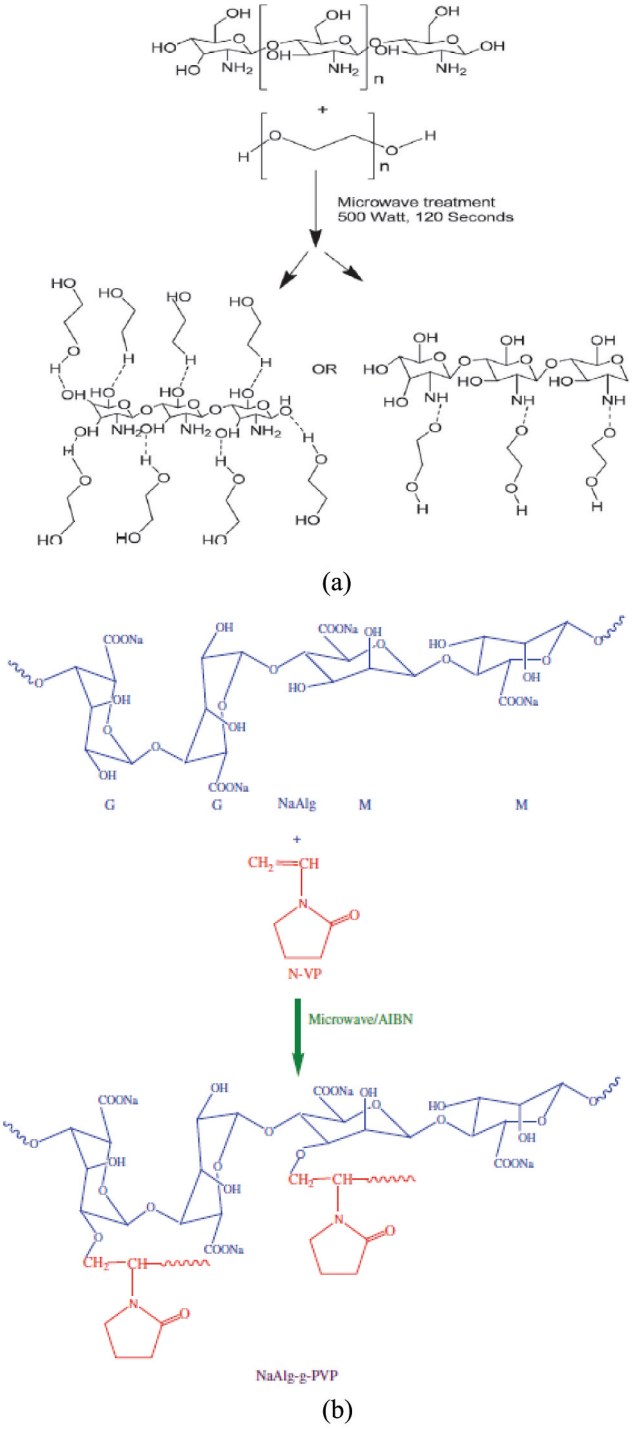

Figure 2. (A) Possible interaction mechanism of CS and PEG following microwave treatment (Reused from [31]) and (b) Proposed scheme for graft copolymerization of NaAlg (Reused from [35]).

the transition temperature and enthalpy (297.2°C and 4.24 J/g) of the chitosan moiety and (18.2 Mpa). The efficacy of the optimized formulation has been showed considerably faster wound healing than a control animal group. At day 14, a significant re-epithelization (87.26%) with a smaller wound size was noted. Therefore, it is recommended that MW aided chitosan- polyethylene glycol hydrogel membrane of curcumin to be used as a notable dosage form for applications in wound healing [32].

Conventional drug delivery systems often have a lower tendency for drug loading, so the model drug atenolol with cyclodextrin was introduced in a 1:1 ratio under MW conditions directly into the hybrid polymer network (HPN) matrix to increase drug loading capacity [33]. A cross-linked network of chitosan and gelatin made of a hybrid polymer called glutaraldehyde. Under the MW's circumstances, this hybrid polymer was developed with optimization. The amount of solvent, pH, and time is considered as process variables optimized with response surface methodology to lower the swelling backbone ratio. As a result, it functions as a drug carrier molecule. Additionally, the HPN matrix was examined for the in situ regulated release of atenolol at 37 °C under different pH settings. The Ritger-Peppas and Peppas-Sahlin and atenolol equations were found to fit together well after their release. Consequently, using MW process confirms the efficacy to design and synthesize HPN with enhanced therapeutic benefit.

