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# KONJAC GLUCOMANNAN, A PROMISING POLYSACCHARIDE FOR COLON RELEASE: A REVIEW

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**ABSTCRAT**
Konjac glucomannan (KGM), a naturally occurring polysaccharide, has in recent years gained chain of β-D-glucose and β-D mannaose with attached acetyl groups in a molar ratio of 1.6:1 with β-1,4 linkages. It is commercially extracted from Kojac (*Amorphophallus konjac* or *Amorphophallus rivieri*) which is native to Asia. The KGM, by itself or by its gelling properties, was employed in pharmaceutical industry, health promotion and treatment. It has been used potentially as a increasingly in importance. The benefits of natural KGM are also more and more appreciated by scientists and consumer due to its biodegradability. KGM consists of a polysaccharide carrier for drug delivery to the colon, such as matrix tablets, gel beads, film-coated dose form. This review will discuss the important chemistry and general properties of glucomannan, and its gel formation mechanism and properties. The example of the pharmaceutical uses of KGM will be given.

**KEYWORDS:** Konjac glucomannan, polysaccharide, controlled release, colon.

## INTRODUCTION

Konjac glucomannan is a high-molecular weight, water soluble, non-ionic, highly viscous, fermentable dietary fiber extracted from the tuber (or) root of the elephant yam, also known as Kojac (*Amorphophallus konjac* or *Amorphophallus rivieri*) which is native to Asia. KGM, is a naturally occurring biopolymer that is finding increasing applications in the pharmaceutical and biotechnology industry. It has been used successfully for many years in the food and beverage industry as a thickening agent, a gelling agent and a colloidal stabilizer. KGM also has several unique properties that have enabled it to be used as a matrix for the entrapment and/or delivery of a variety of drugs, proteins and cells. This review will first describe the source and production, chemical structure and general properties of KGM. The methods of gel formation and properties of the gels will then be discussed. Finally, some examples of the pharmaceutical uses of KGM will be given.

### 1. Glucomannan: origin and structure

Glucomannan (GM) is a polysaccharide of the mannan family, very abundant in nature, specifically in softwoods (hemicellulose), roots, tubers and many plant bulbs.[1-7] Despite the variety of sources, the most commonly used type of GM is named konjac GM, which is extracted from tubers of Amorphophallus konjac.[8,9] Irrespective of its origin, Glucomannan consists of a polysaccharide chain of β-D-glucose and β-D-mannaose with attached acetyl groups in a molar ratio of 1.6:1 with β-1,4 linkages. Because human salivary and pancreatic amylase cannot split β-1,4 linkages, the degree of solubility is controlled by the presence of acetyl groups. Glucomannan passes relatively unchanged form into the colon, where it is highly fermented by resident bacteria. The molecular weight of KGM is ranging from 200,000 to 2,000,000 Da, which varies with origin, method of processing, and storage time. (Fig.1).[10] However, the man-nose/glucose monomer ratio may vary depending on the original source of GM. For example, it has been reported that konjac GM has a molar ratio of around 1.6:1, whereas GMs extracted from Scotch pine and orchid tubers have ratios of 2.1:1 and 3.6:1, respectively.[4,11] These values should be regarded cautiously given the variability observed depending on the studies and, in particular, on the analytical procedures.

In addition regarding the variable glucose/mannose ratio, the diverse types of GM may differ in their acetylation degree. The typical acetylation degree values are 5–10%. On the other hand, it is known that native GM can be easily acetylated with acetic anhydride in the presence of a catalyst.[12-14]

**Fig: 1 Konjac Glucomannan plant**

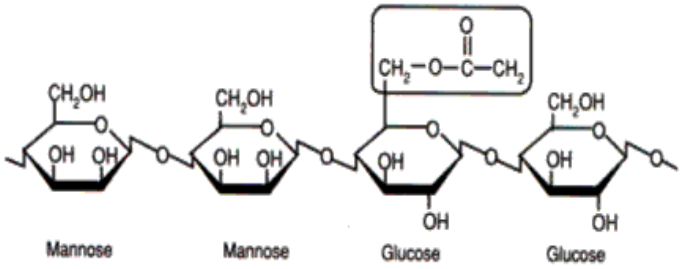


**Fig: 2. Chemical structure of KGM.**

Despite the information on the GM chemical structure, additional work is needed in order to fully understand how its structure and composition affect its physicochemical and pharmaceutical behavior.

