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# Konjac glucomannan, a promising polysaccharide of *Amorphophallus konjac* K. Koch in health care

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ABSTRACT

In recent year, konjac glucomannan (KGM) has attracted more attention due to its non-harmful and non-toxic properties, good biocompatibility, biodegradability and hydrophilic ability. Moreover, KGM and their derivatives have several importances in the multidirectional research areas such as nutritional, biotechnological and fine chemical fields. In the previous article, we have reviewed the nutritional aspects of KGM covering the various aspects of functional foods, food additives and their derivatives. This review aims at highlighting the diverse biomedical research conducted on KGM in the past ten years, covering therapies for anti-obesity, regulation in lipid metabolism, laxative effect, anti-diabetic, anti-inflammatory, prebiotic to wound dressing applications. Moreover, this review deals with global health aspects of KGM and the disparate health related factors associated with diseases and their control measures.



## 1. Introduction

The konjac glucomannans (KGM) is a water-soluble polysaccharide (dietary fibre) [1,2] isolated from tubers of *Amorphophallus konjac* K. Koch, a perennial plant belonging to the family *Araceae* [3]. It has been cultivated for centuries in Asian countries as a source of food and as an ingredient for traditional Chinese medicine (TCM). Konjac products are regarded as one of the "top 10 health foods" by World Health Organization [1,4–6].

The polysaccharide has been largely consumed as a nutritional supplement [5]. The important health benefits of KGM includes in reducing cholesterol [7], normalizing triglyceride (TG) concentration in blood [8], improving blood sugar levels [9], promoting intestinal activity [10] and immune function [11] and wound dressing [12]. KGM is considered as an indigestible dietary fibre being resistant to hydrolysis by the action of digestive enzymes in the human gut [13]. In pharmaceutical industry, KGM is used in the preparation of hydrogel as a DNA-controlled release matrix [14–17]. In addition, it has been used to improve glycaemia and other related risk factors for coronary heart diseases in Type II diabetic patients [18,19]. Therefore, KGM is recognized as a safe biomaterial according to the FDA (Food and Drug Administration, USA) [20,21] for therapeutic uses. Over the last few decades, heteropolysaccharides have gained special importance in the biomedical and drug delivery systems. Among them, KGM is chosen as a preferred biopolymer [16,22].

In a previous review, we have discussed on the global applications of KGM as food for nutritional benefits [23]. The traditional utility and potential health benefits of *A.konjac* K.Koch have been reported by Chua et al. [4]. In this review, we have discussed the potential applications of KGM as health food products and different uses in biomedical sectors in treatment of life style diseases such as Type 2 diabetes, obesity, coronary heart disease (CHD), stroke, hyperlipidemia, hypercholesterolemia, diminution of constipation, treatment of hyperthyroidism, colorectal cancer, wound healing, and as an antioxidant and prebiotic.

## 2. KGM and its chemical structure

The chemical structure of polysaccharides has a great impact on the functional and nutraceutical characteristics and/or on their

*Abbreviations:* ACA, American Cancer Association; ADA, American Diabetes Association; CHD, coronary heart diseases; CMKGM, carboxymethyl konjac glucomannan; eNOS, reduced nitric oxide synthase; FDA, Food and Drug Administration; GR, glutathione reductase; IBD, inflammatory bowel disease; iNOS, inducible nitric oxide synthase; KGM, konjac glucomannan; NCRI, National Cancer Research Institute; OVA, ovalbumin; PKF, purified konjac flour; SCFAs, short-chain fatty acids; TCM, traditional chinese medicines; TNF-α, tumor necrosis factor-alpha; WHO, World Health Organization.

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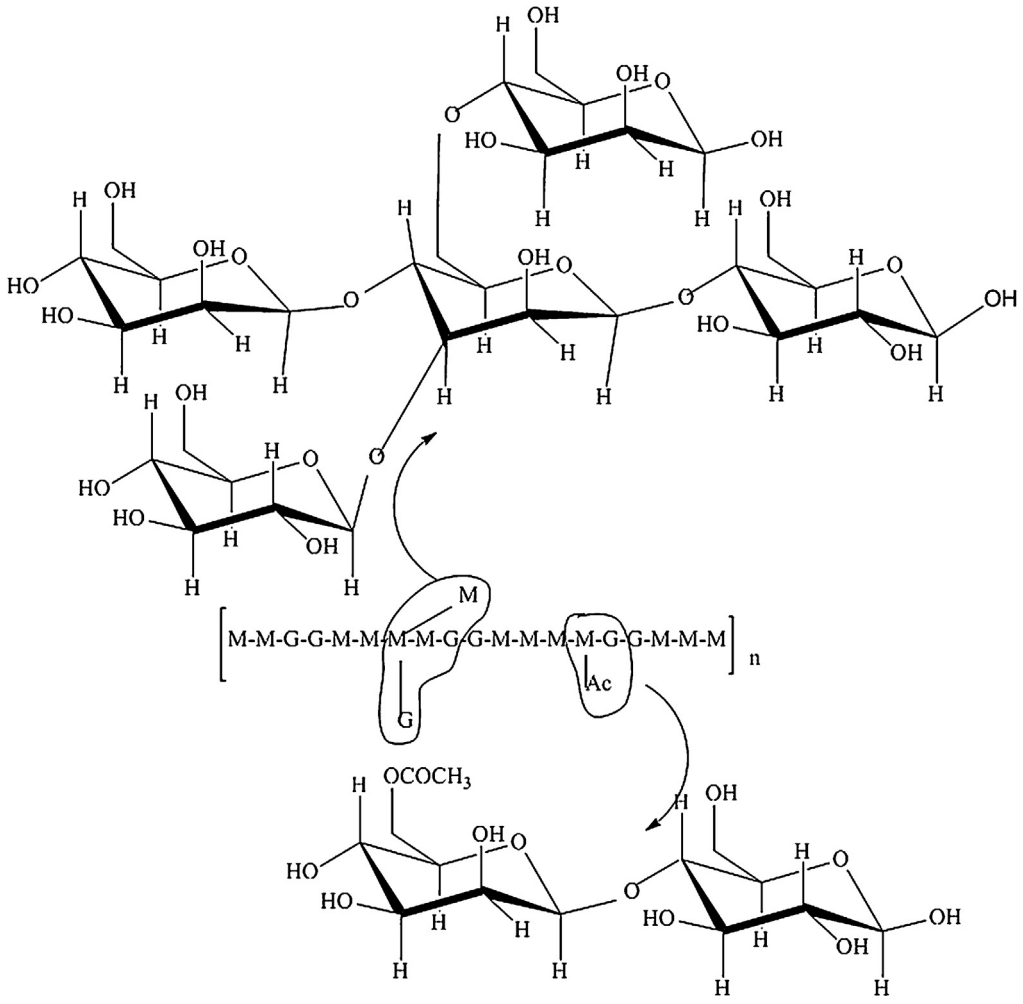


