Chapter 2

Review of Work Done
Chapter 2.1

Review of Work Done – Diltiazem HCl
diltiazem HCl in sigmoid type dissolution pattern, irrespective of the pH of the dissolution media. The study in dogs revealed that higher plasma concentration was maintained for a long time (30 hr) after a lag period of 8 hr.

Ishino et al.\(^{(21)}\) prepared an orally applicable pulsetile drug delivery system in dry-coated tablet form using diltiazem HCl using polyvinyl chloride–hydrogenated castor oil–polyethylene glycol mixture as the outer shell of the tablet. In–vitro drug release from the prepared tablet exhibited a typical pulsetile pattern with a 7 hr lag phase. This dosage form was orally administered to beagle dogs. The results of in–vivo study in non–fasting dogs suggested that the drug could be released in the gastrointestinal tract as in the in–vitro test. However, under the fasting condition, a large difference in the plasma concentration profile was found suggesting that the disintegration time of the tablet tended to be influenced by the feeding condition of subject.

Hendrickson & his team\(^{(22)}\) prepared diltiazem HCl formulation for once–a–day administration containing rapid release diltiazem HCl beads and polymer coated beads for delayed release. Rapid release and delayed release beads were prepared by using various amounts of Eudragit RS 30D and Eudragit RL 30D coatings and capsules were prepared from a mixture of these two beads.

Eichel et al.\(^{(23)}\) prepared a delayed-release pharmaceutical preparation of diltiazem HCl in which two batches were combined in a dosage form, the long acting batch and the short acting batch. A half of beads were coated with a solution containing diltiazem HCl, hydroxypropyl methylcellulose, microcrystalline cellulose and magnesium stearate in water and the other half of beads were coated with a solution containing Eudragit NE 30D, Eudragit RS 30D, sodium lauryl sulfate and magnesium stearate in water. A mixture of the beads showed a two–tired release profile in a dissolution test performed according to USP basket method.

Vasilevska et al.\(^{(24)}\) prepared controlled-release diltiazem HCl using different mixtures of acrylic polymers (Eudragit RS 100, Eudragit RL 100 and Eudragit E 100) as film coating agents and varying the thickness of coating by different amounts of Eudragit. Release profiles of diltiazem HCl from different series were investigated. The ratio of
Eudragit polymers and the coating thickness showed significant effect on drug release.

Timmins & co-workers\(^{25}\) studied the effects of granulation and tableting process variables on the properties of a novel, dual hydrophilic polymer-based controlled release tablets prepared by a simple wet granulation approach. The formulation consisted of 30% sodium alginate and 10% hydroxypropyl methylcellulose as matrix and 50% of diltiazem HCl as a model drug. The granules were evaluated for particle size distribution, Carr's index, density and angle of repose.

Deboeck et al.\(^{26}\) prepared beads made from diltiazem HCl, lactose, microcrystalline cellulose and povidone K-30 (binder) and then coated with a suspension containing Eudragit NE 30D, povidone K-30, magnesium stearate, TiO\(_2\), simethicone, talc and tween 90. In phosphate buffer (pH 5.8), 84% drug dissolution was observed in 12 hr.

Buxton & his team\(^{27}\) prepared a solid oral dosage form comprises diltiazem HCl in controlled-release form and hydrochlorthiazide in normal release form. The controlled-release spheroids were prepared in several steps by mixing diltiazem HCl and microcrystalline cellulose, wet granulating, extruding, and drying to make spheroids; the spheroids were sieved to a particle size of 0.85–1.7 mm and coated with a controlled-release film containing ethylcellulose N10, colloidal anhydrous silica, dibutyl sebacate, polysorbate 80, dichloromethane and methanol. Diltiazem HCl containing controlled-release spheroids were film-coated with a dispersion of hydrochlorthiazide and hydroxypropyl methylcellulose. The hydrochlorthiazide was released in 10 min; the diltiazem HCl release was not affected by the application of hydrochlorthiazide layer.

Buxton & his team\(^{28}\) prepared a controlled-release formulation comprising of spheroids containing diltiazem and a spheronizing agent. Diltiazem HCl and microcrystalline cellulose were mixed, wet granulated and extruded to make spheroids. The spheroids were coated with film of ethylcellulose, colloidal anhydrous silica, dibutyl sebacate and polysorbate 80.

Uekama & co-workers\(^{29}\) evaluated the utility of carboxymethyl ethyl-β-cyclodextrin
successive sequences over 24 hr.

Das et al.\(^{60}\) formulated microparticulate dosage form for diltiazem HCl with Eudragit RS 100 and Eudragit RL 100 using a novel dual polymer technique. In–vitro drug release profiles revealed that dual polymer matrix microparticulate containing Eudragit RS 100 in the inner and Eudragit RL 100 in the outer core exhibit a suitable release profile with an initial release of the drug followed by a plateau level for the test period of 5 hr. DSC analysis showed no interaction of the drug with the polymers.

Sood & Panchagnula\(^ {61}\) investigated the robustness of release of diltiazem HCl from commercially available controlled– or sustained–release preparations (Dilzem\(^ {\text{TM}}\) SR, Dilcontin\(^ {\text{TM}}\) 90, Diltime\(^ {\text{TM}}\) SR and Dilter\(^ {\text{TM}}\) CD), structural integrity and different pH environments in order to evaluate the changes in their drug release properties due to splitting of dosage form and variable pH of gastrointestinal tract. Marked difference in dissolution characteristics of three preparations (Dilzem\(^ {\text{TM}}\) SR, Dilcontin\(^ {\text{TM}}\) 90 and Diltime\(^ {\text{TM}}\) SR) was observed in different dissolution media of pH between 1.2 and 8.0. Whereas product Dilter\(^ {\text{TM}}\) CD, did not show any significant difference in release pattern as a function of pH. Dilzem\(^ {\text{TM}}\) SR and Diltime\(^ {\text{TM}}\) SR showed a higher release profile over time when halved due to broken matrix structure of the tablets and increased surface area, exposed to the dissolution media. Product Dilcontin\(^ {\text{TM}}\) 90, did not show any significant effect of integrity on total amount of drug released, however, the rate of release was found to be significantly higher for the halved tablet. The kinetics of drug release from the selected products at different pH levels were established and drug release was found to be Fickian diffusion controlled from Dilcontin\(^ {\text{TM}}\) 90 and Diltime\(^ {\text{TM}}\) SR, whereas, it followed non–Fickian anomalous diffusion patterns from Dilzem\(^ {\text{TM}}\) SR and Dilter\(^ {\text{TM}}\) CD. Predicted plasma drug concentrations in the case of all four products were found to match the desired characteristics of a therapeutically designed controlled drug release profile. The drug release parameters were not adversely affected due to splitting of the products except for the product Dilcontin\(^ {\text{TM}}\) 90.

