CHAPTER 1 INTRODUCTION

1.0 Monosaccharide

Natural saccharides are generally of simple carbohydrates called monosaccharides with general formula \((\text{CH}_2\text{O})_n\) where \(n\) is three or more. Monosaccharide is polyhydroxy aldehydes or ketones; with more than one hydroxyl group (-OH), and a carbonyl group (C=O) either at the terminal carbon atom (aldose) or at the second carbon atom (ketose). The carbonyl group combined in aqueous solution with one hydroxyl group to form a cyclic compound called as hemi-acetal or hemi-ketal.

Monosaccharides are classified by the number of carbon atoms in the molecule as follows

1. Diose-2
2. Triose-3
3. Tetrose-4
4. Pentose-5
5. Hexose-6
6. Heptose-7

Examples of monosaccharides are glucose, fructose, and glyceraldehyde [1].

1.1 Polysaccharide

Compound which contains more than ten monosaccharide units are called as polysaccharide. Definitions of how large a carbohydrate must be to fall into the categories polysaccharides or oligosaccharides vary according to personal opinion. Polysaccharides, have a general formula of \(\text{C}_x(\text{H}_2\text{O})_y\) where \(x\) is usually a large number between 200 and 2500. Considering that the repeating units in the polymer backbone are often six-carbon monosaccharides, the general formula can also be represented as \((\text{C}_6\text{H}_{10}\text{O}_5)_n\) where \(40 \leq n \leq 3000\). Polysaccharides are an important class of biological polymers. Polysaccharides are polymeric carbohydrate molecules composed of long chains of monosaccharide units bound together by glycosidic linkages and on hydrolysis give the constituent monosaccharides or oligosaccharides. They range in structure from linear to highly branched. Polysaccharides are often quite heterogeneous,
containing slight modifications of the repeating unit. Depending on the structure, these macromolecules can have distinct properties from their monosaccharide building blocks. They may be amorphous or even insoluble in water. [2].

1.1.1 Classification of polysaccharide

Polysaccharides are classified on three basis

1. On the basis of Composition
   a) Storage polysaccharide e.g. starch, glycogen
   b) Structural polysaccharide e.g. cellulose, pectin, chitin

2. On the basis of Function
   a) Homo-polysaccharides
      Glucose e.g. Starch, Cellulose
      Fructosans e.g Inulin
      Galactosans e.g. Ager Ager
   b) Hetero-polysaccharide
      e.g. Hyaluronic acid, chondroitin sulphates.

3. On the basis of Origin
   a) Extracted from plant seed
      Guar gum, Locus bean gum, Tara gum
   b) Tree exudates
      Acacia gum, Tragacanth gum, Karaya gum

1.1.2 Storage polysaccharide

This type of polysaccharide is used as storage polysaccharides in plant. Starch is a one kind of storage polysaccharide.

1.1.2.1 Starch

![Figure: 1 Structure of Starch]
Starch or amylum is a carbohydrate consisting of a large number of glucose units joined by glycosidic bonds. This polysaccharide is produced by most green plants as an energy store. It is the most common carbohydrate in human diets and is contained in large amounts in such staple foods as potatoes, wheat, maize (corn), rice, and cassava.

Pure starch is a white, tasteless and odourless powder that is insoluble in cold water or alcohol. It consists of two types of molecules; the linear and helical amylose and the branched amylopectin. Amylose and amylopectin, exclusively composed of D-glucose residues with α-(1→4) linkages in a linear amylose and α-(1→4) linkages and ~5% α-(1→6) branch linkages in amylopectin. Depending on the plant, starch generally contains 20 - 25% amylose and 75 - 80% amylopectin by weight. Glycogen, the glucose store of animals, is a more branched version of amylopectin [3].

1.1.2.2 Glycogen

Glycogen is storage polysaccharide which of glucose that served as a form of energy storage in animals and fungi. The polysaccharide structure represents the main storage form of glucose in the body. In humans, glycogen is made and stored primarily in the cells of the liver and the muscles, and functions as the secondary long-term energy storage (with the primary energy stores being fats held in adipose tissue). Muscle glycogen is converted into glucose by muscle cells, and liver glycogen is converted to glucose for use throughout the body including the central nervous system.
Glycogen is the analogue of starch, a glucose polymer and energy storage in plants, having a similar structure to amylopectin (a component of starch), but more extensively branched and compact than starch. Glycogen is found in the form of granules in the cytosol/cytoplasm in many cell types, and plays an important role in the glucose cycle. Glycogen forms an energy reserve that can be quickly mobilized to meet a sudden need for glucose, but one that is less compact than the energy reserves of triglycerides (lipids). Glycogen is a branched biopolymer consisting of linear chains of glucose residues with further chains branching off every 8 - 12 glucoses or so. Glucoses are linked together linearly by α(1→4) glycosidic bonds from one glucose to the next. Branches are linked to the chains from which they are branching off by α(1→6) glycosidic bonds between the first glucose of the new branch and a glucose on the stem chain [4].

1.1.3 STRUCTURAL POLYSACCHARIDE

This type of polysaccharides provides strength to plant or animal. Cellulose and chitin are type of structural polysaccharide.

1.1.3.1 Cellulose

![Figure: 3 Structure of Cellulose](image)

Cellulose is structural polysaccharide having general formula of formula \((\text{C}_6\text{H}_{10}\text{O}_5)\text{n}\), a polysaccharide consisting of a linear chain of several hundred to many thousands of β(1→4) linked D-glucose units. Cellulose is an important structural component of the primary cell wall of green plants, many forms of algae and the oomycetes. Some species of bacteria secrete it to form biofilms. Cellulose is the most abundant organic polymer on the Earth. The cellulose content of cotton fiber, wood and dried hemp is 90%, 40-50% and 45% respectively. It is tasteless, odourless, hydrophilic with the contact angle of 20-30. Cellulose is insoluble in water and most organic solvents. It is chiral and biodegradable. It can be broken
down chemically into its glucose units by treating it with concentrated acids at high temperature.

Cellulose is derived from D-glucose units, which condensed through β(1→4)-glycosidic bonds. This linkage motif contrasts with that for α(1→4)-glycosidic bonds present in starch, glycogen, and other carbohydrates. Cellulose is a straight chain polymer: unlike starch, no coiling or branching occurs, and the molecule adopts an extended and rather stiff rod-like conformation, aided by the equatorial conformation of the glucose residues.

Cellulose is mainly used to produce paperboard and paper. Smaller quantities are converted into a wide variety of derivative products such as cellophane and rayon. Conversion of cellulose from energy crops into biofuels such as cellulosic ethanol is an alternative fuel source. Cellulose for industrial use is mainly obtained from wood pulp and cotton [5].

1.1.3.2 Chitin

![Structure of Chitin](image)

Chitin (C\textsubscript{8}H\textsubscript{13}O\textsubscript{5}N\textsubscript{n}) is structural polysaccharide having a long-chain polymer of a N-acetylglucosamine, a derivative of glucose, and is found in many places throughout the natural world. It is a characteristic component of the cell walls of fungi, the exoskeletons of arthropods such as crustaceans (e.g., crabs, lobsters and shrimps) and insects, the radulae of molluscs, and the beaks and internal shells of cephalopods, including squid and octopuses. The structure of chitin is comparable to the polysaccharide cellulose, forming crystalline nanofibrils or whiskers. In terms of function, it may be compared to the protein keratin.
Chitin has also proven useful for several medical and industrial purposes. In butterfly wing scales, chitin is often organized into stacks of nano-layers or nano-sticks made of chitin nanocrystals that produce various iridescent colours by thin-film interference: similar, analogous structures made of keratin are found in iridescent bird plumage.

In its pure, unmodified form, chitin is translucent, pliable, resilient, and quite tough. In most arthropods, however, it is often modified, occurring largely as a component of composite materials, such as in sclerotin, a tanned proteinaceous matrix, which forms much of the exoskeleton of insects. Combined with calcium carbonate, as in the shells of crustaceans and molluscs, chitin produced a much stronger composite. This composite material is much harder and stiffer than pure chitin, and is tougher and less brittle than pure calcium carbonate. Another difference between pure and composite forms can be seen by comparing the flexible body wall of a caterpillar (mainly chitin) to the stiff, light elytron of a beetle (containing a large proportion of sclerotin) [6].

1.2 Natural gums

Natural gums are polysaccharides which are extracted from plant seed or obtained as tree exudates. There seems to be a semantic ambiguity about the very term "gums". Earlier the gum defined as “plant exudates”, the term encompassed also various resins, rubber latex, etc. Now a days the "gums" is somewhat narrower and more specific. It comprises all materials that can be dissolved or dispersed in water to form more or less viscous colloidal solutions or dispersions.

“Gums” have been used in industry and commerce since the beginning of civilization. Gums were also used by the ancient Egyptians for embalming the dead and for glueing together strips of clothing for binding mummies. In different application again gum arabic was for them a convenient adhesive for mineral pigments in paint formulations likewise; gums were used as food and for medicinal purposes by many civilizations up to the present day [7].

In the past uses of gums was restricted to a relatively low number of items, randomly harvested, and of limited quality and property range. Only the last decade, or so, has brought about revolutionary changes. Some gum bearing plants have begun to be cultivated on a commercial scale. Many natural gums are now treated, and, by undergoing various physical and chemical modifications for quality and required properties
improvement. Finally, the creation of new, organic polymers has yielded the whole class of new, synthetic gums.

Gums are available in huge quantities in varieties of plants, animals, marine and microbial sources. Plant gums are very common with different structural and metabolic functions commonly found in family Leguminosae, Sterculiaceae, Bixaceae, Compositae, Combretaceae, Gigarginaceae [8].

Gums have been classified as follows

1. Based on charge
2. Based on the origin
3. Based on the shape

**Based on the ionic charge**

1. *Anionic charged gums*: Tragacanth, arabic, karaya, gellan, agar, pectin, algin, carrgeenans
2. *Cationic charged gums*: Chitosan
3. *Non-ionic charged gums*: Guar gum, locust bean gum, tamarind gum, arabinans, xanthan gum, amylase, cellulose

**Based on the origin**

1. *Marine (sea weeds gum)*: Alginates, agar, carrageenans
2. *Animal origin*: Chitin and chitosan, chondroitin sulfate, hyaluronic acid
3. *Plant origin*:
   a) Seed gums-locust bean, guar, starch, cellulose, amylase
   b) Tree exudates-gum arabia, tragacanth, ghatti, karaya
   c) Tubers-Potato starch
   d) Extracts-pectin
4. *Microbial origin (fungi and bacteria)*: Glycan, pullula, dextran, xanthan, gellan

**Based on the shape**

1. *Linear*: Amylase, pectin, cellulose
2. *Branched*:
   a) Short branched: guar gum, locust bean gum
b) Long branched: amylopectin, karaya gum, gum tragacanth, gum Arabic

1.3 Galactomannas

These polysaccharides or gums were derived from the endosperm of various plants mainly from seeds belonging to family Leguminoseae.

1.3.1 Locust bean gum

Locust bean gum is also known as Carob bean gum, extracted from the endosperm of the leguminous plants, Carob tree (Ceratonia siliqua) mostly grows in Spain and in other Mediterranean countries. Locust bean gum reserved high molecular weight polysaccharide (approximately 50,000-3,000,000) consisting mainly mannose and galactose units as monomers. The mannose element forms a linear chain consisting of (1-4) β-D-mannopyranosyl units and every fourth or fifth chain is substituted on C6 with α-D-galactopyranosy residues as side chain [9]. The ratio of D-galactose to D-mannose differs based on the plant origin and also dependent on the growth conditions of plant during production.

The physicochemical properties of galactomannan polysaccharides are strongly influenced by galactose content. The longer the galactose side chain greater the viscosity. Mannose: galactose content is about 4:1 ratio [16]. Locust bean gum when boiled with water yields thick colloidal solution of high viscosity gets converted to gel on addition of sodium borate. Locust bean gum is insoluble in most of the organic solvents. Locust bean gum used as thickener, stabilizer, emulsifier and gelling agent since ages.
It is used as binding and granulating agent in tablets. Locust bean gum has gained a lot of importance as a controlled release excipient in oral solid dosage forms. Locust bean with combination of xanthan gum showed excellent release profile with zero order release kinetics than individual gum [10].

1.3.2 Tamarind gum

Tamarind gum or tamarind seed polysaccharide (TSP) is a galactoxyloglucan obtained from endosperm of kernels of the tamarind tree, Tamarindus indica (Family Leguminosae).

![Structure of Tamarind gum](image)

The polysaccharide constitutes about 65 % of the seed components. They are highly branched polysaccharide, consists of a main chain of β-D-(1-4)-galactopyranosyl unit with a side chain of single xylopyranosyl unit attached to every second, third and fourth of D-glucopyranosyl unit through α-D-(1-6) linkage [11]. Tamarind seed polysaccharide is a monomer of glucose, galactose and xylose in molar ratio of 3:1:2. Tamarind powder readily hydrates in cold water; on boiling for about 20-30min, required viscosity is achieved. The solution exhibits typical Non-Newtonian flow thixotrophic properties similar to most of the natural
polysaccharides. There is an increase in Non-Newtonian behavior with increase in concentration. Apparent viscosity is about 7000cps [12].

Tamarind polysaccharide gum has a diversified application in pharmaceutical dosage forms. Tamarind gum is used as binder and disintegrating agent in tablets. It is also used as emulsifier, suspending, and gelling agent. Compare to natural tamarind polysaccharide gum, semi-synthetic tamarind gum is mainly used in controlled dosage forms. Tamarind polysaccharide gum is used to enhance the solubility of poorly soluble drugs with a combination of xanthan gum. Tamarind gum can also be used as controlled release excipient in nasal mucosal delivery [13].

1.3.3 Tara gum

![Figure: 7 Structure of Tara gum](image)

Tara gum is also known as Peruvian carob, obtained by grinding the endosperm of the seeds of Caesalpinia spinosa (Family Leguminoseae). Tara gum consists of a linear chain of (1,4)-β-D-mannopyranose units with α-D-galacto-pyranose units attached by (1-6) linkages, the ratio of mannose to galactose is 3:1.

Tara gum hydrocolloid shown good solubility in cold water at low temperature. Tara gum is very stable at chilling and freezing
temperatures. The viscosity is less than guar gum found to be 5000 cps in hot temperature and 3250 cps in cold temperatures.

Tara gum is mainly used as thickening agent and stabilizer in food industry. There is lot of scope for pharmaceutical industry, based on the physico-chemical properties, suitable controlled dosage forms can be investigated [11].

1.4 Plants Polysaccharides

1.4.1 Pectin

Pectin is the methylated ester of polygalacturonic acid. It is commercially extracted from citrus fruits like apple, guava, and gooseberry. Pectins are complex polysaccharides present in the walls that surround growing and dividing plant cells. It is also present between xylem and fibre cells in woody tissue. In recent years, pectin has gained increasingly importance due to its biodegradability. Pectin is a non starch linear polysaccharides that consists of α-1,4-D-galactouronic acid and 1,2-D-rhamnose, with D-galatose, and Darabinose side chains having average molecular weight around 50,000-150,000 daltons. The gelling property of the pectin depends upon the molecular size and degree of esterification [14].

In recent year's pectin which is a biopolymer, found applications in pharmaceutical and biotechnology industry. It is very well known as a thickening agent, gelling agent, and a colloidal stabilizer polysaccharide in food industry. Pectin is highly soluble in water. When it is used alone, in contact with gastrointestinal tract (GIT) fluids it swells and the entrapped drug is released through diffusion [15]. This problem was manipulated with chemical modification without affecting favourable biodegradability properties. Pectin can be chemically modified by saponification catalysed
by acids, bases, enzymes and salts of weak acids. Calcium salts have reduced the solubility of pectin. Pectin showed very good potential in colon specific drug delivery systems for systemic action or a topical treatment of diseases such as ulcerative colitis, Crohn’s disease. Gel forming systems have been widely investigated for sustained drug delivery. Gelling can be induced by mineral acids or by cross-linking with calcium ion or by alginates [16].

1.4.2 Inulin

Figure: 9 Structure of Inulin

Inulin is a natural plant-derived polysaccharide with a diverse range of pharmaceutical and food applications. Inulin is produced by various plants. Inulin belongs to a class of fibers known as fructans. It is used by some plant as a storing energy and is typically found in roots and rhizome. Most of the plants that synthesized inulin do not contained storing material starch. Plants that contain high content of inulin are found in Dandelion (Taraxacum officinale), wild yam (Discora), chicory (Cinchorium intybus), onion (Allium sativum), and garlic (Allium sativum).

Inulin is resistant to digestion in the upper GIT, but it is degraded in colon by colonic microflora specifically by Bifidobacteria [17]. Inulin consists of a mixture of oligomers and polymers that belong to the group of gluco-fructans. α- D- glucopyranosyl - [α-D-fructofuranosyl] (n-1) - D-fructofuranoside, commonly referred to as inulin. The inulin molecules contained 2 - 60 or more β-2-1 linked D fructose molecules [18].
Inulin is a natural renewable polysaccharide with a significant number of pharmaceutical and food applications. In the food industry it is used as a fat or sugar replacement and soluble dietary fibre. Since it is soluble in water, inulin with combination of Eudragit films were prepared in order to resist degradation in upper GIT, but were digested in lower intestine by the action of Bifidobacteria and bacteriods. Methylated inulin hydrogels were developed as colon targeted drug delivery systems and investigated for water take up and swelling [19]. The rate of water transport into inulin was quite high and showed anomalous dynamic swelling behaviour. Inulin derivatised with methacrylic anhydride and succinic anhydride produced a pH sensitive hydrogel that exhibited a reduced swelling and low chemical degradation in acidic medium, but had a good swelling and degradation in simulated intestinal fluid in the presence of its specific enzyme, inulinase [20].

1.5 Marine Polysaccharides

1.5.1 Carrageenans

![Figure: 10 Structure of Kappa Carrageen](image)

![Figure: 11 Structure of Lambda Carrageen](image)

![Figure: 12 Structure of Iota Carrageen](image)
The marine polysaccharides obtained by the extraction from some members of the class Rhodophyceae. It is named after Irish moss Chondrus crispus, also known as Carrageen moss. It was originally isolated from alga in 1844.