**Fig. 1.** Chemical structure of Glucomannan (KGM)(repeating unit); the M-M-G sequence represents β-1, 4 linked of D- glucose (G) and D- mannoses (M) backbone and the backbone is branches through β-1, 6-glucosyl units; the Ac-M-G sequence represents acetyl groups randomly attach at the C-6 position of a D- mannoses (M) unit [Adopted from 6].

bioactivity [24,25]. However, irrespective of its origin, KGM is a β-1, 4 linked polysaccharide composed of a D- glucose (G) and D-mannoses (M) backbone lightly branched, with branches through β-1, 6-glucosyl units [6,26–32]. There may be certain short side branches at the C-3 position of the mannoses and acetyl groups randomly present at the C-6 position of a sugar unit (Fig. 1). The acetyl groups frequently range from 1 per 9 sugar units to 1 per 20 sugar units [4,33]. Moreover, the M (D- mannoses): G (D- glucose) ratio may vary depending on the original source of KGM. For instance, it has been reported that KGM has a M: G molar ratio at around 1.6:1 in acetylated KGM extracted from of *A. konjac* [34,35].

Kobayashi et al. [36] investigated the effects of degree of chemical modifications such as carboxymethylation (introduction of carboxymethyl group) in KGM under various conditions and to develop new applications of KGM. The KGM backbone possesses 5–10% acetyl-substituted residues and the presence of substituted group benefits KGM for the solubility in aqueous solution. However, the KGM losses its acetyl groups with the treatment of alkalis, and is readily transformed into a thermally stable gel called KGM gel [37]. The process of gelation is also enhanced by heating. Therefore, the addition of alkali to KGM not only enhances its solubilisation but also facilitates the deacetylation of the chain [38].

Recently, Xiao et al. [39] reported that the water binding properties of KGM and carboxymethyl KGM (CMKGM) are important for their application in food, pharmaceutical, and bio-engineering fields. The incorporation of carboxymethyl group in the KGM structure has decreased the water adsorption, absorption, and solubility of CMKGM and hence, decreased the hydrophilicity of the molecule. The modification of KGM structure not only provides fundamental information for understanding material functions and applications but also, offers several promising applications such as preparation of biodegradable films [40], biomaterial for enzyme encapsulation [41] and in the drug delivery systems [42].

## 3. Local and traditional uses of KGM

The rounded tuberous root of *A. konjac* K. Koch was discovered by Chinese and listed as early as 206 BCE in Shen Nong's Herbal Classic. It was promptly introduced in Korea, and then in Japan and included as a commodity and planting programme in the 19th century [43]. At the same time, the FDA (1997) and European Union (EU) (1998, 2003) recognized and listed konjac flour as GRAS (Generally Regarded as safe) food additive (nutraceuticals) [44]. It became an important tuber crop of tropical and sub-tropical countries because of its yield potential and culinary properties. It is now widely grown and consumed in all south eastern Asian countries including India, Indonesia, and Malaysia [45].

The tuber of *A. konjac* K. Koch is used as an important source of food and is grown either as wild or cultivated as a vegetable crop in Asian and African countries [46]. The KGM extracted from corm of

*A. konjac* in the form of flour from which foodstuffs such as noodles and spaghetti are prepared. Such foodstuffs increase satiety and are used as an anti-obesity agent [47]. Over the past two decades, KGM has been introduced on a relatively small scale into the United States and Europe as a food additive [47,48]. Being a low caloric content and soluble dietary fiber-rich food, it can delay stomach emptying for considerable time [49]. Further, the tuber is a valuable source for the traditional medicines that are mainly used in China and Korea for the treatment of liver diseases, abdominal pains, piles, enlargement of spleen, asthma and rheumatism [46].

