“Studies on Hydrogels Based on Polyacrylamide and Guar Gum Derivatives”

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CERTIFICATE

This is to certify that Mr. PIYUSH GARG have satisfactorily completed the project work entitled "**Studies on Hydrogels Based on Polyacrylamide and Guar Gum Derivatives"** in partial fulfilment of the requirement of the award of Degree of Master of Technology, Delhi during the academic session 2012-2013. This work has not been submitted in part or full in any other University or Institution for award of any other degree or diploma.

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ABSTRACT

As we all know the importance of green chemistry synthesis and characterization of environmental friendly modified natural polymers is need of time. These natural polysaccharides also eliminates the danger to health and environment. Guar gum is one of the important naturally occurring polymer having wide applications due to its rheological modifying properties in medicinal, pharmaceutical, food, textile and scores of other industrial and commercial sectors. There has been wide study on physiochemical and pharmaceutical properties of guar gum but study on modified guar gum and its derivatives are quite lacking. Unmodified guar gum has certain drawbacks like lack of clarity and free flowing properties, fall in viscosity and turbidity on prolong stay, etc. These draw backs can be overcome by modifying and derivatization of guar gum and can be used in multidiscipline fields.

In this work we are preparing blend biodegradable interpenetrating polymer networks(IPNs) hydrogels using polymers both from natural sources and synthetic ones i.e Carboxymethyl guar gum along with Polyacrylamide with varying concentrations of carboxymethyl guargum and evaluate their properties, characteristics and their potential applications in different areas of biomedical and pharmaceutical applications. Characterization of synthesized hydrogels is carried out using different characterization techniques like FTIR & SEM. Other studies such as swelling studies and their physical properties like compression strength using UTM have also been evaluated.

The blend hydrogels also exhibited the improved mechanical properties compared to those of homopolymers. The Carboxymethylated Guar Gum/Polyacrylamide blended hydrogels with the capacity of absorbing a high amount of water is also evaluated for its drug release profile at different pH. The drug used in this study was the ciprofloxacin hydrochloride. Release kinetics of ciprofloxacin hydrochloride from swollen polyacrylamide/carboxymethyl guargum cross-linked hydrogels in aqueous media have been successfully studied.

OBJECTIVE

Keeping in view the biodegradable behaviour and high viscosity properties of Guar Gum and its various applications, blend biodegradable hydrogels of Carboxymethyl Guar gum and polyacrylamide have been tailored.

The main objectives of the present project are as follows:

1. To prepare Interpenetrating Polymer networks(IPNs) hydrogels of Carboxymethyl Guar gum and Polyacrylamide by free radical polymerization method with varying concentration of carboxymethyl guar gum and were then cross linked with N,N'-methylene-bisacrylamide too.

2. To characterize these blend hydrogels by different physical techniques such as Scanning Electron Microscopy(SEM) and Fourier Transform Infra-Red Spectroscopy(FTIR) for evaluation of structural aspects.

3. To study physical properties like compression strength using Universal Testing Machine(UTM).

4. To study the swelling kinetics of different samples in distilled water.

5. To study the Release kinetics of drug (ciprofloxacin hydrochloride) from swollen polyacrylamide/carboxymethyl guar gum cross-linked hydrogels in aqueous media with varying pH.

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ABBREVIATIONS

GG : Guar Gum

CMGG : CarboxyMethyl Guar Gum

AGU : Anhydroglucose Units

CFX.HCl : Ciprofloxacin Hydrochloride

DNA : DeoxyRibo Nucleic Acid

MIC : Minimum Inhibitory Concentration

IPNs : Interpenetrating Polymer Network

PNIPAM : Poly(N-isopropylacrylamide)

AAm : Acrylamide

KPS : Potassium Per Sulphate

NNMBA : N,N’-methylene-bisacrylamide

FTIR : Fourier Transform Infra-Red

SEM : Scanning Electron Microscope

FEG : Field Emission Guns

ASTM : American Society for Testing Materials

ISO : International Organization for Standardization

UTM : Universal Testing machine

CHAPTER 1

INTRODUCTION

Hydrogels are hydrophilic polymers that swell to an equilibrium volume in the presence of water but preserve their shape[1]. The shape stability and the insolubility in water of hydrogels are the result of the existence of a three-dimensional network. The swollen state is a consequence of the balance between cohesive forces and dispersion forces acting on the hydrated chains. Cohesive forces are usually due to covalent crosslinking (chemical hydrogels) but also can be related to electrostatic, hydrophobic, or dipole–dipole forces (physical gels). Sorption of penetrants into glassy polymers and the consequent release of active ingredients from the swollen matrices have been extensively investigated[2–5].

Also Increasing awareness of environment and ecological problems has led to a paradigm shift on the use of biodegradable materials, especially from renewable agriculture feedstock and marine food processing industry wastes[6]. Consequently, considerable attention has been attracted by natural polymers and their derivatives[7]. Among the several candidates including natural polymers and their derivatives, guar gum (GG), is one of the promising materials for biodegradable plastics. It is a high-molecular weight water-soluble non-ionic natural polysaccharide isolated from the seed endosperm of the guar plant. It is also a versatile biopolymer with immense potential and low price for use in the non-food industries[8].

Guar gum is naturally occurring non-ionic polysaccharide which is derived from the Guar seed *"Gyamposis tetragonolobus"*. Guar is commonly called as "gawar phalli". This leguminous plant has been grown for centuries in India Guar and is mainly being used as food material for both man and animals. It is also used as viscosity builder and water binder in various industries. It is a member of the class of galactomannans, which consist of α (1–4)-linked β-D-mannopyranosyl backbone partially substituted at O-6 with α-D-galactopyranosyl side groups[9]. Because of these associations, guar gum possesses remarkable rheological properties[10] and is widely used in food, personal care[11], and oil recovery. Synergism of GG with other materials, including xanthan gum, agar, carageenan,

starch, etc., is well studied [12]. In addition, GG is also found to exhibit surface, interfacial and emulsification activities [13].

Featuring different physio-chemical properties, GG is a versatile material used for many applications. Galactomannans are often used in different forms for human consumption. It is an excellent stiffener and the absence of toxicity allows its use in the textile, pharmaceutical, biomedical, cosmetic and food industries [14]. In recent years, modified guar gum has been found numerous applications in cartridge explosives, mining, froth flotation, oil recovery, textile printing and waterbased paints [15]. Among many chemically modified methods, chemical crosslinking is a convenient and feasible method to modify the structure of natural polymers and thus makes them attractive biomaterials for further applications. In previous papers, through crosslinking with glutaraldehyde, phosphate, urea–formaldehyde and borax, modified guar gum was applied in various fields, such as controlled drug release [16], colon specific drug delivery [17], liquid pesticide [18], water retention [19] and so on.

However, the high water sensitivity and bad film forming ability of guar gum and its derivatives limit their applications as useful film materials. Guar gum forms viscous colloidal dispersion when hydrated in cold water. These are not very stable due to biodegradation that is why guar gum is rarely used in its natural forms. At present there exists several different ways to overcome these problems, one of them is mixtures of synthetic polymers with natural polymers (preparation of polymer mixtures) which have good biodegradable properties; another option is the synthesis of polymers with use of products from natural sources [20].

So, Polymer blending is an important method for modification or improvement of the physical properties of polymeric materials. Blends of polymers may result in cost reduction and better processing, thus enhancing the properties to be maximized [21]. On several occasions the initial dispersion of the blend component is further promoted by crosslinking, creation of interpenetrating networks, mechanical interlocking comments and use of ‘compatibizing agents’ in order to ensure that no demixing will occur at a later stage [22]. The objective of the present work was to develop blend hydrogels based on Carboxymethylated Guar Gum and acrylamide & to evaluate optical, mechanical, swelling and carrier properties of these hydrogels.

Also the introduction of the N,N'-Methylene-bisAcrylamide cross linking can improve considerably the thermal stability and mechanical properties of the composite hydrogel. The effects of N,N'-Methylene-bisAcrylamide cross linking on structure and properties of the Hydrogel Hybrids of Polyacrylamide and Sodium Alginate have been reported [23]. A basic understanding of the behaviour for N,N'-Methylene-bisAcrylamide cross linked hydrogels is essential for a successful research and development of the new materials. So, in this study, we attempt to introduce N,N'-Methylene-bisAcrylamide into the blend hydrogels of acrylamide and carboxymethylated guargum. The structure and morphologies of the cross linked hydrogels were characterized by FTIR and SEM. Furthermore, the mechanical properties, swelling behaviour and carrier properties of the blend hydrogels were also evaluated.

CHAPTER 2
LITERATURE REVIEW

2.1 GUAR GUM

2.1.1 INTRODUCTION

Until recently, use of gums was restricted to a relatively low number of items, randomly harvested and of limited quality and property range. Only the last few decades or so, has brought about revolutionary changes. Some gum bearing plants have begun to be cultivated on a commercial scale. Guar gum is one of the outstanding representatives of that new generation of plant gums. Guar gum (also called guar) is extracted from the seed of the leguminous shrub *Cyamopsis tetragonoloba*, where it acts as a food and water store. Many leguminous plant seeds contain Galactomannans. Guar Gum is known for its thickening properties. It is obtained from the seeds of *Cyamopsis tetragonolobus*, an annual leguminous plant originating from India and Pakistan. It is also cultivated in the United States. Guar fruit is a pod; its seeds have an average diameter of about 5 mm. The pods are 5-12.5 cm long and contain on the average 5-6 round, light brown seeds. They contain a reserve substance, the albumen. From the outside to the interior, we have:the hull, the albumen or endosperm, which is light cream in colour. It is made up of two hemispherical segments (splits) which surround the germ. Its major constituent is the polysaccharide, the germ, rich in protein.

Interest for Guar Gum is fairly recent: its initial development was due to a lack of Locust Bean Gum in the 1940s. Its large scale industrial production dates from the 1950s [24].

2.1.2 STRUCTURAL UNIT

Guar gum is a galactomannan similar to locust bean gum consisting of α (1, 4)-linked β-D-mannopyranose backbone with branch points from their 6- positions linked to α-D-galactose (*i.e.* 1,6-linked-α-D-galactopyranose) [25,26]. There are between 1.5 - 2 mannose residues for every galactose residue [27]. Various grades of the gour flour are available depending colour (white to greyish), mesh size, viscosity on potential, and rate of hydration. The conclusions from those drawn various studies many by independent investigators in substantial are agreement. The chemical analysis of guar flour shows the following typical composition [24]:

Constituent	**Percentage**
Nitrogen	0.67 corresponding with 3.5-4.0 proteins
Phosphorus	0.06
Ash	1.07
Water sol.polysaccharide	86.50
Water insoluble fraction	7.75
Alcohol sol. Fraction (from 24 hr soxhlet extraction)	1.5

Guar gum (GG) is an edible carbohydrate polymer which is useful as a thickening agent for water and as a reagent for absorption and hydrogen bonding with mineral and cellulosic surfaces. GG is a galactomannan. Guar gum molecule is linear or highly aniso-dimensional carbohydrate polymer with a molecular weight the order 220000 [28].

It is composed on of basically a straight of chain D-mannose of units, linked together by glycoside linkages, and having approximately alternate on every mannose single a D-galactose unit, joined it by an a (1-6) glycoside to linkage. The molecular weight of GG is about 220,000. GG is being used in explosives, foods, cosmetics and pharmaceuticals, and in mining, paper and textile industries, mostly as a water binder.

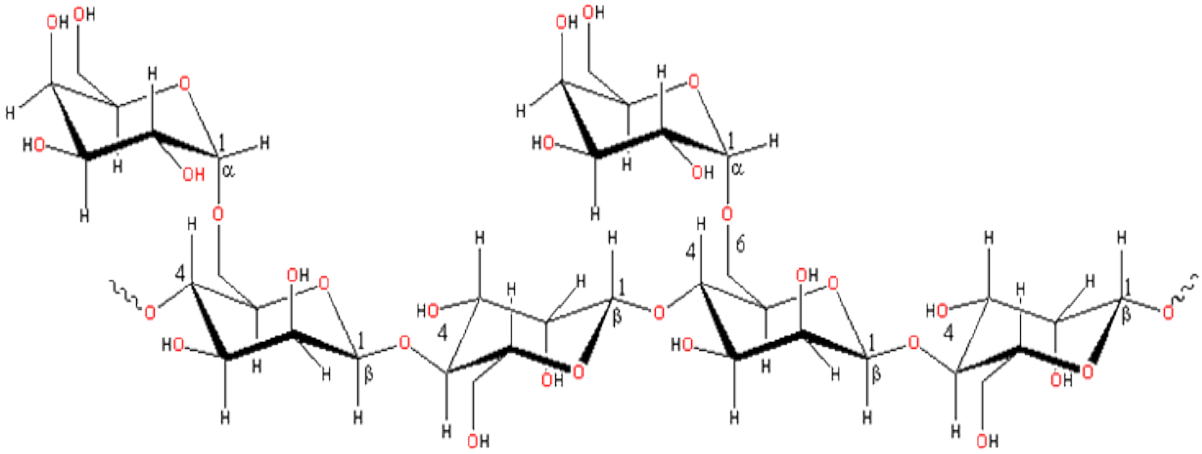

Figure 2.1.1 Structural Unit of Guar Gum Molecule

2.1.3 PHYSICAL AND CHEMICAL PROPERTIES

Guar gum may be identified among others by its perfect solubility in cold water resulting in a viscous which gives a gel-like complex with sol. Further possible processing of guar gum depends on chemical modifications. Various treatments are instrumental in developing functional characteristics that make this gum versatile and useful in a variety of industrial applications. Simplest the change by varying the degree polymerization is of by controlled hydrolysis which is the means of controlling viscosity. Furthermore, the abundance of hydroxyl groups in the galactomannan molecule lends itself - like in cellulose to a variety of chemical reactions [25]. They can be easily esterified, resulting in a variety of interesting compounds.

Guar triacetate - for instance, obtained by reacting the galactomannan with acetic anhydride pyridine, is insoluble water, and can be cast in into strong, flexible films, with properties comparable those cellulose with of acetate. Guar gum, a polymeric galactomannan, has been intrinsically modified to a new guar gum benzamide. Benzoylation is carried out by benzoyl chloride reaction in water medium and a propyl amine spacer is used to impart a high degree of hydrophobicity. The new guar gum benzamide was resistant to water and soluble in non aqueous solvent like dimethyl sulfoxide.

Alkoxylation with ethylene or propylene oxides is also easily carried out producing the corresponding ethers. Carboxyalkyl and cyano alkyl ethers are another example of functional modifications, e.g. o-carboxy-methyl derivative prepared by reacting galactomannan with chloro-acetic acid – forms viscous aqueous solutions that are stable to strongly alkaline reagents[29].

Complexing reactions worth mentioning lead to cross areas linking of the molecules resulting in a three dimensional in network which manifests itself in gel formation. These reactions not peculiar to galactomannans, are being characteristic linear molecules of having an abundance adjacent of hydroxyl groups cis positions. The complexing reaction of polyvinyl alcohol with borax is an example. Among others, copper salts form complexes with galactomannans. Fehling's solution, instance, for does reduce not those polysaccharides even on prolonged boiling. An insoluble, gel-like complex is formed

instead. Salts of Ca, A1, and Cr have the same gel forming capacity at certain pH levels. Perhaps most characteristic, important, is the reaction involving borate ions.

Solutions of most guar gum grades can be dried to form flexible films which resist most organic solvents, but which readily redissolve in water or aqueous solutions. Textile sizings, for instance, use such temporary films for protection of fibres during the weaving process. Some derivatives produce water resistant films, guar triacetate being the most prominent example.

Guar solutions have slightly acidic reaction(pH 5.5-6.1), and if sterile are perfectly stable in storage. They are, however, as are the other natural hydrocolloids, subject to micro biological deterioration, which results in a loss of viscosity as the first tangible manifestation and in a lowering of the pH value. If unpreserved, guar gum solution should be used within 24 h. If its use be delayed preservatives must be employed. In the food industry sodium benzoate and sorbic and benzoic acids are most commonly used for that purpose. Other industries may successfully use formaldehyde, substituted phenols and lauryl sarcosinate.

2.1.4 FUNCTIONALITY

Guar gum is an economical thickener and stabilizer. It hydrates fairly rapidly in cold water to give highly viscous pseudoplastic solutions of generally greater low-shear viscosity when compared with other hydrocolloids and much greater than that of locust bean gum. High concentrations (~ 1%) are very thixotropic but lower concentrations (~ 0.3%) are far less so. Guar gum shows high low-shear viscosity but is strongly shear-thinning. Being non-ionic, it is not affected by ionic strength or pH but will degrade at pH extremes at temperature (*e.g.* pH 3 at 50°C). It shows viscosity synergy with xanthan gum. With casein, it becomes slightly thixotropic forming a biphasic system containing casein micelles. Guar gum retards ice crystal growth non-specifically by slowing mass transfer across solid/liquid interface[29].

2.2 CARBOXYMETHYL GUAR GUM

2.2.1 INTRODUCTION

Guar gum is widely used in a variety of industrial applications because of its low cost and its ability to produce a highly viscous solution even at low concentrations. The high viscosity of guar gum solutions arises from the high molecular weight of guar gum and from the presence of extensive intermolecular association (entanglement) through hydrogen bonding.

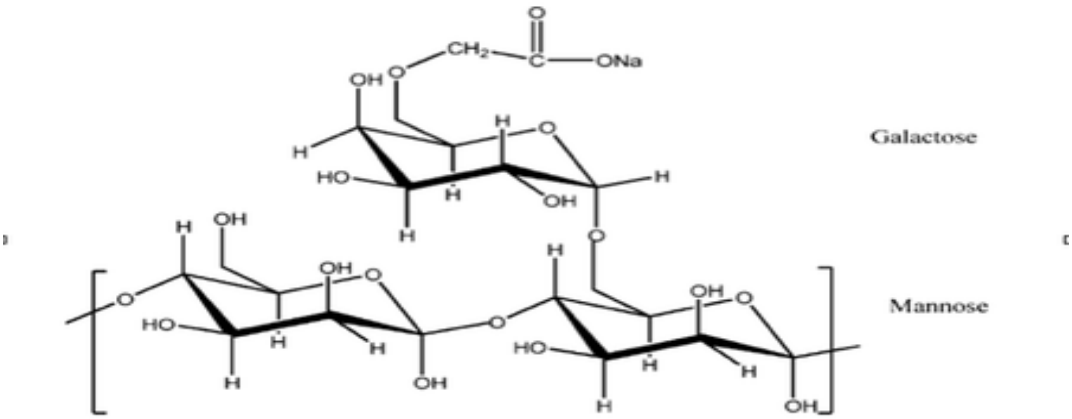

Fig 2.2.1 Structural unit of CarboxyMethyl Guar Gum

However, incomplete hydration of guar gum at room temperature, poor clarity of the solution and the desire for products with modified or particular properties have led to the development of a variety of commercial ether derivatives. Hence it is always reasonable to modify it to suit specific industrial process. Chemical modification of guar gum involves reaction of the hydroxyl groups on the anhydroglucose units (AGU) and these have been used to produce guar gum derivatives based on carboxymethylation, oxidation, grafting and crosslinking. Among the guar gum derivatives, carboxymethyl guar gum (CMGG) is very important because it covers a wide range of industrial applications.

Carboxymethyl guar gum (CMGG) is an anionic semi-synthetic guar gum derivative. The polysaccharide backbone is similar to guar gum which is a galactomannan. It is prepared by reacting guar gum with sodium monochlorate in the presence of sodium hydroxide. Carboxymethyl guar gum (CMGG) is a cheap and easily water soluble commercial polysaccharide.

2.2.2 MANUFACTURING PROCESS

Carboxymethylation of guar gum employed the Williamson ether synthesis procedure, which is a consecutive two-step reaction, proceeding with a strong base – such as sodium hydroxide – that deprotonates the free hydroxyl groups (particularly, the hydroxyl group of (- CH_2OH) in guar gum) to form alkoxides, thereby increasing their nucleophilicity. Carboxymethyl groups are then formed in a reaction between guar alkoxides and chloroacetic acid.

The first step is an alkalization where the hydroxyl groups of the guar gum molecules are activated and changed into the more reactive alkoxide form (GG–ONa).

$GG–OH + NaOH \rightarrow GG–ONa + H_2O$

The carboxymethyl groups are formed in a S_N2 reaction between the guar gum alkoxide and the SMCA. This main reaction is given by

$GG–ONa + Cl–CH_2–CO–ONa \rightarrow GG–O–CH_2–COONa + NaCl$

A side reaction also occurs which competes with the production process of carboxymethyl guar gum. In this side reaction, sodium glyocate is produced at the expense of the guar gum derivative. But this side reaction is significantly slower than the main reaction.

$NaOH + ClCH_2COONa \rightarrow HOCH_2COONa + NaCl$

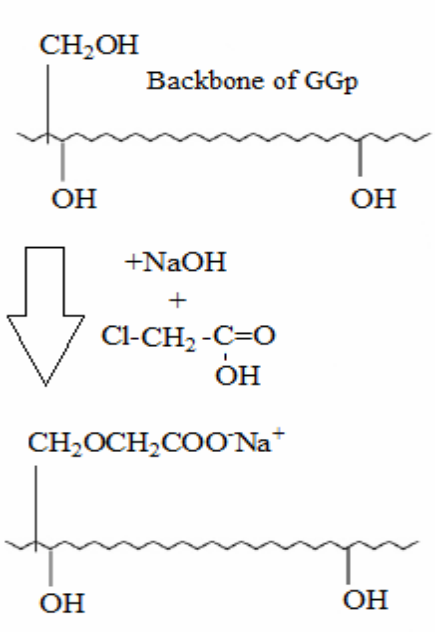

Fig 2.2.2 Overall Reaction scheme for the carboxymethylation process of guar gum

Both native and carboxymethyl guar gum increased the viscosity of water by 10 to 16 fold at 1 g litre. This effect increased with increasing concentration of gum but at every concentration tested carboxymethyl guar gum exhibited a viscosity almost 1.5 times that of native guar gum. It is presumed that this property reflects its ready dispersion in water due to the highly branched nature of guar gum preventing intramolecular interactions and therefore favouring an extended conformation. The presence of like charged carboxymethyl groups throughout the molecule repel each other and therefore favour a highly extended conformation and hence the observed higher viscosity of carboxymethyl guar gum.

Carboxymethyl guar gum can also acts as a drug carrier. Narasimha Murthy S et al investigated the role of carboxymethyl guar gum for drug delivery systems[30].

2.3 CIPROFLOXACIN HYDROCHLORIDE

Ciprofloxacin (1- cyclopropyl - 6 - fluoro - 1,4 - dihydro - 4 - oxo - 7 - (1-piperazinyl)-3 - quinolinecarboxylic acid, $C_{17}H_{18}FN_3O_3.HCl.H_2O$), a member of the fluoroquinolone antibiotic family, is often used to treat and prevent infections caused by bacteria such as enteric, respiratory and urinary tract infections, gastrointestinal surgery and septicemia. Ciprofloxacin inhibits bacterial enzymes, such as DNA gyrase.[31,32]. Ciprofloxacin differs from other quinolones in that it has a fluorine atom at the 6-position, a piperazine moiety at the 7-position, and a cyclopropyl ring at the 1-position.

Its appearance is Faintly yellowish to light yellow crystalline powder. It has a Molecular weight of 385.8 g/mol. Its solubility in water is 3.5 g/dL, in Methanol is 0.21 g/dL, in Acetic acid is 0.14 g/dL & in Ethanol is 0.016 g/dL.

The solubility of ciprofloxacin is low in the range of pH 6-9. On acidic pH 4-5 and basic pH 10-11 scales, the solubility is sensitive to changes in pH. Ciprofloxacin gains a cationic nature below pH 6, whilst it is anionic above pH 9. Ciprofloxacin solubility in water is high. It creates an ionic surface with chloride in water, increasing solubility. Temperature is another factor to increase the solubility.[33, 34]

It has broad antimicrobial activity and is effective after oral administration for the treatment of a wide variety of infectious diseases. The bactericidal action of ciprofloxacin

results from interference with the enzyme DNA gyrase which is needed for the synthesis of bacterial DNA.

Ciprofloxacin is used to treat a number of infections including: infections of bones and joints, endocarditis, gastroenteritis, malignant otitis externa, respiratory tract infections, cellulitis, urinary tract infections, gastrointestinal and abdominal infections prostatitis, anthrax, chancroid, among others. Ciprofloxacin are potent bactericidal agents against E. coli and various species of salmonella, shigella, enterobacter, campylobacter (Hooper, D.C., and Wolfson, J.S., eds.), and chlamydia, mycoplasma, legionella, brucella, and mycobacterium including mycobacterium tuberculosis (Leysen et al., 1989; Alangaden and Lerner, 1997). Ciprofloxacin has MIC90 values from 0.5 to 3 mg/ml for M. fortuitum, M. kansasii, and M. tuberculosis actives in animal [35].

Controlled drug release is to achieve more effective therapies by eliminating the potential for both under- and overdosing with maintaining of drug concentration within a desired range, fewer administrations, optimal drug use and increased patient compliance [36].

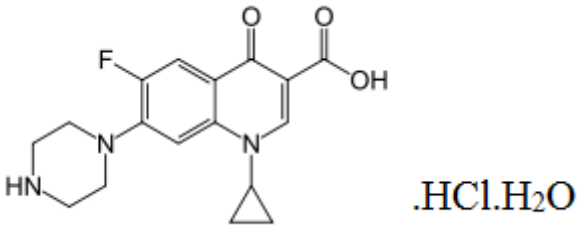

Fig 2.3.1 Structural unit of Ciprofloxacin Hydrochloride

2.4 INTERPENETRATING POLYMER NETWORKS (IPNs)

An interpenetrating polymer network is formed when a second hydrogel network is polymerized within a pre-polymerized hydrogel. This is typically done by immersing a pre-polymerized hydrogel into a solution of monomers and a polymerization initiator. IPNs can be formed either in the presence of a cross-linker to produce a fully interpenetrating polymer network (full IPN) or in the absence of a cross-linking mechanism to generate a network of embedded linear polymers entrapped within the original hydrogel (semi-IPN), as illustrated in figure below. The main advantages of IPNs

are that relatively dense hydrogel matrices can be produced which feature stiffer and tougher mechanical properties, more widely controllable physical properties, and (frequently) more efficient drug loading compared to conventional hydrogels. Drug loading is often performed in conjunction with the polymerization of the interpenetrating hydrogel phase [37].