Gohel et al.\(^ {62}\) investigated feasibility of using succinic acid–treated methylcellulose in matrix–based tablets of diltiazem HCl. A 2\(^ 3\) factorial design was employed to investigate
the effect of ratio of methylcellulose to succinic acid, amount of ethyl alcohol and drying
time on the percentage drug dissolved in 300 min. The tablets were prepared by wet
granulation technique. The ratio of methylcellulose to succinic acid was found to
significantly influence the swelling and gelling characteristics of the polymer. In-vitro
dissolution data of the optimized batch showed zero-order release.

Sharma\textsuperscript{(63)} developed a drug delivery system which delivers diltiazem HCl in a site-
specific, time-controlled manner at the gastrointestinal sites, i.e., duodenum, ileum and
colon. Depending on the rate of absorption and residence time, the time-controlled
delivery of diltiazem HCl achieves a pulsetile release kinetic. A formulation comprises a
fast release fraction containing hydroxypropyl methylcellulose and diltiazem HCl coated
with Eudragit RS 30D, a medium and a slow release fraction, all filled in a capsule.

Sood & Panchagnula\textsuperscript{(64)} developed a matrix based controlled-release pellet formulation
by incorporating hydrophilic materials into a basic formulation for pellets. A basic pellet
formulation consisting of drug and microcrystalline cellulose was used and magnesium
stearate was incorporated as hydrophobic release modifier. The drug release profile was
found to be more sustained when compared to the release of a marketed product
consisting of coated pellets and was more close to the desired theoretically calculated
release profile.

Rao & Diwan\textsuperscript{(65)} evaluated EC–PVP films containing diltiazem HCl and indomethacin for
their potential drug delivery at controlled rate. Drug release studies were carried out
employing the paddle over disk method and drug permeation through full thickness of
the rat abdominal skin was tested using a modified Franz diffusion cell fastened with O-
ring. The content of the film decreased at an apparent first-order rate, whereas the
quantity of drug released was proportional to the square root of time. The release rates of
both drugs decreased linearly with increasing drug concentration and PVP fraction in the
film, both were independent of film thickness. The release of drugs from the films
followed diffusion-controlled model at low drug concentrations. A burst effect was
observed initially, however, at high drug loading levels. The in vitro skin permeation
profiles showed increased flux values with increase of initial drug concentration in the
film and also with the concentration of PVP. Thus, the films composed of EC–PVP–
diltiazem HCl (8:2:2) and EC-PVP-indomethacin (8:2:3) should be selected for the development of transdermal drug delivery system, using a suitable adhesive layer and backing membrane for potential therapeutic use.

Coppi et al.\(66\) designed an intramembrane freely swellable matrix device by enclosing a void space between a crosslinked poly(vinyl alcohol) (PVA) matrix and a calcium alginate membrane in order to control the drug release from coated hydrogels by preventing membrane fractures. The highly swellable PVA matrix loaded with diltiazem HCl was obtained by means of a simplified procedure of the polymer crosslinking reaction using gluteraldehyde in solution with ammonium persulfate. The undried swollen matrix was coated with a calcium alginate membrane employing an ionotropic gelation of sodium alginate induced by calcium ions. After drying process, the resulting calcium alginate membrane, which was uniform and compact in the structure, increased in thickness according to the coating time. After a short burst period, sustained and constant rate phases in both simulated gastric fluid and simulated intestinal fluid. Because the inner hydrogel expanded freely inside the device, the unstressed and intact membrane could act as the rate-controlling factor in the drug release process. Owing to the pH-independent behavior of the membrane, most of the drug was delivered in intestinal fluid. Therefore, the device proposed could be advantageously used for drug targeting to the small intestine.

Altai\(67\) performed a study to examine the use of guar gum to sustain the release of diltiazem under in vitro and in vivo conditions. Guar gum tablet formulations were prepared and evaluated under a variety of in vitro dissolution conditions. Varying the lot of guar gum as well as using guar gum from different suppliers had little effect on dissolution. Also, dissolution of diltiazem from guar gum tablet was essentially independent to stir speed under normal conditions (USP Apparatus II). The stability of guar gum-based formulations under stressed conditions (40/75% RH for 3 months) was also established. The guar gum-based formulations, along with Dilacor XR®, were administered to a group of 8 tested, healthy volunteers in a 4-period crossover study. All four formulations gave similar plasma concentration overtime. Guar gum-based matrix tablets represent a simple and economical alternative to existing diltiazem HCl sustained release dosage forms.
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Shyamala et al.\textsuperscript{68} formulated controlled-release tablets of diltiazem HCl using chitosan as polymer and evaluated for in vitro release kinetics and its therapeutic efficacy in mongrel dog. Different ratios of drug: polymer (1:1, 1:2 and 1:3) were used and tablets were prepared by direct compression technique. The drug release pattern followed Higuchi equation and gave a zero-order release. In-vivo study indicated that hydrogel helped in producing sustained action over the period and thus reducing the frequency of dosing.

Ghosh et al.\textsuperscript{69} prepared sustained-release pellets of diltiazem by pan-coating process using nonpareil sugar cores of appropriate size. The drug was dispersed in melted stearic acid (1:1), and the mixture was loaded on the basic sugar cores using polyvinylpyrrolidone as the binder followed by coating with ethylcellulose solution. Dissolution test was carried out in hydrochloric acid media of pH 1.2 for the first two hours and then the media was replaced by phosphate buffer of pH 7.2. The release pattern was diffusion controlled for the formulations, having lesser amount of ethylcellulose but shifted towards zero order with the increase in the proportion of ethylcellulose in the formulations. A near zero order release profiles were obtained in formulations having higher amount of ethylcellulose, which was able to sustain the drug-release upto 12 hr.

Nagesh et al.\textsuperscript{70} used stearic acid in combination with ethylcellulose and shellac to develop a twice-daily formulation of diltiazem HCl. Diltiazem HCl reservoir was developed around nonpareil sugar then coated with different amounts of ethylcellulose and shellac to produce pellets of various core coat ratios. In vitro release studies in acidic medium of pH 1.2 followed by phosphate buffer of pH 4.5 and pH 7.2 showed prolongation of duration of release when ethylcellulose was used. However, the initial release with these formulations was high. Incorporation of shellac along with ethylcellulose resulted in uniform release throughout the period of study. Analysis of data indicated diffusion was the dominant mechanism in drug release.