## 4. KGM and health benefits

Since early 1960's, many scientists worldwide studied the functional health properties of dietary fibre and their possible role in relation to life style diseases such as cardiovascular disease, coronary heart disease, stroke, sudden death, hyperlipidemia, hypercholesterolemia, diabetes, obesity, and colon cancer [50,51]. While the causes for these life style diseases vary from person to person, the diet is considered to be one of the important factors. There are increasing evidences that intake of dietary fibre has functional benefits in lowering these life style diseases. American Diabetes Association, American Cancer Association, National Cancer Research Institute and other international food and nutrition organizations have published various scientific papers to advocate the advantages of increasing intake of food fibre [52–54].

In China, the *A. konjac* has been used in TCM as an immune-regulation and healthcare food for a long time [18,55]. In TCM, a gel prepared from the purified konjac flour (PKF) has been used for more than 2000 years for detoxification, tumour-suppression, blood stasis alleviation and phlegm liquefaction. This gel has been consumed by the indigenous people of China for the treatment of asthma, cough, hernia, breast pain, burns as well as in curing of haematological and skin disorders [56]. Conventionally, the use of PKF has been related with food applications. On the other hand, KGM, as a health product, is extensively used in Asian countries and in United States for its novel properties. Being a thickening agent, it has extraordinary water retention ability, a unique viscosifying activity and a varying poor (being soluble in alkali) water solubility that leads to the formation of glucomannan derivatives with different solubility [57]. However, more recently this unique biomaterial has gained increasing importance in the biomedical and pharmaceutical fields since KGM controls several functions of organs and organ systems of human beings (Fig. 2). More specifically, these applications include anti-obesity, regulation in lipid metabolism, laxative effect, anti-diabetic, anti-inflammatory, prebiotic, antioxidant, *etc*. [45,58]. The global visions of biomedical applications of KGM are shown in Table 1.

### 4.1. KGM as alternative therapies for type-2 diabetes mellitus/reduction of blood glucose

Diabetes mellitus is a chronic metabolic disease that makes dramatic changes in the lifestyle of patient's well-being leading to reduced physical activity with weakening and life-threatening complications [59,60]. It is one of the common diseases in nearly all countries with China and India are in the forefront. It has been estimated that the world prevalence of diabetes among adults (aged 20–79 years) was 6.4%, affecting 285 million people in 2010 and will increase to 7.7%, and 642 million adults by 2030 [7,61]. Moreover, the percentage of prevalence of type 2 diabetes is higher in the developed than in the developing countries [62,63]. Between 2010 and 2030, there will be 69% increase in numbers of adults with diabetes in the developing countries and a 20% increase in the developed countries [64]. The treatment of diabetes and associated health-risk aspects are often highly complicated and need considerable attentions towards patient's education and repeated medical surveillance [7,63,64].

Despite significant achievements in various treatment approaches and preventive measures during the last few decades, the persistence of diabetes has been rising exponentially and also represents a major healthcare burden throughout the world [64]. Though, there is a lack of evidences supporting the use of herbal supplements for the treatment of diabetes, an increasing number of people are adopting the herbal products such as KGM for remedy [65–69].

Like other soluble fibres (oats, minor millets, guar gum, pectin, and psyllium), KGMhas been advocated for its beneficial effects on the risk of coronary heart diseases [18]. Moreover, KGM is scientifically proven to reduce body weight, decreases the ingestion of foods that increases cholesterol and glucose concentrations, the post-prandial rise in plasma glucose, hepatic cholesterol synthesis, and increases in fecal elimination of cholesterol containing bile acids [70,71]. Several clinical trials have investigated the impact of KGM on total cholesterol, LDL cholesterol (LDL- C), HDL cholesterol (HDL- C), TG, plasma lipids, body weight, fasting blood glucose (FBG), and blood pressure (BP) [72,73]. Although KGM is not considered as a drug, some bio-pharmaceutical effects described in the literature suggest its potential as a bioactive polymer [58]. The KGM has been found to decrease the serum glucose levels following oral administration to type-2 diabetic rats [74].

Huang et al. [55] investigated the effect of konjac food on blood glucose level in patients with diabetes. Seventy-two type 2 diabetic patients were given konjac food for 65 days. The data accumulated by multiple F-test suggested that the FBG and the 2-h postprandial blood glucose (PBG) on the 30th and the 65th days after the food was ingested were significantly reduced. In this context, Vuksan et al. [18] reported that KGM fibre improved the metabolic control as measured by glycaemia, lipidemia, and blood pressure in high-risk type 2 diabetic patients. Eleven patients with hyperlipidemic hypertensive type 2 diabetic males were chosen for participation with intake of KGM fibre enriched biscuits (approx. 0.7 g/412 kJ [100 kcal]) or wheat bran fibre control biscuits. Compared with placebo, KGM significantly reduced metabolic control primary end points such as serum fructosamine (5.7%), TC/HDL-C ratio (10%) and systolic blood pressure (SBP) (6.9%). However, there were no significant changes in secondary end points, including body weight, TC, LDL- C, and HDL-C, TG, applipo-proteins A-1, B, and their ratio, glucose, insulin, and diastolic blood pressure (DBP) of the treated subjects.