Carrageenans are large, highly flexible molecules that curl forming helical structures, ability to form a variety of different gels at room temperature.

They are widely used in the food and other industries as thickening and stabilizing agents.

There are three basic types of carrageenans

1. Kappa (κ) carrageenans
2. Lambda (λ) carrageenans
3. Iota (ι) carrageenans

1. **Kappa (κ) carrageenans**

   It is mainly used as a gelling agent, Kappa forms strong, rigid gels in the presence of potassium ions, it reacts with dairy proteins and mainly used in bakery products. It is mainly obtained from Eucheuma cottonii. Kappa carrageenans form a brittle gel.

2. **Lambda (λ) carrageenans**

   It is non-gelling agent and mainly used as binder and thickener in dairy products. It is obtained from Gigartina from South America.

3. **Iota (ι) carrageenans**

   It forms soft and brittle gels in presence of calcium ions obtained from Eucheuma spinosum. Carrageenans are high-molecular weight polysaccharides made up of repeating galactose units and 3,6-anhydrogalactose (3,6-AG), both sulfated and non-sulfated. The units are joined by alternating α 1-3 and β 1-4 glycosidic linkages. The basic structure of carrageenan is disrupted by a more or less ordered distribution of sulphate hemi ester groups. Carrageenan can also contained some methoxy and pyruvate groups.
All the three types of carrageenans are soluble in hot water, only lambda form is soluble in cold water, while sodium salts of kappa and iota are soluble in cold water. The primary differences that influence the properties of kappa, iota, and lambda carrageenan are the number and position of the ester sulfate groups on the repeating galactose units. Higher levels of ester sulfate lower the solubility temperature of the carrageenan and produce lower strength gels, or contributed to gel inhibition (lambda carrageenan). A particular advantage is that they are thixotropy, became thin under shear stress and recovered their viscosity once the stress is removed.

Carrageenan is a good substitute for gelatine in hard and soft gel capsules. It formed stable emulsions with insoluble drug preparations, enhances homogeneity in colloidal suspension, film forming agent in crystal clear soft capsules, acts as gelling agent in antacid gels. Improved shelf stability, prolongs shelf life of antibiotic suspension [21, 22]. Research showed that carrageenan can be used as suitable excipient in controlled release tablets. In another study, matrix tablets made of lambda and ioto carrageenan showed an excellent dissolution profile that approached zero order kinetics. Hydrogels beads were developed using lambda carrageenan. These beads were incorporated as novel carriers for controlled drug delivery systems [23].

1.5.2 Scleroglucan

Figure: 13 Structure of Scleroglucan
Scleroglucan are non-ionic natural exopolysaccharides of high-molecular-weight polymers that are composed of sugar residues. Scleroglucan is a general term used to designate a class of glucans of similar structure produced by fungi, those of the genus Sclerotium especially Sclerotinum Rolfsii. Scleroglucn is a branched homopolysaccharide that gives only D-glucose upon complete hydrolysis. The polymer consists of a main chain of (1→3)-linked β-D-glucopyranosyl units; every third unit beared a single β-D-glucopyranosyl unit linked (1→6) [24].

Scleroglucan is water soluble at room temperature due to the presence of β-D-(1-6)-glucopyranosyl groups, it is colourless or slightly opalescence liquid, highly stable at wide range of pH and temperatures. Scleroglucan solution exhibited pseudo plastic behaviour, with a high-yield value, resulting in solutions of high suspension power with good pouring properties. Due to its non-ionic characteristic, scleroglucan is not affected by acids and alkalis over a wide pH range (2.5 - 12). It is compatible, without synergism, with other thickeners such as guar gum, locust bean gum and other natural polysaccharides [25].

1.6 Guar gum

Guar gum is one of the outstanding representatives of that new generation of plant gums. Its source is an annual pod-bearing, drought resistant plant, called Guar, or cluster bean (Cyamopsis tetragonolobuos or C. psoraloides) belonging to the family Leguminosae. It has been grown for several thousand years in India and Pakistan as a vegetable, and a forage crop. The guar plant is about 0.6m high, and resembles soyabean plant in general appearance, and in its characteristic arrangement of pods along the vertical stem. The pods are 5-12.5cm long and contain on the average 5-6 round, light brown seeds. It has been found fairly easy to cultivate, undemanding and well adapted to mechanical planting and harvesting. The guar became commercial reality in 1940. The world war caused shortages in supply of locust bean gum, to which guar gum is closely related. The American paper industry began to search for possible replacements. Guar gum was found to be a suitable one and, as a result new plantations of guar bean began to spring up and in 1942. General Mills Inc. is the first company which introduced guar gum to American industry [26].

Guar gum is a high molecular weight hydrocolloidal hetero polysaccharide composed of galactose and mannose units, which are linked
by glycosidic bonds. General structure of guar gum is shown in below structure.

![Figure: 14 Structure of Guar Gum](image_url)

The general structure of guar gum is as shown in figure: 14, which consists of a linear backbone of β (1, 4) - linked D-mannose units with various amounts of α (1, 6) - linked D-galactose side chains. The mannose to galactose ratio is 2:1. As it is non-ionic it is not affected by any pH. It is stable between pH ranges 5-7 and degrades on extreme pH and temperature. The average molecular weight of guar gum is up to 220,000 - 300,000Daltons.

### 1.6.1 Extraction of guar gum

The extraction of gum from guar seed was included splitting of guar, dehusking, falking, hot air grinding, screening etc.

The splitting is also termed as “seed processing”. After splitting of guar, splited seed, germ and undehusked guar split were obtained. The undehusked guar split are nothing but was the endosperm sections with the husk covered the split.

The resulted undehusked guar splits were extremely tough and brittle. The relatively small germs were separated by gravity.
Figure: 15 Extraction of guar gum from guar seed

The oversize of the screens was processed conventionally for separation of endosperm sections and the husk. The process was carried out through extruder having an elongated cylindrical barrel provided with inlet, die opening and outlet. The transportation of undehusked splits were carried out by screw conveyer provided inside the barrel. The step is also called as dehusking or dehulling the unhusked guar splits. The product is called as dehusked guar splits or husk. The husks were separated by screening.

The dehusked splits were relatively large, mostly substantially in the form and shape of the endosperm sections, but still having bits of husk still attached to them. Thus, the dehusked guar splits are actually not completely dehusked.
The dehusked guar splits are then flaked and ground into a powder. The dehusked splits are normally soaked in water from 30min to several hours, at concentrations ranging from in ratio of 1 to 1.2 of water by weight of splits, but 1 to 1.1 parts being preferred. Flaking was then accomplished by passing the wet dehusked guar splits between two counter rotating rollers, one roller moving substantially faster than the other, thus creating high levels of shear causing the wet splits to shred significant mechanical energy that part of the moisture was evaporated and the fiber/flakes heat up several degrees. The flakes were then passed through a hot air grinding or a hammer mill to reduce the flakes to a powder. Hot air was used to transport the flakes into the grinder, as well as to “flash dry cool” the particles during grinding.

The temperature, humidity and mixture ratio of the air and flakes are such that the evaporative cooling during grinding offset the heat generated from grinding so that it prevents the flakes and subsequently the ground powder from exceeding some designated maximum temperature. The powder typically ranges from about 10microns to about 100microns in average particle size. The powder is typically less than 10% water by weight and has a very stable and long shelf life [27].

1.6.2 Properties of guar gum

Guar gum has ability to produce highly viscous, pseudo plastic aqueous solutions even at low concentration, due to it’s high molecular weight [28-31]. Guar gum is soluble in water but insoluble in hydrocarbon, fats, alcohol, esters, ketones in fact with a very few exception (e.g. Formamide) in organic solvents in general [32]. The solution of guar gum in water has the highest viscosity amongst all the natural polysaccharide discovered till the date. Further it has better biodegradability and bio-compatibility compare to other natural polysaccharides [30].

1.6.3 Uses of guar gum

Due to its unique properties guar gum has proved to be a valuable aid in a multitude of industrial applications, as diverse as already mentioned, mining and food, paper, photography, water treatment, cosmetic, beverages and textile etc.
Paper industry

It is used as a dispersant and suspending agent, sizing and coating.

Textile industry

It served as a pigment dispersing aid, as a thickening agent or colour printing pastes [33-34].

Ceramic industry

Sizeable quantity of guar gum was used as a binder, thickener and fixing agent for enamels, porcelain, etc.

Food industry

It is widely used in salad dressing, ice creams, lollipops and sherbets, in bakery products and confections, meats and sausages, cheese spreads, and many other applications [35].

Pharmaceutical industry

Dry guar gum was used as disintegrant and in solution as binder in compressed tablets manufactures [36]. It was also used in liquid dietetic preparations as a low caloric thickener to improve their mouth feel, body and pour characteristics. On account of its hydrophilic property and the ability to form bulky, jelly-like masses, it is used in appetite depressants as a bulking agent in laxatives, and in gastric ulcer treatment. It has also such miscellaneous uses as a thickener for battery electrolytes, printing inks, and as an ingredient in paint, adhesive and polishes [32].

1.6.4 Need of modification

Guar gum had wide applications in various industries like pharmaceutical, cosmetic, food, textile, paper, explosive and toiletries industries etc. Therapeutically it is used as hypoglycaemic, hypolipidemic, antimicrobial, antiproliferative, bulk forming etc. Guar gum was abundantly available at low cost but its uncontrolled rate of hydration decreases its viscosity upon storage and further microbial contamination limited its long term applications [37].
There so, guar gum has been chemically derived to modify into various properties for broaden its industrial applications. A lot of research has been done on guar gum for the changing their physical and chemical properties by grafting, blending and compositing with synthetic and natural polymers [38-40].

1.6.5 Modification of guar gum

Guar gum was modified by various chemical reactions. Some of the reported derivatives of guar gum were carboxymethyl guar gum [38], hydroxymethyl guar gum [41], hydroxypropyl guar gum [42], O-carboxymethyl-O-hydroxypropyl guar gum (CMHPG) [43], O-2-hydroxy-3-(trimethyl ammonia propyl) guar gum (HTPG), O-carboxymethyl-O-2-hydroxy-3-(triethyl ammonia propyl) guar gum (CMHTPG) [44], ammonium hydroxyl propyl trimethyl chloride of guar gum [45], acryloyloxy guar gum [46], methacryloyl guar gum [47], methylated guar gum, sulfated guar gum [48], guar gum esters [49].

The most specific property of the guar gum and their derivatives was that they have hydroxyl groups, which makes them suitable for making changes in their structure formula and functionalization [50].

To improve properties of guar gum modification is carried out. Modification improves property of guar gum viz. viscosity and swelling index.

GG modified by following reaction

1. By grafting
2. By blending
3. By preparing composite and nanocomposite

1.6.6 Grafting

Grafting is the reaction in which one or more species of block are connected to the main chain of a macromolecule as side-chains having constitutional or configurational features that differ from those in the main chain. The processes of grafting "onto", "from", and "through" are all different ways to alter the chemical reactivity of the surface they attach with.
These techniques used for grafting are as follows

1. Free-radical grafting
2. Ionic grafting
3. Photochemical grafting
4. Plasma grafting
5. Enzymatic grafting

The role of initiator was very important in free radical grafting and ionic grafting as it determined the path of the grafting process. In photochemical grafting, when a chromophore on a macromolecule absorbs light, it goes to an excited state, which may dissociate into reactive free-radicals, the grafting process was initiated. If the absorption of light does not lead to the formation of free-radical sites through bond rupture, this process can be promoted by the addition of photosensitizers for the photochemical grafting. In recent years, the plasma polymerization technique has received increasing interest. Plasma conditions attained through slow discharge offer about the same possibilities as with ionizing radiation. The newest technique of grafting is enzymatic grafting. The principle involved is that an enzyme initiates the chemical/electrochemical grafting reaction [51].

Brij Raj Sharma et al. prepared graft co-polymer of methyl methacrylate (MMA) and guar gum (GG) by using ceric ammonium nitrate-nitric acid initiation system. The % grafting (%G) and % grafting efficiency (%GE) were determined as functions of the concentration of ceric ammonium nitrate (CAN), nitric acid, methyl methacrylate, guar gum, polymerization temperature and time. The optimum reaction conditions obtained for grafting of MMA onto guar gum were: amount of GG = 0:01gm/L, CAN= 0:02mole/L, MMA= 0:35mmole/L, HNO₃= 0:2M, reaction time= 3hrs and reaction temperature of reaction= 308°C [52].

Y. Li et al. grafted guar gum on the surface of multiwall carbon nanotube (MWCNT) to obtain GG-MWCNT composite. Then iron oxide nanoparticles were synthesized on the GG-MWNCT to prepare the magnetic GG-MWNCT-Fe₃O₄. GG-MWNCT was composed of about 21.6 wt% GG components, which enhanced the dispersion of GG-MWNCT in aqueous solution and also acted as a template for growth of iron oxide nanoparticles. GG-MWNCT-Fe₃O₄ exhibited superparamagnetic with a saturation magnetization (13.3emug⁻¹), and good adsorption on neutral red and methylene blue. GG-MWNCT-Fe₃O₄ could be easily separated from the aqueous solution in a magnetic field [53].
S. Pala et al synthesized novel polymeric flocculant based on polyacrylamide grafted carboxymethyl guar gum (CMG-g-PAM) by grafting polyacrylamide chains onto carboxymethyl guar gum (CMG) backbone using conventional redox grafting and microwave assisted grafting methods. The flocculation characteristics of grafted and ungrafted polysaccharides had been evaluated in kaolin suspension, municipal sewage wastewater and decolourization efficiency of a dye solution (methylene blue). It was evident from results that CMG-g-PAM synthesized by microwave assisted grafting method was showing best flocculation characteristics [54].

A. V. Singh et al synthesized guaran grafted polystyrene (G-g-Ps) co-polymer using vinyl monomer. The grafting was initiated through the formation of free radical centers on the polymer backbone by oxidation of guaran with cerium (IV) in nitric acid medium. It was concluded that the guaran offers a very regular linear matrix suitable for incorporation the desired physical and chemical properties through appropriate grafting and cross-linkage. The viscosity, hydrophilic-hydrophobic nature of the graft, degree of grafting and chain length of the graft was found of great significance in mineral processing and petroleum industries [55].

E. S. Abdel-Halim et al prepared new sorbent material based on guar gum (GG) by the grafting of acrylamide (Aam) onto guar gum, using potassium bromate/thiourea dioxide redox system for initiating the polymerization reaction. The prepared polyacrylamide/guar gum graft copolymer (PAam-g-GG) was further cross-linked with glutaraldehyde (GA) to obtain the sorbent material in the form of hydrogel. The obtained hydrogel was used for removal of hexavalent chromium ion (Cr (VI)) from its aqueous solution. It was found from the study that the sorption of Cr (VI) by the hydrogel was pH-dependent and maximum sorption was obtained at pH 3. The sorption data obeyed Langmuir and Freundlich sorption isotherm. The Langmuir sorption capacity (Qmax) was found to be 588.24mg/gm. Freundlich constant, KF and n, were found to be 55.03 and 2.835, respectively [56].

Ahmad Bahamdan et al modified guar gum or hydroxypropyl guar by three-step process: carboxymethylation with sodium chloroacetate, esterification with dimethyl sulfate (DMS) and amidation with a series of polyalkoxyleneamines. It was concluded that the solutions of the new derivatives possessed viscosities of approximately ten times less than the viscosities of the parent materials [57].
A. Srivastava et al prepared graft co-polymer of 4-vinyl pyridine onto guar gum initiated by potassium peroxymonosulfate/ascorbic acid redox pair in an aqueous medium. The thermal analysis data showed that the synthesized graft-co-polymer was more thermally stable than the ungrafted guar gum by considering the value of FDT and char yield. It was concluded that the synthesized graft copolymer can be used as a coating material when protection from excessive heat is needed [58].

Y. Zhao et al synthesized p-toluenesulfonate esters hydroxypropyl guar gum. A new guar gum derivatives containing amino group was synthesized through nucleophilic substitution of p-toluenesulfonate activated hydroxypropyl guar gum with ethanolamine [59].

E. S. Abdel-Halim et al prepared guar gum/polyacrylamide graft copolymer in the presence of potassium bromate/thiourea dioxide as initiation system. The prepared and separated guar gum/polyacrylamide graft co-polymer was used for preparation of silver nanoparticles through reduction of silver nitrate under certain conditions. For comparison, guar gum, polyacrylamide and guar gum/polyacrylamide composite were used individually for the preparation of silver nanoparticles under the same conditions. It was concluded that Transmission electron microscopy (TEM) images showed that 85% of silver nanoparticles prepared using the separated graft copolymer fall within the narrow range of 15-20nm, while in case of using the composite for silver nanoparticles preparation, the histogram showed wide range of particle size distribution [60].

P. Adhikary et al prepared graft co-polymers of carboxymethyl guar gum (CMGG) and polyacrylamide (PAam) using a ceric-ion-induced solution polymerization technique. It was found that flocculation efficiency of CMGG graft co-polymer shows better flocculation performance [39].

J. Biswal et al prepared graft co-polymer of guar gum with polyaniline (PANI) using ammonium persulfate (APS) as oxidant/initiator in acidic condition. The solubility of co-polymer in water was not obtained up to 230%G. The grafted materials had hybrid properties of guar gum biopolymer and PANI both. It was concluded that guar gum could be usefully exploited for making environmental-friendly semi-conductor devices by grafting with PANI, and would be novel materials for the fabrication of various electric sensors [61].
D. McLean et al synthesized guar gum-graft-poly(acrylamide-codiallyldimethylammonium chloride) (aka GG-gp(AM-co-DADMAC)) polymer. This new grafted polymer proved to be very effective at adsorbing hydrophobic wood resin particles onto papermaking fibre surfaces and thus removing the troublesome wood resins from the water phase where they have a tendency to aggregate and form troublesome deposits. The new polymer is unique in that it takes advantage of the colloidal stabilizing features of a natural product, guar gum and the wood resin fixative properties of a synthetic polymer p(AM-co-DADMAC). GG-gp-AM-co-DADMAC was effective over the entire pH range as compared to other commercially available polymeric fixatives that were evaluated [62].