3.3. Sodium alginate

Sodium alginate (NaAlg) is a heteropolysaccharide derived from brown seaweed. Na Alg possesses several attractive properties, such as hydrophilicity, high swelling capacity, biocompatibility, and the ability for cell attachment. Regrettably, NaAlg presents disadvantages such as loss of structural integrity and strong hydrophobic character [34]. It is also utilized in manufacturing hydrogels that have further applications in food processing, the cosmetic industry, the textile industry, and other areas because of its good solubility nature, strong affinity towards different resins, and better biodegradability features.

Jin *et al.* aimed to create a NaAlg graft copolymer utilizing MW-assisted synthesis [35] [Figure 2b]. Additionally, a modified polymer [poly(N-isopropylacrylamide)] was used to create pH-responsive beads with increased entrapment effectiveness. Polyvinyl pyrrolidone (PVP) was attached to sodium alginate complex using MW irradiation. Similar attempt was made by Mustafa et al. Using MW assistance, the graft copolymer NaAlg-g-PVP was created [36]. The preparation of the pH-responsive beads with improved entrapment efficiency is another aim of this investigation. To attain this study objective, the PVP was grafting onto sodium alginate using MW radiation. The produced copolymer was evaluated using FTIR, elemental analysis, 1 H-NMR, and thermogravimetric analysis. As a component of the ibuprofen (IB) drug delivery matrix,

the cross-linking series of NaAlg-g-PVP beads was created using glutaraldehyde. The manufacture of the beads was optimized by taking into account several variables, including entrapment effectiveness, swelling capacity, particle size, and information about their drug release. At pH values of 1.2 and 7.4, the effects of several parameters, such as graft yield and drug-to-polymer ratio, were examined. The lengthening of cross-linkage caused by increased drug-to-polymer ratios will reduce IB release. Similar to this, higher graft yield improved IB release.

3.4. Gum karaya

One variety of karaya gum is the sterculia gum, sometimes called kadaya, katilo, kullo, and kuterra [37]. Gum karaya is the dried exudates collected from Sterculiaurens Roxd and other related species of Sterculia (family Sterculiaceae), Cochlo spermumgossypium AP De Candolle, or other species of C kunth (family Bixaceae). Most of the gum's components are high molecular weight acetylated polysaccharides, which, when hydrolysed, yield galactose, rhamnose, galacturonic acid, and a negligible amount of glucuronic acid [38]. In cold water, dispersions can be as concentrated as 5%, whereas in hot water, low-pressure concentrations of between 18 and 20% can be reached. Karaya gum may bind to water molecules very effectively. Still, because the gum particles are not completely dissolved, they can swell, which is described as an increase in total volume relative to the dry mass of up to 60 times the initial volume [39]. MW-assisted grafting was used to combine extracted gum karaya mucilage with acrylamide. Following optimization, a formulation containing 5 g acrylamide, 200 mg ceric ammonium nitrate, and a 2 min irradiation period was chosen. With a grafting effectiveness of 77.59 percent, the optimized formulation yields a percentage grafting of 853.5 percent [40]. The methodology has been optimized using statistical application and the formed grafted polymer can be used in designing various novel drug delivery systems like nanoparticles or microparticles.

3.5. Moringaoleifera gum (MOG)

MOG is an emerging possibility as a natural polymer for creating innovative formulations and pharmaceutical excipients among natural gums [41]. MOG's structure might be customized to meet the needs of applications in a wide range of fields [42]. Several studies have looked into the relevance of various moringa plant components and its phytochemical qualities [43].

The MOG was grafted with N-vinyl-2-pyrrolidone (NVP) by MW-aided graft copolymerization procedure using ammonium persulfate (APS) as initiator [44]. The reaction vessel was exposed to a 30-second burst of 160 W radiation, cooled, and then treated with 80% v/v methanol. The graft copolymer was separated from the mixture as a precipitate. According to several findings, grafting NVP over the MOG lessens its crystallinity and evens its surface. Using the radiation-induced graft copolymerization process, N-vinyl imidazole was also used to graft MOG. A notable changes were noted in the mucoadhesive, antioxidant, and non-hemolytic properties of the grafted copolymer [45]. Despite this, no work has been documented on chemical modifications of MOG and its application [46]. In another research work, MW-assisted free radical modification of MOG has been performed by grafting with acrylamide and varied quantities of acrylamide monomer and ammonium persulphate as redox initiator [47]. The use of free-radical initiators increases the effectiveness of the procedure. The biodegradable graft copolymer made by combining MOG and polyacrylamide was appropriate for use as a tissue-engineered polymeric scaffold and a controlled-release polymeric matrix for the antibiotic metronidazole.