Gallaher et al. [75] studied the hypocholesterolemic effect of a food supplement containing equal amounts of chitosan and KGM (1:1 ratio, w/w). Twenty-one overweight normocholesterolemic (normal concentration of cholesterol in blood) patients were fed with 2.4 g/day of a supplement containing KGM for 28 days. Caloric intake and intake of fat and dietary fibre (excluding the supplement) did not differ significantly between the initial and final period. Serum total, HDL-C and LDL-C were significantly lower on the final day as compared to the initial day. There was a trend towards greater fecal excretion of neutral sterol and bile acids ($p = 0.13$ and 0.16, respectively) at the end of the trial. Chen et al. [9] evaluated the effects of KGM supplement (3.6 g/day) in hyperlipidemic type-2 diabetic patients for 28 days on blood lipid profile and glucose levels. Twenty-two diabetic subjects (age 64.2 + 8.4 years, BMI (Body Mass Index) 25.5 + 3.2 kg/m$^2$) with elevated blood cholesterol levels (FBG) between 6.7–14.4 mmol/L were selected for this study. The fasting blood samples drawn from initial and final days of each period were analyzed for plasma lipids and glucose levels, where as faeces collected at the end of experiment period were analyzed for neutral sterol and bile acid contents. Compared with placebo, KGM effectively reduced the plasma cholesterol (11.1%),

**Table 1**
Global vision of biomedical and pharmaceutical uses of KGM.

| Study design/Duration | KGM dosing and dose forms | Consequence/Result | Reference |
|---|---|---|---|
| Biomedical application | | | |
| Type II diabetes | – | Anti-Diabetic | – |
| 21 subjects; multiple F-test analysis; 64 days | 2.4 g/day; KGM capsule | Reduction of FBG and PBG | [55] |
| 11 males; double blind; placebo controlled; crossover design; 2 successive 21 days | KGM fiber enriched biscuits of 100 kcal equivalent | Significantly declined in serum fructosamine, TC/HDL-C ratio and SBP | [18] |
| 21 overweight; non-placebo controlled; 28 days | 2.4 g/day (KGM + chitosan); capsules | Significantly reduced Serum TC, HDL-C and LDL-C | [72] |
| 22 diabetic subjects; randomized; double-blind; placebo controlled; crossover clinical trial; 28 days | 3.6 g/day; KGM capsules | Significantly reduced TC, LDL-C, TC/HDL-C ratio, ApoB and FBG | [9] |
| 18 subjects; double blind, placebo controlled, cross over; 21 days | 10 g/day; granola bars | Significantly reduced TC, LDL-C, HDL-C | [76] |
| 14 diabetic subjects; random-effects model | KGM capsules | Significantly reduced TC, LDL-C, Triglycerides, body weight, FBG | [19] |
| Swiss albino mice (male) | Corms fine powder; 100 g methanol extracted (1:5, w/v) | Reduced blood glucose levels | [186] |
| Obesity/cholesterol | – | Anti-obesity | |
| 110 elderly people; randomized; placebo controlled; 45 days | Ordinary diet with KGM meal | Significantly decreased TG, TC, and LDL-C | [101] |
| 23 obese children | 2–3 caps (DICOMAN) twice a day | Effective in obese and dyslipidemic children | [103] |
| 63 healthy men; double-blind crossover; placebo controlled design | Gelatin capsules, each containing 0.43 g KGM | Effective as a cholesterol lowering agent | [102] |
| Laxative effect | – | Constipation mitigation | |
| 50 pregnant females; 1–3 months | Sachets with of KGM (1.45 g) | Effective and well tolerated | [96] |
| 20 children; double-blind crossover; placebo controlled design; neurologically impaired | KGM dietary fibre | Improved chronic constipation and stool frequency | [97] |
| 31 children; double-blind crossover; placebo controlled design; 4 wk | GM fiber (DicoFarm) | Beneficial in treatment of constipation | [98] |
