

Ultrasound Assisted Modification of the Polysaccharides

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ABSTRACT

Recent studies focus on the chemical modification of polysaccharides to improve their properties and enhance their applications. Ultrasound assisted chemical modification of two important polysaccharides viz. guar gum and chitosan. Chemical modification of guar gum (GG) under sono-chemical conditions is carried out using epichlorohydrin (EP) as the crosslinking agent.

Similarly, the chemical modification of chitosan (CH) was carried out under sono-chemical conditions employing citric acid (CA) as the crosslinking agent. The resultant cross-linked products obtained in both cases were characterized by scanning electron microscopy (SEM), Fourier transform infrared spectroscopy (FT-IR). It was found that, the temperature of reaction at which modification was done play an important role in the morphology and thermal stability of the modified product.

Keywords: Polysaccharides, guar gum, chitosan, ultrasound, cross-linking.

I. INTRODUCTION

Natural polysaccharides are widely used in the pharmaceuticals to improve the solubility of poorly soluble drugs and to enhance their bioavailability and desired drug release. Chemically modified natural polysaccharides are being used in advanced drug delivery system to fulfill the multitasking functions performed by a drug. Some natural polysaccharides like guar gum and chitosan are of much interest because of their environmental-responsive gelation characteristics in order to achieve controlled drug release according to specific therapeutic needs and chemically classified as galactomannan [1] high molecular weight hydrocolloidal polysaccharide in case of Guar gum. Guar gum is a linear polymer having chain of β -D-mannopyranosyl units linked (1-4) with single member α -D-galactopyranosyl units occurring as side branches [2]. Chitosan is a biodegradable, biocompatible, antimicrobial and nontoxic polysaccharide composed of 1-4 linked D-glucosamine deacetylated unit and N-acetyl-D glucosamine acetylated unit.

The most important property of guar gum is its ability to hydrate rapidly in cold water to attain uniform and very high viscosity at relatively low concentrations but it is insoluble in most organic solvents and has strong hydrogen bonding properties and chitosan is soluble in acidic solution of pH below 6.5 and becomes the only polysaccharide that have property to hold the high density of positive charges [3-8]. Chitosan is used as an excipient in pharmaceuticals as support material for tissue engineering, food, medical and biomedical fields in

drug delivery system[9]. The increase in the thickness of chitosan membrane decreases the rate of release of drug when used in drug delivery system [10]. The advantages of Chitosan has minimum side effects and prolong the efficacy of the drug. Chitosan having low toxicity good biocompatibility has proved to be a good pharmaceutical excipient in both conventional and novel applications [11].

The application of ultrasound has grown rapidly during the recent past in a large number of laboratories across the world. . The chemical effects of ultrasound are significant, and leads to the improvements in chemical reactions. In some cases, ultrasonic irradiation can increase reactivity by nearly a million times. Ultrasonic irradiation differs from traditional energy sources (such as heat, light, or ionizing radiation) in duration, pressure, and energy per molecule. Because of the immense temperatures and pressures and the extraordinary heating and cooling rates generated by cavitations bubble collapse, ultrasound provides an unusual mechanism for generating high-energy chemistry [16]. The application of ultrasound are well known in organic synthesis, environmental protection (the destruction of both chemical and biological contaminants) and process engineering (improved extraction, crystallization, electroplating and new methods in polymer technology), which may have an effective impact in process chemistry and represent a realistic option in industry.

Ultrasound modified chitosan and guar gum improves the aqueous solubility as compared to the native chitosan and it has been a widely used as a drug carrier [12,15]. Chemical crosslinking agent such as glutaraldehyde, formaldehyde, terephthaloyl chloride, epichlorohydrin etc. are used to control the drug release from diffusion controlled polymeric drug delivery matrices [13]. Chitosan and guar gum has been used in the drug delivery system in the form of tablets, gels micro and nano-particles [14].

The aim of the present study is to modify and characterize chitosan and guar gum under sonication conditions for its application in controlled drug release. Modification of these polysaccharides by crosslinking with epichlorohydrin under ultrasonication conditions has been achieved. The biomaterials so obtained are characterized using SEM, FTIR.

II. MATERIALS AND METHODS

2.1 Materials

Guar gum (GG) and chitosan has been obtained from Merck, Mumbai. NaOH and epichlorohydrin are purchased from Himedia, Mumbai. Unless stated otherwise, reagents were used as purchased, without further purification. All solutions are prepared in distilled water. Transducer Digital Sonifier Model 450 (Branson Ultrasonics Corporation, USA) is used for generating the ultrasound with a maximum power input of 400 W and a frequency of 20 kHz.