B. R. Nayak et al studied the ceric-ammonium nitrate initiated graft copolymerization of polyacrylamide onto hydroxyporpyl guar gum by solution polymerization technique. Six grades of graft copolymers were synthesized by verifying catalyst and monomer concentration. The synthesized products were characterized by various instrumental techniques like viscometry, elemental analysis, Infrared spectroscopy (IR), thermal, X-ray diffraction (XRD) and Scanning electron microscope (SEM) studies. The % of grafting increases with increasing catalyst concentration and decreases with monomer concentration taking other parameters constant [63].

A. Bahamdan et al reported that hydrophobically modified hydroxybutyl guar (HMHBG) shows improved rheological properties over native guar, hydroxypropyl guar (HPG) and hydroxybutyl guar (HBG). The HMHBG has 1-2(w/w)% C_{16} alkyl chains randomly distributed. They also illustrate here an alternate route to produce guar derivatives with comparable properties to the system developed by Young and coworkers. This is accomplished by elaborating guar gum derivatives utilizing well known chemical processes and commercially available chemicals. Instead of forming graft polymers using uncontrolled radical polymerization these derivatives are made by combining a graft with established size to an appropriately activated polymer. They reported that treatment of methyl carboxymethyl guar gums with polyalkoxyalkyleneamines is an effective method for preparing the desired guar graft copolymers [64].

A. Tiwari et al prepared amphiphilic guar gum grafted with poly(epsilon-caprolactone) (GG-g-PCL). The structure of the GG-g-PCL copolymer was characterized by proton nuclear magnetic resonance (^{1}H-NMR) spectroscopy. By microwave irradiation, GG-g-PCL with high grafting percentage (>200%) was obtained in a short reaction time. The
GG-g-PCL co-polymer was capable of self-assembling into nanosized spherical micelles in aqueous solution with the diameter of around 75-135nm and 60-100nm, as determined by Dynamic light scattering (DLS) and TEM, respectively. The critical micelle concentration (CMC) of GG-g-PCL was found to be approx. 0.56mg/L in a phosphate buffer solution [65].

M. K. Zaharan at al polymerized acrylamide (Aam) with guar gum (GG) to synthesize poly(acrylamide)-guar gum [PAam-GG] co-polymer using the potassium bromate-thiourea (KBrO₃-TU) redox initiation system. Results obtained indicated that, at a definite rate of shear, the apparent viscosity decreased as the percentage graft yield increased, irrespective of the polymerization conditions applied. Results also indicated that the optimum conditions arrived at for preparation of a Poly(Aam)-GG copolymer were: the KBrO₃ to TU eqimolar ratio, 6:6 mole/100gm GG; [Aam], 30% (based on weight of GG); pH value, 3; polymerization temperature, 50°C and polymerization time, 2hrs. Tentative mechanisms, signifying various chemical events that probably occur throughout the whole course of the polymerization reactions are reported [66].

K. S. Soppirnath et al prepared graft co-polymer of guar gum with acrylamide and cross-linked with glutaraldehyde to form the hydrogel microspheres by the water-in-oil (w/o) emulsification method. The microspheres were loaded with two antihypertensive drugs, verapamil hydrochloride (water-soluble) and nifedipine (water-insoluble) to investigate their controlled release characteristics. The drugs were incorporated either during cross-linking by dissolving it in the reaction medium or after cross-linking by the soaking technique. The microspheres were characterized by Fourier transform infrared spectroscopy (FTIR), thermogravimetry (TGA), differential scanning calorimetry (DSC), equilibrium water uptake and dynamic swelling. Dynamic swelling experiments indicated that with an increase in cross-linking, water transport deviates from Fickian to non-Fickian mechanism. The in vitro drug release showed a dependence on the extent of cross-linking, amount of drug loading, nature of drug molecule and method of drug loading. Even though the release of drugs is swelling controlled in the initial stages, in the later stage diffusion of the solute is dominating. Various transport parameters have been calculated and the results are discussed in terms of the nature of the drug and the polymer [67].
J. Biswal et al synthesized graft co-polymer acrylamide (AAm) and guar gum (GG) using high-energy Co$^{60}\gamma$ radiation to enhance its flocculating properties for industrial effluents. The grafted product was characterized using analytical probes like elemental analysis, thermal analysis, Fourier transformed infrared (FTIR), X-ray diffraction (XRD) and Scanning Electron Microscopy (SEM). The grafting extent was observed to decrease with the dose rate and increase with the concentration of AAm. Thermo gravimetric analysis (TGA) of grafted and ungrafted samples indicated better stability of grafted product. Gamma and microwave radiation effect on grafted and virgin GG has also been reported [68].

Wenbo Wang et al synthesized series of novel guar gum-g-poly(sodium acrylate-co-styrene)/muscovite (GG-g-P(NaA-co-St)/MVT) superabsorbent composites by free-radical grafting copolymerization of natural guar gum (GG), partially neutralized acrylic acid (NaA), styrene (St) and muscovite (MVT) using ammonium persulfate (APS) as the initiator and N,N-methylene-bis-acrylamide (MBA) as the cross-linker. Optical absorption spectra confirmed that NaA and St had been grafted onto the GG main chain and MVT participated in the polymerization reaction. The simultaneous introduction of St and MVT into the GG-g-PNaA matrix could clearly improve the surface morphologies of the composites, and MVT led to better dispersion in the polymeric matrix without agglomeration, as revealed by electron microscopy. Results indicated that the swelling rate and capabilities of the composites were markedly enhanced by the incorporation of the hydrophobic monomer St and inorganic MVT clay mineral. The superabsorbent composite showed a clearer de-swelling characteristic in solutions of multivalent saline, acetone and ethanol, and cationic surfactant than that in the solutions of multivalent saline, methanol and anionic surfactant [69].

Wenbo Wang et al synthesized novel guar gum-g-poly(sodium acrylate)/Na-montmorillonite (GG-g-PNaA/MMT) superabsorbent nanocomposites by graft copolymerization among natural guar gum (GG), partially neutralized acrylic acid (NaA) and Na-montmorillonite (MMT) in the aqueous solution using ammonium persulfate as initiator and N,N'-methylenebisacrylamide (MBA) as cross-linker. Fourier transform infrared spectroscopy confirmed that NaA had been grafted onto GG and the -OH groups of MMT participated in the reaction. The effects of MMT and MBA on water absorbency were investigated. The results show that introducing MMT into the GG-g-PNaA network improved the swelling capability and the swelling rate of the superabsorbent nanocomposite. The
nanocomposites keep water absorbency high, within a wide pH range from 4 - 11 and exhibit better re-swelling capability [70].

S. Thakur et al prepared acryloyl guar gum (AGG) and its hydrogel materials for use as carriers and slow release devices of two pro-drugs, l-tyrosine and 3,4-dihydroxy phenylalanine (l-DOPA). To evaluate their structure-properties relationship, these were characterized by SEM, FTIR and swelling studies. The hydrogel materials responded to the change of pH of the swelling medium, and exhibited reversible transitions in 0.9% saline solution [71].

Xiaofang Wan et al synthesized acrylamide grafted cationic guar gum (CGG-g-PAM), induced by ceric ammonium sulfate, using aqueous polymerization technique at 100°C and the flocculation property was studied with high-turbidity tobacco wastewater (NTU > 4500). Thus five grades of graft copolymers were obtained through alteration of initiator and monomer concentrations in order to understand the effect of molecular weight on flocculation. The grafted copolymer was characterized by FTIR and SEM. Study of DTG demonstrated that CGG-g-PAM had better heat-resistant performance than guar gum, cationic guar gum (CGG) and polyacrylamide. The dosage of polyaluminium chloride (PAC) and CGG-g-PAM, pH value and molecular weight were considered to be the factors that can influence flocculation efficiency. The result showed best flocculation efficiency occurs at pH 5 when the dosage of CGG-g-PAM and PAC are 3.6ppm and 120ppm, respectively. The percentage of turbidity and chemical oxygen demand (COD) removal are 98% and 24% respectively, and its flocculating efficiency prevails over that of CGG and cationic polyacrylamide (CPAM) [72].

Kunj Behari et al studied the effect of reaction conditions on the grafting parameters during the grafting of methacrylamide (MAM) onto guar-gum (GOH) using potassium chromate/malonic acid redox pair under nitrogen atmosphere at different temperatures. On increasing the chromate ion concentration (from 3.5×10^{-3}mole/dm^3 to 20.0×10^{-3} mole/dm^3) grafting parameters were found to increase. Grafting ratio, efficiency, and add on were found to increase with the increase in malonic acid concentration from 3.5×10^{-3}mole/dm^3 to 10.0×10^{-3}mole/dm^3. It was observed that maximum efficiency was obtained when the monomer concentration was 20.0×10^{-3}mole/dm^3. With increasing hydrogen ion concentration, grafting parameters were found to increase. Homopolymer concentration, however, was found to decrease with increasing hydrogen ion concentration. Optimum temperature and time for grafting of MAM
onto guar gum were found to be 35°C and 120min respectively. The graft copolymer was characterized by IR spectroscopy and thermo gravimetric analysis [73].

D. K. Raval et al synthesized graft co-polymer of methyl methacrylate (MMA) and guar gum (GG) in aqueous slurry using hydrogen peroxide (H₂O₂) as initiator. The co-polymer was characterized by infrared spectroscopy. The grafting parameters like % grafting, grafting efficiency, % add-on, and the grafting frequency were determined, and the effect of reaction time, concentration of initiator, and [GG]/[MMA] ratios on the grafting parameters have been discussed. The decrease in % add-on at increasing concentration of H₂O₂ indicated enhancement in the rate of homo-polymerization of methyl methacrylate [74].

A. G. Sullad et al prepared novel type of pH-sensitive hydrogel blend of poly(vinyl alcohol) with acrylic acid-graft-guar gum. Microspheres with a size of 10μm were produced by the water-in-oil (w/o) emulsification method for investigating the controlled release of an anti-tuberculosis drug, isoniazid. These novel carriers were analyzed for surface morphology, size, effect of pH, swelling, drug loading, and in vitro release of isoniazid in pH 1.2 and 7.4 media. The kinetics of drug release was analyzed using empirical equations [75].

A. Srivastava et al synthesized graft co-polymer of N-vinyl-2-pyrrolidone with guar gum and its reaction conditions were optimized for better yield using potassium peroxymonosulfate (PMS) and glycolic acid (GA) as a redox initiator. The effect of PMS, GA, hydrogen ions, guar gum, and N-vinyl-2-pyrrolidone (NVP) along with reaction time and temperature were studied by determining the grafting parameters: grafting ratio, efficiency, conversion, add-on, homo-polymer, and rate of grafting. It was observed that the maximum yield occurred at with a time of 120min at a temperature of 45°C and a guar gum concentration of 0.4gm/L. The graft copolymer was characterized by infrared spectroscopy and thermal analysis. The activation energy for the grafted and un-grafted gum was calculated. It was observed that the graft copolymer was thermally more stable than the pure gum. The swelling and metal ion sorption behavior of guar gum and guar gum-g-N-vinyl-2-pyrrolidone also were studied [76].

Kunj Behari et al synthesized graft co-polymer of guar gum with N-vinyl formamide using potassium bromate/ascorbic acid redox pair. By studying the effect of the concentration of monomer, bromate ion, ascorbic
acid, guar gum along with the effects of time and temperature on the grafting characteristics: grafting ratio (%G), add on (%A), conversion (%C), efficiency (%E), homopolymer (%H) and rate of grafting (Rg), the reaction conditions for optimum grafting have been determined. The maximum grafting ratio, add on, conversion, efficiency and rate of grafting were obtained at minimum concentration of N-vinyl formamide (NVF) i.e. at $10 \times 10^{-2}$ mole/dm$^3$. The maximum values of these parameters were observed at minimum temperature (35°C) and minimum reaction time (120min). On increasing the concentration of ascorbic acid from $0.4 \times 10^{-3}$ - $2.0 \times 10^{-3}$ mole/dm$^3$ the above parameters show increasing trend while on increasing the concentration of bromate ion from 0.2 - $1.8 \times 10^{-2}$ mole/dm$^3$ the parameters show decreasing trend. Infrared spectra of Guar gum and guar gum-g-NVF has been investigated. Thermogravimetric analysis and differential scanning calorimetric analysis showed that guar gum-g-NVF was thermally more stable than guar gum [77].

D. S. McLean et al synthesized and characterized novel fixative, guar gum-graft-poly(acrylamide-co-diallyl di methylammonium chloride) (GG-g-p(AM-co-DADMAC)) polymer. The grafted polymer proved to be effective at adsorbing hydrophobic wood resin particles onto papermaking fibre surfaces, thus removing wood resins from the water phase where they have a tendency to aggregate and form troublesome deposits. The new polymer combines the colloidal stabilizing features of a natural product, guar gum, and the wood resin fixative properties of a synthetic polymer p(AM-co-DADMAC). GG-g-p(AM-co-DADMAC) was effective over the entire pH range as compared to other commercially available polymeric fixatives that were evaluated [78].

Kunj Behari et al studied the effect of reaction conditions on the grafting parameters during the grafting of acrylamide (ACM) onto guar gum (GOH) by using a Cu$^{+2}$-mandelic acid (MA). On increasing the Cu$^{+2}$ ion concentration ($0.5 \times 10^{-2}$ - $1.0 \times 10^{-2}$ mole/dm$^3$), an increase in total conversion of monomer, grafting ratio, efficiency, and add on was observed. Grafting ratios increased with an increase in concentration of mandelic acid and reaches its maximum value at $0.8 \times 10^{-2}$ mole/dm$^3$. It was observed that grafting onto guar gum takes place efficiently when monomer and hydrogen ion concentrations are $20.0 \times 10^{-2}$ and $2.2 \times 10^{-2}$ mole/dm$^3$, respectively. Optimum temperature and time for obtaining a maximum grafting ratio and efficiency was found to be $35 \pm 0.2^\circ$C and 2hrs respectively. The plausible mechanism of grafting was suggested. The graft copolymer was characterized by infrared spectroscopy and thermogravimetric analysis [79].
U. D. N. Bajpai et al synthesized graft co-polymer of guar gum and poly(acrylonitrile) in aqueous medium initiated by the potassium persulfate/ascorbic acid redox and system has been studied gravimetrically at the temperature of 35 ± 0.2°C in the presence of atmospheric oxygen. A plausible mechanism of graft copolymerization had been suggested on the basis of experimental results. The effect of grafting on the water and saline retention capacities had been studied and compared with the values obtained for ungrafted guar gum [80].

E. Chandra Sekhar et al prepared chitosan and guar gum-g-acrylamide (CH-GG-g-AAm) semi interpenetrating microspheres (semi IPNMs) by water-in-oil (w/o) emulsion cross-linking method using glutaraldehyde as a cross-linker. 5-fluorouracil (5-FU) is an anticancer drug was successfully loaded in these semi IPNMs. X-ray diffraction (XRD) and differential scanning calorimetric (DSC) examined the crystalline nature of drug after encapsulation into semi IPNMs. Scanning electron microscopy (SEM) shows the formation of semi IPNMs is spherical with size around 200μm. The encapsulation efficiency of 5-FU was achieved 58%. In-vitro release studies were performed basic (pH 7.4) buffer medium. The release patterns depend on graft polymer composition, effect of cross linker and drug content in the polymer matrices. In vitro release studies indicated the release of 5-FU more than 12hrs [81].

Huan-Ying Shi et al grafted Poly(N-isopropylacrylamide) (PNIPAAm) onto O-carboxymethyl-O-hydroxypropyl guar gum (CMHPG) in aqueous solutions by using potassium persulfate (KPS) and N,N,N,N’-tetramethylethylene diamine (TMEDA) as the initiation system, resulting in new stimuli-responsive grafted polysaccharides. The effects of various factors such as the concentrations of KPS and TMEDA, the feed weight ratio of NIPAAm to CMHPG, and polymerization temperature on the graft copolymerization were studied with respect to the grafting percentage (%G), grafting efficiency of the reaction (%E) and grafting conversion of the monomer (%C). The resulting grafted polysaccharides could exhibit lower critical solution temperatures in aqueous media due to the thermo sensitivity of their PNIAAm graft chains, and their temperature-induced phase transitions were influenced by the grafting percentage, the solution concentration of grafted polysaccharide, as well as the kind and concentration of added salts, as confirmed by determining the optical transmittance of the solutions under various conditions [82].
B. R. Nayak et al synthesized hydroxypropyl guar gum-g-polyacrylamide graft co-polymer by ceric ion induced redox polymerization technique at 28 ± 1°C. The graft co-polymer was characterized by IR and thermal analysis. The flocculation performance of graft copolymer was tested in 1wt% coal suspension [83].

M. Bishop et al investigated reaction product of boric acid and the polysaccharide guaran (the major component of guar gum) by $^{11}$B NMR spectroscopy. By comparison with the $^{11}$B NMR of boric acid and phenylboronic acid complexes of 1,2-diols (HOCMe$_2$CMe$_2$OH, cis-C$_6$H$_{10}$(OH)$_2$, trans-C$_6$H$_{10}$(OH)$_2$, O-C$_6$H$_4$(OH)$_2$), 1,3-diols (neol-H$_2$), monosaccharides (L-fucose, mannose and galactose) and disaccharides (celloboise and sucrose) it is found that the guaran polymer is cross-linked via a borate complex of two 1,2-diols both forming chelate 5-membered ring cycles ([B$_5$2]). $^{11}$B NMR derived pH dependent equilibrium constants and ab initio calculations have been used to understand the reasons for the inefficiency of boric acid to cross-link guaran (almost 2 borate ions per 3 monosaccharide repeat units are required for a viscous gel suitable as a fracturing fluid): the most reactive sites on the component saccharides (mannose and galactose) were precluded from reaction by the nature of the guar structure; the comparable acidity (pKa) of the remaining guaran alcohol substituents and the water solvent, results in a competition between cross-linking and borate formation; a significant fraction of the boric acid is ineffective in cross-linking guar due to the modest equilibrium (Keq). In contrast to prior work, we present evidence for the reaction of alcohols with boric acid, rather than the borate anion. Based upon the results obtained for phenylboronic acid, alternative cross-linking agents are proposed [84].