4. Other polymers

4.1. Colocasia

The Araceae family includes Colocasia esculenta. This plant is a monocot, primarily used for tubers and leaves. The corms have a lower concentration of lipids, vitamins, and proteins but a higher concentration of carbs. The use of crude taro gum as a binding and emulsifying agent has been studied [48,49]. Colocasia has a starch content of 70 to 80%. The grafting of extracted mucilage with acrylamide was done by employing MW-assisted grafting.

Colocasia-g-polyacrylamide was synthesized using an MW-assisted grafting technique. MW power, irradiation time, and gum concentration all affected percent yield, percent grafting, and percent Grafting efficiency, according to the findings. The production of a graft copolymer of Colocasia esculenta and acrylamide was confirmed using Fourier transform infrared spectroscopy, differential scanning calorimetry, X-ray diffractometry, and scanning electron microscopic investigations. As a result, it's possible to conclude that MW-assisted grafting was employed to change natural polymers and would increase their performance in various formulations [50].

4.2. Gellan gum (GG)

GG is a high molecular weight anionic deacetylated exocellular polysaccharide gum produced by a pure culture of Pseudomonas elodea during fermentation [51]. Acrylamide grafted gellan gum was produced using the MW-aided cerric (IV) ion-induced grafting technique (AAm-g-GG). The amount of CAN, the amount of acrylamide, and the duration of the MW irradiation were three different process factors that were used to enhance the synthetic characteristics. When all three parameters were at their highest, the grafted gum's grafting efficiency (GE percent) was higher. It was established that acrylamide was grafted onto gellan gum using FTIR and 13C NMR. SEM showed the modified gum's morphology to be more heterogeneous and lobule-shaped than the native gum. Although the unmodified monomer (acrylamide) is toxic, a toxicity study of AAm-g-GG during the LD50 research in mice showed that there was neither morbidity nor mortality at a dose of 2000 mg/kg body weight. In creating a sustained-release tablet containing metformin hydrochloride, grafted gum was utilized as a rate-controlling polymer. The Higuchi square root kinetic model was used to predict the drug release, which was delayed by up to 8 hours. The releasing mechanism was governed by Fickian diffusion [52].

4.3. Fenugreek seed mucilage

A high percentage of fenugreek seed mucilage (FM) can be isolated from Trigonella foenum graecum L seeds. FM is already described as having various pharmaceutical applications, such as an antidiabetic, mucoadhesive, and binding agent. Galactomannans, a primary component of mucilage that often serves as a hydrophilic/sustaining agent [53].

The graft copolymer of FM with polyvinyl alcohol was prepared by MW irradiation process [54]. The grafting efficacy was enhanced with an increase in the concentration of initiator up to a certain extent and then again declined. However, grafting efficacy was continuously enhanced with monomer concentration. The intrinsic viscosity showed that the modified polymer has longer polymeric chains, thus causing more swelling and controlled drug release. The study was extended to histopathological studies to confirm its non-toxic nature. All these properties made the material a novel excipient for several drug-delivery devices and tissue engineering scaffolds. The polymeric blend of FM was grafted with PVA and used as a tissue scaffold.

4.4. Metallocene

Recent advances in metallocene single-site catalyst technology produced a new variety of polyolefins with enhanced toughness, elasticity, clarity, and sealability. Many of these materials have the potential to replace flexible polyvinyl chloride. Metallocene polyethylene has many medical applications, including blood bags, disposable bags, syringe tubes, storage bottles, etc. Polyethylene (mPE) has an exceptional permeability to oxygen and acts as a barrier for water and ammonia. All these features make mPE a plausible candidate for several medical implants [55]. Grafting of metallocene and Surface modification of mPE was performed by MW-assisted methodology. A decrease in the contact angle of the sample was identified, confirming the enhanced hydrophobicity and biocompatibility. Further, scanning electron microscopy of the sample depicted increased roughness and formation of holes, thus supporting the outcomes. Clotting time was augmented, as evident from the prothrombin time, and activated partial thromboplastin time. The extent of hemolysis was lowered with a modified polymer. Hence the grafting of polymer results in its implication for the fabrication of implants, blood-contacting devices, and vascular prostheses.