## 2. Physicochemical properties

### 2.1. *Solubility*

Although GM is a hydrophilic molecule, its solubility in water can be reduced due to the formation of strong hydrogen bonds after purification or drying processes.[15,16] Among the parameters that affect the aqueous solubility of GM, the acetylation degree appears to be particularly important. More specifically, the presence of acetyl groups in the GM has been described to inhibit the formation of intramolecular hydrogen bonds, thus improving the GM solubility [14]. Moreover, a number of GM derivatives (discussed in Section 5) have been synthesized in order to increase the GM aqueous solubility. This versatile solubility behavior could be of special interest for a variety of pharmaceutical applications that will be later described.

***Method of solubility of Konjac glucomannan***

Glucomannan (1gm) is accurately weighed into 120 ml dry pyrex beaker. The sample is wet with 6ml of 95% ethanol. A magnetic stirrer bar is added followed by 90 ml of distilled water. The slurry is immediately placed on a magnetic stirrer-hot plate and heated and sirred until the solution boils. The beaker is loosely covered with aluminium foil when the solution begins to boil, the beaker is transferred to a second magnetic stirrere, and stirred at rppm temperature until the polymer completely dissolve (about 20 min). The volume is adjusted to 1000ml.

The solution may be very slightly turbid due to the presence of trace amounts of protein. A clear solution is obtained by centrifuging the solution at 12,000g. for 10 min. Glucomannan solution can be stored at room temperature for several weeks in a well sealed storage bottle. Microbial contamination is prevented by adding a few drops of 'toluene' to the storage bottle.

### 2.2. Molecular weight

The molecular weight (Mw) of GM has been determined by light scattering, viscosimetry and Gel Permeation Chromatography (GPC). One of the main problems in the determination of GM Mw relies on its limited water solubility. In fact, some of Mw studies have been performed with GM, which has been chemically modified in order to increase its solubility in water or other solvents.[15] Mark-Howinks parameters were fixed

according to $g = 3.8 \times 10^{-2} \times M_w^{0.723}$ for a solution of konjac GM in water at 25 ± 0.5 $^0$C,[17]

The most frequently used and commercially available GM has a Mw in the range of $1.9 \times 10^6$ -1x $10^4$[15,18,19,20] Nevertheless, there is also the feasibility to depolymerize GM in order to obtain low Mw GM. This strategy may offer interesting possibilities in the pharmaceutical field. In fact, it is known that the polymer Mw has an influence on the physicochemical characteristics of the drug delivery systems.[21,22], as well as on their efficacy in vitro and in vivo. As an example, polymeric nanoparticles based on low Mw chitosan showed higher transfection efficiency in vitro and in vivo, than those prepared with high Mw chitosan.[23,24]

Among the techniques described until now to decrease the GM Mw, acid, alkaline and enzyme hydrolyses are the most important.[3,25,26,27,28] It is well known that certain enzymes can convert polysaccharides into oligosaccharides. The complete degradation of the GM backbone requires the action of b-mannanase, b-mannosidase and b-glucosidase.[29-31]

Finally, the degradation by β-glucosidase occurs only at a terminal glucose unit and stops at terminal oxidized residues or mannose units[32] (Fig. 3).With respect to the influence of GM properties on its enzymatic degradation, some studies have shown that the acetyl groups inhibit b-mannanase and b-mannosidase activity.[33,34]

### 2.3. Gelation properties

The knowledge of the GM gelation mechanism, as well as the variables that affect this process, is useful in the design and understanding of the mechanism of formation of GM-based delivery systems. GM gels can be prepared by heating a GM solution containing alkaline compounds or higher amounts of neutral salt.[18,35] The gelation process occurs due to the interaction of the GM acidic moieties with alkalis.[36] This interaction induces structural changes in the GM molecules, which facilitate the establishment of hydrogen bonds and hydrophobic interactions between the GM chains, consequently, leading to the formation a approximation of the GM molecules. However, at high GM concen network gel structure (Fig. 4).[12,18,20,36,14]

There are a number of parameters which affect the GM gelation behavior and, thus, the properties of the final gel structure. These parameters are the GM acetylation degree, the GM Mw, the temperature and also the concentration of both GM and the alkali involved in the gelation process (see Table 1). The specific influence of each parameter is described as follows.