1.6.7 Blends

The incorporation of some required properties guar gum is also blended with other polymers.

A polymer blend or polymer mixture is a member of a class of materials analogous to metal alloys, in which at least two polymers are blended together to create a new material with different physical properties.

J. Z. Ti et al synthesized blend film of cationic guar gum (GG) and sodium carboxymethylcellulose (NaCMC) by casting method. Differential scanning calorimetry (DSC), FTIR, X-ray Diffraction (XRD), and viscosity
methods were used to examine the miscibility, interaction and degradability of cationic guar gum and sodium carboxymethylcellulose in their blend films. Blend films was degradable quicker than pure GG or NaCMC film. It was concluded that GG/NaCMC blend films have good sustained release performance [85].

A. C. Osvaldo et al used polymer blends of Ethylcellulose (EC)/ inulin (IN), Ethylcellulose (EC)/ Guar gum (GG) or Ethylcellulose (EC)/ Levan (LEV), containing up 30% of the oligo-polysaccharide, for film casting on a Teflon plate. All the films were tested for the thermal analysis. It was observed that Tmax 1 (temperature at which a thermal degradation rate goes up to a maximum) and (OH (wavenumber at which the OH absorption band are centralized)) show similar trends in the composition range of the studied blends [86].

Y. Huang et al prepared films from waterborne polyurethane(WPU) and carboxymethylated guar gum (GMGG) with different contents (20-80wt%) through solution casting method, and then were cross-linked with calcium chloride. The effect of CMGG content on the miscibility, morphology and physical properties of the blend films was investigated. The results revealed that the blend film had higher thermal stability and tensile strength that the of the WPU film, suggesting good miscibility between WPU and CMGG [87].

V. B. Pai et al examined rheological behavior and synergistic character of mixed polysaccharide system blends of xanthan with enzymatically modified guar. Blends of xanthan with enzymatically modified guar gum samples were examined in terms of their dynamic rheological properties and compared to those of xanthan locust bean gum blends. It was found that at constant ionic strength the enzymatically modified guar gum-xanthan blend was more elastic as the temperature of mixing was increased [88].

D. Badamapriya et al synthesized new polymeric film based on blends of cellulose and guar gum blend for coating to colon targeting. It was found that the blend had good film forming properties. It was resulted that guar gum cellulose acetate blends were highly promising film coating material for targeting the colonic site [89].

L-M. Zhang et al investigated shear-dependent viscosity and thixotropic properties of an aqueous polysaccharide blends, formed from 2.5% (w/v) solution of hydroxypropyl guar gum (HPG) and 2.5% (w/v)
solution of carboxymethyl cellulose (CMC) according to different blending ratios. It was found that aqueous HPG/CMC blends behaved as non-Newtonian shear-thinning fluids. Their shear-dependent viscosity behavior could be described using Cross viscosity model with reasonable accuracy [90].

Y. H. Huang et al prepared novel blends from quaternized polysulfone (QPSF) and benzoyl guar gum (BGG) coded as QB with different contents (10-18 wt%) through solution casting method. Simultaneously, other kinds of blends were prepared from chloromethylated polysulfone (CIPSF) and BGG coded as CIB to compare the effect of the substituted groups on the miscibility and properties of the composite materials. The results revealed that QB blends had good or certain miscibility over the entire composition ratio of BGG to QPSF under study. It was found that the composite properties changed considerably with moisture content, which attributed that water molecules had a great effect on the hydrogen bonding between the two polymers [91].

D. Das et al modified guar gum to new guar gum benzamide (GGBA). Benzoylation was carried out by benzoyl chloride reaction in water medium and a propyl amine spacer was used to impart a high degree of hydrophobicity. The ability of GGBA film to limit bacterial growth was assessed in qualitative and quantitative experiments. Large inhibitory halo was observed against both gram positive and gram negative organisms [92].

D. Riscia et al carried out comparative study of the rheological properties of guar (GG), methyl guar (MG), hydroxypropyl guar (HPG) and hydroxypropyl-methyl guar (MHPG) polymers aqueous in semidilute (both unentangled and entangled) and concentrated regimes, using oscillatory and steady shear technique. The storage and loss moduli of guar and guar derivatives aqueous solution had been measured using angular frequencies in the range between 10⁻³ and 10rad/sec. The data has been analyzed using the “blob” model for semidilute solutions and the scaling proposed by Rubinstein, Dobrynin and Colby for concentrated solutions [93].

C. Xiao et al synthesized blends films of chitosan (CH) and hydroxypropyl guar gum (HGG) using a conventional solvent casting technique and were dried at room temperature. A good intermolecular interaction was found because of hydrogen thermal stability than did the other blend and pure CH films. In addition, the best optical transparency
was observed from 500 - 800nm in the blend film containing 60% HGG [94].

W. Xiao et al prepared films by the casting method using sodium alginate (SA) and methacrylol guar gum (MAG) in different ratios. Water vapour transmission rate and oxygen permeability of the films were investigated. Films were evaluated for mechanical and antibacterial properties. The film prepared with the blend containing 85% MAG and 15% MAG (v/v) was found to be the best as it had lower oxygen permeability, better mechanical properties while retaining the similar antibacterial properties of MAG, when compared with MAG film not containing SA [95].

S. K. Bajpai et al studied swelling/degradation behavior of Ba$^{+2}$ ions-cross-linked sodium alginate/carboxymethyl guar gum bipolymeric beads which were intended to exhibit greater stability in the environment of changing pH along the gastrointestinal (GI) tract. Finally, it was concluded that barium ion cross-linked bipolymeric beads demonstrate pH-sensitive swelling and are quite stable in the environment of changing pH, thus offering their strong candidature for possible use in oral delivery of drugs along the GI tract [96].

H. Dong et al studied synergistic interaction between the cationic guar gum (the ammonium hydroxyl propyltrimethyl chloride of guar gum) and sodium alginate was studied. The effect of the mass ratio, mixed temperature, balks salt ion concentration, incubation time and pH value on gelation were investigated. It was concluded that the gel strength was maximum at mass ratio 0.6, temperature 70°C, balk salt ion concentration 1.0mole/L, incubation time 30min and pH 8 [97].

1.6.8 Composites/ Nano composite

The third method for improvement in properties of guar gum is to prepare composite/nano composite. Composite materials are materials made from two or more constituent materials with significantly different physical or chemical properties, that when combined, produce a material with characteristics different from the individual components. The individual components remain separate and distinct within the finished structure.

Nanocomposite is a multiphase solid material where one of the phases has one, two or three dimensions of less than 100nanometers (nm),
or structures having nano-scale repeat distances between the different phases that make up the material.

S. Pandey et al synthesized guar gum-silver nanocomposites for optical sensor to detect ammonia. Aqueous ammonia sensing study of polymer/silver nanoparticles nanocomposites (GG/AgNPs NC) was performed by optical method based on surface plasmon resonance (SRP). It was concluded that in the near future use of room temperature optical ammonia sensor for clinical and medical diagnosis or detecting low ammonia level in human is possible [98].

S. Pandey et al reported low cost eco-friendly method for the synthesis of gold nanoparticles (AuNPs) using guar gum (GG) as a reducing agent. GG/AuNPs nanocomposite (GG/AuNPs NC) was exploited for optical sensor for detection of aqueous ammonia based on surface plasmon resonance (SPR). It was found to have good reproducibility, response times of ~10sec and excellent sensitivity with a detection limit of 1ppb (parts per billion). It was concluded that, this system could be used for the rapid production of an ultra-low-cost GG/AuNPs NC-based aqueous ammonia sensor [99].

S. Pandey et al synthesized ammonia gas sensor from GG/Ag nanocomposite for chemical reaction studies. It was concluded that the nanocomposite could detect ammonia as low as 500ppt at room temperature in a minute time. It was demonstrated by results that such made nanocomposites can be used in several applications including homeland security, environmental pollution and leak detection in research laboratories and many others [100].

R. Mansa et al prepared novel montmorillonite nanocomposites using neutral guar gum and cationic guar gum. It was observed that morphology and structure of the guar-montmorillonite nanocomposites was dependence on the relative amounts of guar and montmorillonite used for their preparation. This was responsible for necessary flexibility for the potential applications of such nanocomposites [101].

T. A. Khan et al synthesized biocomposite of guar gum-nano zinc oxide (GG/nZnO) for enhanced removal of Cr(VI) from aqueous solution. The maximum adsorption was achieved at 50min contact time, 25mg/L Cr(VI) concentration, 1.0gm/L adsorbent dose and 7.0pH. Langmuir, Freundlich, Dubinin-Kaganer-Radushkevich and Temkin isotherm models were used to interpret the experimental data. It was found that GG/nZnO
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Biocomposite adsorbent showed an improved adsorption capacity for Cr(VI) ($q_m=55.56\text{mg/g}$) as compared to other adsorbents reported in the literature. The result suggested that GG/nZnO biocomposite is economical, eco-friendly and capable to remove Cr(VI) from natural water resources [102].

N. R. Gupta et al synthesized AgNPs using a thermo-associating polymer namely, carboxymethyl guar grafted poly(ethylene oxide-co-propylene oxide) [CMG-g-PEPO]. It was found that the polymer was acting as both reducing agent as well as stabilizing/capping agent. The use of these nanoparticles in the controlled release of Doxorubicin hydrochloride (Dox), an anticancer drug was also demonstrated. The binding of Dox onto the polymer and AgNPs was investigated by X-ray photoelectron spectroscopy (XPS) and Raman spectroscopy which indicated that a charge-transfer mechanism was operative between the Dox and polymer holding both the entities together [103].

M. Shenoy et al studied the effect of acetylation of guar gum on its properties as filler in an unsaturated polyester matrix. The rheology of the uncured composition indicated increased polymer-filler interaction with increased ester content. It was found that the tensile and flexural properties increased with the acetylation degree of guar gum; however the impact resistance of the composite was reduced. It was concluded that the treatment of GG particles was not restricted to the particle surface as in the case of natural fibres and changed the nature of the filler itself. Polysaccharides could thus be used as fillers in unsaturated polyester composites as a replacement to mineral fillers making the composites more eco-friendly [104].

Silver (Ag) nanoparticles were synthesized in aqueous GG solution by using gamma radiation. The nanoparticles in solution were prepared by exposing aqueous solution of GG containing AgNO$_3$ and isopropyl alcohol to 60 Co gamma radiations. The aim of the study was to investigate the optical and structural properties of silver nanoparticles as well as the influence of capping agent concentration, precursor concentration along with effect of the other parameters on nanoparticle size and size distribution [105].

R. G. Auddy et al synthesized new cationic biopolymer, guar gum alkylamine (GGAA) silver nanocomposites for wound healing applications. In wound healing experiments, faster healing and improved cosmetic appearance were observed in the new nanobiomaterial treated group.
compared to commercially available silver alginate cream. The nanobiomaterial was observed to promote wound by inducing proliferation and migration of the keratinocytes at the wound site [106].

A. Kumar et al synthesized guar gum stabilized copper nanoparticles catalyst for cyclo-addition reaction. To confirm the morphology of the synthesized nanoparticles, selected area electron diffraction (SAED) analysis of the samples was carried out and it was found that the particles were crystalline in nature which was further confirmed by X-ray diffraction study [107].

S. Tambe et al prepared an electrochemical biosensor using tyrosinase for the determination of catechol. The enzyme was extracted from a plant source *Amorphophallus comanulatus* and entrapped in agarose-guar gum composite biopolymer matrix. Catechol was determined by direct reduction of biocatalytically liberated quinone species at -0.1V versus Ag/AgCl (3M KCl). The response was found to be linear and concentration dependent in the range of 6×10^-5-8×10^-4M with a lower detection limit of 6μM. It has reusability up to 20 cycles and a shelf life of more than 2 months when stored at 40°C [108].

Dingqi Xue et al reported ground water and medical application of iron micro and nanoparticles. Diluted single biopolymer water solutions of guar gum (GG) or xanthan gum (XG) can stabilize these particles for few hours providing steric repulsion and by increasing the viscosity of the suspension. The synergistic effect between GG and XG generates a viscoelastic gel that can maintain 20gm/L iron particles suspended for over 24hrs. This was attributed to (i) an increase in the static viscosity, (ii) a combined polymer structure the yield stress of which contrasts the downward stress exerted by the iron particles, and (iii) the adsorption of the polymers to the iron surface having an anchoring effect on the particles. The XG/GG viscoelastic gel is characterized by a marked shear thinning behavior. This property, coupled with the low biopolymer concentration, determines small viscosity values at high shear rates, facilitating the injection in porous media. Furthermore, the thermo sensitivity of the soft elastic polymeric network promotes higher stability and longer storage times at low temperatures and rapid decrease of viscosity at higher temperatures. This feature can be exploited in order to improve the flowability and the delivery of the suspensions to the target as well as to effectively tune and control the release of the iron particles [109].
M. Sharma et al prepared soft viscoelastic gel from 1-butyl-3-methylimidazolium chloride, an ionic liquid at an optimized concentration of 10% w/v. A nanocomposite gel of the gum with enhanced strength could be prepared with 0.2% w/v of multiwalled carbon nanotubes (MWCNT) in the ionic liquid. When the gels thus prepared were subjected to surface fractures or bisected completely, they found to self-heal at room temperature without any external interventions. The self-healing process could be repeated several times. These viscoelastic gel systems showed thixotropic nature and recovery of the storage modulus with time for several cycles was observed upon rheological investigations. The interaction took place between ionic liquid, guar gum and MWCNT was studied by SEM, TEM, FT-IR, powder XRD and rheometry. The results suggested that, upon standing at room temperature development of electrostatic interactions and the van der waals interactions among the ionic liquid molecules facilitated the formation of reversible noncovalent bonds and eventually activated the self-healing in the gel systems through appropriate chain entanglements [110].

1.7 Guar Gum and its derivatives In Pharmaceutical Industries

1.7.1 Guar gum and its derivatives in control drug release system

Guar gum was used as thickener and stabilizer in pharmaceutical formulation. When mixed with different ingredients in the formulation of tablets it form protective layer and consequently, drug releases out from the guar gum tablet in a sustained manner, achieving the desired kinetics effect, and masked unpleasant taste and odor of drugs and improve its stability and drug release properties.

K. L. K. Paranjothy et al prepared transdermal patches of verapamil HCl by using sodium carboxymethyl guar as a polymer matrix. A comparison of various polymers and plasticizers were also made. In vitro release studied through the mouse skin has shown that sodium carboxymethyl guar as a suitable polymer [111].

Y. V. Rama Prasad et al studied in vitro drug release of guar gum in the form of compression coat applied over indomethacin core tablets protects the drug from being released under conditions mimicking mouth to colon transit. The study clearly established that guar gum, in the form of compression coat, is a potential carrier for drug targeting to colon [112].
Ishihara N et al investigated the effect of partially hydrolyzed guar gum (PHGG) for treatment of the colonization of Salmonella enteritidis (SE) in young and laying. They concluded that ingestion of different rent dose of PHGG decreases the Salmonella enteritidis (SE) due to improvement in the balance of intestinal micro flora. Feed supplemented with 0.025% PHGG was found the most effective [113].

Kumaresh S. Soppimath et al prepared Poly (vinyl alcohol)-guar gum interpenetrating network microspheres by cross-linking with glutaraldehyde. Nifedipine, an antihypertesive drug, was loaded into these matrices before and after cross-linking to study its release patterns. The in vitro release study indicated that the release from these microspheres is not only dependent upon the extent of cross-linking, but also on the amount of the drug loaded as well as the method of drug loading [114].

K. S. Soppimath et al modified guar gum by grafting with polyacrylamide by emulsification. The drug loading capacity of modified guar microspheres were studied at different PH conditions using diltiazem hydrochloride and nifedipine as a model drug. The release followed non-Fickian transport in almost all the cases results show quick release in pH 7.4 buffer than observed in 0.1 N HCl [115].

Y. S. R. Krishnaiah et al prepared three-layer matrix tablets of trimetazidine dihydrochloride by compressing on either side of guar gum matrix tablet granules of trimetazidine dihydrochloride. The three-layer matrix tablets were evaluated for hardness, thickness, drug content uniformity, and were subjected to in vitro drug release studies. The results clearly indicate that guar gum in the form of a three-layer matrix system is a potential hydrophilic carrier in the design of oral controlled drug delivery systems for highly soluble drugs [116].

Y. S. R. Krishnaiah et al studied site-specific delivery of 5-fluorouracil to the colon without the drug being released in the stomach or small intestine using guar gum as a carrier. The study showed that guar gum compression-coated tablets released only 2.5-4% of the 5-fluorouracil in simulated GI fluids [117].

U. S. Toti et al prepared guar gum-g-polyacrylamide polymer. In vitro drug release of diltiazem hydrochloride was studied. The effect of drug loading on release kinetics was evaluated. The nature of drug transport through the polymer matrices was studied by comparing with Higuchi, Hixson-Crowell and Kopcha equations [118].
Narasimha Murthy S et al investigated the role of carboxymethyl guar gum for drug delivery systems. For this terbutaline sulfate (TS) was taken as model drug and the drug loading capacity of carboxymethyl guar gum films was observed at a different pH range [119].

M. Momin et al prepared matrix tablet containing various proportions of guar gum by wet granulation technique using starch paste as a binder and sennosides as model drug. The results of study indicate that matrix tablet containing 50% guar gum and coated with 10% hydroxy propyl methylcellulose phthalate were most suitable for drug like sennosides which are mainly active in the lower GIT [120].

M. K. Chourasia et al studied colon-targeting delivery of metronidazole using guar gum microspheres. *In vitro* drug release studies were performed in simulated gastric fluid and study shows 15.27±0.56% of the drug were released in 5hrs [121].

Pablyana L. R. Cunhaa et al prepared gel by cross-linking guar with glutaraldehyde. The reaction condition utilized leads to a guar gel with viscosity 40 times higher than the original gum viscosity and with 95.6% of water. Study shows that properties viz. low viscosity, small amount of remained glutaraldehyde, and thermal stability indicates that the guar gel has potential to be applied as biomaterial with specific rheological requirements [122].