| 7 constipated subjects; placebo-controlled; diet-controlled trial;21 days | Diet with KGM supplementation (1.5 g/d) | Improved bowel movement and colonic ecology | [99] |
| 80 constipated children; double blind; placebo controlled; randomized trial; 4 wk | KGM (2.52 g/d) | Therapeutic success in constipated children | [100] |
| Inflammatory effect | – | Anti-inflammatory activity | |
| Nc/Nga Mice; 8–9 wk | Diet with PKGM powder | Suppressed scratching behaviour and inflammatory immune responses | [106] |
| Balb/c mice; 8 wk | Diet with highly viscous KGM | Prevented allergic rhinitis-like symptoms and IgE response | [107] |
| Groups of 8 rats; 7 wk | KGM 45 g/kg in G and GC composition | Reduced the oxidative and inflammatory effects | [108] |
| Inflammatory bowel diseases (IBD) | – | – | – |
| Healthy volunteers and patients | KGM hydrolysates | Improved gut pathogens; topical healing; immune system | [112] |
| Dietary Fibre (KGM) on Absorption of Vitamin | – | – | – |
| 6 normal and 5 maturity onset diabetics | Meal with 3.9 g KGM | Reduces Vit-E absorption in the intestine | [116] |
| Prebiotic activity | – | – | – |
| Balb/c mice (n = 48); 4 wk AIN-93 fibre free diet as control | KGM or KGH (both in form of pellets) with 5% (w/w) cellulose | Modulated cecal and fecal micro flora | [118] |
| Wister mice (n = 40); 14 wk; 'Standard diet' as control | 'Standard diet' with 5% (w/v) KGH | Significantly reduced faecal *Clostridum perfringens* and *Escherichia coli* counts | [120] |
| 3 healthy faecal donors male; inulin as control prebiotic substrate | 10% (w/v) KGH with 15 mg/ml cellulase and inulin | Beneficially modulated the faecal microbiota | [121] |
| BALB/c mice; 5 groups (n = 8/group); 10 days | 5% (w/w) unhydrolysed- KGM, and KGH | Provided protective and prebiotic effects | [122] |
| *In vitro* study | 2% (w/v) KGH; peptone water (PW) with 2% (w/v) KGH; lactone (control) | Potential prebiotic and inhibited the growth of pathogenic bacteria (*Staphylococcus aureus* and *S. typhimurium*) | [123] |
| 26 female patients; post antifungal treatment for the *Candida* infection; 30 days | Capsules (200 mg GMH) | Reduced vaginal infections | [5] |
| 26 female volunteers with active lesions of acne vulgaris | KGH at a concentration of 5% (w/v) | Acted as biotherapeutic agent | [125] |
| 89 children; Double-blind, placebo controlled, randomized trial | KGM (dosage of 2.52 g/d); placebo maltodextrin | Effective as therapeutic agent | [126] |
| Wound dressing | – | – | – |
| *In vitro*; *in vivo* (Male Sprague-Dawley rats with wound cut) study | *In vitro* drug release; dressed with pure CS and CS/KGM blend film | Significantly promoted wound healing and hemostatic effect | [129] |
| *In vivo* study (Male Sprague-Dawley rats); 14 days | Dressed with KGM film treated with $Ca(OH)_2$ | Epithelial coverage by post-surgery in wounds | [130] |
| Treatment of hyperthyroidism | – | – | – |
| 48 patients; randomized; placebo-controlled; one-blind study designed; 2 groups; 2 months | Treatment with methimozole (10 mg); propanol (10 mg) with KGM powder | Lowered serum thyroid hormones | [135] |
| Colorectal Cancer | – | – | – |
| Sprague-Dawley rats (n = 8 animals/group); 4 wk | Fed with KGM (5%, w/w) | Reduced colon carcinogenesis | [86] |
| Antioxidant activity | – | Potential antioxidant | – |
| 20 women (BMI: 36.1 ± 4.4 kg/m2) with abdominal obesity; 4 wk | KGM-enriched, Chokeberry (*Aronia melanocarpa*) juice | Stimulated $GP_x$ activity | [188] |
| Male Sprague-Dawley rats (n = 8); 4 wk | Fed a high fat (25% corn oil,w/w) fibre-free diet or with KGM or inulin fiber (5%) | Stimulated local and systemic antioxidative defence system | [189] |