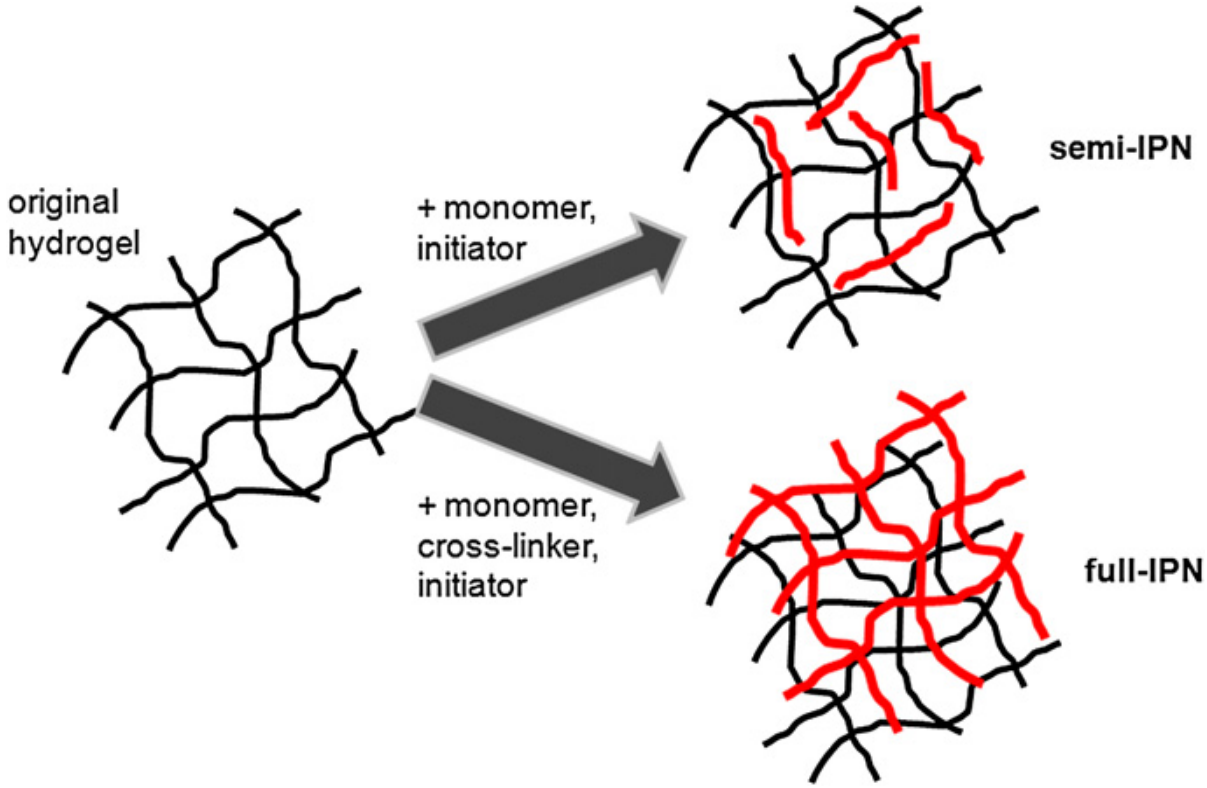

Fig. 2.4.1 Formation and structure of semi and full interpenetrating polymer networks (IPN).

IPN pore sizes and surface chemistries can also be controlled to tune the drug release kinetics, the interactions between the hydrogel and the tissues, and the mechanical properties of the gel [38]. Interpenetrating phases with different degradation profiles and/or different swelling responses to physiological conditions can be used to provide multiple controls over the swelling responses of hydrogels and thus the potential drug release kinetics [39]. IPNs can also moderate the effect of environmental changes on hydrogel responses and burst drug release because of their ability to restrict the equilibrium swelling of either or both of the interpenetrating phases according to the elasticity (i.e. cross-linking density) of either or both gel phases. For example, a highly cross-linked interpenetrating network of a pH-sensitive hydrogel and a hydrolysable hydrogel restricts the typically rapid swelling response of a pH-swelling hydrogel to facilitate linear swelling profiles

following an abrupt pH change from pH 7.4 to 2 [40]. Such responsivity is particularly suitable for minimizing burst release of drugs in oral drug delivery applications. As another example, a lightly cross-linked chitosan-PNIPAM interpenetrating network significantly increased the loading capacity of diclofenac compared to a pure PNIPAM hydrogel while maintaining the sharp thermosensitivity of the PNIPAM phase to regulate the release kinetics [41].

Semi-IPNs can more effectively preserve rapid kinetic response rates to pH or temperature (due to the absence of a restricting interpenetrating elastic network) while still providing most of the benefits of IPNs in drug delivery (e.g. modifying pore size, slowing drug release, etc.). For example, entrapping linear cationic polyallylammonium chloride in an acrylamide/ acrylic acid copolymer hydrogel imparted both higher mechanical strength and fully reversible pH switching of theophylline release [42].

CHAPTER 3

PREPARATION OF HYDROGELS

3.1 MATERIALS REQUIRED

Acrylamide (AAm)	: Monomer
Potassium persulphate (KPS)	: Initiator
CarboxyMethylGuargum(CMGG)	: Co-Polymer
Distilled Water	: Solvent
N,N'-Methylene-bisAcrylamide	: Crosslinking Agent

3.2 SYNTHESIS OF HYDROGEL

3.2.1 PURE ACRYLAMIDE HYDROGEL

- 5 gm of extrapure acrylamide was taken in beaker.
- 50 ml of de-mineralised water was taken and poured into the beaker containing acrylamide and stirred with a magnetic stirrer.
- Than sufficient amount of potassium persulfate (.05 gm) was added into the above solution.
- Again a small amount of N,N'-methylene-bisacrylamide(.10 gm) was added to the solution and mixed.
- Solution prepared was poured into a test tube and the test tube was heated in water bath kept at 65°C, for an hour.
- After an hour solid gel was formed, this was taken out by breaking test tube.
- It was cut into thin equal size slices.
- They were than washed with double distilled water by stirring gently for 2 hours to remove any residual monomer or other reactant.
- These slices were kept in oven for 48 hours set at 50°C for complete drying.
- Half of the slices were broken down to powder form by granite crusher.
- They were than stored in a desicator until further use.

3.2.2 Polyacrylamide - CarboxyMethylGuargum(1%) hydrogel

- 5 gm of extrapure acrylamide was taken in beaker.
- 0.05 gm of carboxymethyl guar gum was weighed and added in beaker.
- 50 ml of de-mineralised water was taken and added to the beaker and is stirred with a magnetic stirrer.
- Than sufficient amount of potassium persulfate (.05 gm) was added into the above solution.
- Again a small amount of N,N'-methylene-bisacrylamide(.10 gm) was added to the solution and mixed.
- Solution prepared was poured into a test tube and the test tube was heated in water bath kept at 65°C, for an hour.
- After an hour solid gel was formed, this was taken out by breaking test tube.
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- Half of the slices were broken down to powder form by granite crusher.
- They were than stored in a desicator until further use.

3.2.3 Polyacrylamide - CarboxyMethylGuargum(2%) hydrogel

- 5 gm of extrapure acrylamide was taken in beaker.
- 0.10 gm of guar gum was added to the beaker.
- 50 ml of de-mineralised water was added to the beaker and the mixture is stirred with magnetic stirrer for an hour.
- Than sufficient amount of potassium persulfate (.05 gm) was added into the above solution.
- Again a small amount of N,N'-methylene-bisacrylamide(.10 gm) was added to the solution and mixed.
- Solution prepared was poured into a test tube and the test tube was heated in water bath kept at 65°C, for an hour.
- After an hour solid gel was formed, this was taken out by breaking test tube.
- It was cut into thin equal size slices.

- They were than washed with double distilled water by stirring gently for 2 hours to remove any residual monomer or other reactant.
- These slices were kept in oven for 48 hours set at 50°C for complete drying.
- Half of the slices were broken down to powder form by granite crusher.
- They were than stored in a desicator until further use.

3.2.4 Polyacrylamide - CarboxyMethylGuargum(5%) hydrogel

- 5 gm of extrapure acrylamide was taken in beaker.
- 0.25 gm of carboxymethyl guargum was added to the beaker.
- 50 ml of de-mineralised water was added to the beaker and the mixture is stirred with magnetic stirrer for an hour.
- Than sufficient amount of potassium persulfate (.05 gm) was added into the above solution.
- Again a small amount of N,N'-methylene-bisacrylamide(.10 gm) was added to the solution and mixed.
- Solution prepared was poured into a test tube and the test tube was heated in water bath kept at 65°C, for an hour.
- After an hour solid gel was formed, this was taken out by breaking test tube.
- It was cut into thin equal size slices.
- They were than washed with double distilled water by stirring gently for 2 hours to remove any residual monomer or other reactant.
- These slices were kept in oven for 48 hours set at 50°C for complete drying.
- Half of the slices were broken down to powder form by granite crusher.
- They were than stored in a desicator until further use.

3.2.5 Polyacrylamide - CarboxyMethylGuargum(7%) hydrogel

- 5 gm of extrapure acrylamide was taken in beaker.
- 0.35 gm of carboxymethyl guargum was added to the beaker.
- 50 ml of de-mineralised water was added to the beaker and the mixture is stirred with magnetic stirrer for an hour.
- Than sufficient amount of potassium persulfate (.05 gm) was added into the above solution.

- Again a small amount of N,N'-methylene-bisacrylamide(.10 gm) was added to the solution and mixed.
- Solution prepared was poured into a test tube and the test tube was heated in water bath kept at 65°C, for an hour.
- After an hour solid gel was formed, this was taken out by breaking test tube.
- It was cut into thin equal size slices.
- They were than washed with double distilled water by stirring gently for 2 hours to remove any residual monomer or other reactant.
- These slices were kept in oven for 48 hours set at 50°C for complete drying.
- Half of the slices were broken down to powder form by granite crusher.
- They were than stored in a desicator until further use.

3.2.6 Polyacrylamide - CarboxyMethylGuargum(10%) hydrogel

- 5 gm of extrapure acrylamide was taken in beaker.
- 0.50 gm of carboxymethyl guargum was added to the beaker.
- 50 ml of de-mineralised water was added to the beaker and the mixture is stirred with magnetic stirrer for an hour.
- Than sufficient amount of potassium persulfate (.05 gm) was added into the above solution.
- Again a small amount of N,N'-methylene-bisacrylamide(.10 gm) was added to the solution and mixed.
- Solution prepared was poured into a test tube and the test tube was heated in water bath kept at 65°C, for an hour.
- After an hour solid gel was formed, this was taken out by breaking test tube.
- It was cut into thin equal size slices.
- They were than washed with double distilled water by stirring gently for 2 hours to remove any residual monomer or other reactant.
- These slices were kept in oven for 48 hours set at 50°C for complete drying.
- Half of the slices were broken down to powder form by granite crusher.
- They were than stored in a desicator until further use.

3.2.7 Polyacrylamide - CarboxyMethylGuargum(15%) hydrogel

- 5 gm of extrapure acrylamide was taken in beaker.
- 0.75 gm of carboxymethyl guargum was added to the beaker.
- 50 ml of de-mineralised water was added to the beaker and the mixture is stirred with magnetic stirrer for an hour.
- Than sufficient amount of potassium persulfate (.05 gm) was added into the above solution.
- Again a small amount of N,N'-methylene-bisacrylamide(.10 gm) was added to the solution and mixed.
- Solution prepared was poured into a test tube and the test tube was heated in water bath kept at 65°C, for an hour.
- After an hour solid gel was formed, this was taken out by breaking test tube.
- It was cut into thin equal size slices.
- They were than washed with double distilled water by stirring gently for 2 hours to remove any residual monomer or other reactant.
- These slices were kept in oven for 48 hours set at 50°C for complete drying.
- Half of the slices were broken down to powder form by granite crusher.
- They were than stored in a desicator until further use.

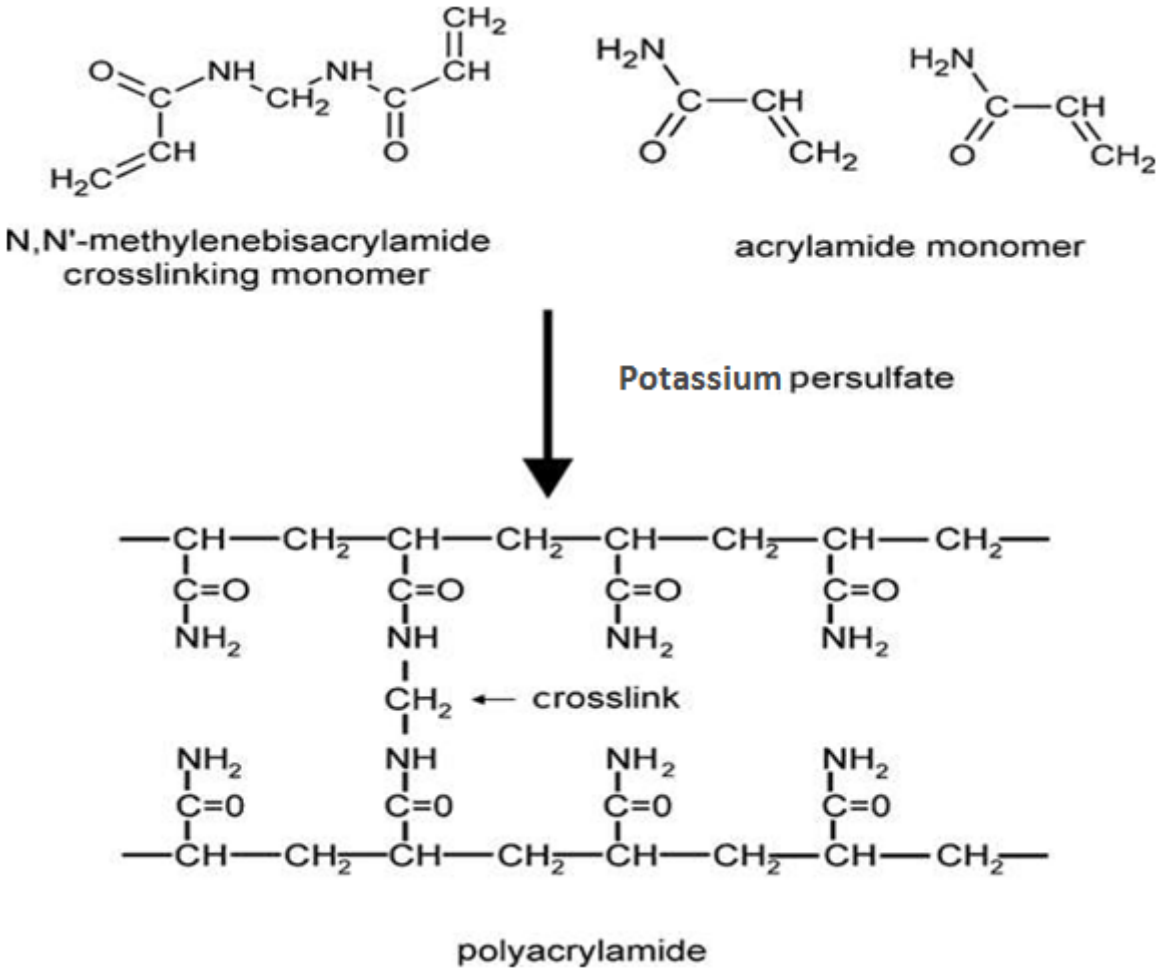


Figure3.2.1 Shows Major Reaction Involved in Polymerization

Fig 3.2.2 Hydrogel Slice Before Drying

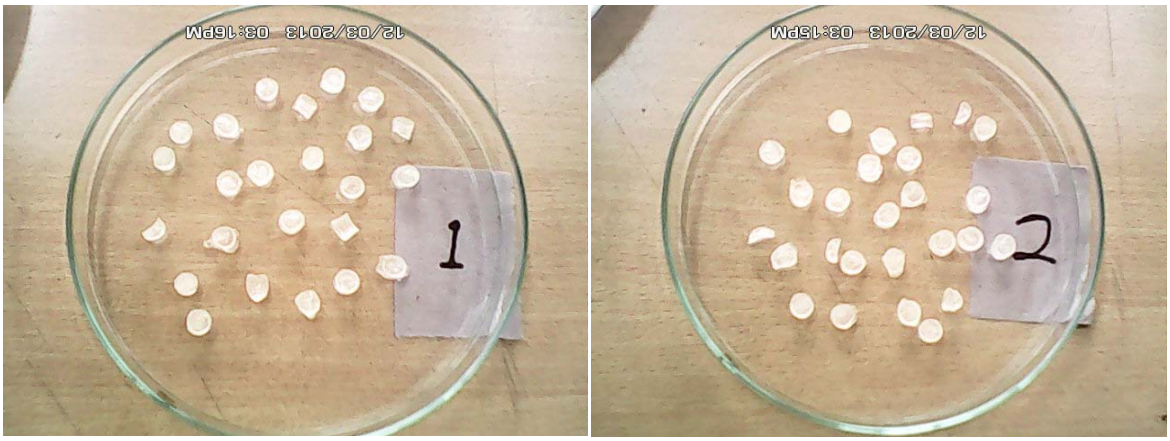


Fig 3.2.3 Hydrogel Slice After Drying

3.3 DRUG LOADING OF HYDROGEL

Ciprofloxacin Hydrochloride was used as a model drug for loading and release experiments. Drugs can be incorporated into hydrogel matrices by two methods[43] i.e post-loading method & in-situ loading method. In this case we are using the post-loading method. In the post-loading method a hydrogel matrix is formed and then the drug is absorbed to this matrix. For an inert hydrogel system diffusion is the major force for drug uptake. Drug release is determined by diffusion mechanism or gel swelling. For hydrogel containing drug-binding ligands the release will be determined by a drug-polymer interaction and drug diffusion.

This method is basically dependent on the soaking technique. In this method a saturated solution of drug(Ciprofloxacin Hydrochloride) is first prepared by dissolving 3.5 gm of Ciprofloxacin Hydrochloride in 100ml of distilled water. Than already prepared and dried hydrogel slices containing 1%, 5% & 15% CMGG are put separately in the prepared drug solution and put in the incubator for 3 days at 37^{o}C. During this period the hydrogel swell and the drug goes inside the pores of the hydrogel along with the water. After 3 days the slices were removed from drug solution and put into oven at 40^{o}C for next 2 days for complete drying. After two days the slices were removed from oven and kept into desicator until further use.

CHAPTER 4

CHARACTERIZATION TECHNIQUES

4.1 Fourier Transform Infra Red (FTIR) Spectroscopy

Introduction

FT-IR stands for Fourier Infra-Red, the preferred method of infrared spectroscopy. In infrared spectroscopy, IR radiation is passed through a sample. Some of the infrared radiation is absorbed by the sample and some of it is passed through (transmitted). The resulting spectrum represents the molecular absorption and transmission, creating a molecular fingerprint of the sample. Like a fingerprint no two unique molecular structure produce the same infrared spectrum. This makes infrared spectroscopy useful for several types of analysis. The information provided by FT-IR is as follows:

1) It can identify unknown materials.
2) It can determine the quality or consistency of a sample.
3) It can determine the amount of components in mixture.

Working of a Spectrometer

Infrared spectroscopy has been a workhorse technique for materials analysis in the laboratory for over seventy years, an infrared spectrum represents a fingerprint of a sample with absorption peaks which correspond to the frequencies of vibrations between the bonds making up the material. Because each different is a unique combination of atoms, no two compounds produce the exact infrared spectrum. Therefore, infrared spectroscopy can result in a positive identification (qualitative analysis) of every different kind of material. In addition, the size of the peaks is a direct indication of the amount of material present. With modern software algorithms, infrared is an excellent tool for quantitative analysis.

The normal instrumental process is as follows:

1. The Source: Infrared energy is emitted from a glowing black-body source. This beam passes through an aperture which controls the amount of energy presented to the sample (and, ultimately, to the detector).

2. The Interferometer: The beam enters the interferometer where the "spectral encoding" takes place. The resulting interferogram signal then exits the interferometer.

3. The Sample: The beam enters the sample compartment where it is transmitted through or reflected off of the surface of the sample, depending on the type of analysis being accomplished. This is where specific frequencies of energy, which are uniquely characteristic of the sample, are absorbed.

4. The Detector: The beam finally passes to the detector for final measurement. The detectors used are specially designed to measure the special interferogram signal.

5. The Computer: The measured signal is digitized and sent to the computer where the Fourier transformation takes place. The final infrared spectrum is then presented to the user for interpretation and any further manipulation.

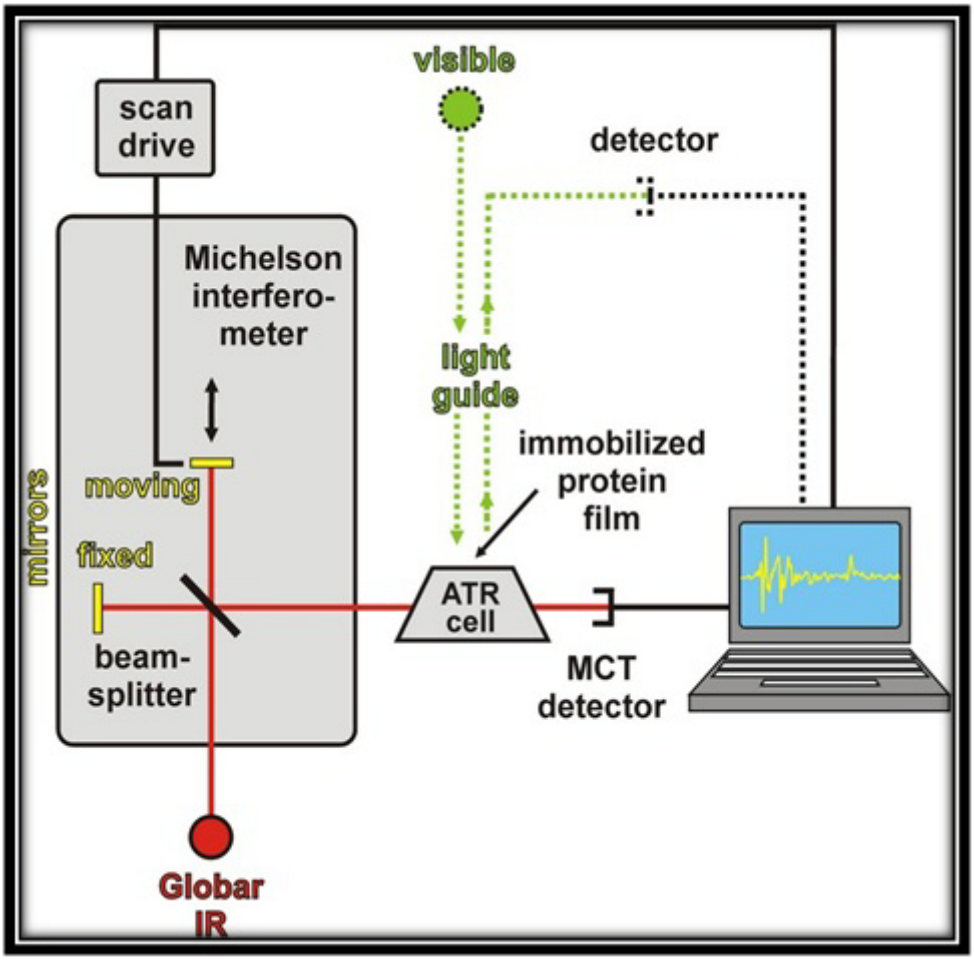


Figure 4.1.1 Model showing working of FTIR

Because there needs to be a relative scale for the absorption intensity, a background spectrum must also be measured. This is normally a measurement with no sample in the beam. This can be compared to the measurement with the sample in the beam to determine the "percent transmittance."This technique results in a spectrum which has all of the instrumental characteristics removed. Thus, all spectral features which are present are strictly due to the sample. A single background measurement can be used for many sample measurements because this spectrum is characteristic of the instrument itself.

The Sample Analysis Process basically involves:

a) Preparation of Potassium Bromide (KBr) Pellet

b) Mounting the sample in the spectrometer

Preparation of Potassium Bromide Pellet:

1) Take a mortar, pestle, pellet holder, 2 bolts and KBr.
2) Measure out 3 spatula loads of KBr. This should be 100-200 mg.
3) Place one spatula-tip of sample in the mortar. It should not be more than a couple of milligrams.
4) Grind the KBr to a very fine powder. Do this all quickly, as the KBr will absorb water from the atmosphere, and this makes it difficult to press a good pellet.
5) Screw one bolt into the pellet holder. Place about 30-50 mg (a small spatula scoop) of the ground mixture into the cavity, and screw the second bolt in.

Mounting the Sample in Spectrometer:

1) First of all collect the background spectrum.
2) Now place the KBr pellet in a sample holder.
3) Mount the holder on to FT-IR spectrometer.
4) Run the spectrometer

Figure 4.1.2 FT-IR Specrophotometer

4.2 SCANNING ELECTRON MICROSCOPY

A scanning electron microscope (SEM) is a type of electron microscope that images a sample by scanning it with a high energy beam of electrons in a raster scan pattern. The electrons interact with the atoms that make up the sample producing signals that contain information about the sample's surface topography, composition, and other properties such as electrical conductivity.