Since acetylation hinders the aggregation of GM, the increase in the GM acetylation degree leads to a delay in the gelation process.[36,14] On the contrary, gelation is favored when the Mw, alkali concentration or temperature increases. This is not only due to the enhancement of the interactions between GM chains[20], but also due to the formation of hydrogen bonds in the junction zones requiring energy.[12,36,20,14]

At low GM concentrations, the formation of the GM gel is impaired by the distance between molecules. In this situation a previous deacetylation process is required in order to facilitate the approximation of the GM molecules. However, at high GM concentrations the proximity of GM molecules promotes the interaction between them, favoring the formation of the network.[18,12,20,36,14]

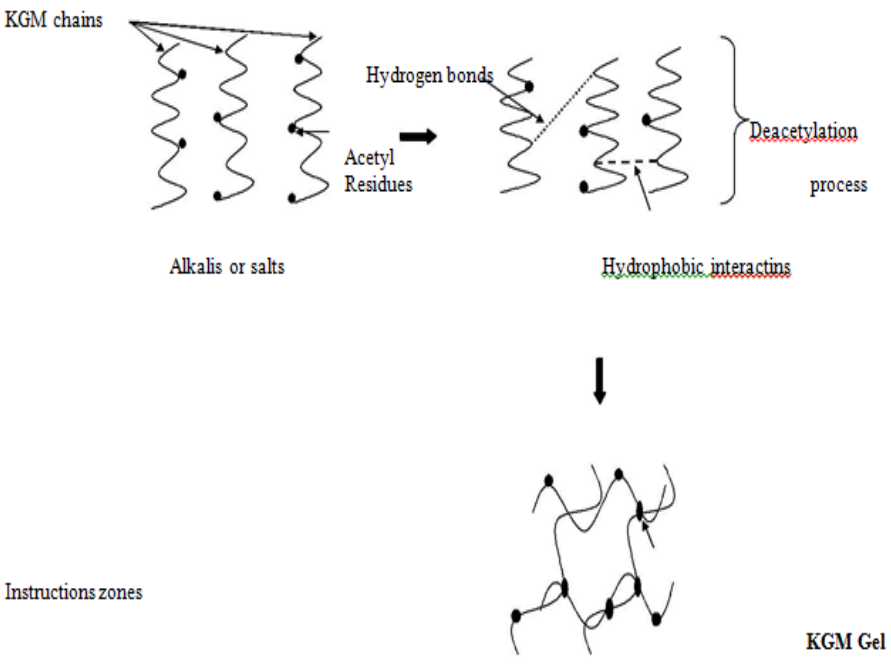


**Fig: 4. Scheme of gelation mechanism of GM.**

## 3. Interaction of glucomannan with other polymers

The possibility to combine GM with other polymers increases its versatility in the drug delivery field. In fact, the interaction of GM with other polysaccharides has been extensively investigated in order to produce new gels with improved gelling properties.[37-39]

Carrageenan, xanthan, acetan, gellam gum, alginate and chitosan are some examples of polysaccharides which were combined with GM.[40,16,41,20,8,9]

### *3.1. Interaction with kappa carrageenan*

Kappa carrageenan forms thermoreversible gels and its gelation depends on the temperature, concentration of counterions or other polysaccharides. More specifically, its interaction with GM gives thermoreversible gels[40], in which the structure is affected by the GM Mw[16] and also by the addition of a small amount of sugars.[19]

The potential of these hydrogels for drug delivery applications has been suggested.[42] However, so far we have not found any evidence of this in the literature.