4.5. Marmelos gum

The gum obtained from ripening fruits of Aegle marmelos is indigenous to India having an astringent taste. Various parts of the Aegle plant were used for several therapeutic purposes, such as for treating fractures, asthma, wound healing, jaundice, etc. In the research work carried out by Bhattacharya, a graft copolymer of marmelos gum was synthesized using poly(acrylamide) as a monomer, and the process was optimized to evaluate the efficacy of modified polymer in drug release characteristics [56].

MW power, exposure time, and gum concentration were identified as variables, and the experimental runs were evaluated for grafting efficiency. Synergistic effects of MW power and exposure time on grafting efficiency were determined. Surprisingly, gum concentration has not contributed much to the selected response. The desirability approach identified modified gum synthesized using 80% MW power, 120 s exposure time, and 2% gum concentration as optimized parameters. The drug release behaviour of modified and unmodified gum was compared by formulating diclofenac matrix tablets. Formulations containing modified gum were shown zero-order kinetic with n value>1, confirming

the super case II transport (with swelling and polymer erosion. Thus, MW-assisted grafting was proven an efficient technique in modifying the release behavior of model drugs [56].

4.6. Gum mastic

Gum mastic is a natural resin found in a wide variety of shrub Pistacia lentiscus, cultivated for its aromatic resin. It has been recognized as a medical agent in treating several gastrointestinal infections. It has also been confirmed for antibacterial and anti-ulcer activity. Gum mastic has its recognition as a controlled release agent, matrix system, and stability enhancer in designing several novel formulations [57].

The grafted copolymer of gum mastic was synthesized using acrylamide as a monomer and the methodology was optimized using the Box-Behnken design [58]. CAN was used as a free radical initiator. The monomer, initiator concentration, and temperature concentrations were selected as process variables to optimize the process for a percentage of yield, grafting, and grafting efficacy. Generally, grafted copolymer shows macromolecular series with core polymeric backbone chains as various side chains. Grafted gum mastic has shown considerable sustained release behavior compared to the unmodified polymer. A copolymer that has undergone grafting displays macromolecular series with one or more block molecule series linked to the main polymeric backbone chain as different side chains. Modified-release formulations can be created using natural polysaccharides like gum mastic via graft polymerization.

4.7. Cashew gum

Cashew gum generally consists of 72% galactose, 15% glucose, 4–5% of glucuronic acid 3–4% of rhamnose, 4–6% of arabinose with branched-chain polymer bonds of β-D-galactose (1→6 and 1→ 3). Cashew gum has many applications in tissue engineering, the food industry, and odontology owing to its admirable physical properties [59]. The high solubility of cashew gum makes it a prised pharmaceutical excipient, especially in designing hydrophilic matrix tablets to promote a controlled drug delivery system. Its application can be extended as a carrier for low-soluble drugs by altering its solubility through simple chemical modifications. The functional group present in its structure (especially to primary hydroxyl groups) provides the required chemical reactivity for functionalization to make cashew gum a versatile excipient [60].

Antonia et al. created MW-aided synthesis of phthalate cashew gum [61]. Three distinct applied voltage and reaction time settings (160 W-3 min, 250 W-3 min, and 250 W-8 min) were used in an MW reactor to irradiate cashew gum and phthalic anhydride, producing three different cashew gum derivatives. It was clear that higher exposure levels and longer exposure times resulted in more hydrophobization of the gum. To ensure the reproducibility and dependability of the methodology used, magnetic agitation and temperature were also controlled. Aa nano specific drug delivery system has been synthesized using benznidazole as a model drug and modified cashew gum as polymer. Prepared nanoparticles have a mean particle size of 288.8 nm, good zeta potential, and exceptional controlled release nature. All these results confirmed that the Phthalated cashew gum could be the best alternative to protect the drug from a stimulated gastric fluid environment.

5. Conclusion

This paper reports the applicability of MW-assisted polymer modifications in designing several novel dosage forms. Selected polymer modifications were discussed to validate this technique's versatility, and various optimized process parameters were summarized. The application of MW technology established promising results owing to its green and sustainable nature. In addition, MW technology has yet to receive industrial application, which is currently uncertain. Hence, more investigations are essential to show the possible cost benefits of MW technology for pharmaceutical, biomedical, and tissue engineering applications

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Disclosure statement

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