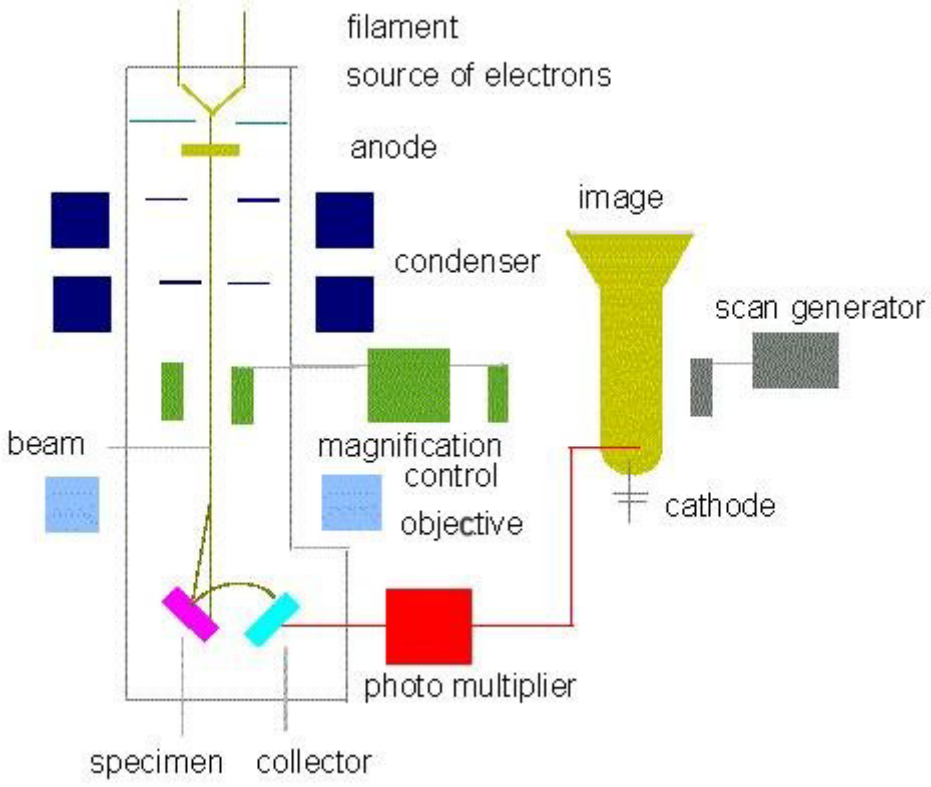


Figure 4.2.1 Model diagram for Scanning Electron Microscope

In a typical SEM, an electron beam is thermionically emitted from an electron gun fitted with a tungsten filament cathode. Tungsten is normally used in thermionic electron guns because it has the highest melting point and lowest vapour pressure of all metals, thereby allowing it to be heated for electron emission, and because of its low cost. Other types of electron emitter include lanthanum hexaboride cathodes, which can be used in a standard tungsten filament SEM if the vacuum system is upgraded and field emission guns (FEG), which may be of the cold cathode type using tungsten single crystal emitters or the thermally assisted Schottky type, using emitters of zirconium oxide.

The electron beam, which typically has an energy ranging from 0.5keV to 40keV, is focussed by one or two condenser lenses to a spot about 0.4nm to 5 nm in diameter. The beam passes through pairs of scanning coils or pairs of deflector plates in the electron column, typically in the final lens, which deflect the beam in the x and y axes so that it scans in a faster fashion over a rectangular area of the sample surface.

When the primary electron beam interacts with the sample, the electrons lose energy by repeated random scattering and absorption within a teardrop-shaped volume of the specimen known as the interaction volume, which extends from less than 100 nm to around 5 µm into the surface. The size of the interaction volume depends on the electron's landing energy, the atomic number of the specimen and the specimen's density. The energy exchange between the electron beam and the sample results in the reflection of high-energy electrons by elastic scattering, emission of secondary electrons by inelastic scattering and the emission of electromagnetic radiation, each of which can be detected by specialized detector. The beam current absorbed by the specimen can also be detected and used to create images of the distribution of specimen current. Electrons amplifiers of various types are used to amplify the signals which are displayed as variations in brightness on a cathode ray tube. The raster scanning of the CRT display is synchronised with that of the beam on the specimen in the microscope, and the resulting image is therefore a distribution map of the intensity of the signal being emitted from the scanned area of the specimen. The image may be captured by photography from a high resolution cathode ray tube, but in modern machines is digitally and displayed on a computer's hard disk.

Figure 4.2.2 Scanning Electron Microscope

4.3 SWELLING STUDIES IN DISTILLED WATER

In order to study the swelling behaviour, the disk samples were immersed in distilled water. The samples were placed in the swelling solution at 37°C and the weight of the swollen samples was measured against time after the excess surface water was removed by gently tapping the surface with a dry piece of filter paper[44].

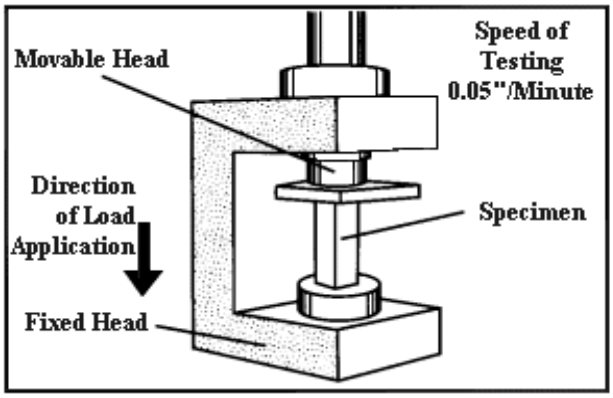
Procedure :

- A measured quantity of dried hydrogel(Wd) slice were immersed in 100ml of distilled water.
- After a regular time interval of 1 hour, sample was taken out of the water and superficial water on the surface of the swollen hydrogel was removed with the help of tissue paper very carefully.
- Weight of the swollen hydrogel (Ws) was taken and percentage swelling was calculated as per equation[45];

$$H = (Ws-W_d)/W_d \times 100 \qquad \ldots\ldots. (1)$$

4.4 COMPRESSION TEST

The **compressive strength** of a material is the force per unit area that it can withstand in compression. This is in contrast to the more commonly measured tensile strength. ASTM D695 is the standard test method. The figure below shows the test geometry.



ASTM D695:

Specimen of known dimensions is placed in the compression apparatus and a known load is applied.

Fig 4.4.1 Model Showing Test Specimen and Machine

Compressive yield strength is the stress measured at the point of permanent yield, zero slope, on the stress-strain curve. **Ultimate compressive strength** or Maximum Compressive Load is the stress required to rupture a specimen. Materials such as most plastics that do not rupture can have their results reported as the compressive strength at a specific deformation such as 1%, 5%, or 10% of the test sample's original height.

The analogous test to measure compressive strength in the ISO system is ISO 604. The values reported in the ASTM D695 and ISO 604 tests seldom differ significantly and are often used interchangably in the early stages of the materials selection process.

In this study the compression test is performed on Instron Universal Testing machine.

The dried hydrogel samples were first put into distilled water for 3 days for complete swelling. Then they are taken out and the excess water from the surface is removed with the help of filter paper. The test specimen is than measured for its dimensions using Vernier caliper. And then it is put on the fixed head of the machine to carry out the test.

Figure 4.4.2 Instron Universal Testing Machine

4.5 DRUG RELEASE STUDY

Ciprofloxacin hydrochloride loaded polymeric hydrogel of CMGG-Polyacrylamide of which prolonged release study was undertaken through UV visible spectrophotometer of Cary, model no UV300.

First of all 6 gm of ciprofloxacin hydrochloride was accurately weighed in to a 50 ml volumetric flask and dissolved in distilled water. The volume made up to 50 ml with distilled water (120 g/L). Working standard solution 5ml of the above solution was pipette out into a 50 ml volumetric flask and volume made up to 50 ml with distilled water to give a concentration of 12 gm/L.

Concentrations of 2-12 gm/L were prepared by suitably diluting working standard solution with distilled water. The optical densities of these solutions were measured at λ max 266 nm using UV visible spectrophotometer. Then the standard plot of absorbance versus concentration was drawn from the data[46,47].

The samples containing variable CMGG content were evaluated for both neutral and acidic medium. The concentration of the samples were then calculated by comparing with the absorbance value of standard solutions directly with the help of instrument[48].

The CFX.HCl release experiments were carried out by transferring previously incubated drug-loaded gels into 50 mL of distilled water at pH 7 & pH 4 and 37 °C at a constant shaking rate. At various time intervals, 3 mL of the drug solution were taken to measure the drug concentration by using a Cary 300, UV-spectrophotometer (λ at 266 nm). The calibration curve based on different concentrations was plotted and the concentration values of unknown solutions were then calculated directly from the instrument.

CHAPTER 5

RESULTS AND DISCUSSION

Blend hydrogels using Carboxymethyl Guar Gum and Polyacrylamide with different concentrations of carboxymethyl guar gum were successfully prepared by free radical polymerization technique. These hydrogels were then characterized using characterization techniques like FTIR, SEM. Mechanical properties like compressive strength, were also determined using Universal Testing Machine. Also, 1%, 5%, 15% carboxymethyl guar gum containing hydrogels were loaded with drug and its release kinetics were studied at different pH. Swelling studies in distilled water at pH 7 were also studied.

5.1 FOURIER TRANSFORM INFRA-RED (FTIR) RESULTS

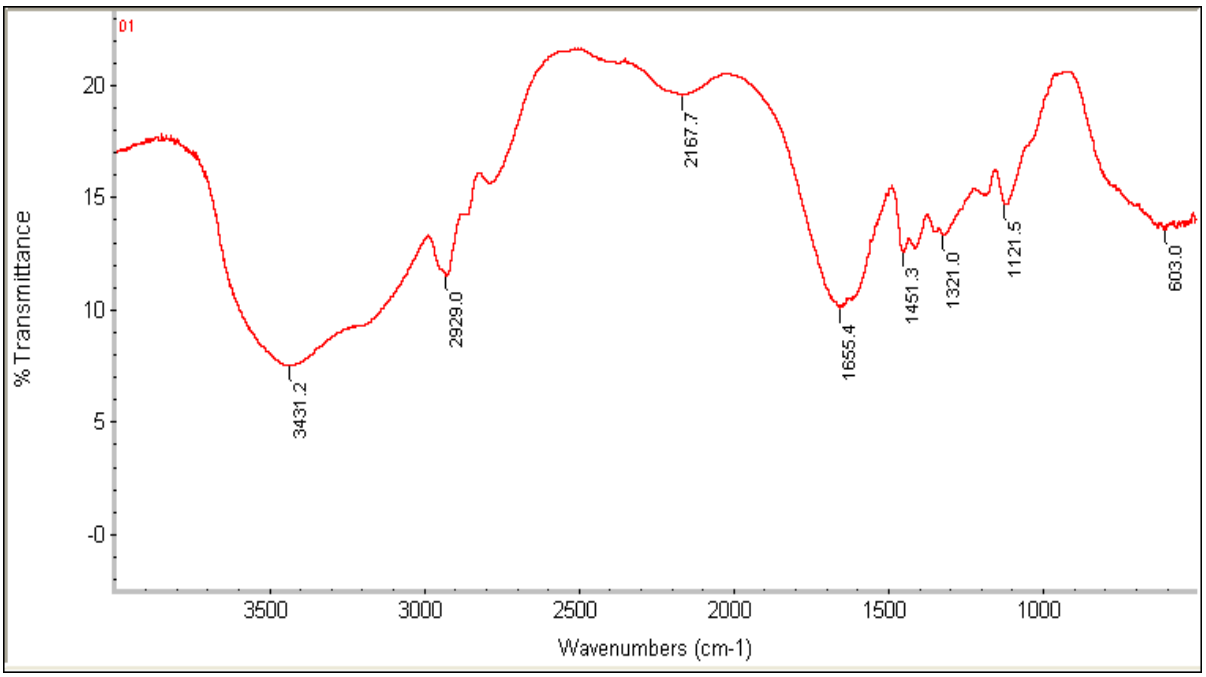


Fig 5.1.1 FT-IR spectra of Pure Polyacrylamide Hydrogel

Absorption(Cm^{-1})	Functional group	Type of vibrations
3431	N-H	Stretching
2929	C-H	Stretching
2167	$O=C-NH_2$	Bending
1655	C-O	Stretching
1451	C-H	Bending
1321	C–N	Bond Stretching
1121	C–C	Stretching

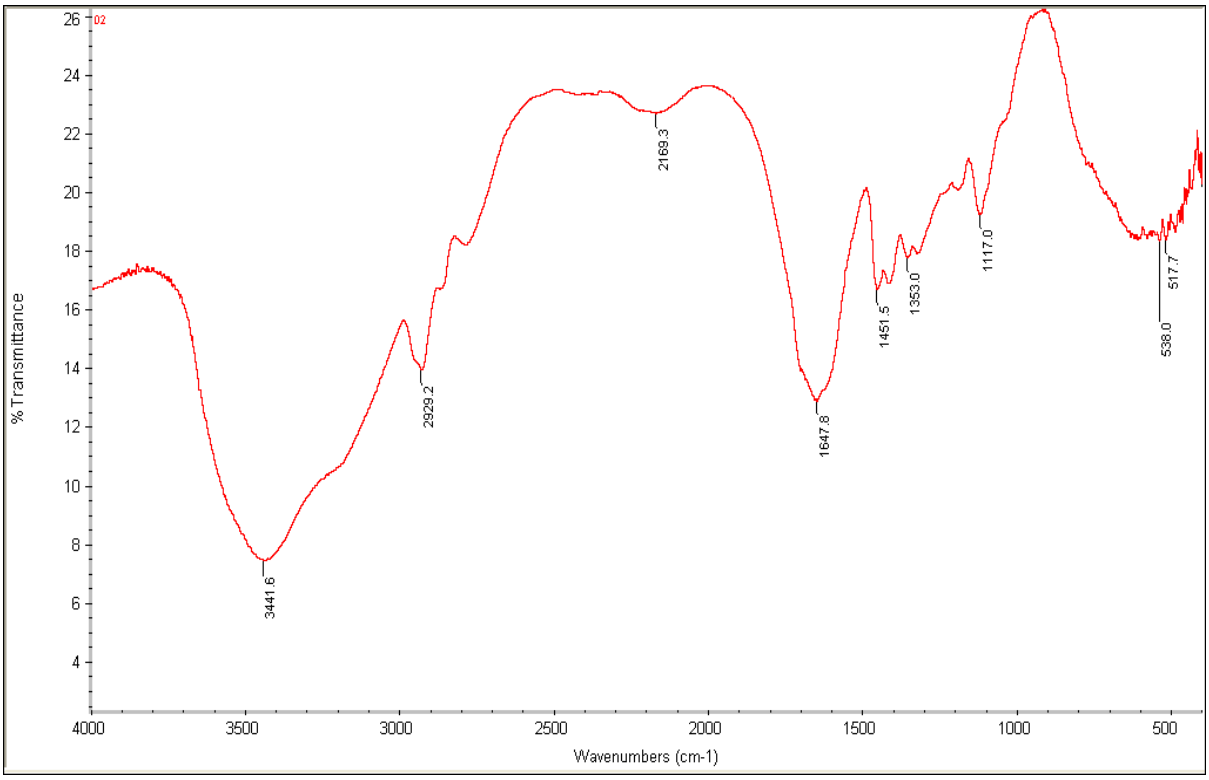


Fig 5.1.2 FT-IR spectra of Polyacrylamide : CarboxyMethylGwargum (1%) Hydrogel

Absorption (Cm^{-1})	Functional group	Type of vibrations
3441	N-H	Stretching
2929	C-H	Stretching
2169	$O=C-NH_2$	Bending
1647	C-O	Stretching
1451	C-H	Bending
1353	C–N	Bond Stretching
1117	C-C	Stretching

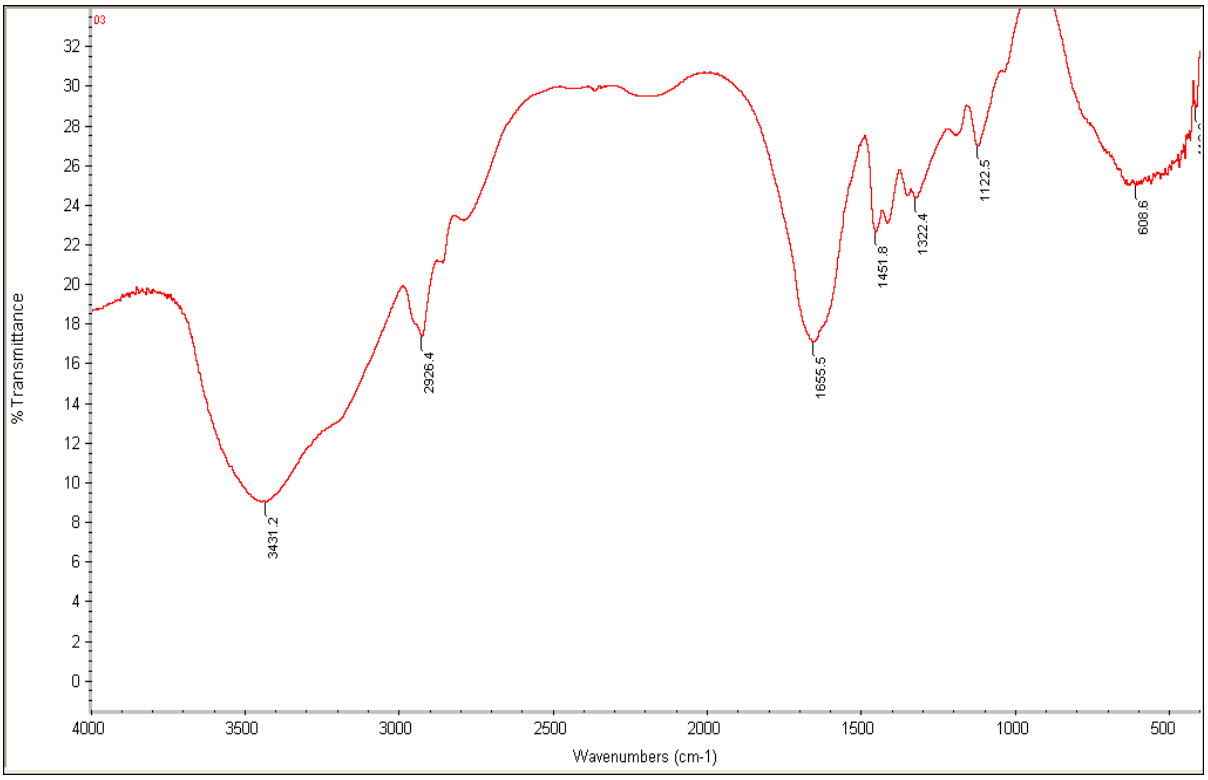


Fig 5.1.3 FT-IR spectra of Polyacrylamide : CarboxyMethylGwargum (2%) Hydrogel

Absorption (Cm^{-1})	Functional group	Type of vibrations
3431	N-H	Stretching
2926	C-H	Stretching
1655	C-O	Stretching
1451	C-H	Bending
1322	C–N	Bond Stretching
1122	C-C	Stretching

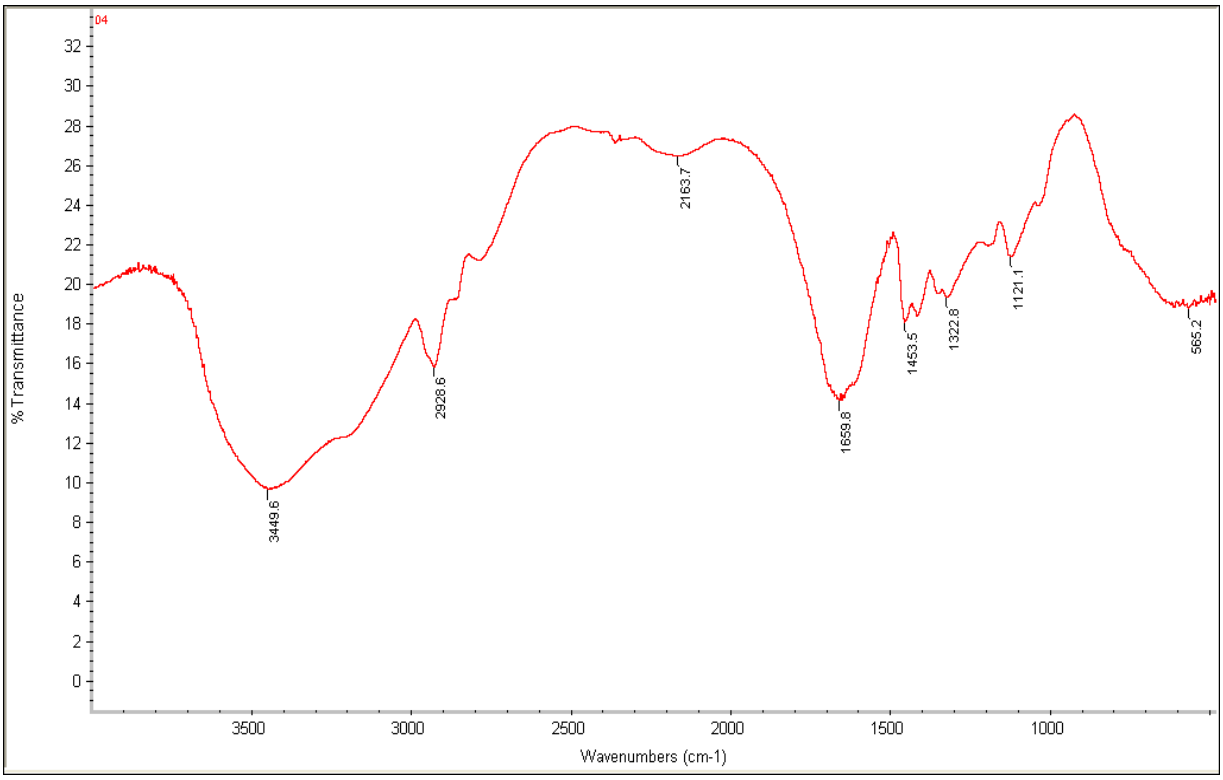


Fig 5.1.4 FT-IR spectra of Polyacrylamide : CarboxyMethylGwargum (5%) Hydrogel

Absorption (Cm^{-1})	Functional group	Type of vibrations
3449	N-H	Stretching
2928	C-H	Stretching
2163	$O=C-NH_2$	Bending
1659	C-O	Stretching
1453	C-H	Bending
1322	C–N	Bond Stretching
1121	C-C	Stretching

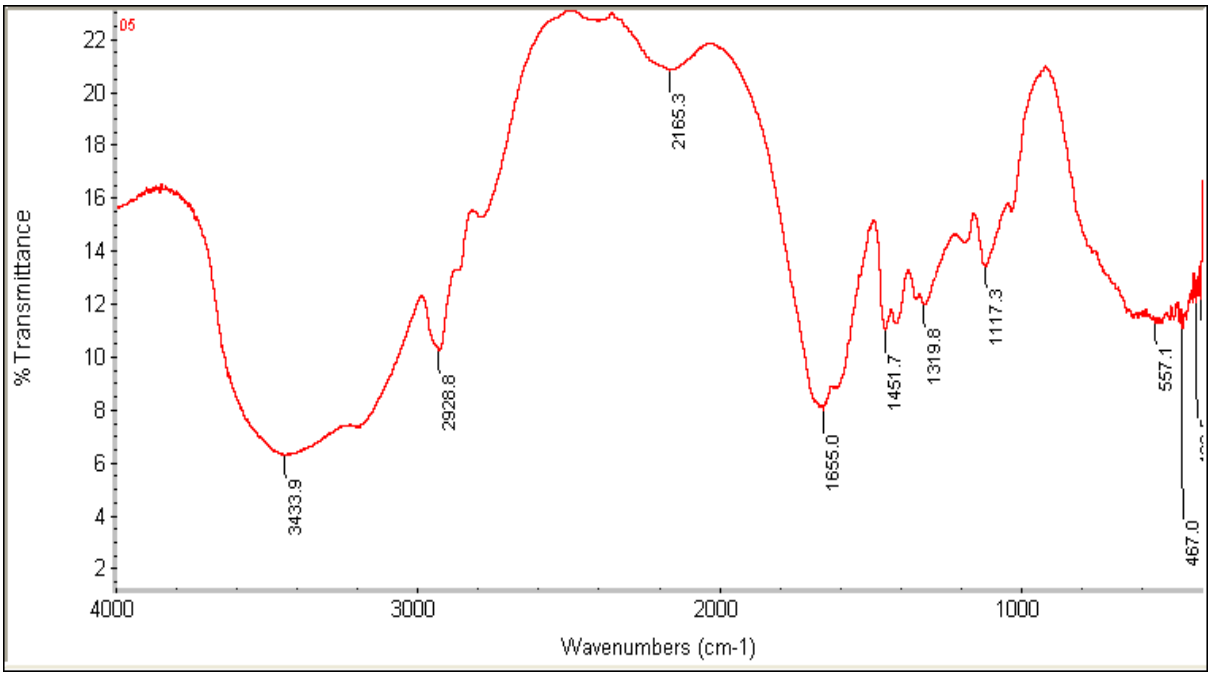


Fig 5.1.5 FT-IR spectra of Polyacrylamide : CarboxyMethylGwargum (7%) Hydrogel

Absorption (Cm^{-1})	Functional group	Type of vibrations
3433	N-H	Stretching
2928	C-H	Stretching
2165	$O=C-NH_2$	Bending
1655	C-O	Stretching
1451	C-H	Bending
1319	C–N	Bond Stretching
1117	C-C	Stretching