M. Chaurasia et al prepared guar gum microspheres containing methotrexate (MTX). MTX-loaded microspheres demonstrated high entrapment efficiency (75.7%). The in vitro drug release was investigated using a US Pharmacopeia paddle type (type II) dissolution rate test apparatus in different media. Guar gum microspheres showed adequate potential in achieving local release of drug in in vitro release studies, and this finding was further validated with in vivo studies [123].

S. Rane et al prepared chemically modified guar gum for improving its film forming properties. The derivatives were evaluated as film coating material by coating dummy tablets. The coated tablets were studied for various tablet parameters such as hardness, friability loss, film adhesion and disintegration. Accelerated stability studies were carried out at 40°C and at 75% relative humidity for a period of 6 months [124].
A. Tiwari et al prepared guar gum grafted with poly (epsilon-caprolactone) (GG-g-PCL). This derivative studied for drug-delivery carrier using microwave irradiation. The drug-release profile showed that the GG-g-PCL micelles provided an initial burst release followed by a sustained release of the entrapped hydrophobic model drug, ketoprofen, over a period of 10-68 hrs. These results suggest that the GG-g-PCL micelles could be used as a nano carrier for In-vitro controlled drug delivery [65].

G. Sena et al synthesized polyacrylamide grafted guar gum (GG-g-PAM) as matrix for controlled release of 5-amino salicylic acid. In-vitro release of this drug from various grades of GG-g-PAM has been studied by USP dissolution method (paddle type). The effect of percentage grafting on the rate of drug release has been investigated [125].

A. S. Yadav et al formulated the oral controlled release zidovudine matrix tablets by using guar gum as rate controlling polymer and to evaluate drug release parameters as per various release kinetic models. The in vitro dissolution study was carried out for 12 hrs using paddle (USP type II) method in phosphate buffer (pH 6.8) as dissolution media. Selected formulation was subjected to stability studies for 3 months, which showed stability with respect to release pattern [126].

R. Malviya et al developed sustained release matrix tablets of diclofenac sodium using guar gum as release modifier. The tablets were evaluated for their hardness, friability, weight variation, and an In-vitro release of drug was performed in phosphate buffer saline pH 7.4 for 24 hrs. Dissolution studies shows the release profile of diclofenac sodium from matrix tablets prepared using guar gum was retarded approximately 24 hrs. Thus guar gum stands as a good candidate for sustained release formulation [127].

H. V. Chavda et al prepared oral controlled drug delivery system for sparingly soluble diclofenac sodium (DCL) using guar gum as triple-layer matrix tablets. Matrix tablets of diclofenac sodium were prepared by compressing three layers one by one. The results clearly indicate that guar gum could be a potential hydrophilic carrier in the development of oral controlled drug delivery systems [128].

P. J. Subrahmanyam developed an oral colon targeted drug delivery system, which consists of theophylline matrix tablets prepared using guar gum and borax cross linked guar gum as rate controlling polymers in
different concentrations. These tablets were evaluated for weight variation, friability, hardness uniformity of content and in vitro drug release under specified conditions. The dissolution data revealed that the tablets containing guar gum and borax cross linked guar gum in higher concentrations each (120mg) showed 87.567±0.42% and 76.186±0.17% of drug release respectively. Selected tablets of borax cross linked guar gum were subjected to in vitro drug release study in presence of rat caecal content medium. Results clearly indicate that there is an increase in the release of the drug to 98.930±0.38% [129].

Vipul V. Jambukiya et al studied the effect of Guar gum (GG) and Modified guar gum (MGG) on the oral bioavailability of a poorly water-soluble drug, Ibuprofen (IBU). Prepared mixtures were evaluated for solubility study and In-vitro dissolution studies using USP XXIII Dissolution apparatus. From the results, it was concluded that the co-grinding mixture with modified guar gum could be useful in developing a dosage form with improved dissolution rate and oral bioavailability of poorly water-soluble drugs [130].

V. E. Bosio et al studied encapsulation of Congo Red (CR) in carboxymethyl guar gum-alginate gel microsphere. CR is a hydrophobic dye commonly used for diagnosis and potentially useful as therapeutic agent of beta amyloid plaques in neurodegenerative diseases. CR, as drug model, was encapsulated on Alginate-Carboxy Methyl Guar Gum (Alg-CMGG) blend microspheres. Guar gum 18% carboxymethylated (CMGG) derivative was synthesized in order to improve aqueous solubility, polymer blending and help reduce surface tension. The derivative was confirmed by FTIR spectroscopy, and elemental analysis. Surface tension of the new CMGG is reduced in about 50% compared with the native polymer. Lowering of Guar Gum (GG) aqueous solutions viscosity from 30,000cps - 350-400cps in case of CMGG is indicating pseudoplastic fluid behavior modifications. Vibrational spectroscopy analysis confirmed interactions among CR molecules in alginate-CMGG matrices ascribed largely to the aromatic motif of the dye and the biopolymer a polar regions. CR was encapsulated on 68/32% alginate/CMGG blend microspheres as the best formulation tested. The release of CR from the microspheres was not detected at pH = 1.2 in 25min, but 62% of CR was found in the supernatant when the pH was raised to 7.4 at 37°C after 8hrs incubation [131].

M. Velimirovic et al studied field assessment of guar gum stabilized microscale zerovalent iron particle for in-situ remediation of 1,1,1-
trichloroethane. A pilot injection test with guar gum stabilized microscale zerovalent iron (mZVI) particles was performed at test site V (Belgium) where different chlorinated aliphatic hydrocarbons (CAHs) were present as pollutants in the subsurface. 100kg of 56μm-diameter mZVI (~70 g/m/L) was suspended in 1.5m$^3$ of guar gum (~7 g/m/L) solution and injected into the test area. The direct push technique was preferred above others (e.g. injection at low flow rate via screened wells) because of the limited hydraulic conductivity of the aquifer, and to the large size of the mZVI particles. A final heterogeneous distribution of the mZVI in the porous medium was observed explicable by preferential flow paths created during the high pressure injection. The maximum observed delivery distance was 25cm. A significant decrease in 1,1,1-TCA concentrations was observed in close vicinity of spots where the highest concentration of mZVI was observed. Carbon stable isotope analysis (CSIA) yielded information on the success of the abiotic degradation of 1,1,1-TCA and indicated a heterogeneous spatio-temporal pattern of degradation. Finally, the obtained results show that mZVI slurries stabilized by guar gum can be prepared at pilot scale and directly injected into low permeable aquifers, indicating a significant removal of 1,1,1-TCA [132].

Guan-Hai Wang et al studied manipulating formation and drug-release behavior of new sol-gel silica matrix by hydroxypropyl guar gum. To develop biocompatible solgel silica matrix for the encapsulation of biomolecules or drugs, a novel water soluble silica precursor, tetrakis (2-hydroxyethyl)orthosilicates (THEOS), was used in combination with a water soluble polysaccharide derivative, hydroxypropyl guar gum (HPGG). We found that the introduction of HPGG could trigger and accelerate the sol-gel transition of THEOS in water and induce rapid formation of homogeneous gel matrix without the addition of any organic solvents or catalysts. Moreover, added HPGG macromolecules had a great influence on the network structure and particle dimension in the silica gel matrix, as confirmed by scanning electron microscope (SEM) observation. From the time sweep rheological measurements, it was found that a higher HPGG amount could lead to shorter gelation time for the sol-gel transition. From the strain and frequency sweep rheological experiments, it was found that the resultant silica matrix containing a higher amount of HPGG exhibited a narrower linear viscoelastic region, a higher dynamic muduli, and greater complex viscosity. In particular, the gel strength of the silica matrix could be modulated by the amount of HPGG. By investigating the controlled release of vitamin B$_{12}$ from the sol-gel silica matrixes, a strong dependence of the release profile on the amount of
introduced HPGG was observed. In this case, a higher HPGG amount resulted in lower release rate [133].

R. T. Thimma synthesized barium chloride cross-linked carboxymethyl guar gum beads for gastrointestinal drug delivery. A mild method for microencapsulation of sensitive drugs, such as proteins, employing a suitably derivatized carboxymethyl guar gum (CMGG) and multivalent metal ions like Ca$^{++}$ and Ba$^{++}$ is reported. Initially, guar gum is derivatized with carboxymethyl groups so that it forms durable, self-standing microbeads when its solution is dropped into CaCl$_2$ or BaCl$_2$ solutions. The swelling data of Ca$^{++}$ and Ba$^{++}$ cross-linked beads suggest that Ba$^{++}$ crosslinks CMGG much more efficiently than Ca$^{++}$. The drug loading efficiency of these Ba$^{++}$/CMGG beads, as a function of concentration of both metal ion as well as drug, was then determined using Bovine Serum Albumin as a model drug. The ability of these beads to protect the drug from the acidic environment of the stomach was investigated. It was found that a very little amount of the drug was released from the beads when they are suspended in NaCl-HCl buffer of pH 1.2 for 6hrs. The beads were also shown to release almost the entire encapsulated drug when exposed to TRIS-HCl buffer of pH 7.4. Thus, the results indicated that Ba$^{++}$ cross-linked carboxymethyl guar gum beads can be used for gastrointestinal drug delivery [134].

A. Tiwari et al studied potential of drug delivery application of an amphiphilic nanocarrier based on guar gum-g-poly(e-caprolactone). Amphiphilic guar gum grafted with poly(e-caprolactone) (GG-g-PCL) was fabricated as a drug-delivery carrier using microwave irradiation. The structure of the GG-g-PCL co-polymer was characterized by ¹H-NMR spectroscopy. By microwave irradiation, GG-g-PCL with high grafting percentage (>200%) was obtained in a short reaction time. The GG-g-PCL co-polymer is capable of self-assembling into nanosized spherical micelles in aqueous solution with the diameter of around 75-135nm and 60-100nm, as determined by DLS and TEM, respectively. The critical micelle concentration (CMC) of GG-g-PCL was found to be approx. 0.56mg/L in a phosphate buffer solution. The drug-release profile showed that the GG-g-PCL micelles provided an initial burst release followed by a sustained release of the entrapped hydrophobic model drug, ketoprofen, over a period of 10-68hrs. Under physiological conditions, the GG-g-PCL co-polymer hydrolytically degraded into lower-molecular-weight fragments within a 7-week period. These results suggest that the GG-g-PCL micelles could be used as a nanocarrier for In-vitro controlled drug delivery [65].
M. Shahida et al modified guar gum through microwave irradiation by varying the time of irradiation. The characterization of the modified products was carried out using FTIR spectroscopic analysis. The FTIR spectrum of the pure guar gum (GG) sample showed a broad peak at 3298 cm\(^{-1}\) while the modified GG sample displayed a peak at 1541 cm\(^{-1}\) which was absent in the crude sample. The X-ray diffraction (XRD) analysis confirmed the increase in crystallinity due to grafting of the sample with polyacrylamide (GG-g-PAM). Scanning electron microscope (SEM) images revealed that granular form of guar gum was changed into fibrillar structure after grafting. Thermo-gravimetric analysis of the modified samples was also carried out and discussed. The role of guar gum as a matrix for controlled release of drug triamcinolone was evaluated. The GG-acrylamide grafted samples presented a correlation between drug release and time of microwave exposure. The results revealed that such modified product has potential applications in colonic drug delivery system [135].

S. C. Angadi et al studied controlled release of Isoniazid through coated interpenetrating blend microparticles of chitosan and guar gum. The matrices have been characterized by X-ray diffraction (XRD) to understand drug distribution, DSC for thermal stability, and Fourier transform infrared spectroscopy (FTIR) for investigating the chemical interactions of drug with the matrices. Surface morphology was investigated by scanning electron microscopy. These microparticles exhibited encapsulation efficiencies from 47 to 58%. Equilibrium swelling as well as in vitro release trends of the formulations studied in pH 1.2 and 7.4 buffer media showed the dependence of drug release on cross-linking, blend ratio of the matrix and coating, all of which affected the release time of drug from 1 - 4hrs to 50hrs. The coated microparticles have reduced the burst release in gastric media to enhance in intestinal media [136].

R. Singh et al studied effect of ionic crosslink on the release of metronidazole from partially carboxymethylated guar gum tablet. Partially carboxymethylated guar gum (PCMGG) was cross-linked in situ by Ca\(^{2+}\) ions during wet massing step of tablet preparation. The resulting tablets were evaluated for the effect of the extent of crosslinking on drug release and matrix swelling. Increase in the concentration of Ca\(^{2+}\) ions increased the viscosity of gel layer and reduced the water penetration velocity into the matrix with subsequent decrease in swelling of the tablets and drug release. Beyond a certain concentration of Ca\(^{2+}\) ions, the viscosity of the gel layer decreased and the drug release rate increased primarily due to erosion of the matrix. The mechanism of drug release...
appeared to be non-Fickian or anomalous transport. The release data also best fitted in zero order equation. The model drug, metronidazole, was compatible with the matrix materials as evident from instrument analysis. Such formulation may provide flexibility in achieving the desired drug release rate from cross-linked matrix tablets [137].

### 1.7.2 Guar gum and its derivatives in treatment of diabetes

The role of guar gum and its derivatives to control blood sugar is well known. Studies showed that guar gum reduced the postprandial rise in blood glucose and insulin concentrations.

D. J. A. Jenkins et al reported that when nine diabetic patients supplemented either their normal home diets (four patients) or metabolic ward diets (five patients) with 25gm guar gum daily for 5 or 7 days their mean urinary glucose excretion fell by 46% (P<0.05) and 54% (P<0.01), respectively. Gel-forming, unabsorbable carbohydrate may therefore be a useful adjunct to anti diabetic therapy, irrespective of the type of treatment or insulin dosage used [138].

G. Biesenbach et al used combination of pectin and guar gum for treatment of hyperlipidemia. They reported that the total-cholesterol level and triglyceride concentration in blood serum is lowered but HDL-cholesterol level remained approximately the same in 15 female patients (52-70yrs) having type-2 diabetes with hypercholesterolemia (total-chol > 240mg/dl and LDL-chol > 130mg/dl). Females were taken fiber mixture at dose level of (17gm + 5.9gm water-soluble fiber) dissolved in 250ml water for the 9 weeks after 3 weeks in dietetics run-in-phase. PHGG is considered as safe and good to use as a food supplement products for lowering of lipids in patients suffering from hyperlipidemia [139].

S. J. Gatenby et al investigated the blood glucose, plasma insulin, C-peptide, and gastric inhibitory polypeptide (GIP) of 14 patients of non-insulin dependent diabetes (NIDDM) after and before intake of modified partial depolymerized guar meal. Results indicate the reduction in the rise in blood glucose, plasma insulin, but no reductions in postprandial plasma C-peptide levels were observed [140].

T. Suzuki et al concluded that guar gum hydrolysate (GGH) increases glucose intolerance and low hypertriglyceridemia in rats fed high-fructose diets. Possible mediators of these beneficial effects of GGH
are the SCFAs produced by microbial fermentation of GGH in the large intestine [141].

S. Saeed et al studied the antihyperglycemic and antihyperlipidemic effects of guar gum on streptozotocin-induced diabetes in male rats. Study result showed that guar gum diet significantly decreased the serum concentration of cholesterol, triacylglycerols and LDL-C and atherogenic index. The most significant result in this study was the reduction of blood glucose in diabetic rats treated with the guar gum diet after 28 days versus non- and glibenclamide-treated rats. The gum promoted a general improvement in the condition of the diabetic rats in body weight and food intake in comparison with non-treated rats [142].

Valesca Dall’Alba et al studied the effect of soluble fibre from partially hydrolysed guar gum (PHGG) on the MetS and cardiovascular risk factors in patients with type 2 diabetes. In these study randomized controlled clinical trial, 44 patients with type 2 diabetes and the MetS underwent clinical, laboratory and dietary evaluations at baseline, 4 and 6 weeks. All patients followed their usual diet and the intervention group received an additional 10gm/day of PHGG. In patients with type 2 diabetes and the MetS, the addition of PHGG to the usual diet improved cardiovascular and metabolic profiles by reducing WC, HbA1c, UAE and trans-FA [143].

Ulf Smith et al studied effect of modified guar gum on glucose and lipid levels diabetics and healthy volunteers. For the study 6 healthy volunteers and 17 diabetics (6 insulin-dependent and 11 diet- and tablet-treated) were treated with a special processed, palatable guar gum (10gm b.i.d. immediately before meals) for periods of one or three weeks or, in some cases, up to 13 weeks. A standardized test meal was given to study the effect of the fiber on postprandial glucose levels. 10gm guar was stirred in water and taken immediately before the test meal. The postprandial blood glucose levels were similar in the healthy volunteers but significantly lower in the diabetics following treatment with guar for 1 and 3 weeks, respectively. Furthermore, the fasting blood glucose levels were significantly lower in the diabetics after three, but not one, weeks of treatment. The lower postprandial glucose levels were coupled with attenuated and delayed insulin levels in accordance with an effect of guar gum on the rate of carbohydrate absorption. The cholesterol levels were on average reduced with 14% in the diabetics following three weeks’ treatment with guar. The higher the initial cholesterol level, the greater the reduction in cholesterol; 26% reduction was achieved in four patients
with initial levels above 7mM. The lipoprotein cholesterol levels were not significantly changed, thus an increase in the cu-lipoprotein cholesterol/total serum cholesterol ratio was obtained. Neither plasma triglycerides nor body weights altered during treatment. The reported side-effects were as expected and were usually mild and transient (e.g. increased flatulence). The data showed that guar gum also reduces postprandial glucose levels on a long-term basis and may improve the diabetic control. Additionally, treatment with this fiber leads to a concentration-dependent decrease in cholesterol levels [144].

P. J. Wood et al studied the effect of Oat bran and guar gum on glycemic index. Healthy subjects consumed D-glucose (glucose) alone or in the presence of oat gum prepared in a pilot plant (PPOG) or commercial guar gum (GG). Both gums significantly and similarly decreased the postprandial glucose rise as indicated by the glycemic index (GI). The effect of PPOG in a normal meal situation was studied by addition to cream of wheat (CW) to mimic oat bran (OB) porridge. Again, PPOG significantly lowered the postprandial glucose rise. Relative to CW alone, the GI of OB (62%) was similar to that of PPOG plus CW (60%). PPOG was less viscous than both GG and a laboratory-prepared sample of oat gum (LPOG). However, apparent viscosity differences between the gums decreased with increasing shear rate and concentration. LPOG was more pseudoplastic than GG, which in turn was more pseudoplastic than PPOG. At the concentration used in the acute meal tests, PPOG and GG reduced the rate of dialysis of glucose to a similar extent [145].