similar chemical structure reported for xanthan and acetan, com-

### *3.2. Interaction with xanthan*

Xanthan gum does not naturally gel at any concentration, however gelification can be induced by temperature, ionic strength of the solution, the pH and the type of electrolyte (K+, Ba2+, Mg2+, Ca2+). The interaction with GM is ruled by a preferred stoichiometry, where the ratio xanthan:GM is 1:2.[43-45] NH4+It has been recently reported the application of xanthan–GM gels and solutions as drug delivery systems of macromolecules and low Mw drugs has been recently reported.[45-47]

### *3.3. Interaction with acetan (xylinan)*

The polysaccharide acetan, secreted by the bacterium Acetobacter xylinum, has a similar chemical structure to xanthan.[48,49] It has been reported that deacetylation of acetan provides stability to the molecule and improves the establishment of intermolecular binding with GM.[41,50,51], obtaining transparent thermoreversible gels at sufficiently high polymer concentrations and theoretical deacetylated acetan/GM ratios above 6/4.[41]

To our knowledge, there are no references on the use of acetan-GM complexes for drug delivery. However, taking into account the similar chemical structure reported for xanthan and acetan, comparable applications could be allocated to both these polymers and to their combination with GM.

### *3.4. Interaction with gellan gum*

The interaction of gellan gum with GM molecules is promoted with increasing concentration of cations, such as sodium or calcium. However, an excessive salt content leads to a separation phase, caused by the formation of aggregates of gellam gum helices with different thermal stabilities.[20,52]

With regard to the drug delivery applications of gellam gumGM mixtures, the only report found in the literature refers to blended films as releasing active agent systems for food packaging purposes.[53]

### *3.5. Interaction with alginate*

Previous studies have shown that the interaction between GM and alginate is mediated by hydrogen-binding and electrostatic interactions. This interaction has been the basis for the formation of GM–alginate beads intended for the controlled delivery of proteins.[54] In this work it was shown that the introduction of GM led to the formation of stronger and more stable gels than those composed only of alginate.

### *3.6. Interaction with chitosan*

Using IR and X-ray spectroscopy it was found that the interaction between chitosan and GM is due to the formation of intermolecular hydrogen bonds between the amine groups of chitosan and the hydroxyl and carboxymethyl groups of GM.[9,54]

The combination of GM with chitosan has been reported to offer an interesting potential in the drug delivery field. In fact, films, beads, micro and nanoparticles have been prepared, based on the combination of these polymers, and presented as new drug and protein carriers.[9,22,54-59] These specific applications will be described in detail at the end of this review article.

## 4. Biopharmaceutical applications

Traditionally, the use of konjac flour has been related with food applications. Indeed, konjac GM is a health product widely used in Asian countries and the United States for its unique properties. This thickening agent presents an extraordinary water absorption capacity, a unique viscosifying action and a synergistic behavior with other gums. In fact, konjac GM has been used to improve the bread texture, as a dietary fiber, etc. However, recently this polymer has gained increasing importance in the biomedical and pharmaceutical fields. More specifically, these applications include (see Table 3):

### *4.1. Glucomannan as a bioactive polymer*

Although GM is not currently considered a drug, some biological effects described in the literature suggest its potential as a bio-active polymer. For example, GM has been found to decrease the serum glucose levels following oral administration to diabetes type 2 rats. This hypoglycemic effect was attributed to the inhibition of carbohydrate absorption[60,61] and also to the decrease of the postprandial insulin flow.[62] On the other hand, some studies performed**.**

**Table 1: KGM biomedical and pharmaceutical applications**

| Applications | | Advantages |
|---|---|---|
| Biomedical | Obesity | Weight loss |
| | Cholesterol | Decrease LDL cholesterol levels |
| | Diabetes type 2 | Decrease the carbohydrate absorption |
| | Cancer | Antitumor activity against sarcoma-180 |
| | | **S**olid tumor |
| Pharmaceutical | Pharmaceutical forms | Sustained release profiles |
| | | Increase of stability |
| | | Improve the interaction between polymers |
| | | Enhance protein association |
| | Coating | Antiseptic coating |
| | Targeting | Recognize mannose receptors |

In rodents have suggested the activity of GM as a growth inhibitor of solid tumors, such as sarcoma.[63-65] Unfortunately, this effect and the corresponding mechanism of action have not been evaluated in further detail.