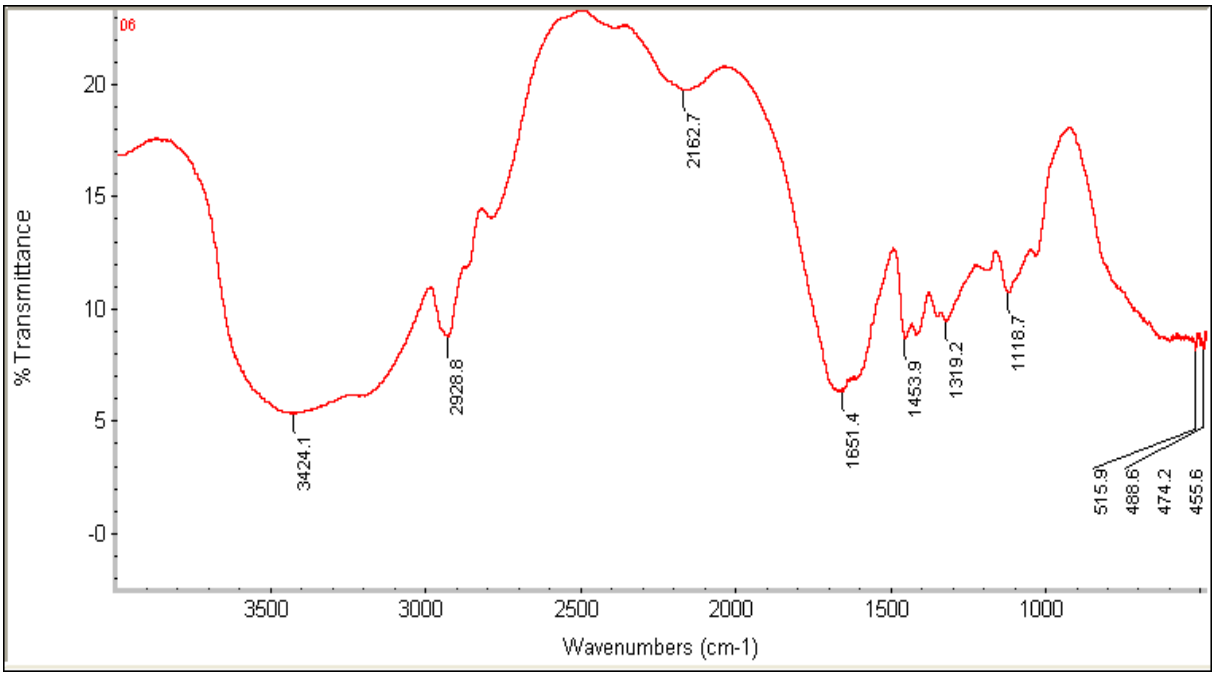


Fig 5.1.6 FT-IR spectra of Polyacrylamide : CarboxyMethylGwargum (10%) Hydrogel

Absorption (Cm^{-1})	Functional group	Type of vibrations
3424	N-H	Stretching
2928	C-H	Stretching
2162	$O=C-NH_2$	Bending
1651	C-O	Stretching
1453	C-H	Bending
1319	C–N	Bond Stretching
1118	C-C	Stretching

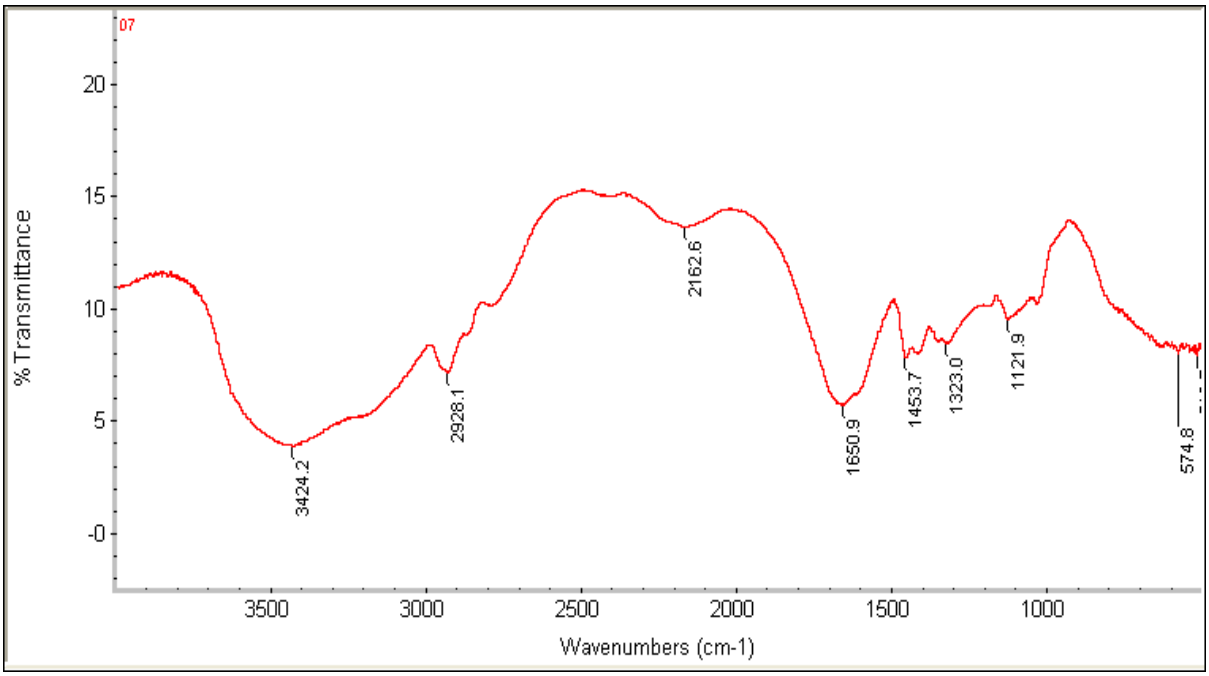


Fig 5.1.7 FT-IR spectra of Polyacrylamide : CarboxyMethylGwargum (15%) Hydrogel

Absorption (Cm^{-1})	Functional group	Type of vibrations
3424	N-H	Stretching
2928	C-H	Stretching
2162	$O=C-NH_2$	Bending
1650	C-O	Stretching
1453	C-H	Bending
1323	C–N	Bond Stretching
1121	C-C	Stretching

In this case the broad bands which can be assigned to the N–H stretching vibration in –NH– group of N,N- methylene bis(acrylamide) or $–CONH_2$ groups of acrylamide in hydrogels appear at 3431 Cm^{-1} [49]. The C–H stretching band is characterized by the peak at 2929 Cm^{-1} due to symmetric or asymmetric stretching vibration of the CH_2 groups of acrylamide or N,N-methylene bis(acrylamide)[50].

The spectra also shows bands at 1651, 1453 and 1319 Cm^{-1}. The characteristic peaks at 1651 Cm^{-1} correspond to the $–COO^-$ asymmetric stretching vibration. 1453 Cm^{-1} and 1319 Cm^{-1} are the $–COO^-$ symmetric stretching vibration[52]. These bands are assigned to carboxymethyl moieties and this indicates that the hydroxyl groups of guar gum molecules were carboxymethylated (Huang et al., 2006).

The bands at 1655 Cm^{-1} are due to the C-O stretching vibrations[51] and aliphatic C–H bending vibrations are observed at 1451 Cm^{-1}. The band at 1321 Cm^{-1} is assigned to the C–N bond stretching vibrations. Other important peaks observed at 1117Cm^{-1} & 1118Cm^{-1} are attributed to C–O–C stretching from glycosidic linkages and O–H bending of GG component. Also C-C stretching vibration gives a peak at 1121 Cm^{-1} [51].

5.2 SCANNING ELECTRON MICROSCOPY (SEM) RESULTS

5.2.1 Pure Polyacrylamide Hydrogel

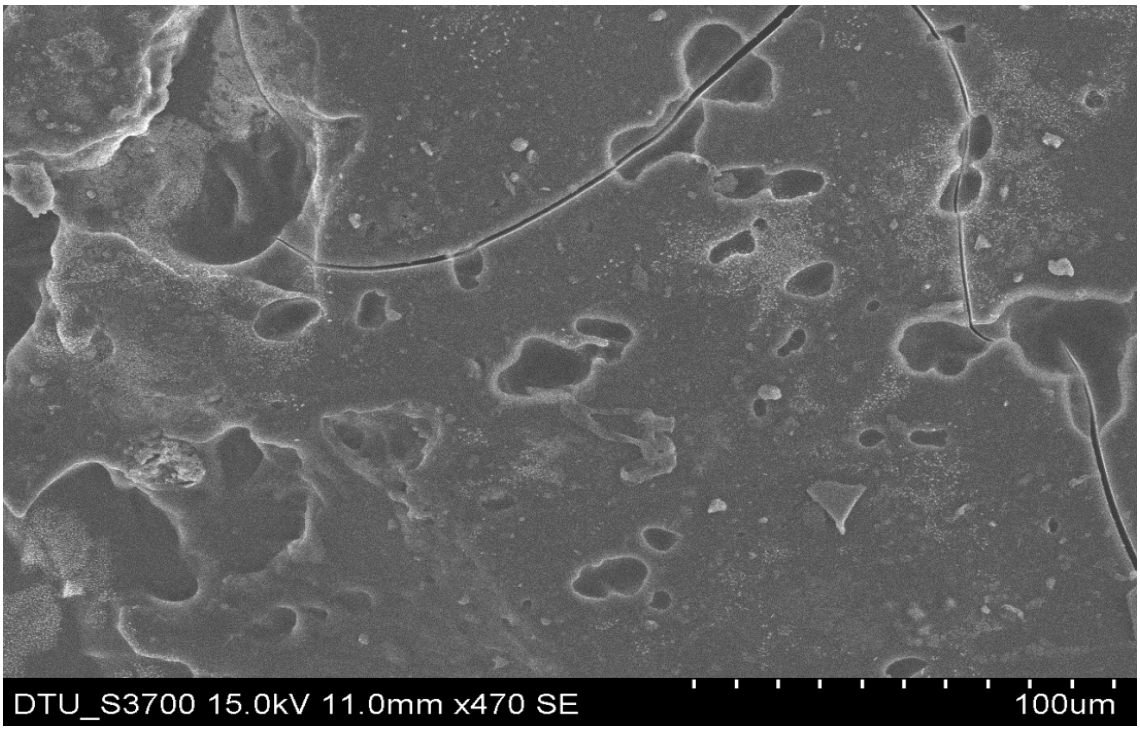


Figure 5.2.1 SEM micrograph of Pure Polyacrylamide Hydrogel at 100µm resolution

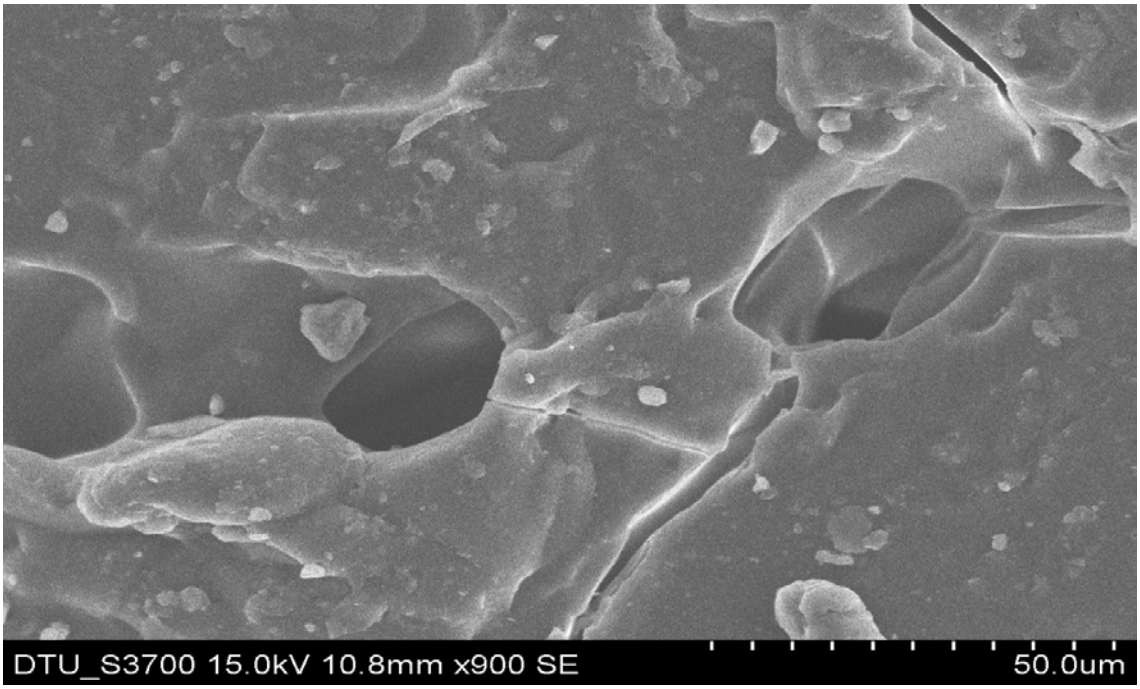


Figure 5.2.2 SEM micrograph of Pure Polyacrylamide Hydrogel at 50µm resolution

5.2.2 Polyacrylamide : CarboxyMethylGwargum (1%) Hydrogel

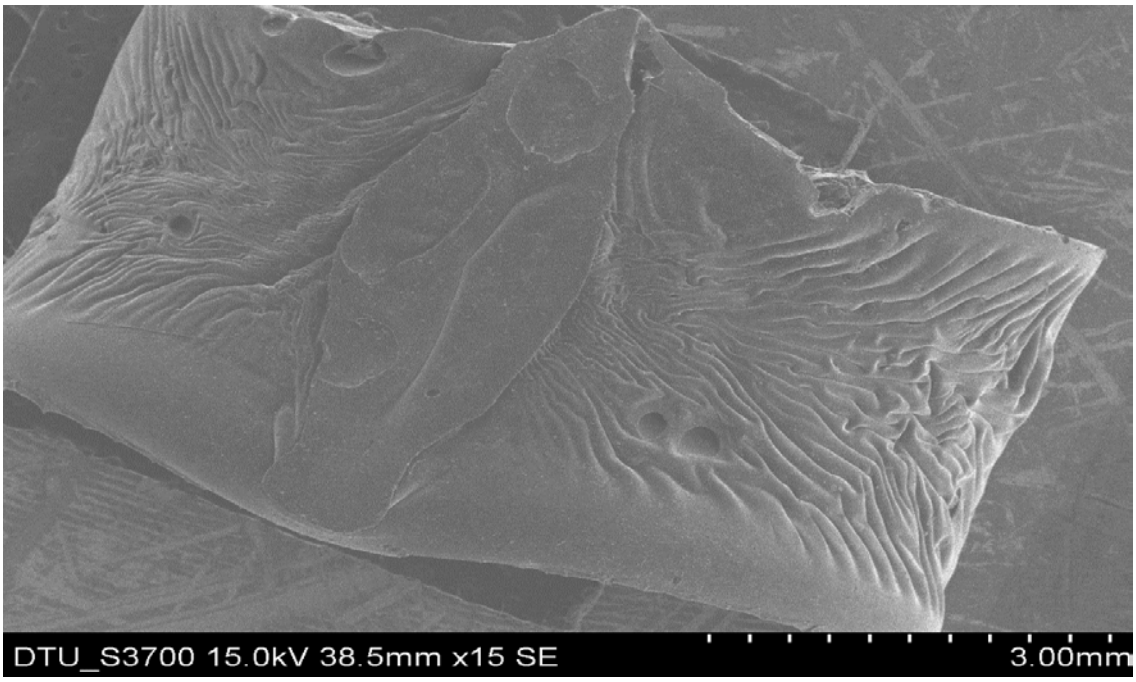


Figure 5.2.3 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(1%) Hydrogel at 3mm resolution

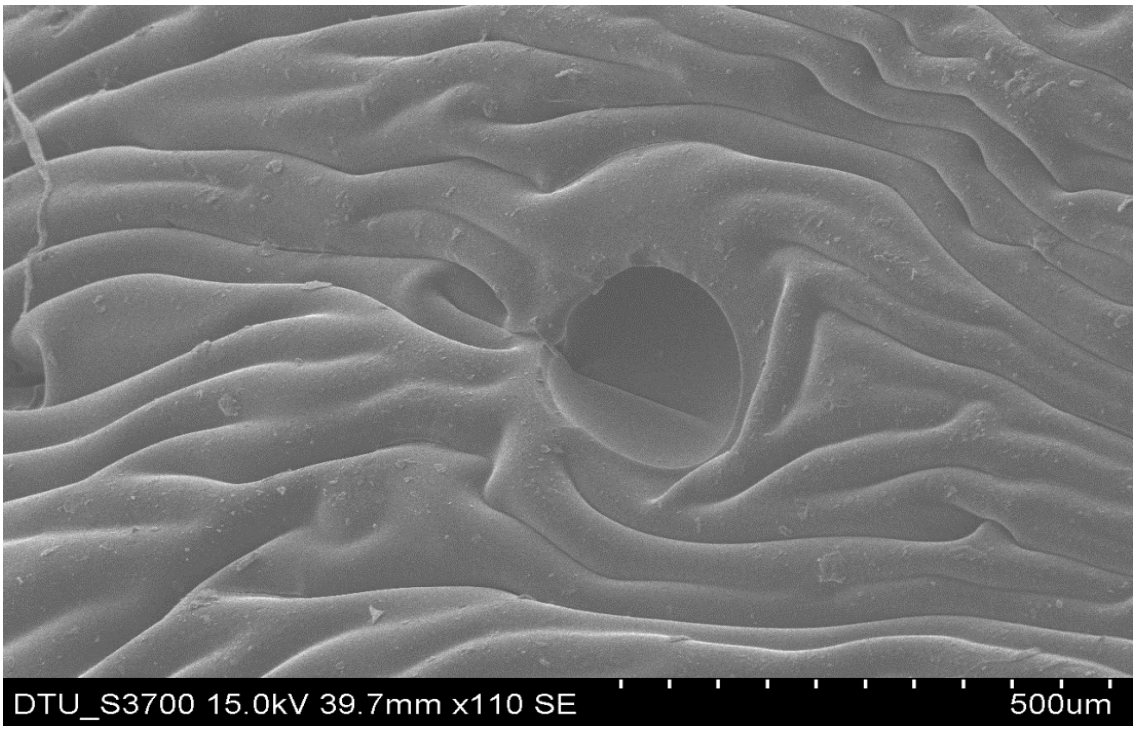


Figure 5.2.4 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(1%) Hydrogel at 500µm resolution

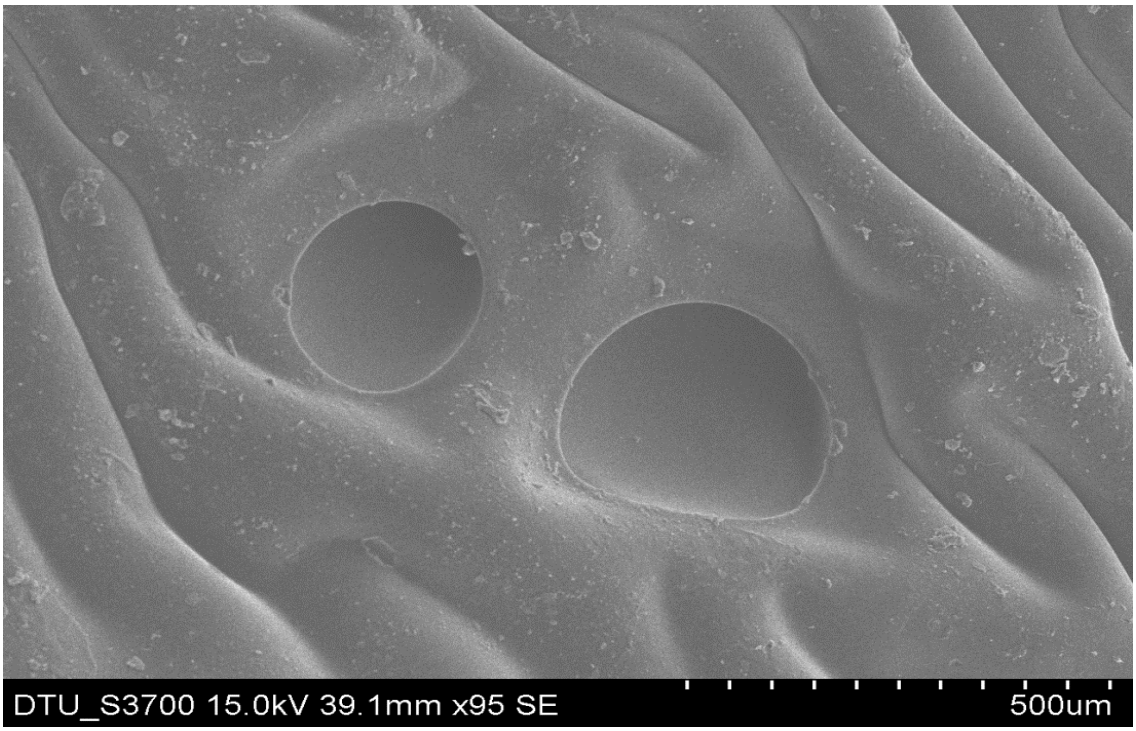


Figure 5.2.5 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(1%) Hydrogel at 500µm resolution

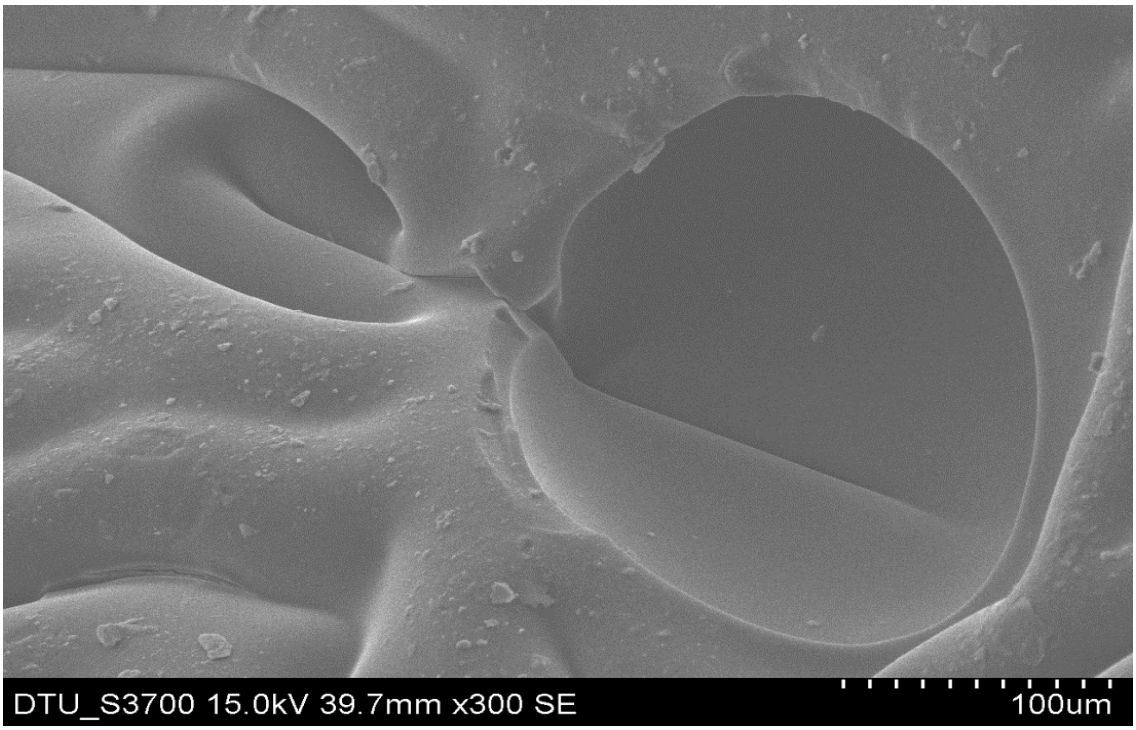


Figure 5.2.6 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(1%) Hydrogel at 100µm resolution

5.2.3 Polyacrylamide : CarboxyMethylGwargum (2%) Hydrogel

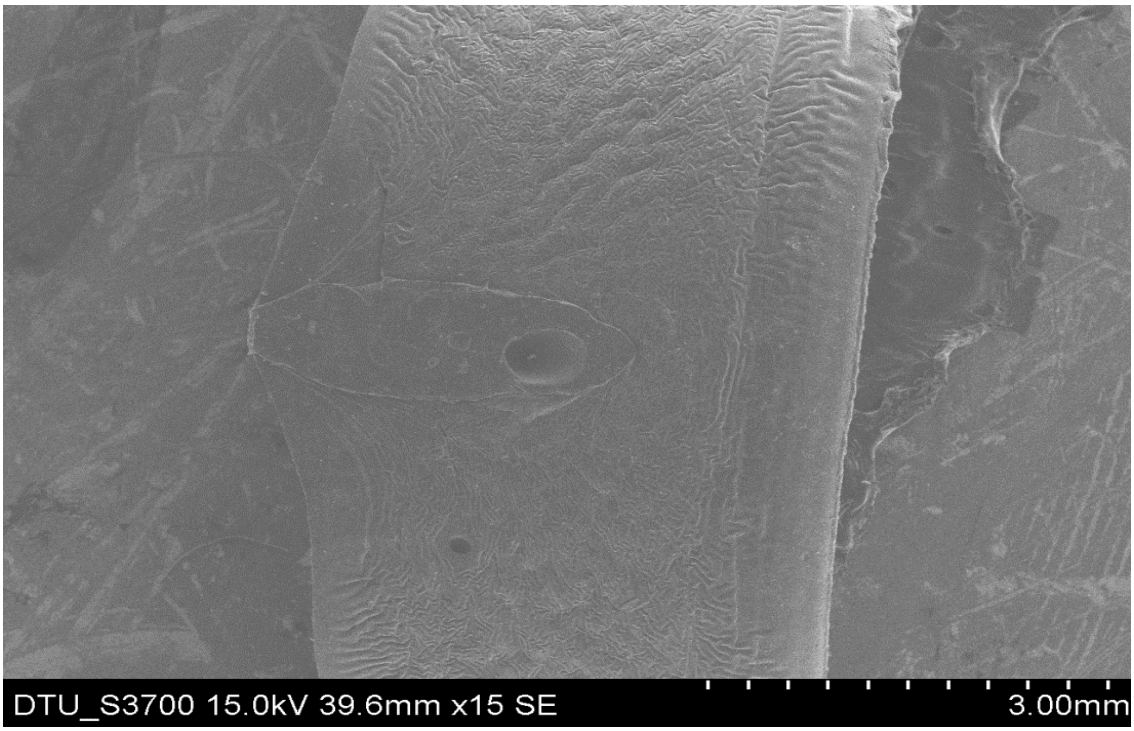


Figure 5.2.7 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(2%) Hydrogel at 3mm resolution