The increased intake of dietary fructose can be associated with alterations on energy homeostasis and lipid/carbohydrate metabolism, such as insulin resistance and dislipidemia. On the other hand, the ingestion of soluble fiber gum guar could improve beneficial mechanism on glucose tolerance and lipids profile. The aim of the present study were to investigate the effects of the supplemental feeding partially hydrolyzed gum guar on glucose and lipid homeostasis, in rats fed with fructose solution. The study was performed on 1 month day-old male Wistar rats randomly assigned into four groups: control (C) or treated with fructose (F-20%), fiber (FB-5%), or fructose plus fiber (F-20% + FB-5% = FF) solution for 30 days on glucose tolerance (OGTT), triacylglycerol concentration in the liver by chloroform/methanol method, glucose, triacylglycerol and total cholesterol serum concentration by assayed by enzymatic colorimetric method, insulin receptor (IR) concentration in the liver by Western Blotting. The total body weight gain was not different between groups; in regards of total caloric intake, in the F group was significantly higher and
in the FB group was lower than other groups. The triacylglycerol concentration in the liver of FF group was significantly higher than F group, the triacylglycerol concentration in the serum was higher the F group compared with other groups. The OGTT reveal impaired on glucose tolerance in the F, FB, FF compared with C. The IR concentration in the liver was lower in the F, FB, FF compared with C, no significant difference was observed between groups for IR concentration in the gastrocnemius muscle. No significant difference was observed between groups for carcass fat content and serum total cholesterol. Fructose induced important alterations on glucose tolerance and lipid metabolism, despite of fiber showed reversion of part this alterations. The association fructose plus fiber to seem decrease insulin receptor concentration in the liver, with consequent impair on glucose tolerance [146].

T. W. Atkins et al studied treatment of poorly controlled non-insulin-dependent diabetic subjects with granulated guar gum. The treatment of poorly controlled, non-compliant non-insulin-dependent diabetic subjects for one month with guar granules (Guarem) was associated with significant improvements in fasting serum glucose and insulin and urinary glucose excretion. No significant change was observed in oral glucose tolerance, erythrocyte insulin receptor binding, serum calcium, cholesterol, triglyceride or HbA1. Subjects reported significant side effects including excessive flatus, increased bowel frequency and fullness. The limited advantages of guarem treatment must be measured against the possibility of these side effects which to a large extent may be avoided by special attention to the means of administration. Prudent supplementation of the diet with guarem has undoubted potential for diabetic control [147].

1.7.3 Guar gum and its derivatives in treatment of Cancer

Guar gum and its derivatives were also helpful in cancer therapy especially colorectal cancer most common form of cancer due to intestinal disorder.

Y. Sakata et al investigated that how much amount of partially hydrolyzed guar gum (PHGG) ingestion can enhances bowel movement and can stop risk of colorectal cancer. They investigated the effect of PHGG intake upon 9 healthy female students by observing weight, moisture and hardness of feces. The result showed that increase in fecal moisture and texture with some variation. The benefit of bowel
movements provided by the PHGG intake has variation among different female students [148].

A. M. Gamal-Eldeen et al prepared the gum c-glycosylated derivative (GG), and its sulphated derivative (SGG) and observed their cancer chemopreventive and anti-inflammatory properties. They reported that modified guar gum has potential to prevent cancer and must be taken as supplement in foods. Results conclude that derivative of guar gum has ability to inhibited the carcinogen activator enzyme, cytochrome P450 1A (CYP1A), and also promote the carcinogen detoxification enzymes glutathione-S-transferases (GSTs) [149].

E. C. Sekhar et al prepared chitosan and guargum-g-acrylamide (CH-GG-g-AAm) semi interpenetrating microspheres (semi IPNMs) by water-in-oil (w/o) emulsion process by using glutaraldehyde as a crosslinker. 5-fluorouracil (5-FU) is an anticancer drug was successfully loaded in these semi IPNMs. In-vitro release studies were performed in basic (pH 7.4) buffer medium. The release pattern depended on graft polymer composition, effect of cross linker and drug content in the polymer matrices. In vitro release studies indicated the release of 5-FU more than 12hrs [150].

E. J. Elias et al studied a suitable polymer (guar gum) based matrix tablet for curcumin with sufficient mechanical strength and promising in vitro mouth-to-colon release profile. Three formulations of curcumin were prepared using varying concentrations of guar gum containing 50mg curcumin by the wet granulation method. Tablets were subjected to evaluation by studying parameter like hardness, friability, drug content uniformity, and in-vitro drug release. In vitro drug release was evaluated using simulated stomach, intestinal and colonic fluids. The susceptibility of guar gum to colonic bacteria was also assessed by a drug release study with rat caecal contents. The 40% guar gum containing formulation (F-1) showed better drug release (91.1%) after 24hrs in the presence of rat caecal contents in comparison with the 50% guar gum containing formulation (F-2) (82.1%). Curcumin could, thus, be positively delivered to the colon for effective colon cancer treatment using guar gum [151].

D. V. Gowda et al synthesized and evaluate phosphate cross-linked guar gum microspheres for improved drug delivery of anticancer drug to colon. The present work aimed to develop and characterize 5-Flourouracil (5-FU) loaded cross-linked Guar gum (GG) microspheres by emulsification method using tri-sodium-tri-meta phosphate (STMP) as a cross-linking
agent for treatment of colon cancer. SEM studies showed that the drug-loaded microspheres were non-aggregated with spherical shape. DSC and FTIR studies showed compatibility of drug excipients used. Release studies showed that drug release was more profound in cecal medium induced with enzymes causing degradation of the GG than that of the release showed in SIF. Stability studies showed that there were no significant [152].

M. Kaur et al developed and characterized guar gum nanoparticles for oral immunization against tuberculosis. The main aim of this study was to develop an effective carrier system containing Ag85A-loaded guar gum nanoparticles for oral vaccination against tuberculosis. Nanoparticles were prepared by Nanoprecipitation method. The developed particles with mean diameter 895.5±14.73nm and high antigen entrapment seem to be optimum for oral vaccine delivery. The acid protection assay, Peyer’s patch uptake study and in-vitro antigen study confirmed that the developed formulations can protect the antigen from harsh gastric environment and can safely deliver the antigen to the intestinal region. In vivo studies data indicated that the developed nanocarriers can induce a strong mucosal as well as systemic immune response. Therefore, the experimental evidence suggests that guar-gum nanoparticle can be utilized for safe and effective vaccine delivery via oral route [153].

1.7.4 Guar gum and its derivatives as hydrogel

Hydrogels were prepared by crosslinking guar gum with different monomer. These hydrogels were incorporated with different drugs to study their release pattern. Guar gum hydrogels were also useful in the control drug delivery system.

Gliko-Kabir I et al prepared a cross-linked low swelling guar gum (GG) hydrogel by reacting it with trisodium trimetaphosphate (STMP) and its function as possible colon-specific drug carriers was analyzed in the rats. It was concluded that cross-linked guar (biodegraded enzymatically) is an effective vehicle for colon specific drug delivery systems [154].

K. S. Soppirnath et al studied drug release ability of polyacrylamide-guar gum copolymer, cross-linked with glutaraldehyde. These guar gum hydrogel microspheres were incorporated with two antihypertensive drugs, verapamil hydrochloride (water-soluble) and nifedipine (water-insoluble) to investigate their controlled drug release capacity. In vitro study shows dependence of drug release on the extent of
crosslinking of guar copolymer, concentration of drug, type of drug molecule and method of drug loading [66].

A. Das et al examined the effect of glutaraldehyde cross-linked guar gum for delivery of colon specific drug system. The ability of this hydrogel discs for drug loading capacity, buffer intake ability, drug release efficiency were investigated in different medium and pH. They concluded that crosslinking decreases swelling (buffer intake) of guar gum. % drug release capacity increased with increasing glutaraldehyde concentration [155].

M. George et al prepared pH sensitive alginate-guar gum hydrogel cross-linked with glutaraldehyde for the controlled delivery of protein drugs. The cross-linked alginate-guar gum matrix is novel and the drug loading process used in the study was mild and performed in aqueous environment. The release profiles of a model protein drug (BSA) from test hydrogels were studied under simulated gastric and intestinal media. Protein release from test hydrogels was minimal at pH 1.2 (~20%), and it was found to be significantly higher (~90%) at pH 7.4. Presence of guar gum and glutaraldehyde crosslinking increases entrapment efficiency and prevents the rapid dissolution of alginate in higher pH of the intestine, ensuring a controlled release of the entrapped drug [156].

A. Tiwari et al prepared photo polymerized guar gum-methacrylate derivative having molecular weight range from 74-210Da and different degree of methacrylation. These hydrogels exhibit excellent endothelial cell proliferation capacity just like that of matrigel control. The human endothelial cell line EA.hy926 was photo-encapsulated in the GG-MA hydrogels. Cells remained viable at low macro monomer concentrations, but cell viability decreased sequentially as the macro monomer concentration increased [157].

S. Thakura et al synthesized acryloyl guar gum (AGG) and its hydrogel materials for use as carrier and slow release devices of two pro-drugs, l-tyrosine and 3,4-dihydroxy phenylalanine (l-DOPA). The hydrogel materials responded to the change of pH of the swelling medium, and exhibited reversible transitions in 0.9% saline solution. These were loaded with two pro-drugs, and their cumulative release behavior was studied at pH 2.2 and pH 7.4. The hydrogel materials exhibited structure-property relationship in the release of these pro-drugs. The % cumulative release of l-tyrosine was the maximum from the AGG-g-poly (methacrylic acid),
while the maximum release of l-DOPA was observed from AGG-g-poly (AAc) in both the media [70].

A. G. Sullad et al prepared pH-sensitive hydrogel blend of poly(vinyl alcohol) with acrylic acid-graft-guar gum. Microspheres with a size of 10μm were produced by the water-in-oil (w/o) emulsification method for investigating the controlled release of an anti-tuberculosis drug, isoniazid. These novel carriers were analyzed for surface morphology, size, effect of pH, swelling, drug loading, and in vitro release of isoniazid in pH 1.2 and 7.4 media. The kinetics of drug release was analyzed using empirical equations. Release times of the drug were increased to 8 h from its nascent plasma half-life of 0.5-1.6hrs. [74].

G. S. Chauhan et al prepared guar gum (GG) based hydrogel, by grafting GG with acrylic acid (AAc) using simultaneous gamma radiation technique. Swelling behavior of hydrogels was studied at various temperature, pH, and the salt sensitivity of the hydrogels was studied by swelling the hydrogels in 0.9% NaCl solution. The hydrogels exhibited fast swelling and stimuli-responsiveness at the technologically significant pH or temperature. These stimuli-responsive hydrogels being cost-effective, biocompatible, and biodegradable are easy to synthesize. The hydrogels are technologically important and have potential applications in drug delivery and separation processes [158].

Hiroyuki Kono et al synthesized and characterized guar gum hydrogels as carrier materials for controlled protein drug delivery. Hydrogels were prepared from guar gum (GG) via esterification with 1,2,3,4-butane tetracarboxylic dianhydride (BTCA). Detailed spectroscopic analysis using FTIR and solid-state NMR revealed that an increase in the BTCA feed amount in the preparation mixture led to an increased degree of crosslinking, which affected the swelling behavior and rheological properties of the hydrogels. The hydrogels exhibited enzyme degradability, and after incubation with β-mannanase and α-galactosidase, 30-57% of the hydrogels were degraded. In addition, the hydrogels adsorbed bovine serum albumin and hen egg white lysozyme thorough electrostatic and hydrophobic interactions. The protein-adsorbed GG hydro-gels exhibited a slow and steady release of the proteins over a 24hrs period in buffer solutions after a fast release of proteins in the first hour. As such, GG hydrogels are expected to be efficient drug delivery carriers for protein-based drugs [159].
G. Bocchinfuso et al theoretically studied of an unexpected similarity between guar gum and Scleroglucan interaction with borax. Guar gum is a galactomannan that assumes a very flexible conformation in solution, while scleroglucan is a very rigid polysaccharide that dissolves in water as triple helices. Both polymers can form gels in the presence of borax. Despite their structural differences, the freeze-dried gel systems of both polymers, when compressed to form tablets, show a peculiar anisotropic swelling in water that reflects an amazing similarity in terms of their molecular properties. In this paper the behavior of the guar/borax gel was compared with that of scleroglucan/borax. The macroscopic properties of the two systems were characterized in terms of rheological measurements. Atomic force microscopy images and molecular dynamics simulation allowed evaluating, at molecular level, the effect of borax addition to the Guar polymer. Both experiments show that an increasing of the polymer rigidity is produced by borax. The role played by galactose in the side chain was also discussed [160].

P. B. Kajjari et al synthesized Novel Interpenetrating Polymer Network hydrogel microspheres of chitosan and poly(acrylamide)-grafted-Guar Gum for controlled release of Ciprofloxacin. Acrylamide-grafted-guar gum (pAAm-g-GG) was prepared and blended with chitosan (CS) to form interpenetrating polymer network (IPN) hydrogel microspheres by the emulsion cross-linking method using glutaraldehyde (GA) as a cross-linker. The microspheres encapsulated up to 74% of ciprofloxacin (CFX), an antibiotic drug, having a plasma half-life of 4hrs and the release of CFX was extended up to 12hrs. Scanning electron microscopy (SEM) confirmed their spherical structure with smooth surfaces; Fourier transform infrared spectroscopy (FTIR) confirmed the grafting reaction as well as chemical stability of CFX in the blend IPN hydrogel microspheres. Differential scanning calorimetry (DSC) and X-ray diffraction (XRD) techniques confirmed the molecular level dispersion of CFX in the matrix. Swelling of microspheres performed in pH 7.4 buffer media was used to understand the drug release kinetics. In vitro release of CFX in pH 1.2 and 7.4 media showed a dependence on blend composition of the IPN, extent of cross-linking as well as initial drug loading. In vitro release data was analyzed using empirical equations, namely, KorsmeyerPeppas, to compute the diffusion exponent (n), whose value ranged between 0.19 and 0.33, indicating non-Fickian transport of CFX through the blend IPN hydrogel microspheres [161].

P. Thanikaivelan et al developed thermoresponsive magnetic nanoparticle- aminated guar gum hydrogel system for sustained release of
doxorubicin hydrochloride. Hydrogel based sustained drug delivery system has evolved as an immense treatment method for solid tumors over the past few decades with long term theranostic ability. An injectable hydrogel system comprising biocompatible aminated guar gum, Fe₃O₄-ZnS core-shell nanoparticles and doxorubicin hydrochloride was synthesized. Amination of guar gum resulted in attraction of water molecules thereby forming the hydrogel without using toxic crosslinking agents. Hydrogel formation was observed at 37°C and is stable up to 95°C. The prepared hydrogel is also stable over a wide pH range. The in-vitro studies show that the maximum de-gelation and drug release up to 90% can be achieved after 20 days of incubation. Studies reveal that the drug and the core-shell nanoparticles can be released slowly from the hydrogel to provide the healing and diagnosis of the solid tumor thereby avoiding several drug administrations and total excision of organs [162].

1.7.5 Guar gum and its derivatives in treatment of other disease

Guar gum and its derivatives were also used in treatment of other disease like cholera, functional constipation, and diarrhea. Guar gum and its solution were also used in eye-drop formulations.

J. W. Lampe et al had given 11 healthy men three different fed enzymatically modified guar gum, maltodextrin and soy polysaccharides for 18 days trial. They demonstrated improvement in gastrointestinal function [163].

H. Takahashi et al confirmed the role of partially hydrolyzed guar gum (PHGG) for prevention of constipation on 15 constipated women for 3 weeks. Most favored reason for constipation is lack of dietary fibers in our diet. In the experiment female were taken an average diet of 9.7±0.1gm/day then weight, texture, moisture and bacterial flora ion feces were observed. Results confirmed beneficial effect of PHGG for treatment of constipation [164].

N. H. Alam et al evaluated the effect of partially hydrolyzed guar gum (BENEFIBER) on the rate of normal absorption of glucose, amino acid (arginine) and fat and their side effects was also investigated. 10 healthy male volunteers in a double blind trial were given to two different dietary supplements (with fibers, without fibers) for a period of two weeks. The results of the study demonstrated that PHGG did not interfere with the normal absorption of glucose, amino acid and fat and shows no side effects so its use is safe for health [165].
A. F. Heini et al evaluate the effects of hydrolyzed guar gum on fasting and postprandial hormone levels, respiratory quotient (RQ) and postprandial satiety during a controlled weight-loss program and found it useful for weight reduction [166].

K. Yamada et al observed the role of partially hydrolyzed guar gum (PHGG), glucomannan, highly methoxylated (HM) pectin and water-insoluble cellulose on the serum lipid level and immunoglobulin (Ig) production of Sprague-Dawley. They reported decrease in serum total cholesterol, phospholipids and triglyceride levels and increase in immunoglobulin IgA productivity in rats fed on water soluble dietary fibers (guar gum, pectin) as compared to cellulose (water insoluble fiber) [167].

O. Watanabe et al investigated the effect of phosphorylated guar gum hydrolysate (P-GGH) on intestinal calcium absorption of overiectomized (OVX) rats. Rats were fed on P-GGH (50gm/kg of diet) for six week. Result showed that in the condition of estrogen deficiency P-GGH may be useful for prevention of the reduction of intestinal calcium absorption and bone [168].

E. M. Kovacs et al reported the effect of modified guar on appetite and body weight loss. For this purpose 28 fatty male (age 19-56) were given semisolid meal along with modified guar gum in different amount for specified time period. GG addition to a semisolid meal prevented an increase in appetite, hunger and desire to eat, which was increase in the other treatments as a result significant decrease in body weight taken place [169].