### 4.2. Pharmaceutical applications of glucomannan

GM has been investigated as a pharmaceutical excipient in tablets, films, beads and hydrogels, due to its gelling, solubility and biodegradable properties.[9,54,66] Interestingly, recent work in this field has highlighted the potential of GM for the targeting of nanocarriers to specific receptors, i.e., the mannose receptors on the cell surface.[67] This mannose receptor is a 180-kDa transmembrane protein with five domains, able to recognize several sugars, such as mannose.[68] This hypothesis is supported by previous reports which have shown that the presence of mannose residues on the particle surface increases their uptake by the M cells[69,70] and macrophages[71], where the mannose receptors are over expressed.

**Pharmaceutical Applications**

1. KGM has been studied for its effects on constipation, serum cholesterol, blood glucose, blood pressure and insulin resistance syndrome.
2. KGM could be hydrolyzed by β-mannanase to manufacture manno-oligosaccgharides, which play important roles in biological systems.
3. KGM has the ability to lower blood cholesterol and sugar level, help with weight loss, promote intestinal activity and immune functions etc.
4. KGM can also be used for modification of carbohydrate in diabetes metabolism and also used in the preparation of composite materials, edible films, coating packaging films, biodegradable films and controlled release matrix.
5. KGM may be very promising polysaccharide with respect to colon specific drug delivery systems but only limited drug delivery systems have been tried till date.

**Industrial Applications**

1. More recently, purified konjac flour or KGM has been used as a food stabilizer, gelling agent and supplement.
2. It was approved for use as a binder in meat products by the US Department of Agriculture in 1997.
3. Konjac tubers are considered food by the US Food and Drug Administration.
4. Konjc glucomannan has been recognized as GRAS (Generally Recognized as safe) by a consensus of scientific opinion since1994.
5. It is widely utilized in areas of the food industry, chemical engineering and petroleum drilling.
6. KGM has been utilized as a raw material in the food and polymer industries in China since ancient times.
7. Natural health products containing the ingredient glucomannan in tablet, capsule or powder form, which are currently on the Canadian market (Health Canada Advisory, 2010).

#### *4.2.1. Glucomannan-based films*

A number of recent articles have described the preparation of films made of GM or its derivatives in combination with other polymers.[53,72-78] Among them, GM methylcellulose and GM-poly(acrylic)acid films have been found particularly promising for drug delivery.[53,72] The role of GM in these films is the modulation of their swelling properties and, hence, their ability to control drug release.

#### *4.2.2. Glucomannan-based beads*

Beads made of GM in combination with other polymers have been prepared in order to be used for protein delivery.[54] The results have shown that the incorporation of GM into the alginate beads causes, not only the modification of the particle surface, but also the different disposition of the components inside the network. The resulting beads exhibited an improved protein-loading capacity and also a pH-dependent swelling behavior.

#### *4.2.3. Glucomannan-based hydrogels*

Due to the fact that GM is degraded by the enzymes secreted by the colonic bacteria, some authors have underlined the potential of GM-based hydrogels for colonic drug delivery.[74,75,79] These hydrogels were prepared using combinations of GM with acrylic acid or sodium tripolyphosphate. In addition, in order to achieve a selective colonic drug delivery, GM hydrogels were also formed using azo polymers as cross-linkers. It was

concluded that GM is responsible for the enzymatic degradation of hydrogels, and thus, for the resulting drug release from the systems. The formation of hydrogels from oxidized konjac GM and chitosan has been reported very recently.[72] In this gel GM works as a crosslinker agent for chitosan, thus improving the controlled release properties of the resulting hydrogels.