Kim\textsuperscript{71} developed a coated donut-shaped controlled release tablets of diltiazem HCl. The tablet core comprises diltiazem HCl and a water-soluble hydrophilic polymer-hydroxypropyl methylcellulose. The tablet core is coated with hydrophobic water-
insoluble material covering the entire core except the cylindrical hole. The results of release kinetic showed parabolic and zero-order release pattern.

Kim\(^{(72)}\) designed coated, donut–shaped tablets (CDST) to achieve parabolic and linear drug release profiles for diltiazem HCl. When rapidly erodible polymers (HPMC E3, HPC, PEG 8000, PEO) were used, the release profiles from the tablets became parabolic whereas zero-order release was achieved by using slowly erodible polymers (HPMC E5, HPMC E15, and PEO). As drug loading was increased from 10% to 39% w/w, the drug release rate from CDST based on HPMC E3 became faster and parabolic whereas that from CDST based on HPMC E5 was linear. The drug release rate of diltiazem HCl from HPMC E3 and E5 was significantly influenced by stirring rate and hole size.

Gendrat et al.\(^{(73)}\) developed a multiparticulate pharmaceutical form with delayed– and time–release for diltiazem HCl. Neutral spherical carrier (300–400 μm), 0.7 kg were pulverized with a suspension comprising Eudragit RS 100 0.525, diltiazem 7.000, and alcohol 18.760 kg. The particles that obtained were coated with a suspension containing Eudragit RS 100 2.000, Eudragit RL 100 0.100, Et phthalate 0.192, Aerosil 0.320, talc 0.400, alcohol 10.500 and acetone 4.500 kg. Capsules containing 400–500 microspheres were prepared. The amount of diltiazem HCl released after 8 and 12 hr was 40.4 and 99.4%.

Nagesh et al.\(^{(74)}\) developed and evaluated extended–release formulation of diltiazem HCl. Diltiazem reservoir was developed around the nonpareil sugar then coated with different amounts of ethylcellulose and shellac to produce pellets of various core coat ratios. In–vitro release studies in acidic medium of pH 1.2 followed by phosphate buffer of pH 4.5 and pH 7.2 showed prolongation of duration of release when ethylcellulose was used. However, the initial release with these formulations was high. Incorporation of shellac along with ethylcellulose resulted in uniform release throughout the period of study. Analysis of data incorporated diffusion was the dominant mechanism in drug release.

Gohel et al.\(^{(75)}\) developed sustained–release tablets of diltiazem HCl using modified guar gum. Guar gum was modified using lactic, citric or tartaric acid. The lactic acid modified guar gum exhibited improved swelling characteristics at pH 1.2 and 7 as compared to
that of untreated guar gum and citric or tartaric acid treated guar gum. For the optimization of the formulation, simplex lattice design was employed taking the amount of modified guar gum, untreated guar gum and dicalcium phosphate dihydrate as independent variables. The kinetics of drug release was best explained by the Korsmeyer and Peppas model.

Siepmann et al.\(^{(76)}\) investigated the effect of the composition of diffusion-controlled release devices on the drug diffusivity and the resulting release kinetics in a quantitative way. Diltiazem HCl and theophylline were investigated in ethylcellulose and Eudragit RS 100 plasticized with various amounts of acetyltributyl citrate, acetyltriethyl citrate, dibutyl phthalate, dibutyl sebacate, diethyl phthalate and tributyl citrate. Thin drug-containing films were used to determine the diffusion coefficients experimentally. The effect of the type and amount of plasticizer on the drug diffusivity was found to be significant, whereas the chain length of the polymer only played a minor role in the investigated systems. Interestingly, a quantitative relationship between the diffusion coefficient of the drug and the plasticizer level could be established. The release patterns from microparticles were calculated and the significant effect of the composition of the device on the resulting release rate was simulated. The latter could be effectively modified by varying the type and amount of plasticizer. The practical benefit of the presented method is to calculate the required composition of diffusion-controlled drug delivery systems to achieve desired drug release profiles.

Cheng et al.\(^{(77)}\) prepared simple uncoated compressed tablets with a central hole (donut shape) or multi-hole tablets. Theophylline and diltiazem HCl were used as model drugs to investigate in-vitro drug release from donut-shaped tablets. As for the donut-shaped tablets, the duration of zero-order drug release could be upto 80–90%. When the hole size was increased, the release rate increased, and the duration of linear drug release was longer. The duration of linear drug release of two-hole and three-hole tablets were longer than that of the single-hole tablets. As the drug solubility increased, the duration of linear drug release was shortened. However, three stirring rates (50 rpm, 100 rpm, 150 rpm) had little effect on the drug release.

Kawasaki et al.\(^{(78)}\) assessed the potential, as sustained release vehicles, of gels formed
in situ following the oral administration of dilute aqueous solutions of a xyloglucan polysaccharide derived from tamarind seed by in-vitro and in-vivo studies. Aqueous solutions of xyloglucan that had been partially degraded by β-galactosidase to eliminate 44% of galactose residue formed rigid gels at concentration of 1.0 and 1.5% w/w at 37°C. The in-vitro release of indomethacin and diltiazem from the enzyme-degraded xyloglucan gels followed root-time kinetics over a period 5 hr at 37°C at pH 6.8. The results of this study suggest the potential of the enzyme-degraded xyloglucan gels as vehicle for oral delivery of drugs.

Yang & Zhu\(^{(79)}\) prepared sustained-release tablets of diltiazem HCl. Sustained-release tablets containing hydroxypropyl methylcellulose and ethylcellulose as carriers, lactose and sodium alginate as fillers to adjust the release rate and 15% ethanolic polyvinyl pyrrolidone solution as adhesive were prepared by wet granulation and indirect compression technique. Uniform design method was used to optimize the formulae and process. A multivariate regression equation was applied to predict the factors affecting drug release. The release mechanism was fitted to the first order kinetics.