G. Parisi et al also observed useful effects of partially hydrolyzed guar gum for treatment of irritable bowl syndrome in an open clinical trial different dose of PHGG was given to different patients and their gastrointestinal symptoms GSRS), physiochemical symptoms (HADS) and quality of life (SF-36) was observed in six month. Results show beneficent effect of this modified guar gum on patient’s health [170].

M. L. Stewart et al observe fruitful physiological effects of partially hydrolyzed guar gum (PHGG) to human health. They investigated the variation in intestinal fermentability by changing molecular weight of modified guar gum. For trial guar gum of four different molecular weights (15, 20, 400, and 1,100 kDa) was fermented using a batch In vitro fermentation system. The result showed that molecular weight of guar
gum was positively influenced on the acetate production and negatively influenced on the propionate production. They conclude that 400-kDa guar gum is suitable for intestinal fermentability [171].

De Cássia Freitas K et al reported the effect of partially hydrolyzed guar gum towards intestinal iron absorption in rats with iron deficiency. 24 male wistar rats having iron deficiency anemia was divided in three groups and fed with partially hydrolyzed guar (100kg/day) diet, cellulose (100kg/day) diet, and without dietary fiber diet for each group respectively. Maximum intestinal absorption of iron, regeneration of hemoglobin and hepatic levels of iron observed in first group fed on PHGG containing diet [172].

G. N. Foulks studied the role of HP-Guar as gelling agent in polyethylene glycol (PEG) 400/propylene glycol 9(PG) eye drops used for the treatment of dry eye diseases. A literature review prior to july 2007 was conducted and founded efficacy of HP-Guar as gelling agents in PEG/PG eye drops [173].

S. Nakamura et al studied the role of dietary fiber especially partially hydrolyzed guar gum on transitory diarrhea caused by ingestion of malitol and lactitol (sugar substitute). PHGG effect was evaluated by injection of different dose of malitol to volunteers female until they experienced diarrhea. Then observation confirmed suppressive effect on diarrhea of partially hydrolyzed guar [174].

Y. Zhu et al prepared sulfonated degraded guar gum by reaction of guar gum with chlorosulfonic acid under different conditions. Structure of this modified guar was confirmed by infrared spectrometry. They concluded that about 2500mg/L concentration of sulfated guar can be reduced to about 60-66% cholesterol, about 76-89%LDL and almost 100% of fibrinogen [175].

G. M. Belo et al evaluated the effect of partially hydrolyzed guar gum for treatment of functional constipation among different hospitalized patient. They found it beneficial for reduction of functional constipation [176].

D. C. Kuo et al evaluated the role of partially hydrolyzed guar gum for prevention of FeCl₃-induced arterial thrombosis and hyperlipidemia in the high fat-diet fed hamsters. Based on their results, they conclude that
PHGG supplement can increase antioxidant protein expression and thus decrease oxidative stress induced arterial injury [177].

D. Polymeros et al investigated the effect of guar gum on colonic transit time (CTT) and symptoms of chronic constipation. We enrolled patients fulfilling Rome III criteria for chronic constipation. CTT was measured before and at the end of treatment. After a 2-week run-in period, patients received 5mg PHGG daily for 4 weeks. During study period, patients kept daily symptoms, stool and laxative usage diaries. They also recorded their symptom-related satisfaction weekly and treatment adverse events. Forty-nine patients received treatment; 39 (80%) completed the study. Treatment significantly reduced colon transit time, from $57.28 \pm 39.25$ to $45.63 \pm 37.27$ hrs ($p = 0.026$), a reduction more prominent in slow transit patients (from $85.50 \pm 27.75$ to $63.65 \pm 38.11$ hrs $p = 0.016$). Overall, the weekly number of complete spontaneous and spontaneous bowel movements increased significantly ($p < 0.001$); the latter correlated significantly with the acceleration of CTT in the overall population and in slow transit patients ($B = 0.382; p = 0.016$ and $B = 0.483; p = 0.023$, respectively). In addition, the number of bowel movements with straining decreased ($p < 0.001$) and stool form improved ($p < 0.001$), while days with laxative intake and days with abdominal pain decreased ($p = 0.001$ and $p = 0.027$, respectively). 4 week PHGG use accelerates colon transit time in patients with chronic constipation, especially in those with slow transit, and improves many of their symptoms including frequency of bowel movements [178].

Z. V. Potkins et al studied effects on ileal apparent digestibility in the growing pig of replacing barley with bran, oatmeal by-product, guar gum and pectin. In two experiments using a total of nine growing pigs initially about 25kg live weight and 10 weeks of age and tilted with simple T-shaped cannulae about15cm from the ileo-caecal junction, studies were made of the effects on ileal apparent digestibility of replacing barley, in barley-based diets, with 225gm/kg diet of either bran (BR) or oatmeal by-product (OB) and 50gm/kg diet of either guar gum (G) or pectin (P). All replacements depressed the apparent digestibility of the dry matter, ether extract. Nitrogen, nitrogen-free extract and gross energy fractions but only the OB replacement effect on dry matter was significant. The BR significantly depressed the apparent digestibility of praline but all other amino acids were not significantly affected by diet and showed no consistent trend of either increase or decrease [179].
M. E. McIvor et al studied long term effect of guar gum on blood lipids. While guar gum has been shown to lower total cholesterol and low density lipoprotein cholesterol (LDL-C) in diabetic patients over the short-term, the long-term effects are less well studied and may be unpredictable. Granola bars with and without 6.6gm guar gum were developed and fed to 16 adult volunteers with Type II diabetes mellitus who had been randomized in a double-blind fashion into guar and placebo groups of equal size. Four to six bars were consumed daily with an ad lib diet over a 6-month period. Total cholesterol, total high density lipoprotein cholesterol (HDL-C), subfractions HDL2-C and HDL3-C, LDL-C, and β-apoprotein were measured at 0 and 6 months. Although LDL-C was lower and triglycerides higher at 6 months than at baseline, these changes were of equal magnitude and direction in both guar and placebo groups. Using each subject as his own control, only the change in triglycerides was statistically significant (P < 0.025). When male subjects alone were analyzed, the guar group showed a statistically significant decrease in LDL, while the placebo group did not. Other lipid parameters were not significantly changed during the study, despite a positive effect on carbohydrate metabolism from the guar bars. The data suggest either that the hypolipemic effects of guar gum in patients with Type II diabetes mellitus are not sustained for 6 months, or the effects occur only in men [180].

D. E. Mcdonald et al studied adverse effects of soluble non-starch polysaccharide (guar gum) on piglet growth and experimental colibacillosis immediately after weaning. This study evaluated the effects of adding soluble fibre to the diet of healthy weaner pigs and weaner pigs experimentally infected with enterotoxigenic Escherichia coli (ETEC) in a model of post-weaning colibacillosis. Bodyweight gain, intestinal changes and proliferation of ETEC were measured 7 days following weaning. The basal diet consisted of pregelatinised rice fortified with animal protein. Addition of guar gum to this diet elevated the soluble fibre content from 1 - 6%, and was associated with reduced bodyweight gains, increased large intestinal weights and fermentation, and increased proliferation of ETEC in the small intestine. The optimal levels and type of dietary fibre used for weaner pig diets require further evaluation [181].

P. R. Turner et al studied hypolipidaemic effect of guar gum. The hypolipidaemic effect of guar gum (30gm/day) was examined in a double blind placebo-controlled crossover study in 9 patients with primary hyperlipidaemia. The treatment periods were of six weeks duration. Cholesterol levels in low density lipoprotein (LDL) were decreased by
11.5% and in intermediate density lipoprotein (IDL) by 10.7%. Plasma cholesterol levels were reduced by 9.6% ($P < 0.05$). Kinetic studies using autologous $^{125}$I-labelled LDL showed a decrease of 21.6% in plasma LDL apo B pool size ($P < 0.05$) that resulted from a 39.1% increase in its fractional rate of catabolism. The kinetic effects of guar gum on LDL metabolism appear similar to that of bile acid binding resins in that LDL apo B fractional catabolism is greatly increased while there is a slight increase in production rate [182].

J. Tuomilehto et al studied effect of guar gum and gemfibrozil in the treatment of hypercholesterolaemia. 29 hypercholesterolaemic patients, treated for one year with gemfibrozil but being still hypercholesterolaemic (serum total cholesterol ≥ 6.25mmole/L) were included in a double-blind trial to evaluate the hypocholesterolaemic effects of gemfibrozil-guar gum combination (GE + GU) vs. gemfibrozil-placebo combination (GE + PL) using a cross-over study design. The patients were treated with gemfibrozil on a constant dosage (range 900-1200mg/day) during the entire trial. After a 4-week run-in period on GE + PL treatment the patients were randomly allocated to 2 groups: one received GE + GU 15 g/day, and the other GE + PL for 3 months and after those groups were crossed over. Guar gum and placebo were administered as granules taken 3 times a day during meals. Serum total cholesterol was 8.61±0.17 mmole/L before gemfibrozil therapy, and 7.29±0.15 mmole/L at the end of the run-in period on GE + PL ($P < 0.01$). During the double-blind phase serum total cholesterol values were 6.28±0.19 mmole/L at the end of the GE + GU treatment period and 7.21±0.16 mmole/L at the end of the GE + PL treatment period ($P < 0.01$). At the end of the GE + GU treatment period serum total cholesterol was 27% lower and LDL-cholesterol 39% lower than before gemfibrozil treatment. A marked improvement (23%) was found in HDL/LDL ratio during GE + GU treatment compared with GE + PL treatment. The HDL/LDL ratio was remarkably higher (95%) at the end of GE + GU treatment than before gemfibrozil. It is concluded that combination therapy with gemfibrozil and guar gum is effective in lowering elevated serum total and LDL cholesterol levels and in particular in increasing HDL/LDL ratio [183].

L. A. Simons et al developed long-term treatment of hypercholesterolaemia with a new palatable formulation of guar gum. Nineteen patients with primary hypercholesterolaemia previously stabilized on diet alone were treated with a new formulation of guar gum (6gm t.d.s. with meals) in a placebo-controlled, single-blind study. Seventeen patients completed 3 months treatment without serious side
effects, while 2 patients withdrew immediately because of severe diarrhoea. Thirteen patients have completed 12 months treatment with guar gum. There have been no significant changes in safety parameters. Plasma cholesterol was reduced by a significant 15% during the first 3 months of treatment (7.9±0.8 vs 6.7±1.0 mmole/L, P < 0.001) and this effect has been sustained for 12 months. The fall in plasma cholesterol was associated with a significant 20% fall in LDL cholesterol, but with no change in HDL cholesterol. Plasma triglycerides did not change significantly. Percentage cholesterol absorption was reduced by guar gum in 4/5 normal subjects examined [184].

H. lashkari et al studied effects of incorporating guar gum (GG) and gum arabic (GA) in cheese-making milk with various fat contents (0.4, 0.9, and 1.4 %) on chemical and rheological properties of Iranian white cheese were evaluated by response surface method (RSM). As GG concentration increased, dry matter content of cheese samples decreased due to the high water binding capacity of this gum. A similar trend was also observed for GA at concentrations less than 150ppm. The higher the GG concentration, the higher was the free fatty acid content of cheese samples. GA at concentrations more than 150ppm, increased the storage modulus (G′), causing an undesirable hard texture for the product. The G′ and stress at fracture (σf) of samples decreased by the increasing concentration of GG incorporated into the cheese-making milk. Response surface minimization of rheological indices for Iranian white cheese showed that combination of two hydrocolloids (GG in the concentration range 75-170ppm and GA at concentrations <75 ppm) would provide the softest texture [185].

K. Rochus et al evaluated the potential of affecting amino acid metabolism through intestinal fermentation in domestic cats, using dietary guar gum as a model. Apparent protein digestibility, plasma fermentation metabolites, faecal fermentation end products and fermentation kinetics (exhaled breath hydrogen concentrations) were evaluated. 10 cats were randomly assigned to either guar gum- or cellulose supplemented diets that were fed in two periods of 5 weeks in a crossover design. No treatment effect was seen on fermentation kinetics. The apparent protein digestibility (P = 0.07) tended to be lower in guar gum-supplemented cats. As a consequence of impaired small intestinal protein digestion and amino acid absorption, fermentation of these molecules in the large intestine was stimulated. Amino acid fermentation has been shown to produce high concentrations of acetic and butyric acids. Therefore, no treatment effect on faecal propionic acid or plasma propionyl carnitine was observed in the present study. The ratio of faecal butyric
acid:total SCFA tended to be higher in guar gum-supplemented cats ($P = 0.05$). The majority of large-intestinal butyric acid is absorbed by colonocytes and metabolized to 3-hydroxy-butyrlycoenzyme A, which was then absorbed into the bloodstream. This metabolite was analysed in plasma as 3-hydroxy-butyrlycarnitine, which was higher ($P = 0.02$) in guar gum-supplemented cats. In all probability, the high viscosity of the guar gum supplement was responsible for the impaired protein digestion and amino acid absorption. Further research is warranted to investigate whether partially hydrolyzed guar gum is useful to potentiate the desirable in vivo effects of this fibre supplement [186].

F. E. Wood et al studied the effect of dietary guar gum and cellulose on mineral excretion and status in young male fischer 344 rats. A 31-day feeding study in young, male Fischer 344 rats was conducted to compare the effect of guar gum, a representative soluble fiber, with that of cellulose, a widely used insoluble fiber, on calcium excretion and status. Calcium was fed at a marginally sufficient level (0.25%) to maximize the potential for observing effects, and at 0.5%, the NRC Requirement. Effects on the excretion of P, Mg, Cu, Fe, Mn, and Zn, all fed at NRC levels, where also investigated. Diets were fiber free, or supplemented with guar, cellulose, or mixtures of the two. The addition of fiber to the 0.5% calcium basal diet generally resulted in directionally or significantly decreased fecal excretion of minerals. Fecal excretion of Ca, P, Mg, and Cu was significantly decreased with increasing gum in groups receiving 0.25% calcium; this was reflected in increased serum, but not bone, levels of these minerals except P. Serum and bone P and Zn increased with increasing guar and 0.5% calcium, while serum Zn showed the same dependence among groups fed 0.25% calcium. Bone ~m was negatively correlated with guar level in groups fed 0.5% calcium, but serum levels in all groups were similar [187].

R. L. Hood et al studied effect of guar gum and tocotrienols on cholesterol metabolism on the japanese quail. The effects of dietary fibre (α-cellulose or guar gum) and tocotrienols from palm oil were studied in young and mature Japanese quail. The diets were based on ingredients of vegetable origin with equal amounts of saturated and unsaturated fatty acids. In young quail, dietary guar gum plus tocotrienols was effective in reducing plasma cholesterol and liver size in comparison to quail fed α-cellulose. Tocotrienol had no effect on cholesterol metabolism when included in the α-cellulose treatment. In mature quail tocotrienols were not effective in reducing blood cholesterol. Neither guar gum nor tocotrienol altered the propensity of Japanese quail to develop
atherosclerosis in the aortic arch. The Reflotron proved to be a good instrument for providing quick and reproducible results for blood cholesterol and the results are comparable to those obtained from analyses with an enzymatic kit. The small quantity (30μl) of blood required for the Reflotron enables serial samples to be taken from small animals [188].

H. Takahashi et al studied the effect of partially hydrolyzed guar gum on fecal output in human volunteers. Partially hydrolyzed guar gum (PHGG, average M. W. 20,000) digested by β-D-mannanase was given as a beverage after every meal (36gm/3times/day) to eight healthy men for 4 weeks. Diet with PHGG increased fecal weight and output frequency while lowering the pH of feces without an influence on fat, protein or mineral excretion. Among the fecal volatile fatty acids (VFA), only acetic acid significantly increased. Total serum cholesterol was reduced (P < 0.05) by a diet with PHGG compared with the controlled diet period, while other serum lipid parameters were unaffected during the study. In conclusion, PHGG increased the bulking capacity without any influence on utilization of other nutrients [189].

M. G. Papich et al developed guar gum-coated colon-targeted tablets of Ronidazole (RDZ) and to determine the pharmacokinetics of this delayed-release formulation in cats. Guar gum-coated tablets were administered orally once to five healthy cats (mean dose 32.3mg/kg). The tablets were then administered once daily for 5 days to four cats (mean dose 34.5mg/kg), and absorption studies repeated on day 5. Plasma was collected and analyzed for RDZ concentration, and pharmacokinetic noncompartmental and deconvolution analysis were performed on the data. There was negligible RDZ release until after 6hrs and a delayed peak plasma concentration (mean C_{max} 28.9μg/mL) at approximately 14.5hrs which coincides with colonic arrival in cats. Maximum input rate (mg/kg per hour) occurred between 6 and 16hrs. This delayed release of ronidazole from guar gum coated tablets indicates that release of RDZ may be delayed to deliver the medication to a targeted area of the intestine. Repeated dosing with guar gum tablets to steady-state did not inhibit drug bioavailability or alter the pharmacokinetics. Such targeted RDZ drug delivery may provide improved efficacy and reduce adverse effects in cats [190].

H. Takahashi et al studied effect of guar gum on growing rats were fed on the diets containing intact guar gum (GG, 5%) and varying amounts of partially hydrolyzed guar gum (PHGG, 5 and 10%) for 3 weeks. Food consumption was almost similar to that of the control rats, except that the
rats fed on GG gradually declined. The weight of gastro-intestinal tract was found to be remarkably increased in case of caecum and large intestine of the rats fed on the diet containing GG and PHGG. The value for digestible and metabolizable energy and efficiency of energy utilization declined in the rats fed on the experimental diets but protein utilization remained unchanged. It is concluded that PHGG was effective in decreasing body fat and energy deposition without reduction of protein utilization [191].