#### *4.2.4. Glucomannan-based microparticles*

We have recently developed GM and chitosan–GM microparticles intended for pulmonary drug delivery using a spray-drying technique. The results showed that the morphology and surface appearance of the microspheres, as well as their densities and aerodynamic diameters, are closely dependent on their composition (presence and amount of GM) (Fig. 10). Furthermore, studies performed on well-differentiated Calu-3 cells showed the ability of these chitosan–GM microspheres to closely interact with the mucus layer, remaining adhered to the epithelium.[80]

#### *4.2.5. Glucomannan-based nanoparticles*

Nanoparticles made of carboxymethylated-GM and chitosan have been prepared by electrostatic interaction between the negativecarboxylic groups of carboxymethylated-GM and the positive amino groups of chitosan, followed by a sonication step.[57] These nanoparticles exhibit a positive charge, and a size that can be modulated within the range of 50–1200 nm, depending on the polymer concentration. Additionally, these nanoparticles elicited an ability to entrap and release bovine serum albumin (BSA).[56-58] The introduction of GM in these formulations was intended to increase their stability and their controlled release properties.

Similarly, in our lab, we have developed a new protein particulate carrier made of GM and chitosan. The difference with the above-mentioned nanoparticles relies on the preparation technique, which, in our case, was based on an ionotropic gelation process.[22] These nanoparticles are obtained spontaneously by the simple mixing of the components. These very mild conditions make this approach very attractive for the association of delicate macromolecules to the nanoparticles. The interaction between both polymers, GM and chitosan, is expected to be driven by hydrophobic interactions and hydrogen bonds. Moreover, the presence of TPP (sodium tripolyphosphate) helps to build up the nanostructure, resulting in round and homogeneous nanoparticles.

As expected, these nanoparticles exhibited an improved stability in ionic media and a delayed protein release.[22,55] This delay could be explained by the higher crosslinking degree of chitosan nanogels impaired by the presence of GM [54,66]. Furthermore, the results from our group have shown that the introduction of GM into the nanoparticles leads to a facilitated interaction with the intestinal epithelium both in vitro and in vivo.[81,82] In summary, GM–chitosan nanoparticles offer attractive features as carriers for transmucosal drug delivery applications (Fig. 11).

## 5. Colonic role of Konjac glucomannan

Konjac glucomannan has a promising pharmaceutical uses and is presently considered as a carrier material in colon-specific drug delivery systems (for systemic action or a topical treatment of diseases such as ulcerative colitis, Crohn's disease, colon carcinomas), as indicated by the large number of studies published over the last few years (Table 2). The potential of pectin or its salt as a carrier for colonic drug delivery was first demonstrated by two studies, i.e.[83,84] The rationale for this is that konjac glucomannan will be degraded by colonic bifidobacteria enzymes, but will retard drug release in the upper gastrointestinal tract due to its insolubility and because it is not degraded by gastric or intestinal enzymes.[83][85] demonstrated that konjac glucomannan-chitosan degrading bacteria, *E. coli*, could adhere to beads casted of low methoxylated KGM. The ability of the bacteria to adhere to the beads, however, was not correlated with their ability to degrade glucomannan. When the dissolution of Konjac glucomannan matrix tablets was analysed with and without *E. coli*, a significant retardation in the dissolution rate was observed in the presence of *E. coli*, suggesting the formation of a bio-film on the matrix.[86]

## 6. Toxicity of Konjac glucomannan

It is well known that GM has been traditionally used as a food additive in China and Japan, most specifically as a dietary fiber and, hence, considered good for health.[20] Despite this long-lasting tradition, the results of the toxicity studies are very promising but still limited. For example, several authors have found no evidence of toxicity in rats after the long-term feeding of rats with a GM dose equivalent to an intake of 500 mg/kg body weight per day.[87,98] Other authors have performed more detailed toxicity studies aimed at identifying signs of toxicity such as oral toxicity, sensitization studies in the skin, sub-acute and sub-chronic intestinal toxicity studies, cell-aging, embryocitoxicity and genotoxicity studies.[89,90] Interestingly, none of these studies has revealed significant signs of toxicity and only minor side-effects, such as diarrhea, abdominal pain and flatulence, were reported at doses higher than 5 g/day.[91-93]

Finally, concerning the regulatory aspects, in 1996 the European Commission in its ‘‘Report of the scientific committee for food" (41st series) considered that even when the GM toxicity studies were not enough to establish an Acceptable Daily Intake (ADI) ‘‘the use of konjac gum as an additive at intended levels up to 1% in food is acceptable provided that the total intake from all sources did not exceed 3 g/day".