Pillay & Fassih\(^{(80)}\) devised a new approach for in situ interactions between drug and electrolytes to controlled the release of diltiazem HCl from oral hydrophilic monolithic systems. Electrolytes such as sodium bicarbonate or pentasodium triphosphate were used to modulate intragel pH dynamics, swelling kinetics and gel properties. Through in situ ionic interactions a compositionally heterogeneous structure referred to as a "metamorphic scaffold" was established which results in the inhibition of drug dissolution, induction of a differential swelling rate and attainment of "matrix stiffening" and axially provides a uniform gel layer. Presence of such phases in matrix structure and its influence on swelling dynamics enabled control of diltiazem HCl release in a zero-order manner in different pH environments over a 24-hr period. From kinetic analysis using the power law expressions and Hopfenberg model, it became apparent that the dynamics of matrix relaxation and controlled erosion were major factors involved in the release mechanism, while the composite rate constant decreased by approximately 2-fold in the presence of electrolytes. These findings indicated that the dynamics of swelling and gel formation in the presence of ionizable species within hydrophilic matrices provide an attractive alternative for zero-order drug delivery from a
simple monolithic system.

Kim & Fassihi\(^81\) developed a new simple polymeric matrix tablet containing diltiazem HCl that delivers highly soluble drugs over long periods of time and which is easy to manufacture. The drug was first granulated with or encapsulated in a swellable polymer, such as gum. This granule was disposed in a matrix of a more swellable, erodible polymer, such as HPMC or PEO and optionally included pectin. The more swellable erodible polymer had a diffusion rate coefficient which was greater than the different rate coefficient of the relatively less swellable polymer. It was this difference in diffusion rate coefficients between first and second polymers, which controlled the rate of drug release and allowed the system to approach zero-order drug delivery over the drug release period.

Sripathy & co-workers\(^82\) developed a sustained-release dosage form of diltiazem HCl using Pulsincap technique. The powder formulation was placed in the formaldehyde treated capsules and closed with a Na CMC plug. Various combinations of diltiazem HCl and polymer mixture were prepared and filled into these capsules and in-vitro release studies were carried out. The plug ejects out releasing the drug into the gastrointestinal tract.

Bonferoni et al.\(^83\) studied the influence of buffer composition pH and ionic strength on the release of diltiazem HCl from a complex of the drug with \(\lambda\)-carrageenan. Two viscosity grades of carrageenan were compared. A factorial analysis was used to evaluate the influence of individual variables and their interactions. The increase of ionic strength significantly increased complex solubility in all the buffer systems. A significant effect of polymer grade on complex solubility was evidenced only in phosphate buffer with a pH of 6.8, indicating lower solubility of the complex when higher polymer molecular weight was involved. In most cases, drug release rate decreased when high polymer grade was involved in the complex. Ionic strength especially affected the drug release profiles. At higher ionic strength drug release was no longer, but decreased with time, probably because of lower polymer solubility.

Vishnubhotla & Himadri\(^84\) have developed a pharmaceutical composition in the form
of a tablet or a capsule for the controlled release of diltiazem, comprises about 30–97% by wt. of a hydrophilic polymer, about 0.5–30% by wt. of an enteric (pH-dependent) polymer and about 2.5–60% by wt. of diltiazem HCl. The ratio of hydrophilic polymer to enteric polymer is in the range of about 1:1 to about 15:1. Such pharmaceutical composition releases diltiazem at a rate that allows effective plasma levels of diltiazem to be maintained over a period of 24 hr after administration to human adult subjects.

Tianyuan et al.\textsuperscript{[85]} developed a method of press-coating to prepare the pulsatile tablets of diltiazem HCl. The tablet with a core of 30 mg diltiazem HCl and an outer shell of hydrophobic material were prepared by a compression method. The pulsatile-release tablets with the lag time of 2, 4, 6 and 8 hr were prepared by changing the composition, the thickness of the coating material and the pressure used. The pH media less influenced the release of diltiazem HCl. The pulsatile release of diltiazem HCl was controlled by adjusting the composition of the outer shell materials and the manipulation conditions.

Bonferoni et al.\textsuperscript{[86]} studied the interaction between \(\lambda\)-carrageenan and diltiazem. Dialysis equilibrium in buffered media showed that the interaction is quite insensitive to the pH of the medium (in the range 1.8–6.8), while it is reduced by increasing ionic strength. In the basis of the calculated binding capacity, the complex was prepared, dried and milled. The amount of drug going into solution from the complex was not significantly affected by the pH of the medium (in the range of 1.8–6.8), while it is increased with increasing ionic strength.

Miyazaki et al.\textsuperscript{[87]} investigated the potential of tablets containing 1:4, 1:1 and 4:1 wt ratios of pectin and HPMC for the sustained release of diltiazem by sublingual administration. Measurement of maximum adhesive force to rat peritoneal membrane indicated satisfactory bioadhesive strength. An in vitro sustained release of diltiazem over 5 hr was achieved with bilayer tablets compressed of a drug-release ethylcellulose layer in addition to the pectin/HPMC layer containing drug. Plasma concentration–time curves obtained following sublingual administration to rabbits of single and bilayer tablets with 1:1 wt ratios of pectin and HPMC showed evidence of sustained release of diltiazem was 2.5–fold that achieved by oral administration for single layer tablets and
1.8-fold for the bilayered tablets.

Gohel et al.\textsuperscript{[88]} investigated feasibility of using succinic acid-treated ispaghula husk in matrix-based tablets of diltiazem HCl. The succinic acid-treated ispaghula husk showed improved swelling and gelling. A $3^2$ factorial design was employed to investigate the effect of amount of succinic acid-treated ispaghula husk and dicalcium phosphate (DCP) on the percentage drug dissolved from the compressed tablets. The results of multiple linear regression analysis revealed that the significance of the amount of succinic acid–treated ispaghula husk was greater in magnitude than that of the amount of DCP in controlling the drug release. The tablets showed considerable radial and axial swelling in distilled water. It was concluded that succinic acid–treated ispaghula husk can be used as an economical hydrophilic matrixing agent.

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Chapter 2.2

Review of Work Done — Guar Gum
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2.2.1. **As a Sustained–Release Agent**

**Bhalla & Sanzgiri**\(^{(1)}\) found that guar gum alone did not retard the release of salbutamol sulfate from controlled-release. However, a 40:60 combination of guar gum and hydroxypropyl methylcellulose yielded a better release pattern. Stability study showed that guar gum–hydroxypropyl methylcellulose combination formulation showed faster drug release on storage at higher humidity.

**Bhalla & Rajasingh**\(^{(2)}\) found that a combination of sodium carboxymethyl cellulose and guar gum gave a satisfactory release pattern of quinidine sulfate and adequate stability to accelerated storage conditions.

**Bhalla & Gulati**\(^{(3)}\) reported the use of guar gum as a release controlling material for the sustained release tablets of theophylline. The results showed that the formulation based on 5% guar gum gave an appropriate release pattern over a period of 12 hr. Also the in–vivo performance of guar gum formulation was good, both in terms of levels of drug obtained and minimal fluctuations over the 12 hr period.