*Abbreviation:* BMI: mean body mass index; G: KGM-enriched squid-surimi; GNP-CS/KGM: gentamicin- nanoparticles with chitosan/konjac glucomannan; $GP_x$ activity: glutathione peroxidise activity; GS: KGM–spirulina enriched squid-surimi; LDL-C: low-density lipoprotein cholesterol; MF, modified fat; NA, not available; KGH, *konjac* glucomannan hydrolysate; NCEP, National Cholesterol Education Program Step 2 guidelines; PKGM, pulverized konjac glucomannan; SBP, Systolic Blood Pressure; Standard diet = "rat and mouse standard diet"; TC: total cholesterol; TG: Triglycerides.

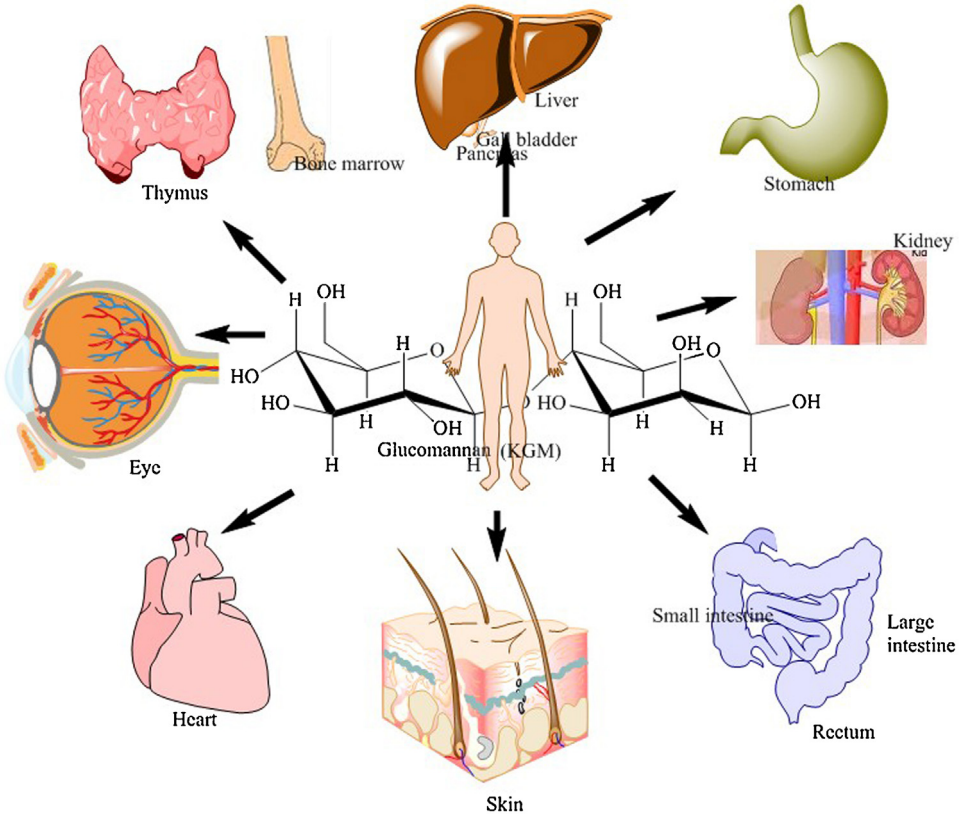


**Fig. 2.** Effects of Glucomannan (KGM) on organs and organ systems of human being; KGM act on Liver (controls lipid metabolism); Stomach (regulates Inflammatory bowel diseases-IBD); Kidney (affected from type –II diabetes); Large intestine (Constipation Mitigation), Small intestine (Inflammatory bowel diseases-IBD), Rectum (Constipation Mitigation); Skin (wound dressing); Heart (affected from severe type –II diabetes); Eye (affected from severe type –II diabetes); Thymus and Bone marrow (control immune system).

LDL-C (20.7%), total/HDL- C ratio (15.6%), ApoB (12.9%) and fasting glucose (23.2%). Fecal neutral strol and bile acid concentrations were increased by 18.0% and 75.4%, respectively, with KGM supplements. From these studies, it is evident that KGM can be an adjunct for the treatment of hyperlipidemic diabetic subjects.

Yoshida et al. [76] studied the supplements of plant sterols and/or KGM on the status of lipid profile and cholesterol biosynthesis in hypercholesterolemic type 2 diabetic and non-diabetic subjects. Eighteen non-diabetic individuals and sixteen type 2 diabetic individuals were supplemented in their diet with plant sterols, KGM (10 g/day) and mixture of both (sterol+ KGM). The overall total cholesterols decreased after feeding with the mixture (sterol+ KGM) ($4.72 \pm 0.20$ mmol/L) as compared to the control (no supplements) ($5.47 \pm 0.18$ mmol/L). Plasma LDL-C concentration was also lowered ($p < 0.05$) after KGM ($3.16 \pm 0.14$ mmol/L) and combined treatments (sterol+ KGM) ($2.95 \pm 0.16$ mmol/L) as compared to control ($3.60 \pm 0.16$ mmol/L). However, there was no significant variation in lipid profile in the subject groups. Chen et al. [77] developed microcapsule composed of sulphate-glucomannan-alginate barium (SGA) for the treatment of diabetes. This microcapsulation technique was more effective compared to the traditional microencapsulated APA (alginate-poly-L-lysine-alginate) and Aba ($Ba^{2+}$) microencapsulated islets for the treatment of diabetes. The three types of microencapsulated islets were cultured *in vitro* and their morphology and biochemical activities were studied. SGA microencapsulated islets had higher activity and produced more insulin and cytokine (such as MCP-1. IL-1, IFN-γ, TNF-α) than the APA and ABa microencapsulated islets after transplantation. More recently, Shah et al. [78] reported that dietary fibre like KGM improved satiety by providing bulk and increasing digestion time to slow postprandial glucose uptake, thereby lowing blood glucose and insulin levels. Thus, KGM has the ability to improve insulin sensitivity in individuals with type 2 diabetes.

To sum up, KGM is considered as a potentially emerging alternative therapy for treatment of type 2 diabetes. KGM is useful in improving diabetes control, reducing associated risk factors such as hyperlipidemia and hypertension, and ameliorating insulin resistance [79,80]. These hypoglycaemic effects were attributed to the inhibition of carbohydrate absorption as well as decrease in the postprandial insulin flow [55,81–83].

### 4.2. Anti-Obesity

Obesity is a medical condition in which excess fat has accumulated in the body to the extent that it may have detrimental effect on human health, leading to reduced life expectancy and/or increased health problem [84]. KGM is reported to reduce the absorption kinetics of obesity fat [85,86]. Li et al. [87] studied the effect of high frequency oscillatory type ball-mill treatment or grain size effect on structure and anti-obesity potential of konjac flour on obesed rats. The grain size of konjac flour changed from 657.3 μm ($d_{50}$) to 23.7 μm ($d_{50}$). The structural changes of grain sizes are characterized by using X-ray diffraction and differential scanning calorimeter. With a decrease of the grain size and crystallinity after 4 h of treatment, the milled konjac flour swelled more quickly. The resultant konjac flour induced significantly the antiobesity properties, such as decrease in body weight, glucose, TG, and LDL-C concentrations in blood of nutritional obese rats. Vasques et al. [88] extracted a compound, hydroxycitric acid from *Garcinia cambogia* and mixed it with KGM and studied the pharmacotherapeutic efficiency of double-blind randomized sample for the treatment of obesity. A significant reduction was observed in total cholesterol

level (−32.0 ± 35.1 mg/dl) and LDL- C levels (−28.7 ± 32.7 mg/dl) in the treated obese group.