**Konjac principles**

- As a soluble dietary fiber, it can form a protective layer around the food to prevent the food from interfering with digestive enzymes.
- Swelling (can enlarge up to 80-100 times,) can suppress appetite; promote satiety, so that overall food intake can be decreased.
- It can delay and prevent cholesterol levels from rising, simple sugars and other nutrients, making them fat and reduce acid synthesis in the body.
- Bowel function- it can increase the amount of bowel movements; so it has the role of intestinal cleansing.

**Table 2: Controlled release formulation using KGM.**

| S.No | Dosage form | Application | References |
|---|---|---|---|
| 1 | Tablets | KGM /xanthan gum mixtures as sustained release | Fan, J et al., 2008[94] |
| 2 | Tablets | KGM/xanthan gum mixtures as excipients for controlled drug delivery systems. | Mancenido F et al., 2008[95] |
| 3 | Tablets | KGM matrix tablet for extended release | Shevkar B et al., 2014 [96] |
| 4 | Tablets | KGM matrix tablet for extended release of diclofenac sodium | Bhagyashree shevkar et al., 2014 [97] |
| 5 | Tablets | KGM and chitosan matrix system | Gallaher CM et al., 2000[98] |
| 6 | Tablets | The potential use of hydrolysed KGM as a prebiotic. | Al-Ghazzewi FH et al., 2007 [99] |
| 7 | Tablets | Effects of KGM hydrolysates on the gut microflora | Elamir AA et al., 2008 [100] |
| 8 | Tablets | Interaction in Xanthan–KGM mixtures and the influence of electrolyte. | Annable P et al., 1994 [101] |
| 9 | Tablets | KGM and xanthan gum mixture as the sustained release material of matrix tablet. | Jiangyang Fan et al., 2008 [102] |
| 10 | Tablets | Effect of degree of acetylation on gelation of KGM. | Gao, S. J et al., 2004 [103] |
| 11 | Tablets | KGM hydrolysate beneficially modulates bacterial composition | Connolly ML et al., 2010 [104] |
| 12 | Tablets | Controlled release of matrix system oxidized KGM. | Korkiatithaweechai S et al., 2011 [105] |
| 13 | Tablets | Drug diffusion in neutral and ionic hydrogels assembled. | Voepel J et al., 2009 [106] |
| 14 | Tablets | KGM/xanthan gum mixtures as controlled drug delivery systems. | F. Alvarez-Manceñido et al., 2008 [107] |
| 15 | Tablets | KGM matrix system. | Vuksan V et al., 1999 [108] |
| 16 | Tablets | *In-vitro* evaluations of KGM and xanthan gum matrix system as the sustained release | Jiangyang, F et al., 2008 [109] |
| 17 | Tablets | KGM matrix system as sustained release | Ahmad ainurofiq et al., 2004 [110] |
| 18 | Tablets | KGM controlled release matrix system. | Vuksan, V et al., 2000 [111] |
| 19 | Films | Blend films from chitosan and KGM solution. | Xiao C et al., 2000 [112] |
| 20 | Films | KGM-based films by alkali and sodium carboxymethylcellulose | L. Cheng et al., 2002 [113] |
| 21 | Films | KGM–quaternized poly(4-vinyl-N-butyl) pyridine blend films | Ch. Liu et al., 2004 [114] |
| 22 | Films | Biocompatibility of KGM/chitosan blend films, | X. Ye et al., 2006 [115] |
| 23 | Films | Preparation and optimization of KGM coated soluble drug | Wang Chao et al., 2008 [116] |
| 24 | Gels | Release characteristics of dibucaine dispersed in konjac gels. | Nakano M et al., 1979 [117] |
| 25 | Gels | Investigation of sustained releae property of KGM-borate composite gel to salicylic acid. | Li, B et al., 2003 [118] |
| 26 | Nanoparticles | KGM-coated nanoparticles | Z. Cui et al., 2003 [119] |
| 27 | Nanoparticles | Novel polyelectrolyte carboxymethyl KGM–chitosan nanoparticles for drug delivery. | Du, J et al., 2005 [120] |
| 28 | Nanoparticles | Formation of glucomannan-chitosan nanoparticles. | Alonso-Sande M et al., 2006 [121] |
| 29 | Nanoparticles | phosphorylated glucomannan-coated chitosan nanoparticles as nanocarriers for protein delivery | M. Cuña et al., 2006 [122] |
| 30 | Hydrogels | KGM hydrogels as DNA controlled release matrix. | Wen, X et al., 2008 [123] |
| 31 | Hydrogls | Novel hydrogels from oxidized KGM cross-linked chitosan | H.Q.Yu et al., 2007 [124] |
| 32 | Hydrogels | KGM–poly(acrylic acid) IPN hydrogels for controlled release | Xian Wen et al., 2009 [125] |