**Bhalla & Shah**\(^{(4)}\) found that combinations of guar gum, hydroxypropyl methylcellulose (HPMC) and ethyl cellulose could provide tablets with suitable characteristics and appropriate drug release for ketoprofen. Stability study revealed that no marked changes were observed in the drug release pattern from the ethyl cellulose and guar gum–HPMC matrix tablets under all conditions of storage.

**Waaler & Arsensen**\(^{(5)}\) investigated the influence of xanthan gum and guar gum on the property of hydrocolloid matrix tablet containing naftidrofuryl. The effects of the two independent variables (amount of each hydrocolloid) on dissolution rate, friability and crushing strength were examined. Tablets containing at least 1% guar gum and 4% xanthan gum showed the best technical properties. Drug release was mainly dependent on the amount of guar gum when at least 2% xanthan gum was included.

The study of **Jain et al.**\(^{(6)}\) suggested the potentiality of guar gum and karaya gum as
release retarding materials in combination with hydroxypropyl methylcellulose for controlled release tablets of isoniazid. The authors found burst effect of drug in case of both the natural gums. The tablets containing either guar gum or karaya gum showed faster release of drug because of the low viscosity of these two gums as compared to hydroxypropyl methylcellulose.

Parasrampuria et al.⁷ evaluated and compared the pharmacokinetic profiles of guar gum–based three diltiazem (240 mg) formulations and a commercially available sustained release product–Dilacor™ XR. Crossover study was carried out on eight healthy volunteers. All the three guar gum–based formulations provided prolonged diltiazem release very similar to Dilacor™ XR.

Altaf et al.⁸ prepared once-daily sustained-release tablets of diltiazem HCl (240 mg) using guar gum. The drug release profiles were found to be similar with that of commercial product–Dilacor™ XR. The release patterns were independent of stirring speed and batch-to-batch variability of guar gum. Also, the results of accelerated stability study showed no significant change in dissolution profiles and assay content.

Kuhrts et al.⁹ developed an oral delivery pharmaceutical formulation for achieving sustained-release of diltiazem HCl. The formulation included 20–90% of a pharmaceutically acceptable hydrocolloid gum obtainable from higher plants (guar gum), 5–30% another excipient that aid in sustained-release (hydroxypropyl methylcellulose) and a drug (diltiazem HCl).

Kuhrts et al.¹⁰ developed an oral composition for reducing the gastric irritation effect of an NSAID. The composition comprised of a mucosal protective amount of a pharmaceutically acceptable hydrocolloid gum (guar gum), a dispersion-enhancing amount of another excipient and a drug. In-vivo tests were conducted in the aspirin-induced gastric ulcer model rats. In rats receiving guar gum at 0.1, 1.0 and 5%, reductions in ulcer severity were 30, 38, and 59% respectively.

Altaf et al.¹¹ made a comparison between two USP in-vitro dissolution apparatus (USP
apparatus 2 and apparatus 3) on two hydrocolloid based tablets, i.e., guar gum and hydroxypropyl methylcellulose (HPMC) containing two different drugs: a water-soluble (verapamil HCl) and a relatively water-insoluble (ketoprofen). This comparison was made to correlate dissolution results from the two apparatus for their potential exchange in prescreening of formulations. The guar gum–based tablets showed a better correlation between two setups, as they were less susceptible to varying hydrodynamic conditions than were the HPMC matrix tablets. The authors concluded that this finding might be due to formation of a relatively strong gel when guar gum hydrates.

Khullar et al.\textsuperscript{[12]} prepared controlled-release tablets of niacin using guar gum as a matrix forming agent. The effect on in-vitro dissolution profile was examined using variables such as guar gum content, pH of dissolution medium and moisture content of the granules. It was observed that the dissolution profile declined with the increase in the guar gum content in the tablet. However, the pH of the dissolution medium and moisture content of granules did not cause any considerable change in dissolution profile. The formulation was not affected when subjected to different stability conditions. Thus, the authors suggested guar gum as a suitable matrixing agent for low- or high-dose drugs.

Khullar et al.\textsuperscript{[13]} studied the drug release mechanism from guar gum–theophylline matrix. The drug release was found to be controlled by matrix swelling and/or dissolution/erosion of guar gum. The swelling behavior of guar gum matrix, dependent on the concentration of drug and viscosity grade of the guar gum, is controlled by the rate of water uptake into the matrices. A close to linearity relationship was found between weight loss of matrix tablet and theophylline release indicating that the drug release followed the erosion mechanism also.

Altatf\textsuperscript{[14]} performed a study to examine the use of guar gum to sustain the release of diltiazem under in-vitro and in-vivo conditions. Guar gum tablet formulations were prepared and evaluated under a variety of in-vitro dissolution conditions. Varying the lot of guar gum as well as using guar gum from different suppliers had little effect on dissolution. Also, dissolution of diltiazem from guar gum tablet was essentially independent to stirring speed under normal conditions (USP Apparatus II). The stability
of guar gum–based formulations under stressed conditions (40/75% RH for 3 months) was also established. The guar gum–based formulations, along with Dilacor™ XR, were administered to a group of eight healthy volunteers in a 4–period crossover study. All four formulations gave similar plasma concentration overtime. Guar gum–based matrix tablets represent a simple and economical alternative to existing diltiazem HCl sustained release dosage forms.

Aminabhavi et al.\(^{(15)}\) studied the controlled–release of neem seed oil using a polymeric system based on different combinations of starch urea–formaldehyde and guar gum. Starch mixture was more effective in soil applications especially if the moisture content was very low. In the case of higher moisture containing soil applications, guar gum is a preferred matrix for the effective release of neem seed oil. In the absence of actual soil condition data one can use effectively the 1:1 combination of the starch and guar gum system.

Soppimath et al.\(^{(16)}\) prepared polyvinyl alcohol–guar gum loaded microspheres containing nifedipine. The release of nifedipine sustained for \( \geq 8 \) hr from the microspheres. The study indicated that the release could be governed by both concentration of cross–linking agent and the initial drug loading.