2.2 Modification of polysaccharides

To crosslink guar gum (GG), 2.00 g of native GG is mixed with 10 ml of 5 M NaOH and 1.4 ml of distilled water until a uniform paste is obtained. The epichlorohydrin (0.8 ml) is added to the mixture and kneaded thoroughly in order to get a homogeneous mixture. the mixture is heated 12 h under ultrasonication condition at

40 °C.. The modified gels are dried in an oven at 50 °C till no further change in weight of polysaccharides are observed.

2.3 Scanning electron microscopy (SEM) characterization

A JEOL JSM-1610 scanning electron microscope (SEM) is used to perform textural characterization of native and modified polysaccharides. For SEM studies, the samples are mounted on metal stubs using double-sided adhesive tape and submitted to a JOEL gold sputtering coater for 6 min to make them conducting before analysis. different Magnifications are applied for each sample in order to estimate the morphology.

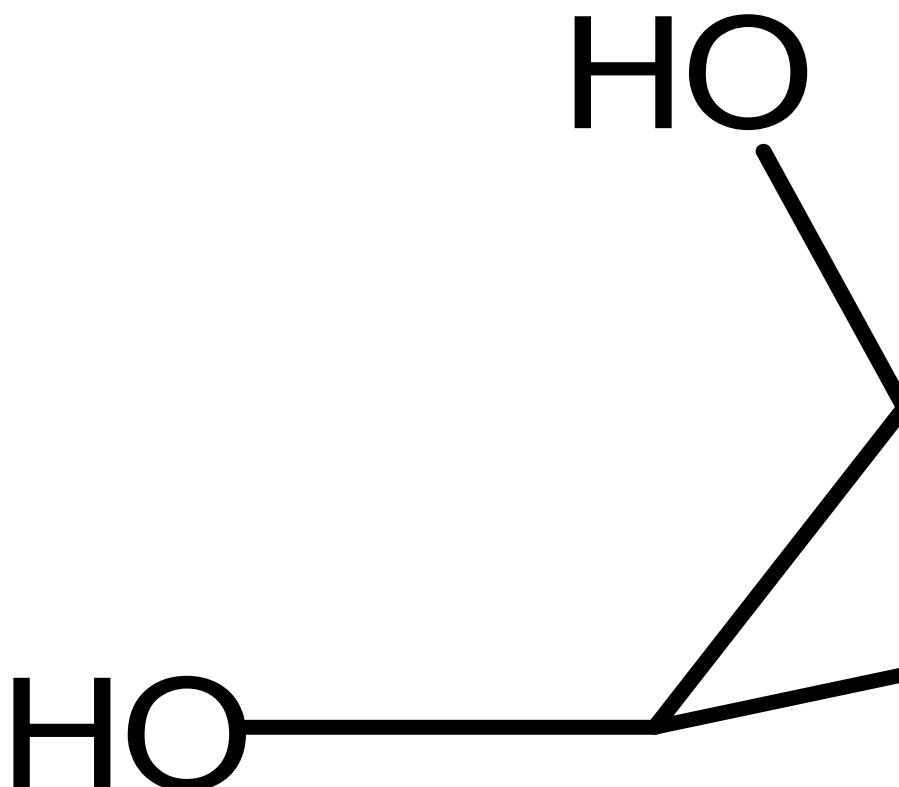
2.4 FTIR analysis

The Fourier Transformation IR spectra (FTIR) of native and modified polysaccharides are recorded with Bruker tensor 27 spectrophotometer between 400 and 4000 cm^{-1} . The samples are thoroughly grounded with dry KBr and tablets are prepared by compression under vacuum.