Several groups of researchers evaluated the safety and efficacy of KGM for achieving weight loss in overweight and obese individuals [9,89,90]. More recently, Zalewski et al. [91] evaluated the effects of KGM on body weight and BMI in otherwise healthy obese children and adults. The results concluded that the short term KGM feeding may help to reduce body weight. The mechanism of action of KGM is to promote satiety due to delaying in gastric empting caused by "mass effect" of gel-like viscous mass forming in the stomach and delaying gastrointestinal transmit time.

Zalewski and Szajewska [92] evaluated the efficiency of KGM consumption on body weight in overweight and obese children. Children (aged 6–17 years) were randomly assigned to receive KGM or placebo (maltrodextrin) for 3 months and followed-up for 3 months with a dose of 3 g/day. The results did not provide a definite answer on effectiveness of KGM of overweight and obesity in children. However, the study envisaged a research gap in the field of konjac research.

In contrast, Onakpoya et al. [93] reviewed the efficacy of KGM in body weight reduction. Evidence from available randomized clinical trials did not show that KGM intake generated statistically significant weight loss. In otherwise healthy overweight or obese adults, there are some evidences to suggest that in the short term KGM may help to reduce body weight [91].

### 4.3. Laxative effect/constipation mitigation

Constipation and encopresis are common problems in people particularly at the old age. It has been reported that dietary fibre has a pivotal role to play in the management of constipation, and an average intake of about 18–27 g/day of fibre has shown to be useful in reducing constipation [94,95].

Signorelli et al. [96] investigated the use of a combination of KGM with lactose in the constipation of pregnanant women. Fifty pregnant females affected by constipation were treated with sachets containing a preparation of KGM (1.45 g) and glucose (4.2 g), in a posology of 2(1–4) sachets/day for 1–3 months. The treatment induced a return to normal frequency of weekly number of evacuations (4.9–5.8/week) and a parallel control of weight gain (within 20% of initial body weight).The latter finding seems to be related to hunger control induced by KGM at the gastric level which prevents an excessive food intake.

Staiano et al. [97] evaluated the efficacy of KGM as a treatment for chronic constipation in children with severe brain damage. They designed a study with 20 children with severe brain damage and chronic constipation by randomly assigning in a double blinded study with either KGM or placebo for 12 weeks. Stool habits, total and segmental gastrointestinal transit times, and anorectal mobility were evaluated in all the children before and after the treatment period. The experiment revealed that KGM significantly increased stool frequency as compared with placebo. Clinical scores of stool consistency were significantly improved, whereas the occurrences of painful defecations per week were significantly reduced by KGM but not by placebo. However, neither KGM nor placebo had a measurable effect on total and segmental transit times.

Loening-Baucke et al. [98] evaluated the effect of KGM fibre in the treatment of children with functional constipation with or without encopresis. Forty-six chronically constipated children were recruited into the study, but only 31 children (aged between 4.5–11.7 years) could complete. KGM fibre (DicoFarm, Rome, Italy) and placebo were given as 100 mg/kg body weight daily (maximal 5 g/day) with 50 mL fluid/500 mg for four week each. The result confirmed that KGM was beneficial in the treatment of children with functional constipation.

Chen et al. [95] investigated the gastrointestinal response of KGM in volunteers and their stools were fully collected to determine the fecal mass, components, microflora, and short-chain fatty acid content. They found that the KGM supplement notably increased the mean defecation frequency (number/day), dry and weight stool weight (g/d) by ~27.0%, 21.7%, and 30.2%, respectively. The increased dry fecal mass was due to the presence of plant- and soluble materials. However, with the supplement of KGM the bacterial biomass such as lactobacilli, bifidobacteria and total bacteria found elevated in fecal mass (log counts/g wet feces) as examined by the fluorescence In Situ Hybridization methods. Moreover, KGM supplement also increased colonic fermentation as confirmed by decrease in fecal pH and increase in fecal short-chain fatty acids. Chen et al. [99] further investigated the supplementation of KGM into low-fibre-fed Chinese diet had promoted bowel movement and improved colonic ecology in constipated adults. A total of seven constipated subjects had participated in the diet controlled linear study that consisted of a 21 days of placebo period, seven days of adaptation period, and a 21 days of KGM supplement (1.5 g/d) period. Stools were collected from individual subject for analysis of colonic indices such as fecal microflora, pH, and short-chain fatty acid content. It was observed that KGM supplement slightly but significantly increased the weekly defecation frequency from 4.1 ± 0.6 to 5.3 ± 0.6 and slightly eased the bowel movement. The fecal weight (g/d) and percent moisture content were not significantly altered with fibre supplement. Moreover, the KGM intake increased the fecal concentration (log counts/g wet feces) of lactobacilli, bifidobacteria and total bacteria. In addition, fermentation of KGM resulted in greater concentrations of fecal acetate, propionate and butyrate and thus lowers the fecal pH. Chmielewska et al. [100] investigated the efficacy of KGM as a sole treatment for functional constipation. Children (aged between 3 and 16 years) with functional constipation were randomly assigned to receive KGM (2.52 g/day) or placebo for 4 weeks. It was observed that the primary outcome and treatment success (≥3 stools per week with no soiling) were similar in the KGM and placebo groups (relative risk 0.95). In the KGM group, the stool consistency score was higher at week 1, lower at week 3 and similar at weeks 2 and 4. Stool frequency was higher only at week 3 and week 4 but was similar among groups at weeks 2 and 3. No difference was observed in the frequency of any other secondary outcome of adverse effects.