S. G. Kumber et al synthesized graft co-polymer of acrylamide onto guar gum by Ce(IV) induced free-radical polymerization to prepared interpenetrating polymer network (IPN) beads of polyacrylamide-g-guar gum with sodium alginate by crosslinking with glutaraldehyde. Two widely used pesticides, solid chlorpyrifos and liquid fenvelarate, are loaded up to 60-70% efficiency in the IPN beads. The polymer and beads are characterized by Fourier transform IR spectroscopy to confirm grafting and to understand the possible interactions between the pesticides and the polymer matrix. Scanning electron microscopy was used to study the morphology of the beads. Equilibrium swelling experiments indicate that the swelling of the beads decreases with an increase in crosslinking, as well as an increase in pesticide loading. The in vitro release studies are performed under static conditions, and the release data are fitted to an empirical relationship to evaluate the transport parameters. Diffusion coefficients were calculated for the transport of pesticides through the polymeric beads using the initial and later time approximation methods. These values show a decrease with increasing crosslinking and increasing pesticide loading. Long-term diffusion coefficients as computed by Fick’s equations are found to be smaller in magnitude when compared to the initial time diffusion coefficients [192].

K. Narsaiah et al studied optimizing conditions for microencapsulation of nisin using calcium alginate as primary wall material and guar gum as filler at different air pressures using response surface methodology. Nisin is a widely used bacteriocin active against gram positive bacteria and is also reported to be active against some gram negative bacteria. Incorporation of nisin into food systems is another challenge as directly added nisin is prone to inactivation by food constituents. Encapsulation of nisin has been done so far in liposomes which is rather an expensive technology involving multiple processes. Other cost effective alternatives with good encapsulation efficiency and better control release properties were sought. Alginate was useful as a matrix for entrapment of bioactive compounds. The optimum conditions
were: sodium alginate concentration (2\%w/v), guar gum concentration (0.4\%w/v), and air pressure (0.5 bar gauge). The encapsulation efficiency of nisin in microcapsules produced under optimal conditions was 36.65\% [193].

S. G. Kumber at al reported preliminary experimental data on the release kinetics and encapsulation efficiency of urea formaldehyde (UF) cross-linked matrices of starch (St), guar gum(GG), and starch 1 guar gum (St1GG) for the controlled release of solid (chlorpyrifos) and liquid (neem seed oil) pesticides. The data reveal variable release rates in relation to the polymer type and especially the pesticide type. It is possible to slow the release rates of pesticides using cheaply available materials such as starch and guar gum [194].

1.8 Guar gum in Food industries

In food industry, guar gum was used as a novel food additive in various food products for food stabilization and as fiber source. It is liked by both manufacturer and consumer because it is economical as well as natural additive. It was used in variety of foods as an additive because it changes the behaviour of water present as a common component in various foods viz. chapatti, bread, fried products, yoghurt, cake, sausage, pasta, ice-cream [195].

1.8.1 Beverages

Guar gum was used in beverages for thickening and viscosity control because of its several inherent properties. The important property of guar gum was its resistance to breakdown under low pH conditions present in beverages. Guar gum is soluble in cold water which makes it easy to use in beverage processing plants. It improved the shelf life of beverages.

1.8.2 Processed cheeses

In cheese product, syneresis or weeping was a problem of serious concern. Guar gum prevents syneresis or weeping by water phase management and thus also improves the texture and body of the product. In cheese products it was allowed upto 3\% of the total weight. Guar gum in the soft cheeses enhances the yield of curd solids and gives a softer curve with separated whey. Low-fat cheese can be produced with addition
of guar gum (at concentration 0.0025-0.01% w/v) without changing the rheology and texture compared with full-fat cheese [196].

1.8.3 Dairy products

Main purpose of using guar gum in frozen products is stabilization. Guar gum has important role in ice cream stabilization because of its water binding properties. Its use in high temperature short time (HTST) processes is very favorable because such processes require hydrocolloids that can fully hydrate in a short processing time. According to McKiernan locust bean gum has all the properties of an ideal gum but it hydrates slowly which is not favorable in HTST process [197]. Julien obtained satisfactory results with guar as stabilizer in continuous ice cream processing [198]. Guar gum should be used in ice cream mix at a concentration level of 0.3% [199]. It was also used in combination with carrageenan in a mixed guar carrageenan system developed for HTST process. Like locust bean gum its performance can be improved when used in combination with other stabilizers [175]. Guar gum in ice cream improves the body, texture, chewiness and heat shock resistance. Partially hydrolyzed guar gum (at 2-6% concentration level) decreased syneresis and improved the textural and rheological properties of low fat yoghurt comparable with full-fat yoghurt [200].

1.8.4 Processed meat products

Guar gum had strong water holding capacity in both hot and cold water. Hence, it is very effectively used as a binder and lubricant in the manufacturing of sausage products and stuffed meat products. It performs specific functions in processed meat products like syneresis control, prevention of fat migration during storage, viscosity control of liquid phase during processing and cooling and control of accumulation of the water in he can during storage. Guar gum also enhanced the creaming stability and control rheology of emulsion prepared by egg yolk [201].

1.8.5 Bakery products

Addition of guar gum in cake and biscuit dough improved the machinability of the dough that is easily removed from the mold and can be easily sliced without crumbling. At 1% addition of in batter of doughnuts, it gives desirable binding and film-forming properties that decreases the penetration of fats and oils. Guar gum in combination with
starch is found to be effective in prevention of dehydration, shrinking and cracking of frozen-pie fillings [202]. In wheat bread dough, addition of guar gum results in significant increase in loaf volume on baking [203]. Guar gum along with xanthan gum retard staling in gluten-free rice cakes by decreasing the weight loss and retrogradation enthalpy [204]. Similarly, guar gum also retards staling in chapati at room temperature as well as refrigerated temperature by controlling retrogradation of starch [205].

1.8.6 Salad dressings and sauces

Guar gum’s cold water dispersibility and compatibility with high acidic emulsions enable it to use as thickener in salad dressing at about 0.2-0.8% of total weight. In salad dressings, it acts as an emulsion stabilizer by enhancing the viscosity of water phase and hence decreasing the separation rate of the water and oil phase [206]. Guar gum has been found useful as a thickener in place of tragacanth in pickle and relish sauces [207]. Guar gum enhanced the consistency of tomato ketchup more prominently than other hydrocolloids like carboxy methyl cellulose, Sodium alginate, gum acacia and pectin. On addition of guar gum serum loss and flow values of tomato ketchup decreases which makes it a novel thickener for tomato ketchup [208].

1.9 Drug delivery system

Drug delivery was the method or process of administering a pharmaceutical compound to achieve a therapeutic effect in humans or animals. Drug delivery was often approached via a drug's chemical formulation, but it may also involve medical devices or drug-device combination products. Drug delivery was a concept heavily integrated with dosage form and route of administration, the latter sometimes even being considered part of the definition.

Drug delivery technologies modify drug release profile, absorption, distribution and elimination for the benefit of improving product efficacy and safety, as well as patient convenience and compliance. Drug release was from: diffusion, degradation, swelling, and affinity-based mechanisms.

Most common routes of administration are as follows
1. Non-invasive peroral (through the mouth)
2. Topical (skin)
3. Transmucosal (nasal, buccal/sublingual, vaginal, ocular and rectal)
4. Inhalation routes

Many medications such as peptide and protein, antibody, vaccine and gene based drugs, in general may not be delivered using these routes because they might be susceptible to enzymatic degradation or cannot be absorbed into the systemic circulation efficiently due to molecular size and charge issues to be therapeutically effective. For this reason many protein and peptide drugs have to be delivered by injection or a nano-needle array. For example, many immunizations are based on the delivery of protein drugs and are often done by injection [209].

1.9.1 Novel drug delivery system

The method by which a drug was delivered can have a significant effect on its efficacy. Some drugs have an optimum concentration range within which maximum benefit is derived, and concentrations above or below this range can be toxic or produce no therapeutic benefit at all. On the other hand, the very slow progress in the efficacy of the treatment of severe diseases, has suggested a growing need for a multidisciplinary approach to the delivery of therapeutics to targets in tissues. From this, new ideas on controlling the pharmacokinetics, pharmacodynamics, non-specific toxicity, immunogenicity, biorecognition, and efficacy of drugs were generated. These new strategies, often called drug delivery systems (DDS), were based on interdisciplinary approaches that combine polymer science, pharmaceutics, bioconjugate chemistry, and molecular biology.

To minimize drug degradation and loss, to prevent harmful side-effects and to increase drug bioavailability and the fraction of the drug accumulated in the required zone, various drug delivery and drug targeting systems are currently under development. Among drug carriers one can name soluble polymers, microparticles made of insoluble or biodegradable natural and synthetic polymers, microcapsules, cells, cell ghosts, lipoproteins, liposomes, and micelles. The carriers can be made slowly degradable, stimuli-reactive (e.g., pH- or temperature-sensitive), and even targeted (e.g., by conjugating them with specific antibodies against certain characteristic components of the area of interest). Targeting is the ability to direct the drug-loaded system to the site of interest.

Two major mechanisms can be distinguished for addressing the desired sites for drug release
1. Passive
2. Active targeting

An example of passive targeting was the preferential accumulation of chemotherapeutic agents in solid tumors as a result of the enhanced vascular permeability of tumor tissues compared with healthy tissue. A strategy that could allow active targeting involves the surface functionalization of drug carriers with ligands that are selectively recognized by receptors on the surface of the cells of interest. Since ligand-receptor interactions can be highly selective, this could allow a more precise targeting of the site of interest.

1.9.2 Drug Delivery Carriers

Colloidal drug carrier systems such as micellar solutions, vesicle and liquid crystal dispersions, as well as nanoparticle dispersions consisting of small particles of 10-400nm diameter show great promise as drug delivery systems. When developing these formulations, the goal is to obtain systems with optimized drug loading and release properties, long shelf-life and low toxicity. The incorporated drug participates in the microstructure of the system, and may even influence it due to molecular interactions, especially if the drug possesses amphiphilic and/or mesogenic properties.

Different types of drug carriers are as follows

1. Micelles
2. Liposomes
3. Dendrimers
4. Liquid crystal
5. Nanoparticles

1.9.2.1 Micelles

Micelles formed by self-assembly of amphiphilic block copolymers (5-50nm) in aqueous solutions are of great interest for drug delivery applications. The drugs can be physically entrapped in the core of block copolymer micelles and transported at concentrations that can exceed their intrinsic water-solubility. Moreover, the hydrophilic blocks can form hydrogen bonds with the aqueous surroundings and form a tight shell around the micellar core. As a result, the contents of the hydrophobic core
are effectively protected against hydrolysis and enzymatic degradation. In addition, the corona may prevent recognition by the reticuloendothelial system and therefore preliminary elimination of the micelles from the bloodstream. A final feature that makes amphiphilic block copolymers attractive for drug delivery applications is the fact that their chemical composition, total molecular weight and block length ratios can be easily changed, which allows control of the size and morphology of the micelles. Functionalization of block copolymers with cross-linkable groups can increase the stability of the corresponding micelles and improve their temporal control. Substitution of block copolymer micelles with specific ligands is a very promising strategy to a broader range of sites of activity with a much higher selectivity.

1.9.2.2 Liposomes

Liposomes are a form of vehicles that consist either of many, few or just one phospholipid bilayers. The polar character of the liposomal core enables polar drug molecules to be encapsulated. Amphiphilic and lipophilic molecules were solubilized within the phospholipid bilayer according to their affinity towards the phospholipids. Participation of nonionic surfactants instead of phospholipids in the bilayer formation results in niosomes. Channel proteins can be incorporated without loss of their activity within the hydrophobic domain of vesicle membranes, acting as a size-selective filter, only allowing passive diffusion of small solutes such as ions, nutrients and antibiotics. Thus, drugs that are encapsulated in a nanocage-functionalized with channel proteins are effectively protected from premature degradation by proteolytic enzymes. The drug molecule, however, is able to diffuse through the channel, driven by the concentration difference between the interior and the exterior of the nanocage.

1.9.2.3 Dendrimers

Dendrimers were nanometer-sized, highly branched and monodisperse macromolecules with symmetrical architecture. They consist of a central core, branching units and terminal functional groups. The core together with the internal units, determine the environment of the nanocavities and consequently their solubilizing properties, whereas the external groups the solubility and chemical behaviour of these polymers. Targeting effectiveness was affected by attaching targeting ligands at the external surface of dendrimers, while their stability and
protection from the Mononuclear Phagocyte System (MPS) was being achieved by functionalization of the dendrimers with polyethylene glycol chains.

1.9.2.4 Liquid crystals

Liquid Crystals combine the properties of both liquid and solid states. They can be made to form different geometries, with alternative polar and non-polar layers (i.e., a lamellar phase) where aqueous drug solutions can be included.

1.9.2.5 Nanoparticles

Nanoparticles (including nanospheres and nanocapsules of size 10-200nm) are in the solid state and are either amorphous or crystalline. They were able to adsorb and/or encapsulate a drug, thus protecting it against chemical and enzymatic degradation. Nanocapsules were vesicular systems in which the drug was confined to a cavity surrounded by a unique polymer membrane, while nanospheres are matrix systems in which the drug was physically and uniformly dispersed. Nanoparticles as drug carriers can be formed from both biodegradable polymers and non-biodegradable polymers. In recent years, biodegradable polymeric nanoparticles have attracted considerable attention as potential drug delivery devices in view of their applications in the controlled release of drugs, in targeting particular organs / tissues, as carriers of DNA in gene therapy, and in their ability to deliver proteins, peptides and genes through the peroral route.

Development of new drug molecule was expensive and time consuming. Improving safety efficacy ratio of “old” drugs has been attempted using different methods such as individualizing drug therapy, dose titration, and therapeutic drug monitoring. Delivering drug at controlled rate, slow delivery, targeted delivery are other very attractive methods and have been pursued vigorously. There were a number of factors stimulated interests in the development of these new devices, concepts, and techniques.

Conventional drug administration methods, while widely utilized, have many problems that may be potentially overcome by these methods. Equally important, these advances may appear attractive relative to the costs of new drug development. Rising research and development costs,
alternative investment opportunities for drug firms, fewer firms conducting pharmaceutical research, and erosion of effective patent life have resulted in a decline in the introduction of new chemical entities since the late 1950s.

Numerous animal and human investigations have provided an increased understanding of the pharmacokinetic and pharmacodynamic principles that govern the action and disposition of potent opioid analgesics, inhalation anesthetic agents, sedative/hypnotics, and muscle relaxants. These studies suggest that skin and buccal and nasal mucous membranes may have use as alternate routes of analgesic and anesthetic delivery. Similar developments with other compounds have produced a plethora of new devices, concepts, and techniques that have together been termed controlled-release technology (CRT). Some examples of CRTs are transdermal and transmucosal controlled-release delivery systems, nasal and buccal aerosol sprays, drug-impregnated lozenges, encapsulated cells, oral soft gels, iontophoretic devices to administer drugs through skin, and a variety of programmable, implanted drug-delivery devices. There were number of factors stimulating interest in the development of these new devices, concepts, and techniques. Conventional drug administration methods, while widely utilized, have many problems that may be potentially overcome by these methods. Equally important, these advances may appear attractive relative to the costs of new drug development. [210-213].

1.9.3 Control drug delivery

Controlled drug delivery is one which delivered the drug at a predetermined rate, for locally or systemically, for a specified period of time. Continuous oral delivery of drugs at predictable and reproducible kinetics for predetermined period throughout the course of GIT. Controlled drug delivery employed drug-encapsulating devices from which therapeutic agents may be released at controlled rates for long periods of time, ranging from days to months. Such systems offer numerous advantages over traditional methods of drug delivery, including tailoring of drug release rates, protection of fragile drugs and increased patient comfort and compliance [214].
1.9.3.1 Advantages of control drug delivery

- Maintained drug levels within a desired range
- Fewer administration required
- Optimal use of the drug
- Increased patient compliance

1.9.3.2 Disadvantages of control drug delivery

- Possible toxicity or non-biocompatibility of the material used
- Undesired by-product of degradation
- Surgery required to implant or remove the system
- Patient discomfort from the delivery device
- Higher cost

The ideal drug delivery system should be inert, biocompatible, mechanically strong, comfortable for the patient, capable of achieving high drug loading, safe from accidental release, simple to administer and remove, and easy to fabricate and sterilize. The goal of many of the original controlled-release systems was to achieve a delivery profile that would yield a high blood level of the drug over a long period of time. With traditional drug delivery systems, the drug level in the blood follows the in which the level rises after each administration of the drug and then decreases until the next administration. The key point with traditional drug administration is that the blood level of the agent should remain between a maximum value, which may represent a toxic level, and a minimum value, below which the drug is no longer effective [215].

Controlled Drug Delivery (CDD) occurred when a polymer, whether natural or synthetic, was judiciously combined with a drug or other active agent in such a way that the active agent was released from the material in a predesigned manner. The released of the active agent may be constant over a long period, it may be cyclic over a long period, or it may be triggered by the environment or other external events. In any case, the purpose behind controlling the drug delivery is to achieve more effective therapies while eliminating the potential for both under and overdosing [216].
1.9.4 Control Release Dosage Form

The United States Pharmacopoeia (USP) defined the modified-release (MR) dosage form as “the one for which the drug release characteristics of time course and/or location were chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms such as solutions, ointments, or promptly dissolving dosage forms”. One class of MR dosage form is an extended-release (ER) dosage form and is defined as the one that allows at least the 2-fold reduction in dosing frequency or significant increased in patient compliance or therapeutic performance when compared with that presented as a conventional dosage form (a solution or a prompt drug-releasing dosage form).

The terms “controlled release (CR)”, “prolonged release”, “sustained or slow release (SR)” and “long-acting (LA)” have been used synonymously with “extended release”.

Nearly all of the currently marketed monolithic oral ER dosage forms fall into one of the following two technologies

1. Hydrophilic, hydrophobic or inert matrix system
2. Reservoir (coated) systems

**Hydrophilic, hydrophobic or inert matrix systems**

These consist of a rate controlling polymer matrix through which the drug is dissolved or dispersed.

**Reservoir (coated) systems**

In this system drug containing core was enclosed within a polymer coating. Depending on the polymer used, two types of reservoir systems are considered.

a) Simple diffusion/erosion systems
b) Osmotic system

a. **Simple diffusion/erosion system**

In this system drug-containing core was enclosed within hydrophilic and/or water-insoluble polymer coatings. Drug release was achieved by
diffusion of the drug through the coating or after the erosion of the polymer coating.

b. Osmotic systems

The drug core was contained within a semi-permeable polymer membrane with a mechanical/laser drilled hole for drug delivery. Drug release was achieved by osmotic pressure generated within the tablet core.

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