III. RESULTS AND DISCUSSIONS

3.1 Sonochemical modifications of polysaccharides

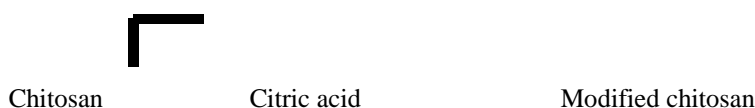
Modification of guar gum is carried out in order to improve its properties. The reaction of guar gum with epichlorohydrin occurs with formation of guar gum alkoxide by addition of NaOH. When epichlorohydrin is added to the system, the epoxy ring opens, resulting in a new macromolecular epoxy. In the next stage, the macromolecular epoxy reacts with other guar gum alkoxide forming a bridge between chains (**Scheme 1**). Crosslinking drastically reduces the segmental motion in a polymer and formation of inter-chain linkages leads to the formation of three-dimensional network⁷. Ultrasonic irradiation, as a new technology, has been widely used in chemical reactions. When ultrasonic waves pass through a liquid medium, a large number of micro bubbles form, grow, and collapse in very short span of time, about a few microseconds. Ultrasonication generates alternating low-pressure and high-pressure waves in liquids, leading to the formation and violent collapse of small vacuum bubbles. This phenomenon is termed cavitations and causes high-speed impinging liquid jets and strong hydrodynamic shear-forces. These effects are used for the deagglomeration of nanometer-size materials. In this aspect, ultrasonication is an alternative to high-speed mixers and agitator bead mills. Ultrasonication has been used as a technique to disperse nano-materials in different matrices[17-23].



Scheme 1: Ultrasound assisted modification of guar gum

Modification of chitosan by surface grafting is an efficient technique to produce chitosan with enhanced physico-chemical properties and biocompatibility. Citric acid (which is commonly used in food, beverage, chemical and medical industries) is considered as potential molecule for the modification of chitosan. Surface grafting with citric acid leads to enhanced hydrogen bonding, and balanced hydrophilicity of the biomaterials. Citric acid modified chitosan is used as nucleation catalyst and for the removal of heavy metals etc. Chemical modification of chitosan under ultrasonicator, using 0.1 mol acetic acid and 1% citric acid (CA) solution was prepared in deionized water. Then, both the solutions were mixed and the mixture was sonicated for 6 hours at temperatures viz. 40°C to get the modified chitosan. The schematic representation is shown in **Scheme 2**.

From the **Scheme 2** it is evident that, the citric acid molecules attack on the $-NH_2$ group of the chitosan and led to grafting of citric acid on the chitosan moiety. The modification was authenticated by using some advanced analytical techniques like FT-IR spectroscopy, SEM etc. The modification of chitosan can be verified by comparing the FT-IR spectrum of pure chitosan and citric acid treated chitosan.



Scheme 2: Chemical modification of chitosan under ultrasonication

3.2 FTIR analysis

The overlaid IR spectra of native and modified polysaccharides are represented in Fig.1. The spectra exhibit the typical bands and peak characteristic of polysaccharides. An IR band at 870-899 cm^{-1} appears due to the presence of β - glycosidic linkage in backbone chain of GG. The presence of a very strong and broad absorption band at 3430 cm^{-1} is assigned to OH bond stretching¹⁵. The peak obtained at 2930 cm^{-1} results from stretching modes of the C-H bonds of methyl groups (-CH₃). The absorption band appearing at 1649 cm^{-1} is due the OH bend belonging to water molecules. CH₂ group bending is assigned to an absorption band located at 1423 cm^{-1} , and the bending of CH₂-O-CH₂ appears in the 1018 cm^{-1} frequency region. A significant modification can be observed in the well defined spectrum of modified guar gum. The IR spectra of the modified guar gum (S1) show a reduced intensity of the absorption band located at 3430 cm^{-1} , due to OH stretching, indicating that some OH groups are crosslinked. Thus, the decrease in band intensity confirms the substitution of epichlorohydrin. Further, the FTIR spectra of modified GG exhibit decrease in intensity of peak is observed in the samples modified by ultra-sonication (S1) technique. This shift in peaks suggests breakage of hydrogen bonds, originally present in native guar gum . Natural gums usually contain fractions of sugar acid units which would usually impart a weakly anionic character to the gum macromolecule. The wave numbers between 800 and 1200 cm^{-1} represents the finger print region for carbohydrates.

Fourier Transformation Infrared Spectroscopy (FTIR) is a powerful tool for the identification of functional groups present in an organic compound. FT-IR spectra of pure and Chitosan modified at different temperatures presented in Fig 2. The spectrum of pure Chitosan (CH) shows an O-H stretching band at 3464 cm^{-1} The C-N stretching band appears at 1384 cm^{-1} and peak at 1068 cm^{-1} is due to C-O vibrations.

The FT-IR spectrum of citric acid modified Chitosan (CA-CHM) at 40 °C exhibits, band at 1639 cm^{-1} due to stretching vibrations of the carbonyl group (C=O) group of amide. The band at 3363 cm^{-1} is due to O-H stretching vibrations. The C-O-C vibration band appears at 1079 cm^{-1} and the band at 1016 cm^{-1} is due to C-O bond vibrations.