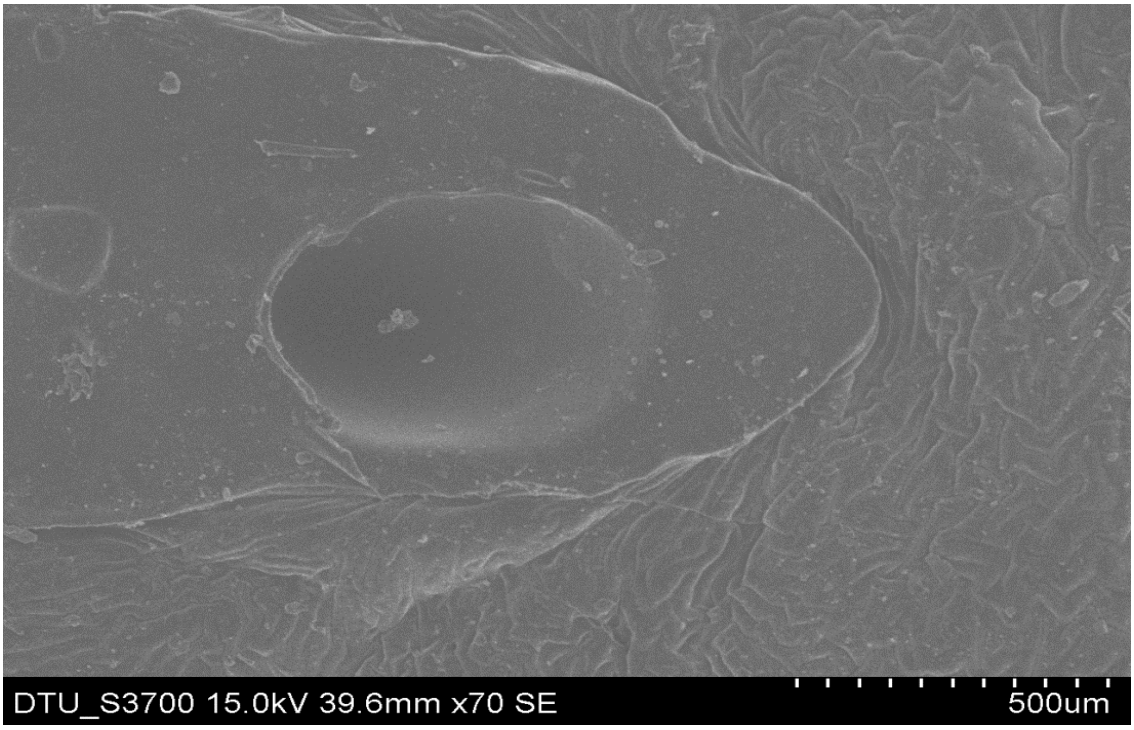


Figure 5.2.8 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(2%) Hydrogel at 500µm resolution

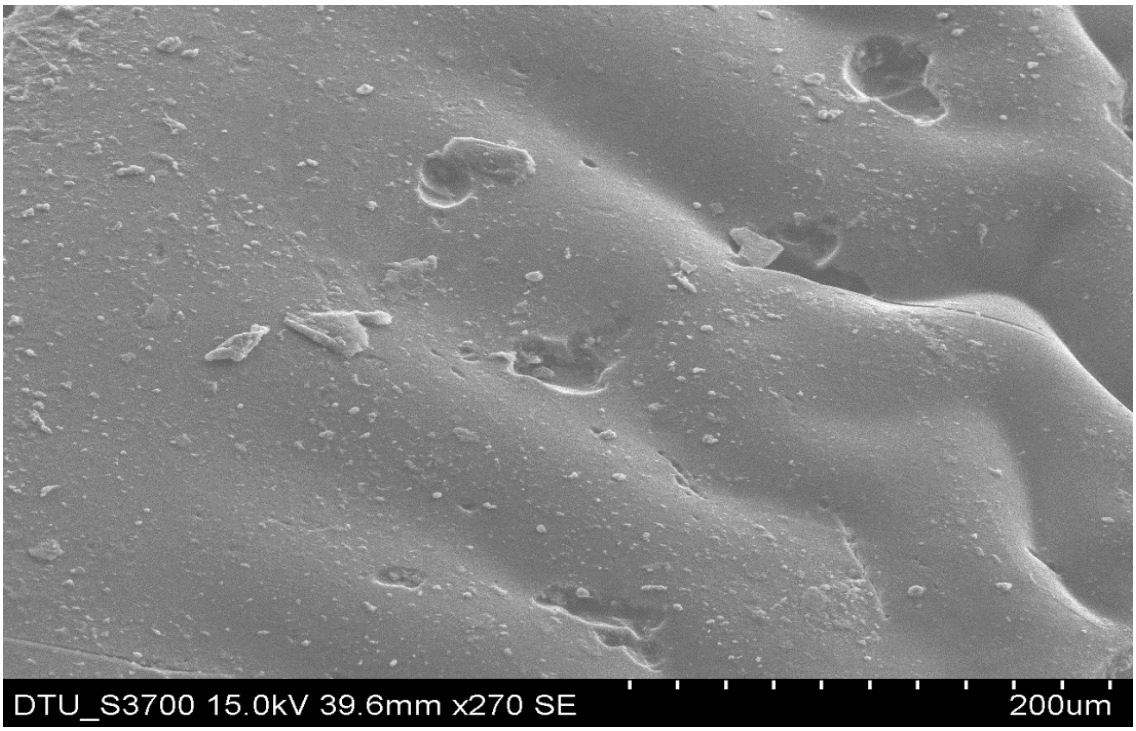


Figure 5.2.9 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(2%) Hydrogel at 200µm resolution

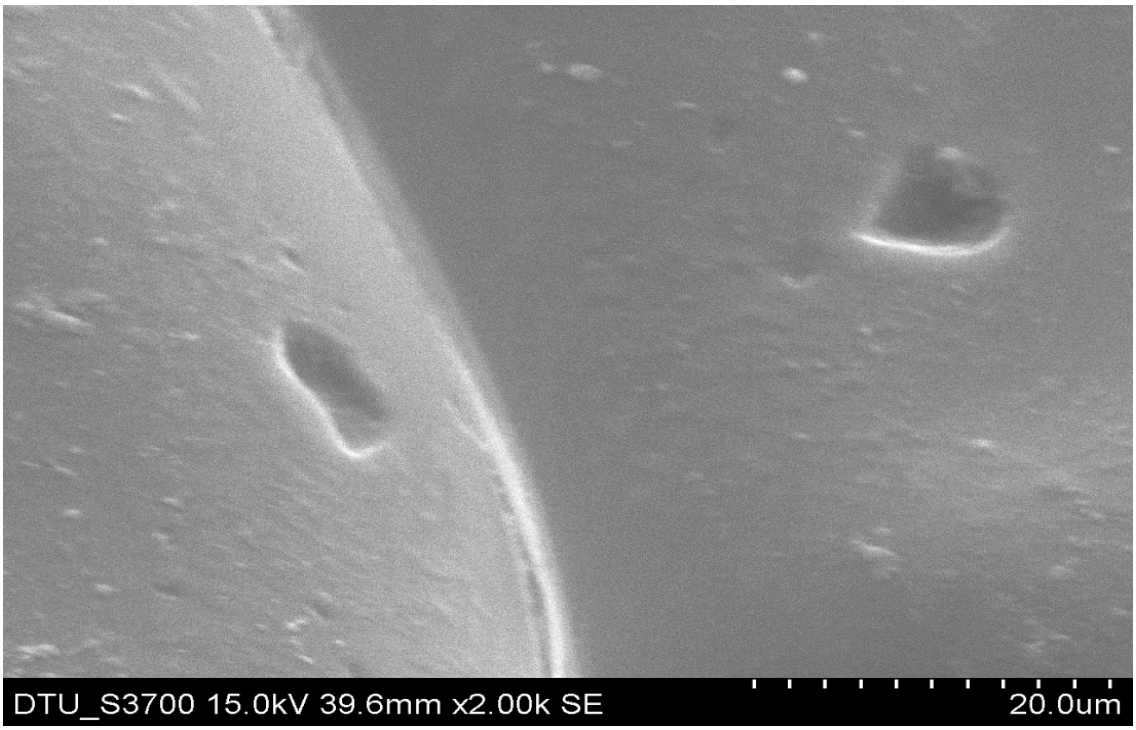


Figure 5.2.10 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(2%) Hydrogel at 20µm resolution

5.2.4 Polyacrylamide : CarboxyMethylGwargum (5%) Hydrogel

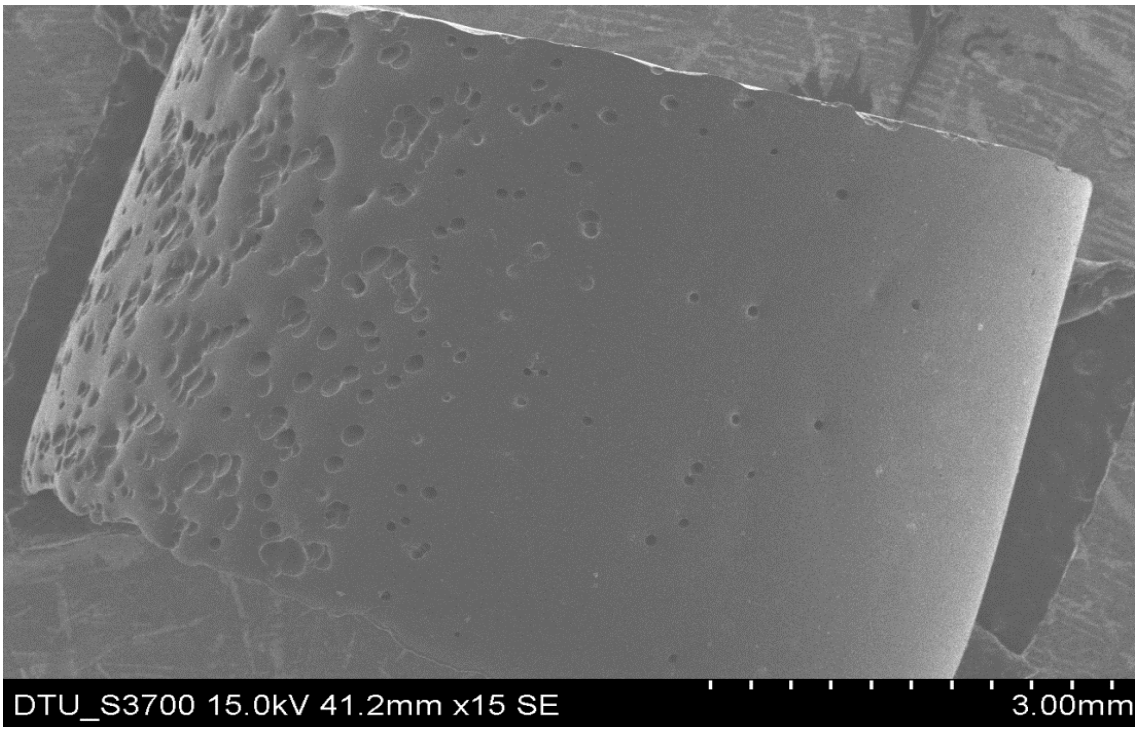


Figure 5.2.11 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(5%) Hydrogel at 3mm resolution

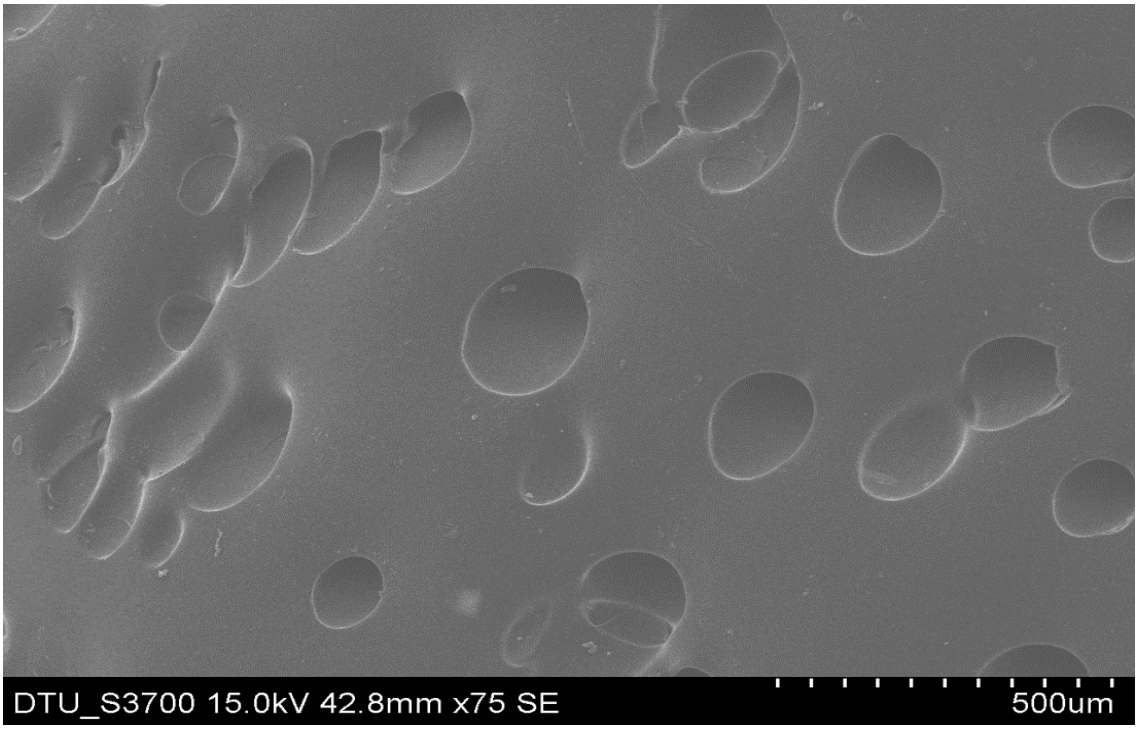


Figure 5.2.12 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(5%) Hydrogel at 500µm resolution

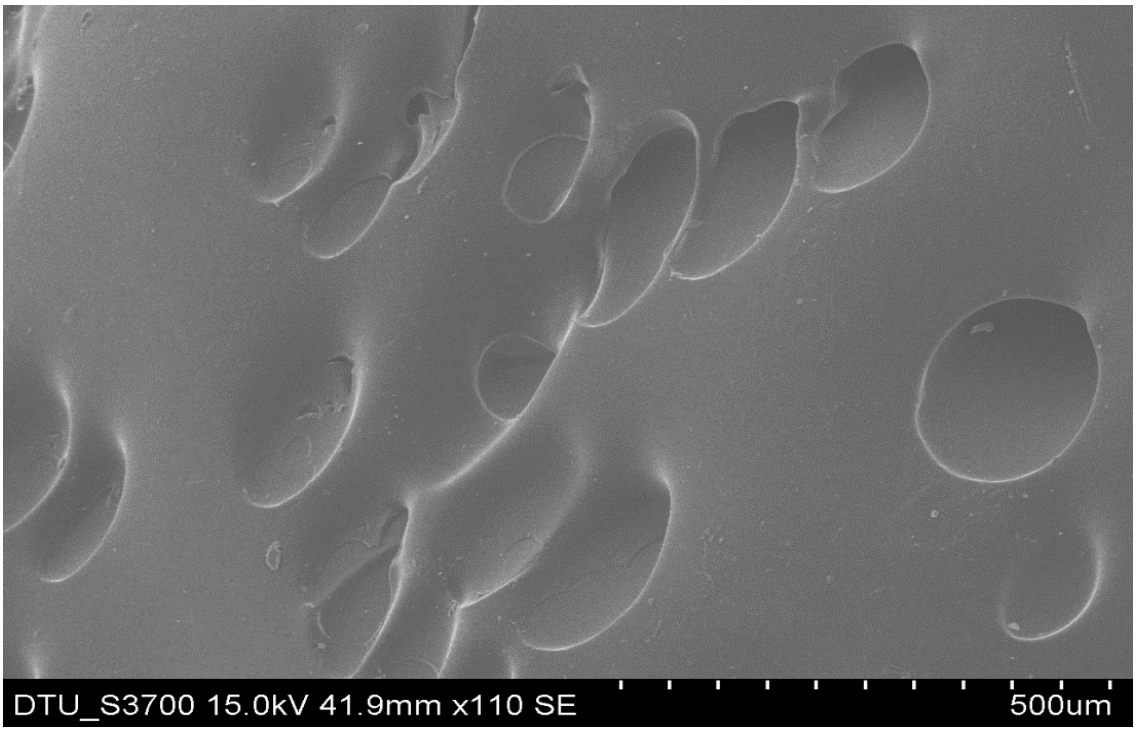


Figure 5.2.13 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(5%) Hydrogel at 500µm resolution

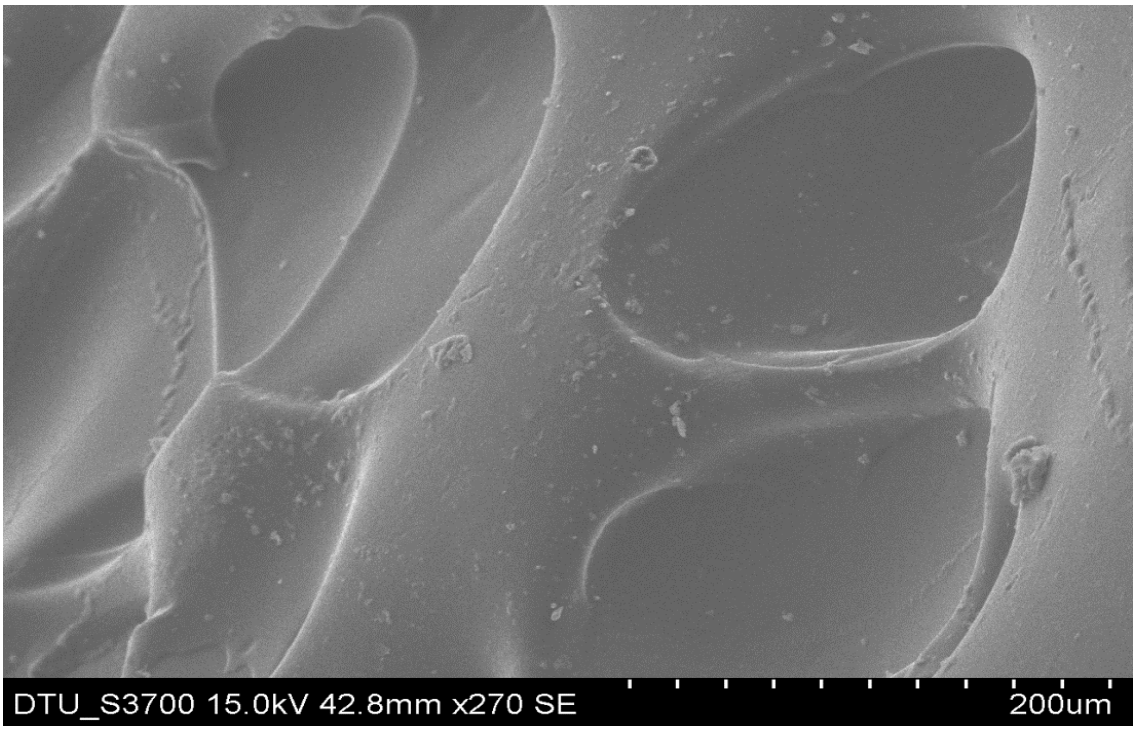


Figure 5.2.14 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(5%) Hydrogel at 200µm resolution

5.2.5 Polyacrylamide : CarboxyMethylGwargum (7%) Hydrogel

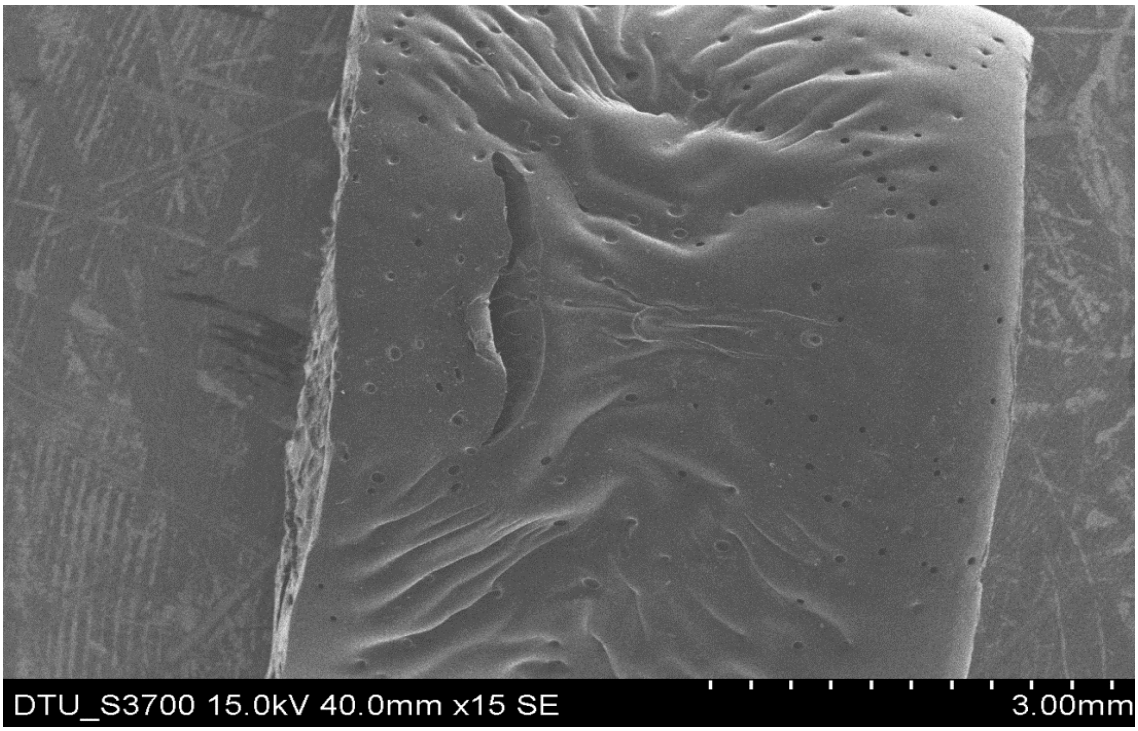


Figure 5.2.15 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(7%) Hydrogel at 3mm resolution

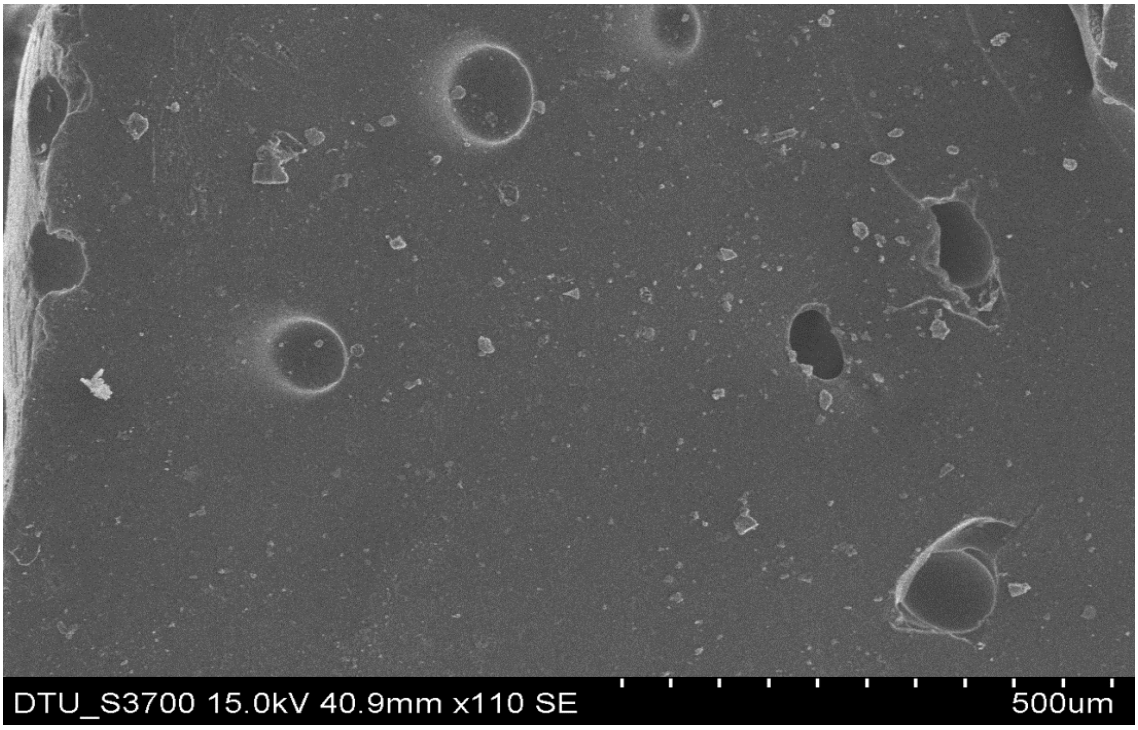


Figure 5.2.16 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(7%) Hydrogel at 500µm resolution