| | | | |
|---|---|---|---|
| 33 | Hydrogels | Protein release from galactoglucomannan hydrogels | A.A. Roos et al., 2008 [126] |
| 34 | Hydrogels | Effects of KGM hydrolysates on the gut microflora | Abdulmnem, A et al., 2008 [127] |
| 35 | Beads | Alginate-KGM-chitosan beads as controlled release matrix. | Wang K et al., 2002 [128] |
| 36 | Beads | Alginate-KGM-chitosan beads as controlled release matrix. | He et al., 2002 [129] |
| 37 | Beads | The potential of enzyme entrapment in konjac cold-melting gel beads. | Perols, C et al., 1997 [130] |

**Table 3 Colon-specific drug delivery using KGM.**

| S.No | Dose form | Application | References |
|---|---|---|---|
| 1 | Tablets | Compression coat for colonic drug delivery: | Kang Wang et al., 2010 [131] |
| 2 | Tablets | Xanthan in synergistic gelation with KGM | Goycoolea FM, et al., 1995 [84] |
| 3 | Tablets | binary mixtures for colonic drug delivery. | Felipe AM et al., 2008 [132] |
| 4 | Tablets | novel pH sensitive drug carrier for colon delivery | Dong-Ying Xu et al., 2009 [133] |
| 5 | Tablets | compression coated tablets for colonic delivery | Zhang Y et al., 2006 [86] |
| 6 | Tablets | Dextran and cross-linked galactomannan as coating materials for sitespecific drug delivery to the colon. | Hirsch, S., et al., 1999 [83] |
| 7 | Hydrogels | phosphated cross-linked KGM hydrogels for colon-targeted drug delivery | Liu M.M et al., 2007 [134] |
| 8 | Hydrogels | KGM grafted acrylic acid for colon-specific drug delivery. | Chen LG et al., 2005 [135] |
| 9 | Hydrogels | KGM hydrogels containing azo crosslinker for colon-specific delivery. | Liu et al., 2004 [136] |
| 10 | Hydrogels | phosphated cross-linked KGM hydrogels for colontargeted drug delivery. | Meimei, L. et al., 2007 [137] |
| 11 | Beads | calcium alginate/KGM beads as colon drug delivery system | Hajaratul Najwa et al., 2015 [138] |
| 12 | Beads | Novel pH-sensitive polyelectrolyte carboxymethyl KGM–chitosan beads as drug carriers. | Du J et al., 2006 [139] |

## CONCLUSION

The chemistry and gel-forming characteristics of KGM have enabled this naturally occurring biopolymer to be used in pharmaceutical industry, health promotion and treatment. It has also been used potentially in pharmaceutical preparation and drug formulation as a carrier of a wide variety of biologically active agents, not only for sustained release applications but also as a carrier for targeting drugs to the colon for either local treatment or systemic action. By selection of the appropriate type of KGM, gelation conditions, added excipients, and coating agents, the dosage forms of various morphology and characteristics can be fabricated. As research and development continues with delivery system using KGM, we expect to see many innovative and exciting applications in the future.

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