3.3 SEM Analysis

Scanning electron micrographs of native GG and modified GG are shown in Fig. 3. It is clear from both the micrographs of the native guar gum magnified 500 times has a flakes in bulk . After modification of 1500 the native guar gum, there is a loss of particulate morphology as observed in native form as indicated by exfoliated surface. Exfoliated morphology can be attributed to mechanical effect of ultrasound. The SEM image of pure Chitosan magnified 500 times exhibit the presence of Chitosan flakes in bulk. SEM image of the Chitosan modified at the 40⁰C shows relatively smooth surface at a magnification of 1500. This is due to the fact that grafting of chitosan with citric acid molecules leads to the binding of polymer chains with hydrogen bonds due to the presence of amine and hydroxyl sites in the Chitosan chains and the presence of carboxylic group in the citric acid moiety. As a result of this, the polymer chains will flip on each other which leads to surface smoothness.

IV. CONCLUSION

In conclusion, the modification of polysaccharides has improved their properties which has been confirmed by FTIR spectroscopy and SEM analysis. the modification of the guar gum was carried out by using epichlorohydrin; the SEM studies indicate the change in morphology from a regular to disintegrated surface. Dynamic mechanical analysis has shown that the modified GG samples exhibit shear thinning behavior at higher shear rates due to reduced inter chain bonding.

The chitosan has also been successfully modified with citric acid at 40 °C temperature . The various characterization techniques show that citric acid has been grafted to the Chitosan backbone. The modified Chitosan exhibit high stability and better hydrophilicity in comparison to native chitosan .