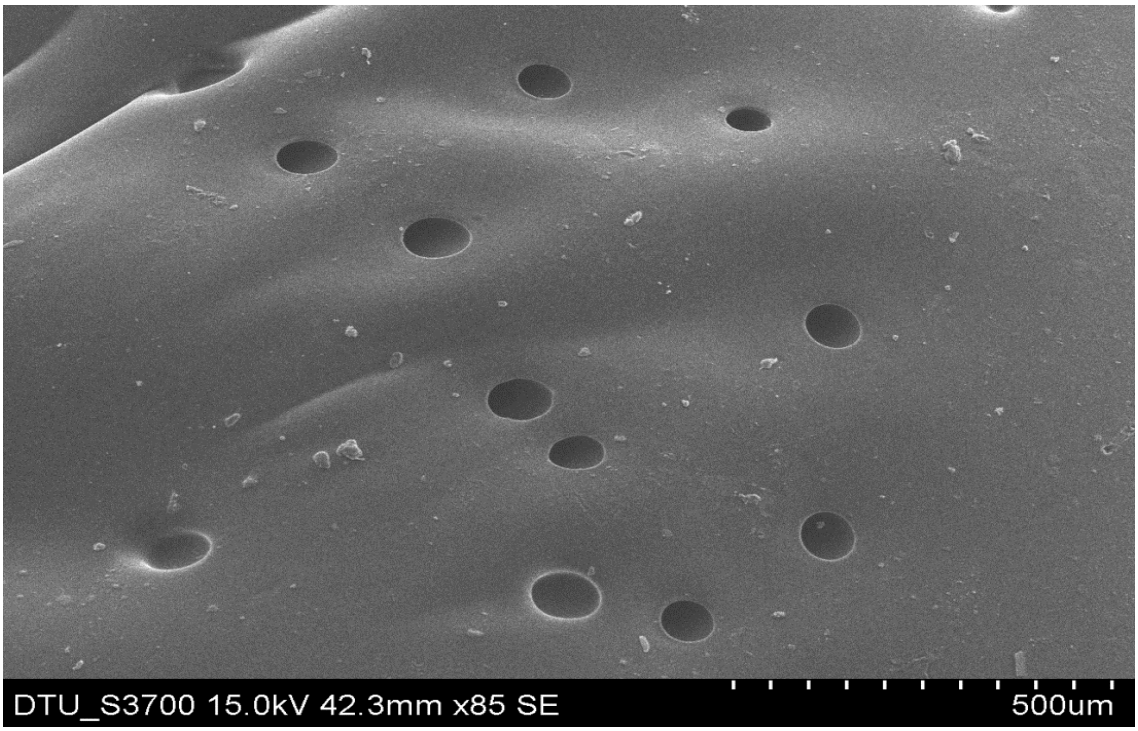


Figure 5.2.17 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(7%) Hydrogel at 500µm resolution

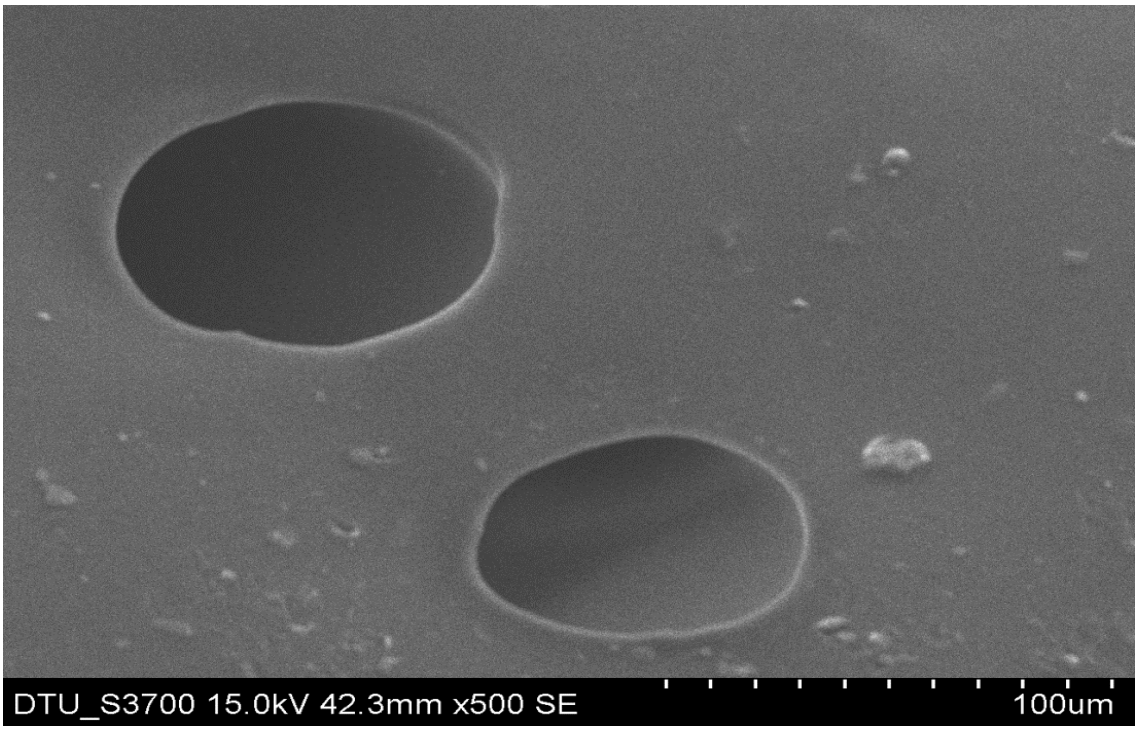


Figure 5.2.18 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(7%) Hydrogel at 100µm resolution

5.2.6 Polyacrylamide : CarboxyMethylGwargum (10%) Hydrogel

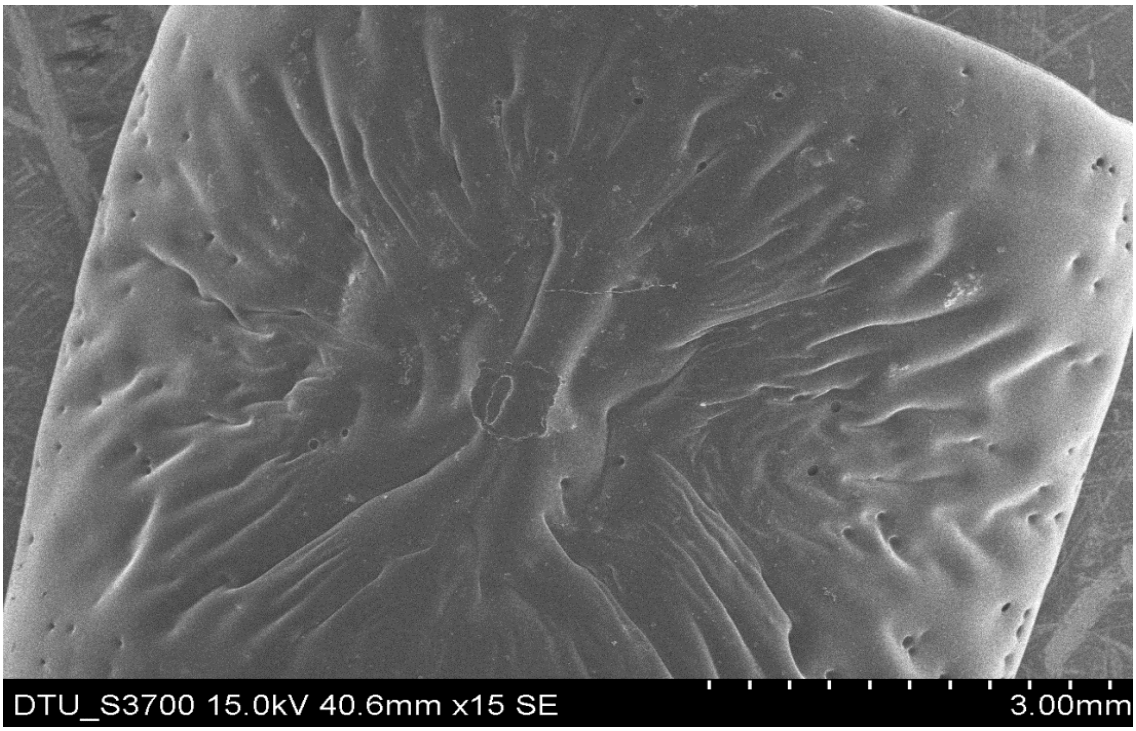


Figure 5.2.19 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(10%) Hydrogel at 3mm resolution

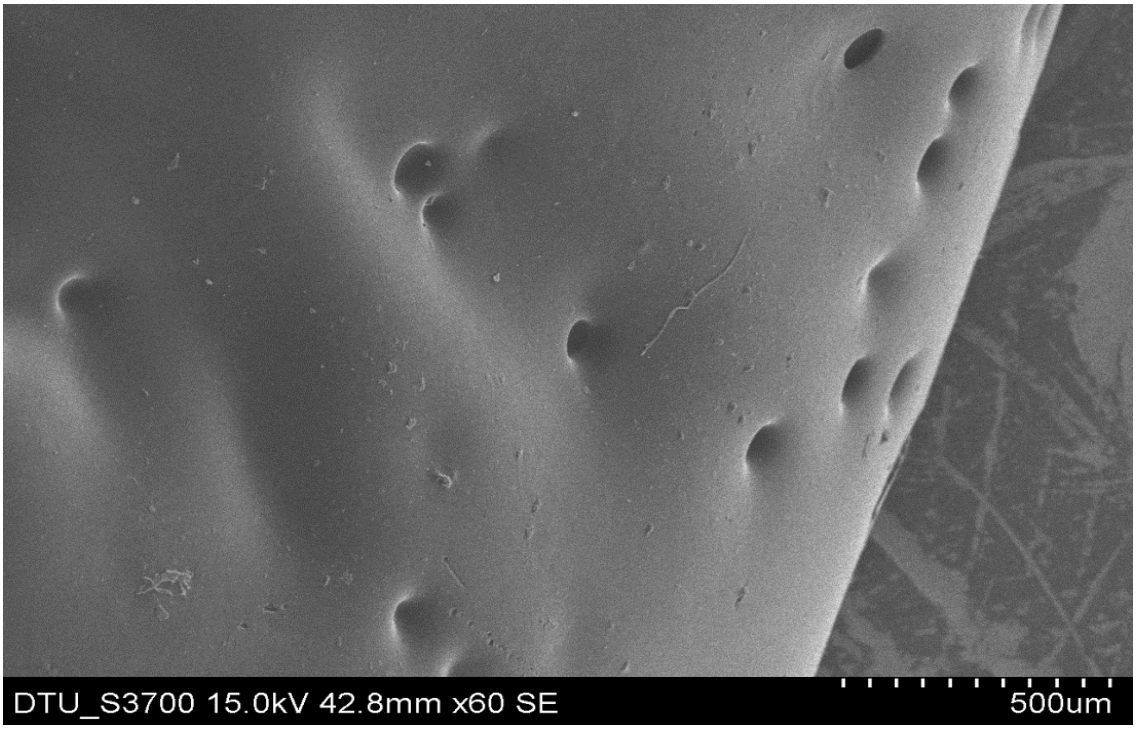


Figure 5.2.20 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(10%) Hydrogel at 500µm resolution

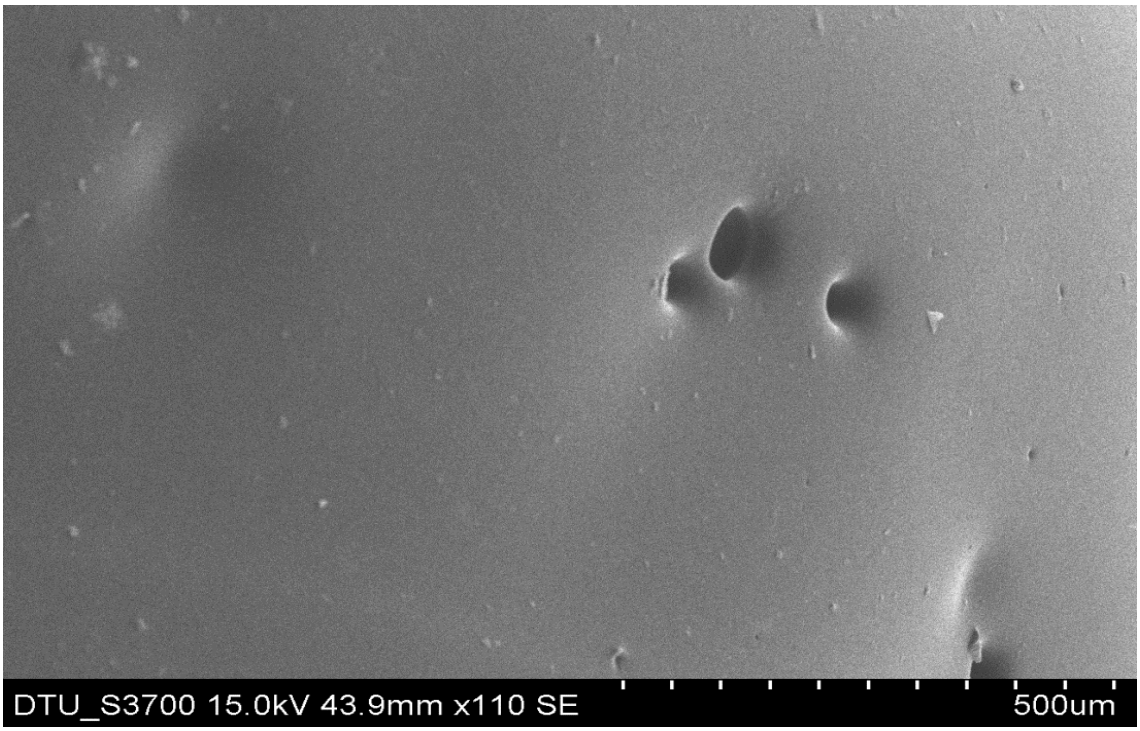


Figure 5.2.21 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(10%) Hydrogel at 500µm resolution

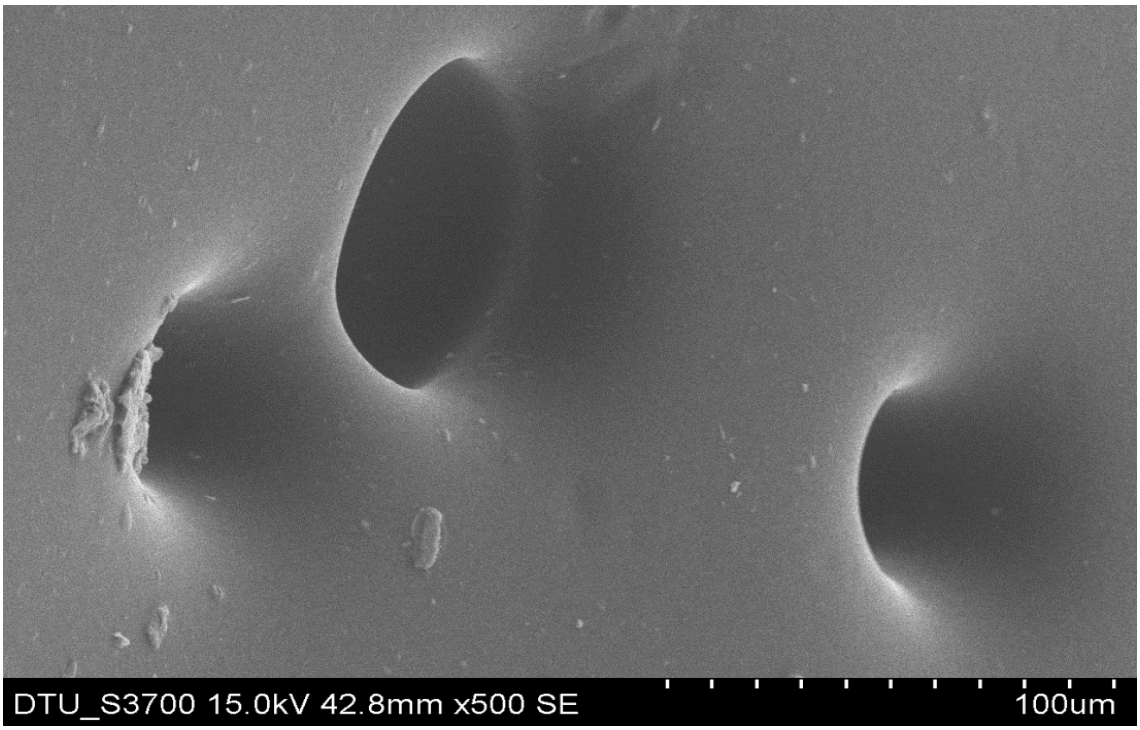


Figure 5.2.22 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(10%) Hydrogel at 100µm resolution

5.2.7 Polyacrylamide : CarboxyMethylGwargum (15%) Hydrogel

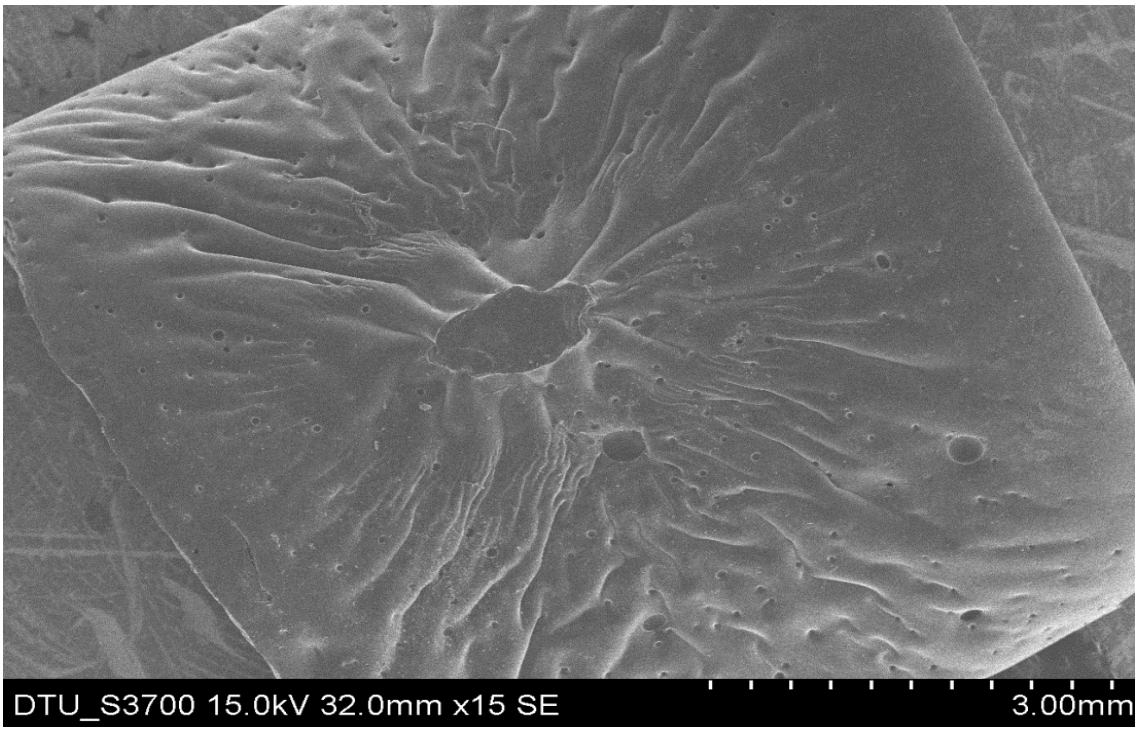


Figure 5.2.23 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(15%) Hydrogel at 3mm resolution

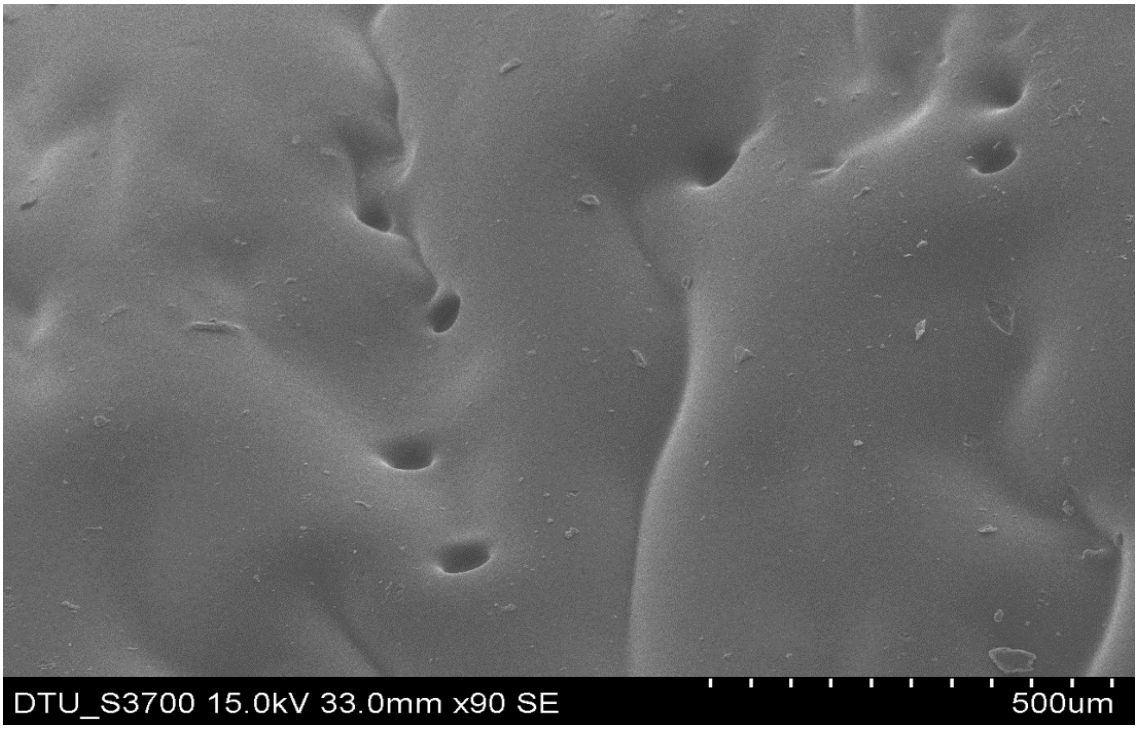


Figure 5.2.24 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(15%) Hydrogel at 500µm resolution

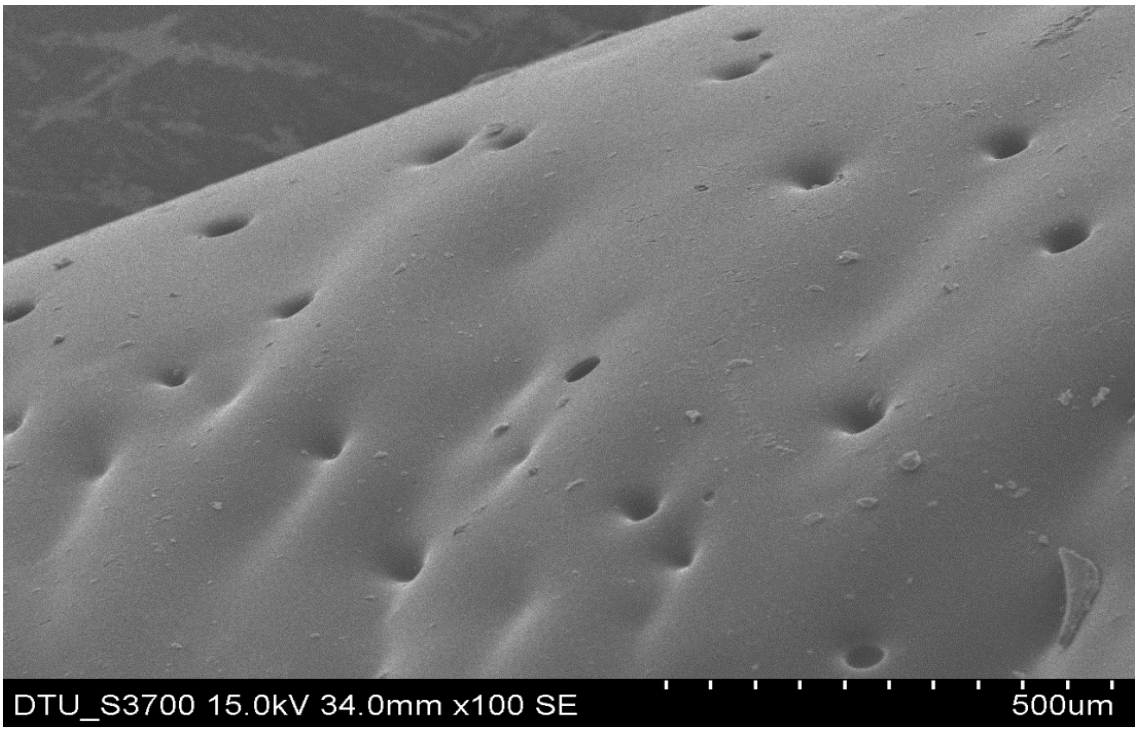


Figure 5.2.25 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(15%) Hydrogel at 500µm resolution

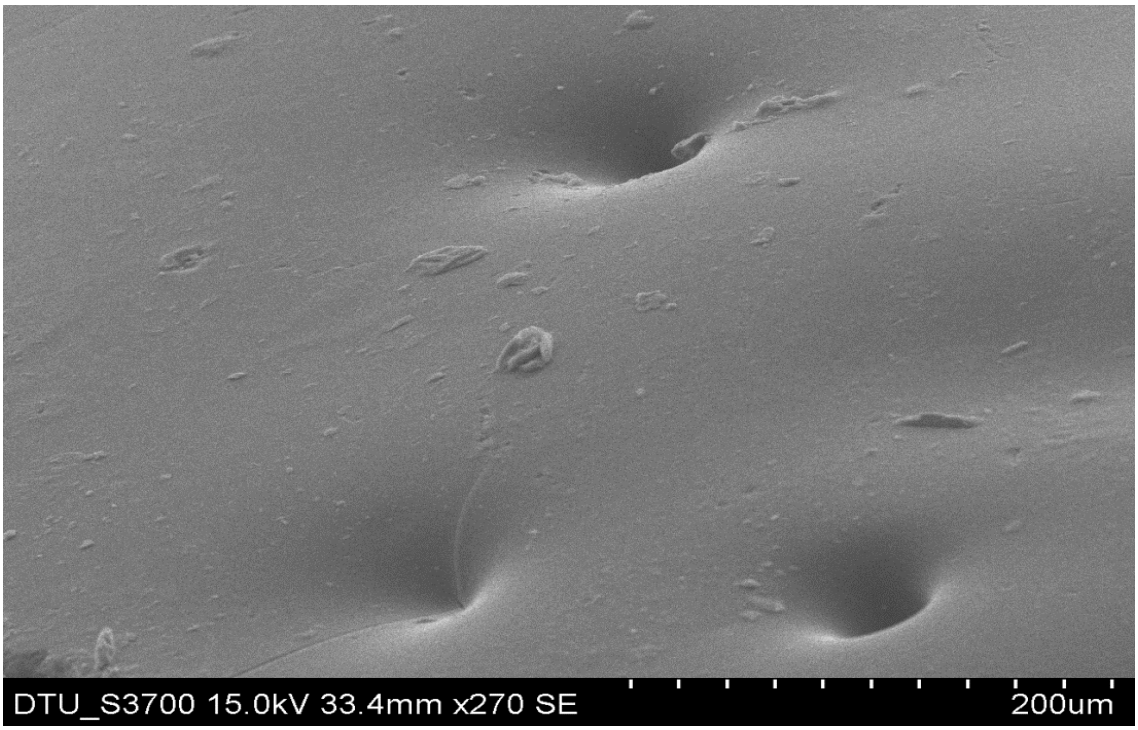


Figure 5.2.26 SEM micrograph of PolyAcrylamide : CarboxyMethyl Guargum(15%) Hydrogel at 200µm resolution

From SEM micrographs it has been observed that carboxymethyl guargum containing hydrogels showed less deterioration of surface i.e they have a smooth surfaceas compared to pure polyacrylamide containing hydrogel. The improvement in structure with addition of carboxymethyl guar gum has also been confirmed through compression test.