Soppimath et al.\(^{(17)}\) prepared poly (vinyl alcohol)–guar gum interpenetrating network microspheres by crosslinking with gluteraldehyde. Nifedipine, an anti–hypertensive drug, was loaded into these matrices before and after crosslinking to study its release patterns. The extent of crosslinking was analyzed by Fourier transform IR spectroscopy and differential scanning calorimetry. Furthermore, the microspheres were characterized for drug entrapment efficiency, particle size, transport of water into the matrix and drug release kinetics. The molecular transport phenomenon, as studied by the dynamic swelling experiments, indicated that increase in crosslinking affected the transport mechanism from Fickian to non–Fickian. The in vitro release study indicated that the release from these microspheres is not only dependent upon the extent of crosslinking, but also on the amount of the drug loaded as well as the method of drug loading.
2.2.2. **Modification of guar gum**

In order to explore the pharmaceutical applications of guar gum Paranjothy\(^{18}\) synthesized various derivatives of guar gum such as guar acetate, guar phthalate, guar acetate phthalate, guar succinate, oxidized guar gum, hydroxypropyl guar, guar benzoate and sodium carboxymethyl guar. The author had concluded that sodium carboxymethyl guar seems to be the promising derivative.

Paranjothy\(^{19}\) synthesized sodium carboxymethyl guar (Na CMG) by different methods in order to overcome the disadvantages of guar gum. The rheological study showed that Na CMG solution might be more controllable than guar gum with regard to its thickening, suspending, viscosity building, clear gel forming and emulsifying properties. The toxicity studies reported that Na CMG can be used as a safe excipient in pharmaceutical and food formulations.

2.2.3. **Modified guar gum as a sustained-release agent**

Baweja & Misra\(^{20}\) prepared methylated guar gum using sodium hydroxide and dimethyl sulfate. Guar gum and methylated guar gum were evaluated as hydrophilic matrices for controlled release tablets of chlorpheniramine maleate. In case of guar gum, decreased drug release was observed after burst effect in dissolution studies. The authors assumed that this is due to poor interaction coefficient, which leads to slow rate of hydration. In case of methylated guar gum, slower drug released was observed as compared to guar gum. Methylation of guar gum increased the rate of hydration and hence faster formation of obstructive gel layer. Increase in degree of methylation, increased the rate of drug release because of reduction in viscosity of the methylated guar gum. Addition of water-soluble diluent (lactose) or water-insoluble diluent (microcrystalline cellulose) to the guar gum or methylated guar gum matrix tablets changed the drug release significantly. A significant reduction in drug release in first half an hour was observed from direct compression to wet granulation method of preparation of matrix tablets. The authors concluded that desired drug release rate can be obtained without any burst effect by controlling the degree of methylation, changing the
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composition and method of preparation of methylated guar gum matrix tablets as compared to guar gum matrix tablets.

Misra & Baweja (21) made an attempt to improve the interaction coefficient by controlled hydrolysis of guar gum using hydrochloride acid. Hydrolyzed guar gum was characterized by sugar characterizations and gel strength. Phenylpropanol amine was selected as a model drug for the preparation of hydrophilic matrix tablets. The results of dissolution studies suggested that controlled hydrolysis produced guar gum with improved interaction coefficient and dissolution profile.

Gebert & Friend (22) recently found that purification of guar galactomannan results in enhancement in physicochemical and pharmaceutical property. The purification of guar galactomannan has better physicochemical characteristics such as 40–50% increase in viscosity and 100% increase in hydration rate compared to that of unpurified guar galactomannan. These physicochemical changes resulted in improvements in pharmaceutical properties like better stirring speed independence in tablet and capsule dissolution profile, gel integrity and improved tablet hardness. The improvement in pharmaceutical characteristics also resulted in to decrease in amount of guar galactomannan required for sustaining the release of water-soluble drug.

Gohel et al. (23) used succinic acid treated guar gum as a pH-independent matrixing agent for the development of modified release tablets of diclofenac sodium. The swelling and gelling properties were found to be improved after succinic acid treatment to the guar gum. The tablets containing succinic acid treated guar gum showed less wetting time as compared to that of untreated guar gum, as a result, faster swelling and faster drug release were observed. A 2^3 full factorial design was adopted for the optimization of the formulation containing succinic acid treated guar gum. Zero-order drug release kinetic was observed from a formulated batch.

Gohel et al. (24) developed sustained release tablets of diltiazem HCl using modified guar gum. Guar gum was modified using lactic, citric or tartaric acid. The lactic acid modified guar gum exhibited improved swelling characteristics at pH 1.2 and 7 as compared to that of untreated guar gum and citric or tartaric acid modified guar gum. For the
optimization of the formulation simplex lattice design was employed taking the amount of modified guar gum, untreated guar gum and dicalcium phosphate dihydrate as independent variables. The kinetics of drug release was best explained by the Korsmeyer and Peppas model.

2.2.4. GUAR GUM IN COLON–SPECIFIC DRUG DELIVERY

As a pharmaceutical adjuvant, guar gum may be used for oral colonic drug delivery because of its reported degradation in the human colon by polysaccharidases. However, its poor film–forming property limits its use as a matrix tablet rather than enteric-coating material\(^{25, 26}\).

Wong et al.\(^{27}\) suggested that guar gum–based tablets may be useful biodegradable polymeric matrix for delivery and release in distal ileum, cecum and colon. They studied the reciprocating cylinder dissolution apparatus (USP dissolution apparatus III) to evaluate performance of guar gum–based colonic drug delivery and they found that the dissolution setup may have predictive in-vivo colonic delivery using guar gum based colonic dosage forms.

Prasad et al.\(^{28}\) investigated guar gum as a carrier for colon–specific drug delivery of indomethacin using in–vitro methods. Drug release studies showed that guar gum protects the drug from being released completely in the stomach and small intestine. Studies in phosphate buffer saline (pH 6.8) containing rat caecal contents demonstrated the susceptibility of guar gum to the colonic bacterial enzyme action with consequent drug release. The pretreatment of rats orally with 1 ml of 2% aqueous dispersion of guar gum for 3 days induced enzymes specifically acting on guar gum. Thereby increasing drug release. The results illustrate the usefulness of guar gum as a potential carrier for colon–specific drug delivery.

Krishnaiah et al.\(^{29}\) evaluated a novel colon–specific drug delivery system based on a polysaccharide, guar gum, by conducting gamma scintigraphic studies using technetium–99m–DTPA as tracer, in six healthy male volunteers. Scintigraphs taken at
regular intervals showed that some amount of tracer present on the surface of the tablets was released in stomach and small intestine and the bulk of the tracer present in the tablet mass was delivered to the colon. The colonic arrival time of the tablets was found to be 2 to 4 hr. On entering the colon, the tablets were found degrade in five out of six volunteers thereby releasing a larger amount of the tracer. The study clearly demonstrates that guar gum, in the form of directly compressed matrix tablets, is a potential carrier for colon-specific drug delivery.