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Figure Captions

Fig. 1. FTIR graph of native and modified GUAR GUM

fig.2. FTIR graph of native and modified Chitosan

Fig. 3. SEM images of native and modified polysaccharides

FIGURES

fig 1

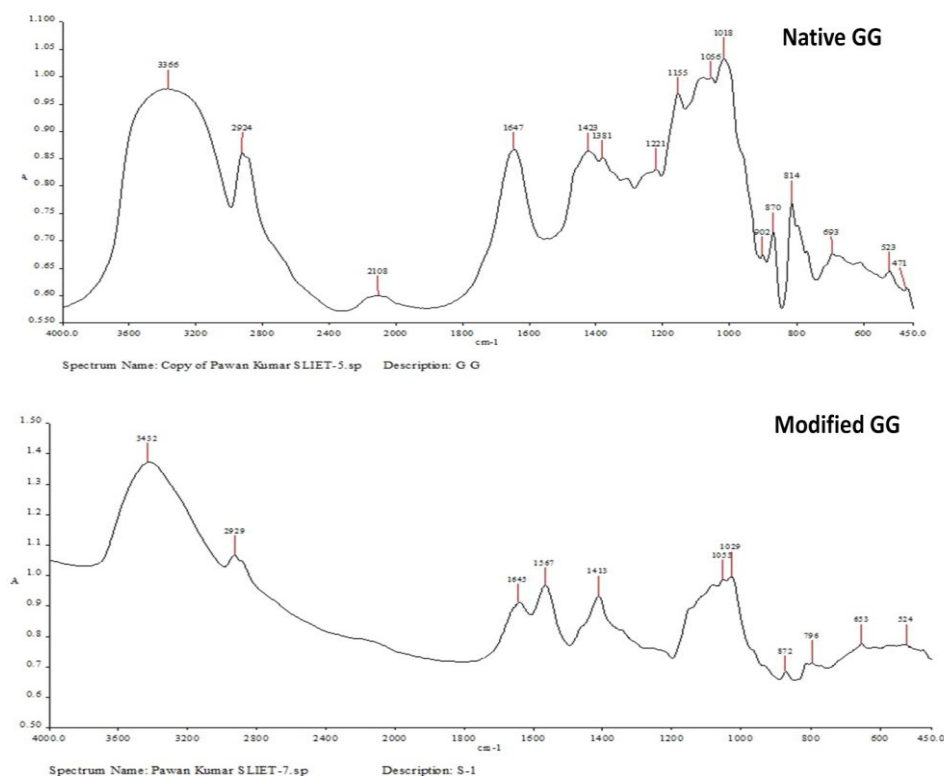


fig 2

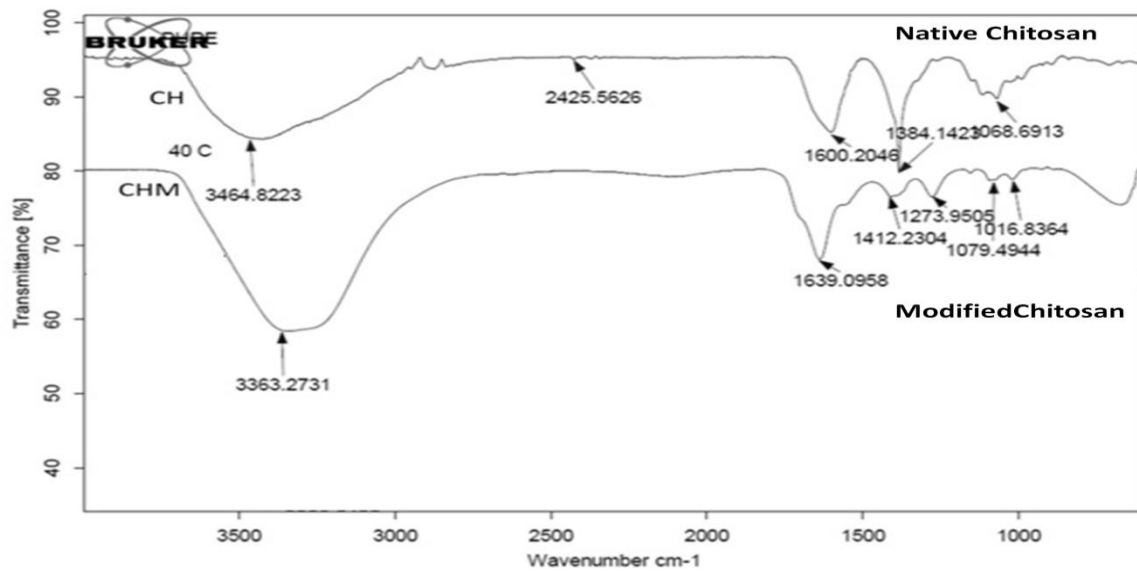
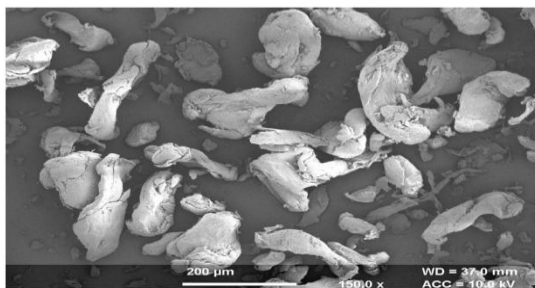
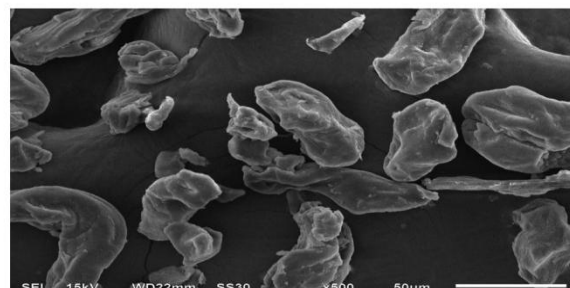


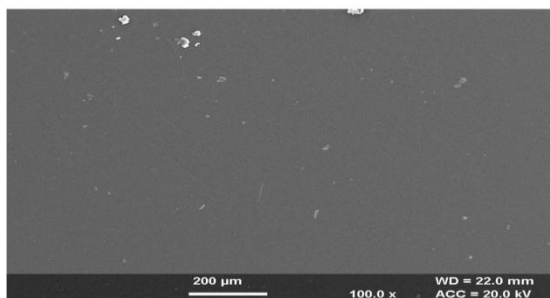
fig 3



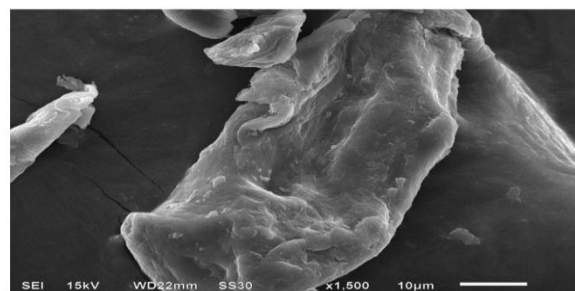
Native Chitosan



Native Guar Gum



Modified Chitosan



Modified Guar Gum