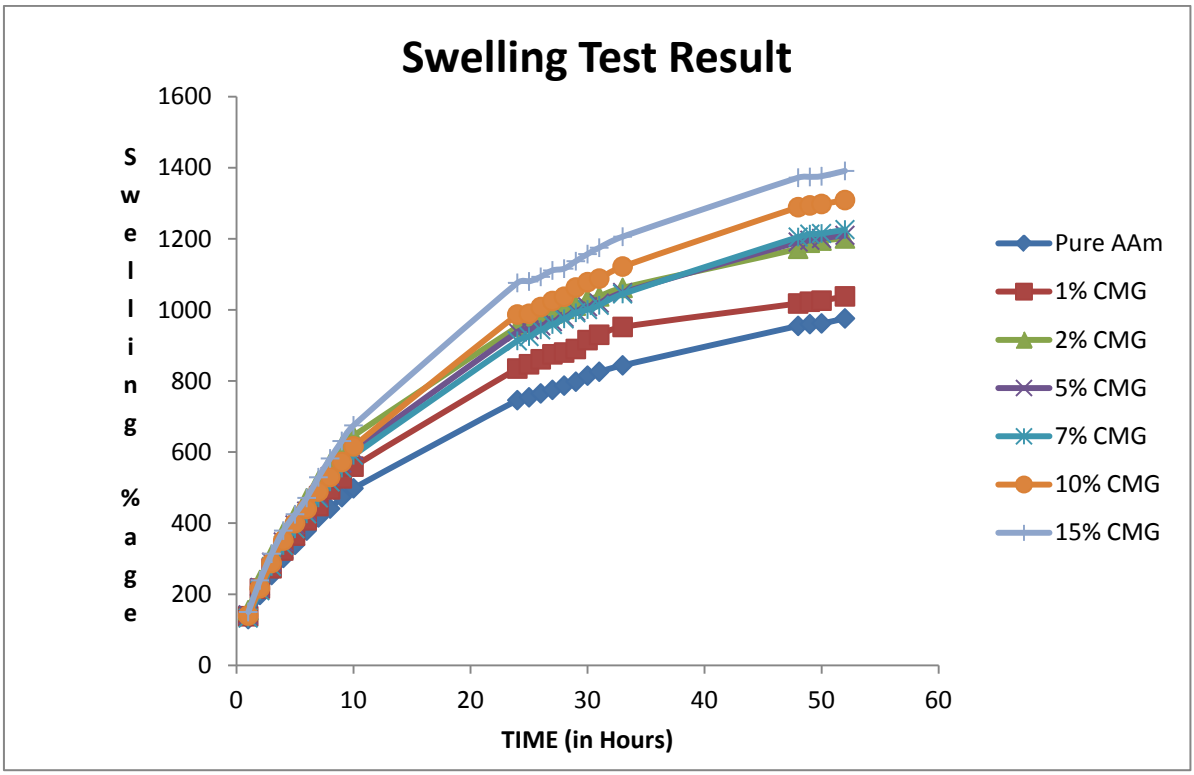
Also the micropores which are absent in the pure acrylamide hydrogel are available in carboxy methyl guargum containing hydrogel.

Also the pore density increases with the increase in the carboxy methyl guargum content in the hydrogel. This can also be a reason for the increase in uptake of water with the increase in the carboxymethyl guar gum content in the hydrogel.

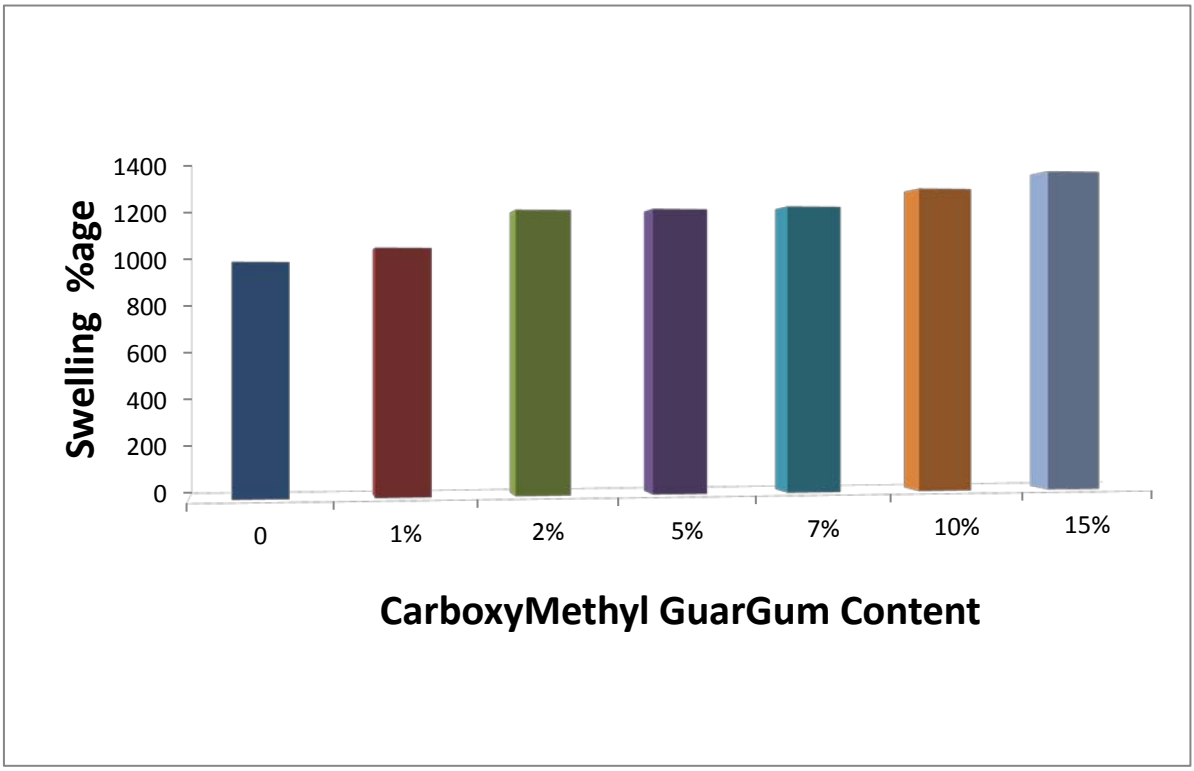
5.3 SWELLING RESULT

TABLE 5.3.1 Value of Swelling %age with change of Time

	Swelling %age						
Time (in hours)	Pure Acrylamide hydogel	AAm : CMG (1%)	AAm : CMG (2%)	AAm : CMG (5%)	AAm : CMG (7%)	AAm : CMG (10%)	AAm : CMG (15%)
		Hydro gel	Hydro gel	Hydro gel	Hydro gel	Hydro gel	Hydro gel
1	130	138	155	142	133	140	150
2	198	216	240	219	210	217	239
3	254	273	311	290	278	288	314
4	302	323	374	347	337	351	379
5	339	365	422	395	384	400	425
6	379	408	470	434	426	440	471
7	416	448	519	477	471	489	529
8	441	495	569	531	516	530	582
9	473	526	617	569	555	572	631
10	498	559	646	605	591	616	675
24	746	835	952	938	913	987	1076
25	754	847	962	944	925	989	1080
26	765	861	977	955	944	1008	1093
27	775	875	990	967	959	1025	1111
28	787	880	1003	979	975	1037	1116
29	798	890	1012	996	992	1063	1137
30	815	915	1030	1009	1001	1078	1157
31	826	930	1038	1019	1013	1088	1175
33	844	952	1062	1049	1045	1122	1206
48	955	1018	1172	1191	1205	1289	1372
49	960	1023	1189	1196	1213	1294	1374
50	962	1026	1195	1201	1215	1298	1376
52	976	1038	1201	1210	1226	1309	1391



Graph 5.3.1 – Swelling Studies : Swelling %age v/s Time



Graph 5.3.2 – Swelling Studies : Swelling %age v/s CMGG Content

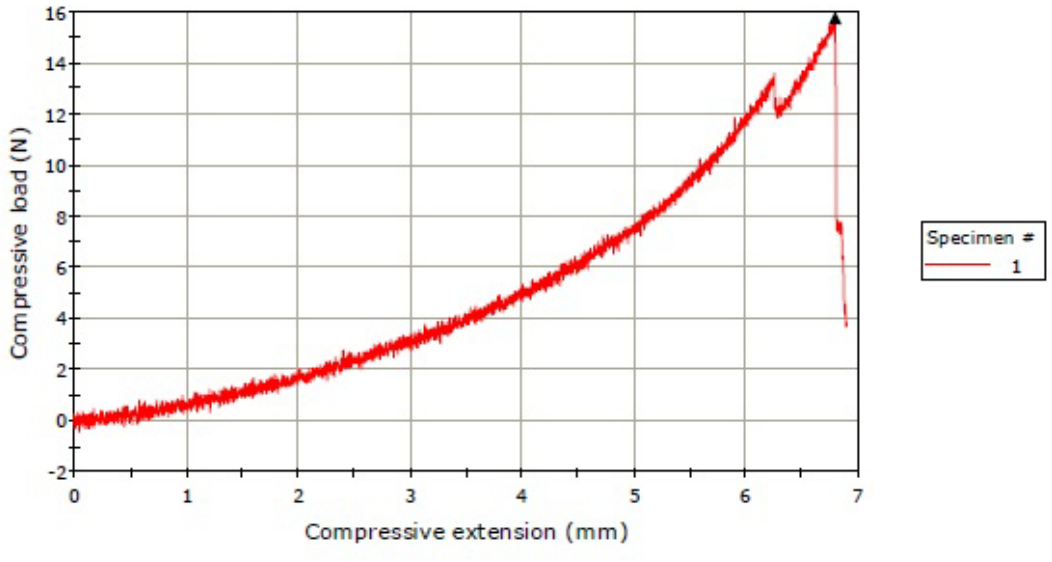
The Swelling Percentage of the hydrogels prepared of Carboxymethylated guar gum-Polyacrylamide blends is evaluated by immersion method where pre-weighed hydrogel samples are immersed into water for a fixed time at a specific temperature, then removed from the water and soaked the surface water with filter paper to measure the final weight. Swelling Percentage is expressed as a fraction of increase in weight against initial weight of the films.

Iniatially the % increase in weight of hydrogel was proportional to time. But with further passage of time, the rate of increase in weight started showing decreasing trend, which later became constant. After 48 hours there was no significant change in weight of the sample.

In this case, swelling percentage of the hydrogel shows an upward curve versus CMGG content. With increase in CMGG content the hydrogel shows a considerable increase in equilibrium swelling percentage.

The Swelling ratio increases from 9.7 for pure acrylamide hydrogel to 13.9 for 15% CMGG containing hydrogel.

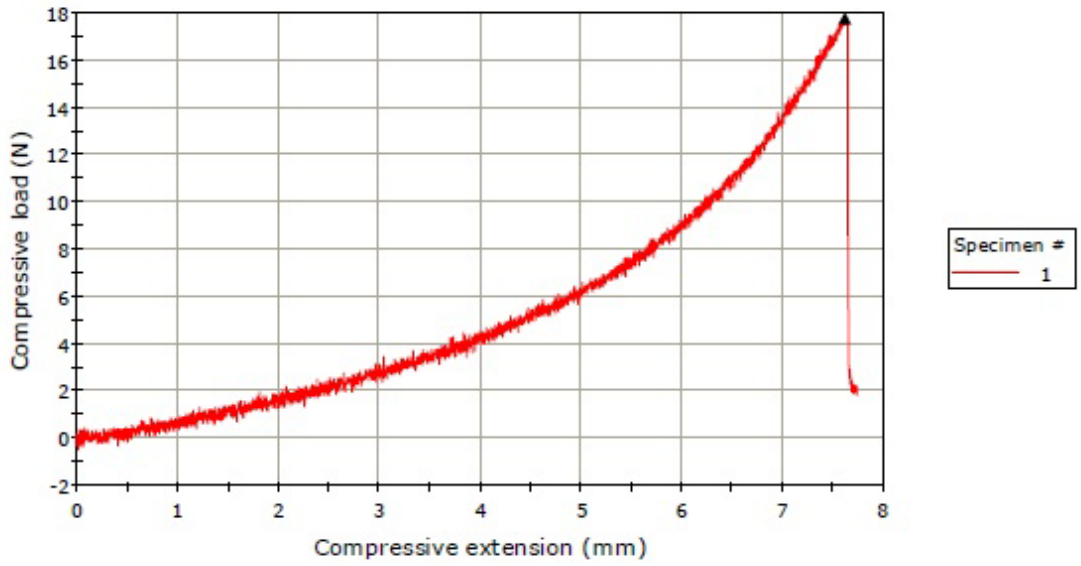
5.4 COMPRESSION TEST



Results Table 1

	Maximum Compressive load (kgf)
1	1.60651

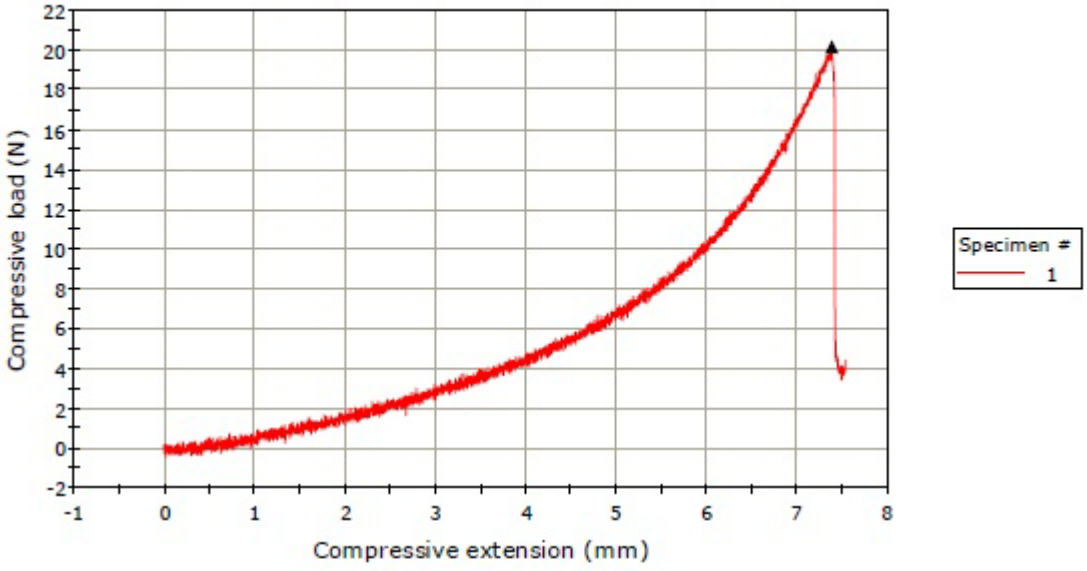
Figure 5.4.1 - Compression Test : Pure Polyacrylamide Hydrogel



Results Table 1

	Maximum Compressive load (kgf)
1	1.80916

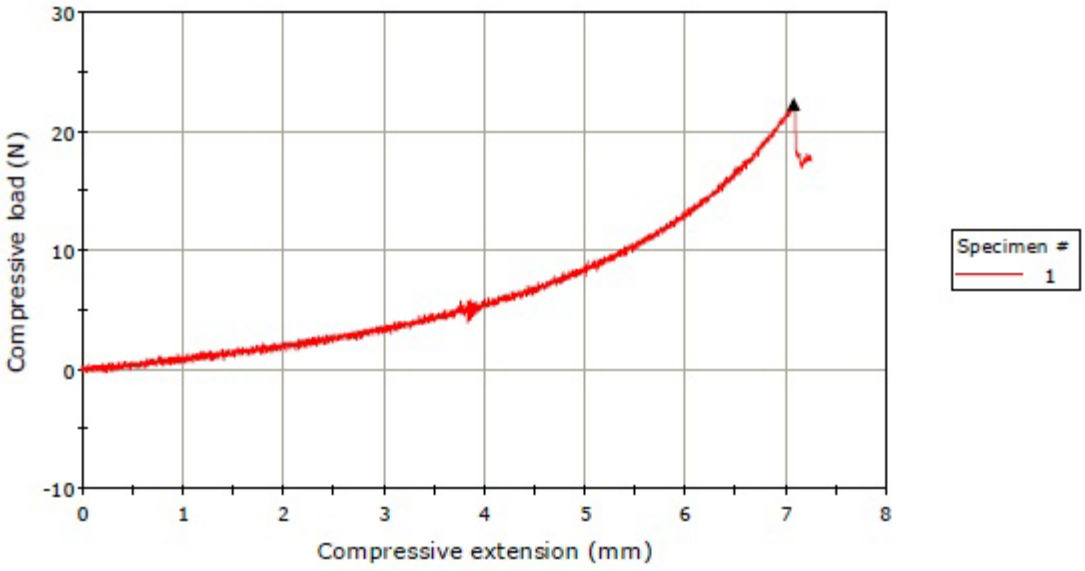
Figure 5.4.2 - Compression Test : Polyacrylamide-CarboxyMethylGwargum (1%) Hydrogel



Results Table 1

	Maximum Compressive load (kgf)
1	2.05637

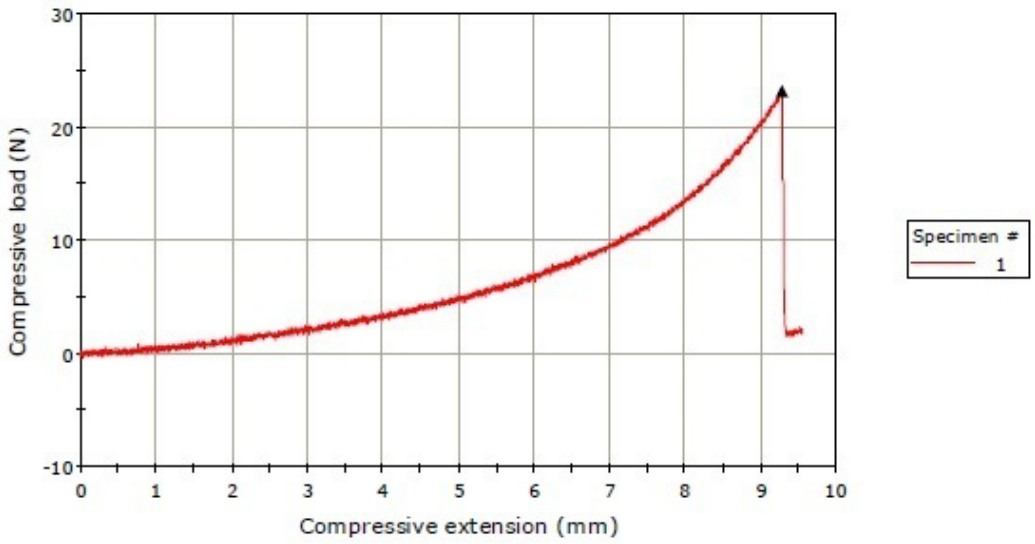
Figure 5.4.3 - Compression Test : Polyacrylamide-CarboxyMethylGwargum (2%) Hydrogel



Results Table 1

	Maximum Compressive load (kgf)
1	2.27186

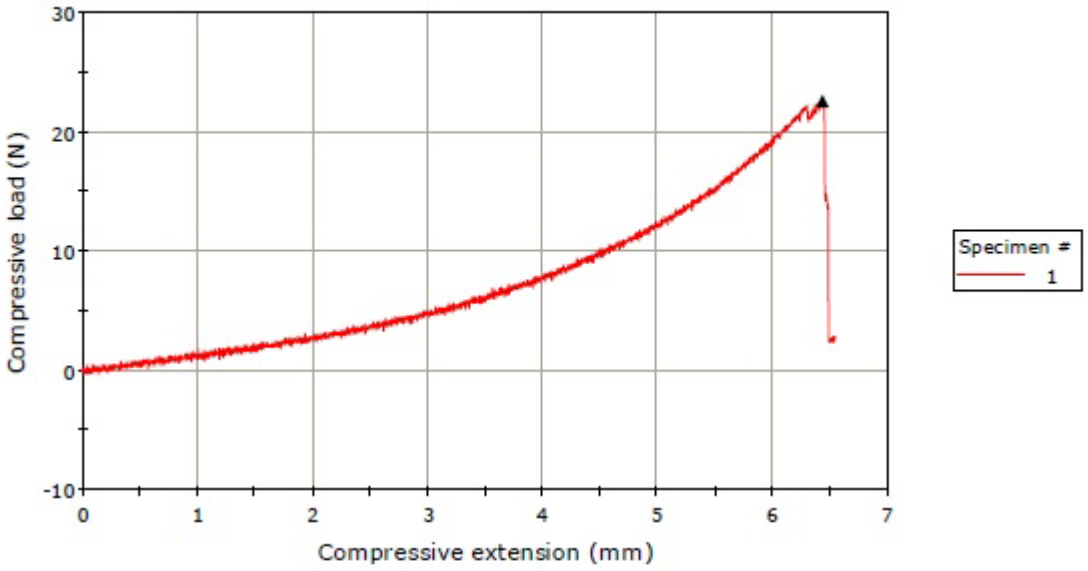
Figure 5.4.4 - Compression Test : Polyacrylamide-CarboxyMethylGwargum (5%) Hydrogel



Results Table 1

	Maximum Compressive load (kgf)
1	2.28465

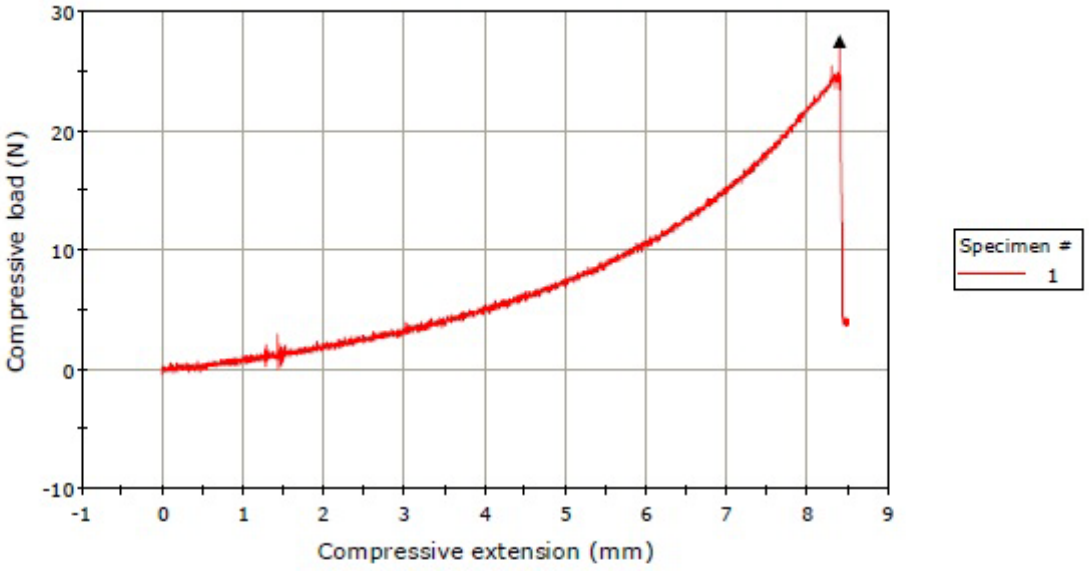
Figure 5.4.5 - Compression Test : Polyacrylamide-CarboxyMethylGwargum (7%) Hydrogel



Results Table 1

	Maximum Compressive load (kgf)
1	2.29912

Figure 5.4.6 - Compression Test : Polyacrylamide-CarboxyMethylGwargum (10%) Hydrogel