Krishnaiah & his team\(^{(30)}\) evaluated colon-specific drug delivery systems based on a polysaccharide, guar gum, using in-vitro and in-vivo methods. In-vitro drug release studies showed that 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. Studies in pH 6.8 phosphate buffer saline containing 4% w/v rat caecal contents demonstrated the susceptibility of guar gum to the colonic bacterial enzyme action with consequent drug release. Gamma-scintigraphic studies in healthy human volunteers with technetium-99m-DTPA as a tracer in sodium chloride core tablets compression coated with guar gum have shown that the gum coat protect the drug (tracer in the present study) from being released in the stomach and small intestine. On entering the ascending colon, the tablets commenced to release the tracer indicating the breakdown of the gum coat by the enzymatic action of colonic bacteria. The tablets disintegrated in the ascending colon of all volunteers, resulting in the distribution of released tracer across the entire colon. The study clearly established that guar gum, in the form of compression coat, is a potential carrier for drug targeting to colon.

Krishnaiah & coworkers\(^{(31)}\) developed colon-specific delivery systems for 5-aminosalicylic acid (5-ASA) using guar gum as a carrier. Core tablets containing 5-ASA were prepared by wet granulation with starch paste and were compression coated with coating formulations containing different quantities of guar gum (300, 200, 150 and 125 mg). In-vitro drug release studies showed that the application of 175 mg of coating formulation containing 150 mg of guar gum over 5-ASA core tablets resulted in the release of less than 2% drug in simulated gastric and intestinal fluids and about 93% of 5-ASA in pH 6.8 buffer containing rat cecal contents. Differential scanning calorimetric
(DSC) studies showed the absence of any interaction between 5-ASA and the excipients on storage at 45°C for 12 weeks. The study confirmed that selective delivery of 5-ASA to the colon can be achieved using guar gum as a carrier in the form of a compression coating over the core.

Lee et al.\(^{(32)}\) developed a colonic drug delivery containing polysaccharides, which are degradable by colonic enzymes. Capsules filled with budesonide pellets were coated with a composition containing pectin and guar gum at the ratio of 4 to 1 (pH 8), to a thickness of 15 mg/cm\(^2\). The capsules disintegrated in 60 min in simulated colonic fluid, but not disintegrated in simulated gastric or intestinal fluid during 24 hr studies.

### 2.2.5. Modified Guar Gum in Colon-Specific Drug Delivery

Rubinstein & Gliko-Kabir\(^{(33)}\) modified guar gum by borax to increase the exposed surface area of the delivery system to the enzyme-rich environment of the large intestine upon arrival at that organ. They found that borax-modified guar gum maintained its ability to degrade by galactomannanase. The borax-modified guar gum was found to possess better swelling property and higher fluid uptake, and as a result, better enzymatic degradation.

Rubinstein et al.\(^{(34)}\) reported the ability of crosslinked guar gum as a potential drug carrier for the local treatment of ulcerative colitis. Crosslinking of guar gum with gluteraldehyde caused a sharp decrease in the swelling properties of guar gum. However, the ability of guar gum to degrade in in-vivo (in the cecum of the rat) and in in-vitro (in enzyme containing buffer) was not decreased. The hydrogel of crosslinked guar gum release budesonide as a result of enzymic degradation.

Gliko-Kabir et al.\(^{(35)}\) evaluated low swelling, crosslinked guar gum and its potential use as a colon-specific drug carrier. Guar gum was crosslinked with increasing amounts of gluteraldehyde under acidic conditions to obtain different products with increasing crosslinking densities. Significant reduction in guar gum swelling properties in both simulated gastric fluid and simulated intestinal fluid was observed. The crosslinking
degree of the modified guar gum products was gluteraldehyde concentration dependent. The potentiality of the crosslinked guar gum to serve as a colon-specific drug carrier was assessed using drugs with different water-solubilities (sodium salicylate, indomethacin and budesonide). The release of sodium salicylate from crosslinked guar gum disks was completed within 2 hr. While the release of indomethacin and budesonide was negligible for more than 10 hr. However, the release rate increased when galactomannase and α-galactoside were added to the dissolution media. The crosslinked guar gum maintained its degradation properties in the presence of typical colonic enzyme.

Gliko-Kabir et al. modified guar gum to increase its use for colon-specific drug delivery. Guar gum was cross-linked with increasing amounts of trisodium trimeta phosphate to reduce its swelling properties for use as a vehicle in oral delivery formulations, especially drug delivery systems aimed at localizing drugs in the distal portions of the small bowel. Swelling of guar gum in artificial gastrointestinal fluids was reduced from 100 to 120-fold (native guar gum) to 15-35-fold depending on the amount of crosslinker used, showing a bell-shape dependency. As a result of the crosslinking procedure guar gum lost its non-ionic nature and become negatively charged. Effective network and elasticity measurement showed that the crosslinking degree of the new products was linearly dependent on the amount of the crosslinker used in the reaction.

Gliko-Kabir et al. analyzed the functioning of trisodium trimetaphosphate (STMP) crosslinked guar gum products (GGP) as a colon-specific drug carrier. It was found that the product GGP-0.1 (loosely crosslinked with 0.1 equivalent of STMP) was able to prevent the release of 80% of its hydrocortisone load for at least 6 hr in phosphate buffer (pH 6.4). When a mixture of α-galactosidase and β-mannase was added to the buffer solution, an enhanced hydrocortisone release was observed. In-vivo degradation studies in the rat cecum showed that despite the chemical modification of guar gum, it retained its enzyme degrading properties in a crosslinker concentration dependent manner. Eight days of guar gum diet prior to study increased α-galactosidase activity in the cecum of the rat three-fold, compared to its activity without the diet. However, this increase in the enzyme activity was unable to improve the degradation of the different GGP products. It is concluded that because guar gum crosslinked with STMP can be biodegraded enzymically and is able to retard the release of a low water-soluble drug, this polymer
could potentially be used as a vehicle for colon-specific drug delivery.

### 2.2.6. As a Disintegrant

Feinstein & Bartilucci\(^{(38)}\) evaluated five tablet disintegrants using two specially formulated bases (a highly soluble formulation and an insoluble one) alone and with active ingredients. Among five disintegrants tested (Veegum WG, Solka Floc BW-200, Jaguar A-20-B (guar gum), Purity 825 (corn starch) and Landalgine P), Jaguar A-20-B and Purity 825 at 10% levels were found to be the most effective.

As a disintegrant, guar gum has been found to be superior to some common disintegrants such as corn starch, cellulose, algins and magnesium aluminium silicates\(^{(39)}\).