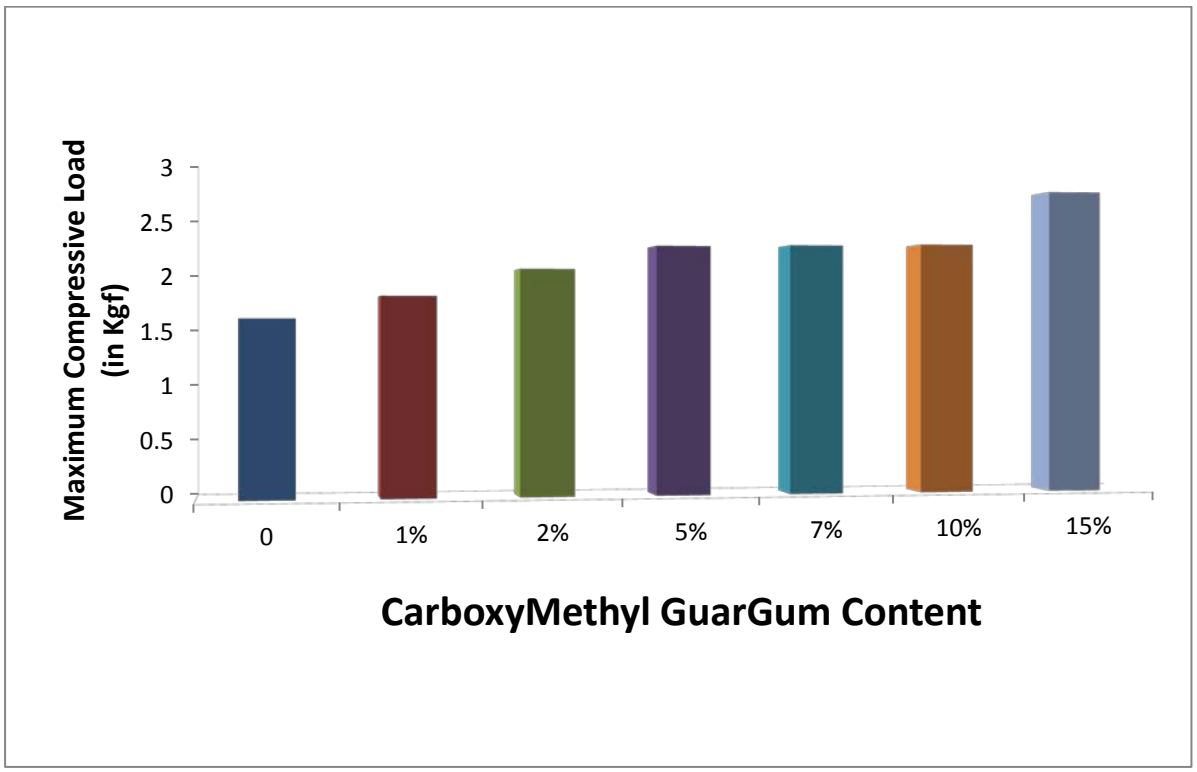
Results Table 1

	Maximum Compressive load (kgf)
1	2.80103

Figure 5.4.7 - Compression Test : Polyacrylamide-CarboxyMethylGwargum (15%) Hydrogel

Table 5.4.1 Value of Maximum Compressive Load v/s CMGG Content

SAMPLE	Maximum Compressive Load (in Kgf)
1. Pure Polyacrylamide Hydrogel	1.60651
2. Polyacrylamide : CMGG (1%) Hydrogel	1.80916
3. Polyacrylamide : CMGG (2%) Hydrogel	2.05637
4. Polyacrylamide : CMGG (5%) Hydrogel	2.27186
5. Polyacrylamide : CMGG (7%) Hydrogel	2.28465
6. Polyacrylamide:CMGG (10%) Hydrogel	2.29912
7. Polyacrylamide:CMGG (15%) Hydrogel	2.80103



Graph 5.4.1 – Compression Test Studies : Maximum Compressive Load v/s CMGG Content

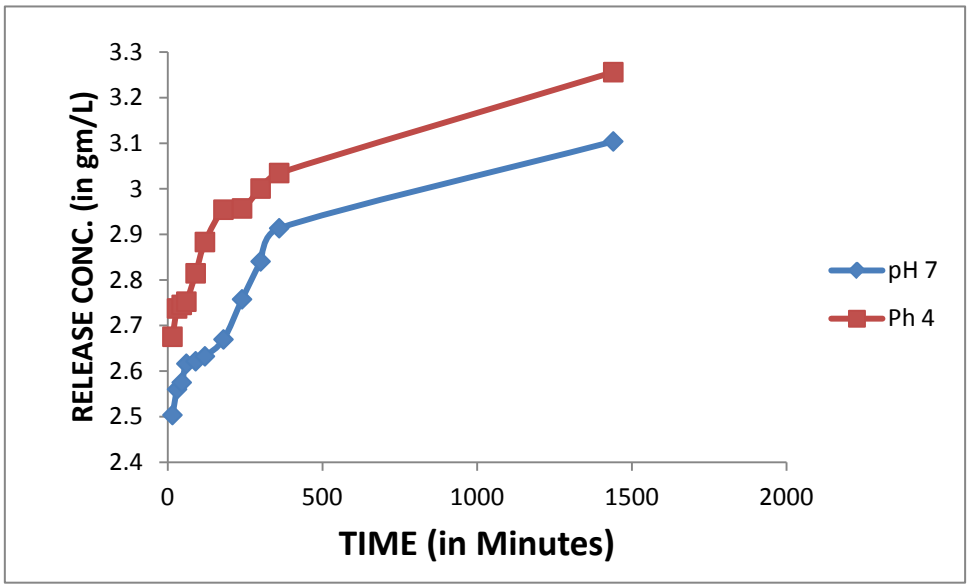
Pure Polyacrylamide hydrogel shows the lowest value of compressive strength of all hydrogels. The hydrogel containing highest content of carboxymethyl guar gum exhibits highest compression strength at break of all hydrogels prepared. On blending carboxymethyl guar gum with Polyacrylamide, the compression strength of the hydrogels increases with the increasing content of carboxymethyl guar gum. Compression strength of the hydrogels improved significantly as it shows nearly two fold increase in the compression strength from 1.6 Kgf to 2.8 Kgf as the carboxymethyl guar gum content increases from 0 to 15%.

15% Carboxymethyl Guar Gum containing hydrogel of 20mm thickness has a compression strength of 2.8 Kgf. The higher value is on account of increased intra molecular hydrogen bonding in case of carboxymethylated guar gum.

5.5 DRUG RELEASE STUDIES

Table 5.5.1 Concentration v/s Time values for samples containing 1% CMGG in acidic & neutral medium

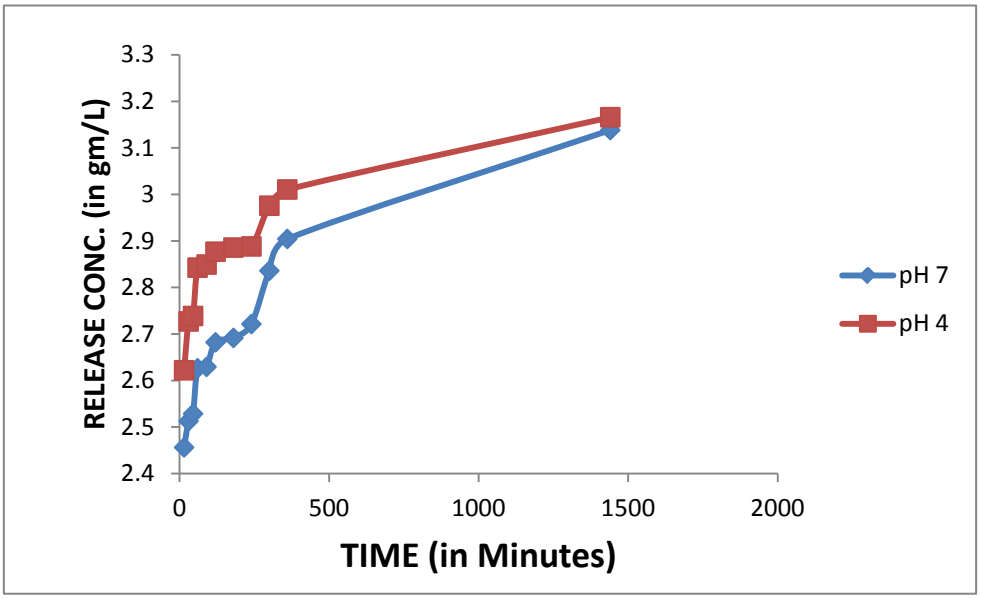
TIME	CONCENTRATION (in gm/L)	
(in minutes)	at pH 7	at pH 4
15	2.5035	2.6754
30	2.5601	2.7375
45	2.5750	2.7452
60	2.6162	2.7523
90	2.6216	2.8146
120	2.6325	2.8832
180	2.6695	2.9541
240	2.7575	2.9569
300	2.8406	3.0006
360	2.9135	3.0346
1440	3.1039	3.2560



Graph 5.5.1 – Drug Release Study : Release Concentration v/s Time graph for samples containing 1% CMGG in acidic & neutral medium

Table 5.5.2 Concentration v/s Time values for samples containing 5% CMGG in acidic & neutral medium

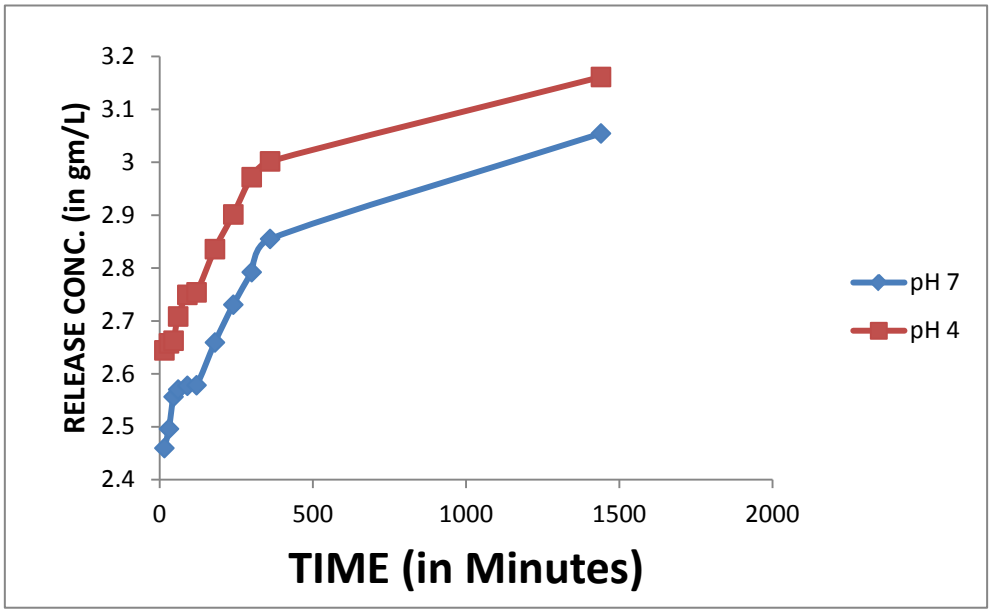
TIME	CONCENTRATION (in gm/L)	
(in minutes)	at pH 7	at pH 4
15	2.4561	2.6219
30	2.5127	2.7268
45	2.5284	2.7386
60	2.6263	2.8425
90	2.6293	2.8491
120	2.6820	2.8768
180	2.6915	2.8856
240	2.7213	2.8881
300	2.8358	2.9756
360	2.9042	3.0105
1440	3.1381	3.1658



Graph 5.5.2 – Drug Release Study : Release Concentration v/s Time graph for samples containing 5% CMGG in acidic & neutral medium

Table 5.5.3 Concentration v/s Time values for samples containing 15% CMGG in acidic & neutral medium

TIME	CONCENTRATION (in gm/L)	
(in minutes)	at pH 7	at pH 4
15	2.4595	2.6443
30	2.4959	2.6576
45	2.5566	2.6626
60	2.5703	2.7084
90	2.5774	2.7493
120	2.5784	2.7540
180	2.6592	2.8357
240	2.7307	2.9013
300	2.7921	2.9717
360	2.8550	3.0016
1440	3.0544	3.1612



Graph 5.5.3 – Drug Release Study : Release Concentration v/s Time graph for samples containing 15% CMGG in acidic & neutral medium

Drug release from a hydrogel is closely related to many factors such as swelling behaviour of the hydrogel, drug affinity for the polymer structure and solubility of the drug in water. Graph 5.5.1, 5.5.2 & 5.5.3 depict the *in vitro* release profile of ciprofloxacin hydrochloride from hydrogels at pH 4 & 7 at 37 °C. The drug release study was also performed for samples containing 1%, 5%, 15% CMGG content.

Generally, all hydrogels showed an initial burst release within the first 15 min. The explanation for this sudden release is possibly due to the drug absorbed at the gel surface. It has been found that the ciprofloxacin hydrochloride release increased rapidly at first and then gradually reached the equilibrium value in approximately 7 h.

From the graph it has been observed that the release of ciprofloxacin hydrochloride is more in acidic medium as compared to neutral medium for all the samples.

CHAPTER 6

APPLICATIONS AND FUTURE PROSPECTS

The hydrophilic nature of synthesised hydrogel permits drug delivery of therapeutic materials that would otherwise denature due to hydrophobic interactions, and the protective structure also prevents destruction of cells or proteins by host immune responses, since matrix pore size can be made small enough to prevent the entry of large immune cells and antibodies.

They can be used as scaffolds in tissue engineering. When used as scaffolds, these hydrogels may contain human cells to repair tissue.

These hydrogels have the ability to sense changes of pH, temperature, or the concentration of metabolite and release their load as result of such a change. So they can found a number of applications where such a change should be sensed like in the case of biosensors.

Since the obtained hydrogel have good water retention capacities, so they can be used in disposable diapers where they absorb urine, or in sanitary napkins.

These hydrogels can also be used as dressings for healing of burn or other hard-to-heal wounds. Wound gels are excellent for helping to create or maintain a moist environment.

Therapeutic protein administration usually faces the need of frequent doses due to the small residence time in blood of the protein. A promising strategy to overcome this drawback is the development of sustained drug release systems based on hydrogel matrices loaded with the therapeutic drug and the tailored hydrogel is a good candidate for this use.

CHAPTER 7

CONCLUSION

In this work, we have successfully prepared the blend hydrogels of Guar Gum by combining both natural and synthetic polymer with a clean, cheap and dry method using free radical polymerization method. The natural polysaccharide used was carboxymethyl guar gum and the blend hydrogels of polyacrylamide-guar gum due to non-toxic nature, biocompatibility and biodegradability of guar gum can be used as drug carrier in pharmaceutical industry and even in cosmetics and water purification fields. The carboxymethyl guar gum containing hydrogels show compression strength of 2.8 Kgf and showed significant water swellling capabilities in distilled water at room temperatures.

The synthetic polymer, Polyacrylamide and the derivative of guar gum, carboxymethylated guar gum, were also used to prepare the blend IPNs hydrogels containing varying amount of CMGG and it has been found that as the concentration of CMGG in the hydrogel increases, the water swelling capacity and compression strength of the hydrogel also increases.

Swelling ratio increases from 9.7 for pure polyacrylamide hydrogel to 13.9 for 15% CMGG containing hydrogel and Compression strength of the hydrogels shows nearly two fold increase in the compression strength from 1.6 Kgf to 2.8 Kgf as the carboxymethyl guar gum content increases from 0 to 15%.

The tailored hydrogels were successfully loaded with drug (Ciprofloxacin Hydrochloride) and their release kinetics were studied in neutral and acidic medium.

The results illustrated that the blend hydrogels were a good candidate for drug carrier in pharmaceutical and cosmetic industries owing to their biodegradable, biocompatible and low toxic nature. The synthesis process of the hydrogel is convenient, low cost and eco-friendly, which might be expected to have wide applications in lots of industries.

REFERENCES

[1] I. Katimea,*, R. Novoaa, E. Dı´az de Apodacaa, E. Mendiza´balb, J. Puigb,"Theophylline release from poly(acrylic acid-co-acrylamide)hydrogels" , Journal of Polymer Testing 18, (1999) 559–566.

[2] Hopfenberg HB, Hsu KC. Polym Eng Sci 1978;18:1186.

[3] Peppas NA, Franson NM. J Polym Sci, Polym Phys Edn 1983;21:983.

[4] Davidson CWR, Peppas NA. J Controlled Release 1986;3:259.

[5] Hopfenberg HB, Apicella A, Saleeby DB. J Membr Sci 1981;8:273.

[6] Tharanathan, R. N. (2003). Biodegradable films and composite coatings: past, present and future. Trends in Food Science & Technology, 14(3)

[7] Chandra, R., Rustgi, R. (1998). Biodegradable polymers. Progress in

Polymer Science, 2(7), 1273–1335.

[8] Cheng, Y., Brown, K. M., & Prud'homme, R. K. (2002). Characterization

and intermolecular interactions of hydroxypropyl guar solutions. Biomacromolecules, 3(3), 456–461.

[9] Wientjes, R. H. W., Duits, M. H. G., Jongschaap, R. J. J., & Mellema, J.(2000). Linear rheology of guar gum solutions. Macromolecules, 33(26),9594–9605.

[10] Whitcomb, P. J., Gutowski, J., & Howland, W. W. (1980). Rheology of guar solutions. Journal of Applied Polymer Science, 25(12), 2815–2827.

[11] Brode, G. L., Goddard, E. D., Harris, W. C., & Salensky, G. A. (1991). Cationic polysaccharides for cosmetics and therapeutics. In C. G. Gebelein, T. C. Cheng, & V. C. Yang (Eds.), Cosmetic and pharmaceutical applications of polymers (pp. 117–128). New York: Plenum.

[12] Cui, W., Eskin, M. A. M.,Wu, Y., & Ding, S. (2006). Synergisms between yellow mustard mucilage and galactomannans and applications in food products – A mini review. Advances in Colloid and Interface Science, 128–130, 249–256.

[13] Garti, N., Madar, Z., Aserin, A., & Sternheim, B. (1997). Fenugreek galactomannans as food emulsifiers. Food Science and Technology, 30, 305–311.

[14] Srivastava, M., & Kapoor, V. P. (2005). Seed galactomannans: An overview. Chemistry and Biodiversity, 2, 295–317.

[15] Lapasin, R., & Pricl, S. (1995). Applications of guar gum derivatives. In Rheology of industrial polysaccharides: Theory and applications (pp. 145–149). London: Blackie Academic and Professional.

[16] Soppirnath, K. S., & Aminabhavi, T. M. (2002). Water transport and drug release study from cross-linked polyacrylamide grafted guar gum hydrogel microspheres for the controlled release application. European Journal of Pharmaceutics and Biopharmaceutics, 53(1), 87–98.

[17] Xiao, C., Weng, L., & Zhang, L. (2002). Improvement of physical properties of crosslinked alginate and carboxymethyl konjac glucomannan blend films. Journal of Applied Polymer Science, 84(14), 2554–2560.

[18] Anandrao, R. K., Kumaresh, S. S., Tejraj, M. A., Ashok, M., & Mahesh, H. M. (1999). Urea–formaldehyde crosslinked starch and guar gum matrices for encapsulation of natural liquid pesticide [azadirachta indica a. juss. (neem) seed oil]: swelling and release kinetics. Journal of Applied Polymer Science, 73(12), 2437–2446.

[19] Tayal, A., Pai, V. B., & Khan, S. A. (1999). Rheological and microstructural changes during enzymatic degradation of a guar-borax hydrogel. Macromolecules, 32(17), 5567–5574.

[20] Arvanitoyannis, I. (1999). "Totally-and-partially biodegradable polymer blends based on natural and synthetic macromolecules:preparation and physical properties and potential as food packaging materials", Journal of Macromolecular Science, C39 (2), 205–271.

[21] Alperin, C., Zandstra, P. W., & Woodhouse, K. A. (2005). Polyurethane films seeded with embryonic stem cell-derived cardiomyocytes for use in cardiac tissue engineering applications. Biomaterials, 26(35), 7377–7386.

[22] Arvanitoyannis, I., Kolokuris, I., Nakayama, A., & Aiba, Sei-ichi; Preparation and study of novel biodegradable blends based on gelatinized starch and 1,4-transpolyisoprene for food packaging or biomedical applications(1998), Carbohydrate Polymers, 34(4), 291–302.

[23] Omidian Hossein, G. Rocca Jose, Park Kinam, (2006) "Elastic, Superporous Hydrogel Hybrids of Polyacrylamide and Sodium Alginate", Journal of Macromolecular Bioscience, 703–710.

[24] ChudZikowaski R. J., "Guar gum and its applications", Journal of Society of Cosmetic Chemists of Great Britain, 22 : 43-60 (1971).

[25] Ahmed, Z. F. and Whistler, R. L. J. Am. Chem. Soc. 9. 2524 (1950)

[26] Swanson, J. W. J. Am. Chem. Soc. 71 1510 (1945).

[27] Ratna Sharma; Guar Gum Grafting and Its Application in Textile and Clothing Sarojini Naidu Govt. Girls' College Bhopal (M.P.) Asian J. Exp. Sci., Vol. 19, No. 2, (2005), 77-81

[28] Rafique, C. M. and Smith, F. J. J. Am. Chem. Soc. 9., 4684 (1950)

[29] Whistler R.L.,Hymowitz T., "Guar Agronomy, Production, Industrial Use & Nutrition", Purdue University Press,West Lafayette, IN, 1979.

[30] Narasimha Murthy S., Hiremath S.R., Paranjothy K.L., "Evaluation of carboxymethyl guar films for the formulation of transdermal therapeutic systems". Int J Pharm.(2004 Mar 9); 272(1-2):11-8.

[31] Pisal, S.; Zainnuddin, R.; Nalawade, P.; Mahadik, K.; Kadam, S.; AAPS PharmSciTech **2004**, 5, 84.

[32] Efe, H.; Bicen, M.; Kahraman, M. Vezir; Kayaman-Apohan, N.; "Synthesis of 4-Acryloylmorpholine-based Hydrogels and Investigation of their Drug Release Behaviors", Journal of Braz. Chem. Soc., 2013.

[33] Melo, M. J. P.; Varanda, F. R.; Dohrn, R.; Marrucho, I. M.; Solubility of Ciprofloxacin and Moxifloxacin in Different Solvents: The effect of the HCl group, Aveiro, Portugal, 2007, p. 3810.

[34] Dunn, D. S.; Raghavan, S.; Vokt, R. G.; Journal of Applied Biomaterials. **1994**, 5, 325.

[35] Laurence L. Brunton, Text book of Goodman & Gilman's, The Pharmacological Basis Of Therapeutics - Sulfonamides, Quinolones, And Agents For Urinary Tract Infections - William A. Petri, Jr., ISBN: 0-07-146892-7, 11th Ed. (2006), Chapter 43.

[36] Le Bourlais C. A., Treupel-Acar L., Rhodes C.T., Sado P. T, Leverge R, New ophthalmic drug delivery systems, Drug Dev. Ind. Pharm. 1995, 21, 19– 59.

[37] Mohamadnia Z, Zohuriaan-Mehr AJ, Kabiri K, Jamshidi A, Mobedi H. Journal of Bioactive and Compatible Polymers 2007;22(3):342-56.

[38] Yin LC, Fei LK, Cui FY, Tang C, Yin CH. Biomaterials 2007;28(6): 1258-66.

[39] Li SF, Yang YJ, Yang XL, Xu HB. Journal of Applied Polymer Science 2007;105(6):3432-8.

[40] Chivukula P, Dusek K, Wang D, Duskova-Smrckova M, Kopeckova P, Kopecek J. Biomaterials 2006;27(7):1140-51.

[41] Alvarez-Lorenzo C, Concheiro A, Dubovik AS, Grinberg NV, Burova TV, Grinberg VY. Journal of Controlled Release 2005;102(3): 629-41.

[42] Zhang YX, Wu FP, Li MZ, Wang EJ. Polymer 2005;46(18):7695-700.

[43] Lin C.C. and Metters A.T.: Hydrogels in controlled release formulations: Network design and mathematical modeling. Adv. Drug Deliv. Rev., 2006, **58**, 1379-1408.

[44] Martínez-Ruvalcaba1 A., Sánchez-Díaz J. C.,"Swelling characterization and drug delivery kinetics of polyacrylamide-co-itaconic acid/chitosan hydrogels", eXPRESS Polymer Letters Vol.3, No.1 (2009) 25–32.

[45] Nagasawa, N., Yagi, T., Kume, T. & Yoshii, F. (2004) Radiation crosslinking of carboxymethyl starch. *Carbohydrate Polymers* 58, 109-113.

[46] Parida P., Dash D., Behera A., Mishra S.C., "Preparation and characterisation of graft biopolymer to improve sustained release property", Department of Pharmaceutical Sciences (2012).

[47] Yoo MK, Cho KY, Song HH, Choi YJ, Kwon JW, Kim MK, Lee JH, Wee WR, Cho CS, "Release of ciprofloxacin from chondroitin 6-sulfate-graft-poloxamer hydrogel in vitro for ophthalmic drug delivery", Drug Development and Industrial Pharmacy (2005), 31(4-5):455-463.

[48] Affo W., Mensah-Brown H., Awuku J.F., Markwo A., "Quantitative Analysis of Ciprofloxacin Sodium Chloride Pharmaceutical Infusions Using Ultraviolet-visible Spectroscopy", ARPN Journal of Science and Technology(2013), VOL. 3, NO. 3.

[49] Özeroglu C., Birdal A., "Swelling properties of acrylamide-N,N′-methylene bis(acrylamide) hydrogels synthesized by using meso-2,3-dimercaptosuccinic acid-cerium(IV) redox couple", eXPRESS Polymer Letters Vol.3, No.3 (2009) 168–176.

[50] Dodi G., Hritcu D., Popa M. I., "Carboxymethylation of guar gum:synthesis and characterization", Cellulose Chem. Technol., **45** (3-4), 171-176 (2011)

[51] Murugan R., Mohan S., Bigotto A., "FTIR and Polarised Raman Spectra of Acrylamide and Polyacrylamide", Journal of the Korean Physical Society, Vol. 32, No. 4, April 1998, pp. 505_512.

[52] Gong, Honghong; Liu, Mingzhu; Zhang, Bing; "Synthesis and characterization of carboxymethyl guar gum and rheological properties of its solutions", Journal of Carbohydrate Polymers, Volume88 Issue3, 2012.