Particle size can affect disintegration, with finer particle sizes having greater disintegrating capabilities. The reason for the superiority of guar gum as a disintegrant may be related to its strong affinity for water, with the finer grade guar being a more effective disintegrant due to a better distribution within the tablet\(^{(40)}\).

A patented combination of guar gum and microcrystalline cellulose known as Avicel® CE-15 is marketed by FMC Corporation. According to the manufacturer, Avicel® CE-15 imparts unprecedented sensory characteristics to the chewable dosage forms. Avicel® CE-15 is designed to perform in direct compression formulations, producing comparably softer tablets that are less friable and disintegrated rapidly\(^{(41)}\).

### 2.2.7. Modified Guar Gum as a Disintegrant

Holinej\(^{(42)}\) evaluated HCl-crosslinked carboxymethyl guar as a disintegrant. A tablet formulation contained crosslinked carboxymethyl guar 2–10, magnesium stearate 1–5, lactose 100–140, DCP 100–140 and hydrochlorothiazole 30–80 mg. The results showed that disintegration efficiency of crosslinked carboxymethyl guar is equivalent to that of tablets containing Na CMC. The author reported that the tablets containing crosslinked
carboxymethyl guar can be made at lower cost while meeting pharmacopoeial standards.

Guar gum was chemically modified by periodate oxidation to improve its utility as a disintegrant\(^4\). It was found that the modification improved the water uptake and swelling characteristics of the guar gum. Therefore, the tablets containing oxidized guar gum showed a noticeable reduction in disintegration time compared to the tablets containing guar gum. The degree of oxidation showed effect on water uptake and swelling characteristics of the oxidized guar gum and hence the disintegration time of the tablets containing oxidized guar gum. The results with other disintegrants (starch, microcrystalline cellulose, sodium carboxymethyl cellulose–Cl, PVP–Cl, sodium starch glycolate) showed that the oxidized guar gum can be suitable or even better alternative as a tablet disintegrant.

2.2.8. **As a Viscosity Builder**

Kovacs\(^{44}\) studied the compatibility of guar gum with xanthan gum. The results showed that in presence of guar gum, the viscosity of xanthan gum solution increased considerably. The effect is most pronounced in deionized water and reduced by the presence of salt. The optimum synergistic effects were obtained with xanthan gum: guar gum ratios of 3:7 and 1:9.

Rao et al.\(^\text{45}\) studied the effect of heat treatment on the viscosity of aqueous guar gum and sodium carboxymethyl cellulose (Na CMC) solutions and reported that prolonged heat treatment of 1% solutions of guar gum and Na CMC solutions resulted in permanent loss of their viscosity.

Goswami & Derian\(^4\) reported the methods for enhancing the stability of guar solutions by sterilizing the solutions with UV light and/or adding a surfactant to the solutions. A solution of 0.5% guar was heated at 90°C for 15 min then cooled and exposed to UV light for 2 hr. There was no change in the viscosity of the solution and there was no sign of presence of any microorganisms.
2.2.9. **AS A BINDER**

Elsabbagh *et al.*\(^{(47)}\) studied the effect of guar gum in comparison with other commonly used binders on in-vitro release of ephedrine HCl (water-soluble) and sulfadimidine (water-insoluble) from tablets. At 3% and 5% level, guar gum was shown to retard drug release better than other excipients such as gum acacia, Carbopol 934®, sodium carboxymethyl cellulose and Explotab®.

2.2.10. **MISCELLANEOUS**

Vemuri\(^{(48)}\) studied the flow index and consistency values for aqueous solutions of guar gum. The effects of particle size, ionic strength and pH variation on rheological parameters were investigated. The viscosity of the guar gum solutions was found to increase with decrease in particle size. Since guar gum is non-ionic material, it was expected to have no pH dependency. However, in all experiments, the rheological parameters (viscosity, flow index and consistency) were influenced by pH. The metal ions (Sodium, potassium, magnesium and calcium) showed variable effects on flow index and consistency.

Some research has also been conducted regarding the use of guar gum in gels for ophthalmic and skin infection preparations\(^{(49)}\).

Sateesh *et al.*\(^{(50)}\) formulated flocculated suspensions of paracetamol and hydrotalcite using sodium carboxymethyl guar as a suspending agent. The formulated suspensions were evaluated for their stability parameters such as sedimentation volume, pH changes, viscosity changes, compactness and redispersibility etc. The paracetamol suspension was subjected to dissolution studies and hydrotalcite suspension was evaluated for acid neutralizing capacity. The formulations showed constant features in all aspects.

Kuhrts\(^{(51)}\) developed an oral antihyperlipidemic pharmaceutical or supplement composition comprising a combination of niacin and a gel-forming dietary fiber such as guar gum. The composition does not have the usual undesirable flushing and itching
side effects of niacin, while effectively lowering cholesterol level. Five capsules each containing niacin 74, guar gum 470 and MgCO₃ 74 mg were given 3 times/day to a patient with high cholesterol level for 23 days. The serum concentration of cholesterol and triglyceride decreased from 387 and 357 to 293 and 198 mg/dL, respectively.

Bahraini\(^{(52)}\) developed a viscoelastic system, for the use during eye surgery, comprising a viscous galactomannan polysaccharide containing liquid composition, which forms a gel on contact with a borate containing composition. The galactomannan like guar gum, locust bean gum, tara gum or hydroxypropyl guar gum is injected first into the anterior chamber of the eye followed by addition of the borate composition. The gel formed has a greater viscosity and cohesiveness than those of the galactomannan alone; thus it is able to coat the tissue to be protected in situ and can be removed by aspiration following termination of surgery. The system may also include drugs such as antihypertensives, antiglucoma agents, neuroprotectants and antimicrobial agents.

One of the commercially available guar gum is SUPERCOL® Guar Gum. It is available in two grades: SUPERCOL® G3 NF Guar Gum and SUPERCOL® U NF Guar Gum. SUPERCOL® G3 NF Guar Gum is a coarse-granulation, high-purity, low-microbial-content guar gum. It is developed for use in systems where fast dispersion, high viscosity, and gradual hydration rate are desired. It exhibits excellent thermal stability and compatibility with other components. Its free-flow characteristics and low content of fines contribute to its uniqueness. SUPERCOL® U is fine-granulation, high-purity, low-microbial-content guar gum with outstanding characteristics. It exhibits very fast hydration, high viscosity, excellent thermal stability, and good compatibility with other components\(^{(53)}\).

2.2.11. **List of References**

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