Recently, Chiu and Stewart, [10] investigated the digestibility and fermentability of two different preparations of KGM *in vitro*, and studied their impact on human health. *Konnyaku* (yam cake made from *A. Konjac*), inulin, and guar, gum were subjected to *in vitro* digestion and fermentation. The fragmentated samples were investigated for gas volume, pH, and short chain fatty acid (SCFA) measurements. Organic acids like acetate, butyrate and propionate were measured with gas chromatography. The results of *in vitro* digestion confirmed that KGM and *Konnyaku* were resistant to degradation by digestive enzymes. In addition, fermentation patterns presented in this study provided a mechanism for the health benefits of KGM.

Supplementation of KGM has shown to relive constipation, which could be associated with increased stool bulk and promotion of the growth of lactic acid bacteria in colon; thus improved the colonic ecology [10,78,95].

### 4.4. Regulation of lipid metabolism, reduce blood lipid and cholesterol

The preventive effects of KGM have been observed in a number studies and found to regulate the metabolic parameters of blood lipids and cholesterol levels [7].

Zhang et al. [101] investigated the effect of food containing refined konjac meal on human lipid metabolism. A total of 110

elderly people with hyperlipidemia were randomly assigned to one of the two groups. The 'experimental' group consumed an ordinary diet plus foods containing refined konjac meal, and the 'control group' consumed only the ordinary diet. The experiment was carried out for 45 days. The results indicated that in the experimental group, blood levels of TG, TC, and LDL-C were significantly decreased at the end of the trial, whereas HDL-C and apoprotein (AI) levels were significantly increased. In contrast, for the control group, the changes in the above parameters were insignificant. It was observed that the effects of refined konjac meal on lipid levels in the blood were somewhat different between patients with hyperlipidemia and those with high risk critical values. For the former, TG and TC were decreased by $83.8 \pm 133.5$ mg/dl, and $42.4 \pm 23.4$ mg/dl, respectively; whereas for the latter, these values decreased by $-1.1 \pm 23.1$ mg/dl and $8.3 \pm 18.2$ mg/dl, respectively; the difference mentioned above was statistically significant.

Arvill and Bodin [102] investigated the effects of KGM on serum cholesterol concentrations in 63 healthy men (aged between 25 and 65 years) in a double-blinded crossover, placebo controlled design. The subjects were given identical gelatin capsules, each capsule containing 0.43 g KGM (active) or corn starch (placebo) in addition to 66 mg lactose and 10 mg magnesium stearate. Three capsules were given three times daily half- one hr before the meals (total daily amount 3.9 g KGM) with a glass of water. It was observed that intake of KGM fibre reduced the TC concentrations by 10%, LDL-C concentrations by 7.2%, TG by 23%, and systolic blood pressure by 2.5%. But, HDL-C and the ratio of LDL-C to HDL-C did not change significantly. In addition, no change in diastolic blood pressure or body weight was observed.

Livieri et al. [103] investigated the effectiveness of KGM on childhood obesity. The study has been carried out in 23 obsessed (aged 5.2–15.8 years) children with excess weight of $51 \pm 16\%$, treated with 2–3 capsules twice a day of KGM fibre (DICOMAN 5:2-3 gr/die), and in 30 obesed children (aged 5–18 years) with similar excess weight studied as control. In KGM-treated obsessed children, excess weight and TG levels had decreased drastically more than in obsessed controls, concomitant with decrease of cholesterol levels, but serum iron, calcium, copper and zinc contents remain unchanged.

More recently, Martino et al. [104] reported, "a low-fat, fiber-rich diet" is the first step in the management for hypercholesterolemic children. KGM has been demonstrated to lower the total and LDL-C.

The ability of KGM, especially in regulation of lipid metabolism, reduces blood lipid and cholesterol and can be a candidate for use as possible therapeutic tools for the treatment of several diseases such as diverticulitis, Crohn's disease or ulcerative colitis [5].

### 4.5. Anti-inflammatory activity

Anti-inflammatory refers to the property of a substance or treatment that reduces inflammation or swelling. Inflammation is a biological response to noxious stimuli such as pathogens that cause tissue and cell damage [105].

Onishi et al. [107] examined the effects of dietary pulverized KGM powder on scratching behaviour and skin inflammation in mice (4 week-old NC/Nga), a model of atopic dermatitis. They were fed with diet containing KGM and effects of cutaneous inflammation were evaluated (every 2 weeks) by histopathological analysis. Continuous KGM feeding caused significantly decreased eczematous skin lesion including hyperkeratosis, dermal mastocytosis and eosinophilia. Moreover, cutaneous over- productions of substances P, IL-10, IL-4, and TNF-α were restrained in KGM-fed mice. In a further study, Onishi et al. [108] investigated that feeding with KGM powder could prevent skin inflammation in a murine model of atopic dermatitis. KGM feeding suppressed allergic rhinitis-like symptoms in mice upon immunization and nasal sensitization with ovalbumin (OVA). The KGM-fed mice showed a much lower frequency of sneezing than in control animals. In addition, KGM-fed mice exclusively suppressed OVA-specific IgE response without affecting IgG1/IgG2 responses as well as systemic Th1/Th2 cytokine production. The result suggested that KGM supplementation could be a beneficial foodstuff in preventing nasal allergy such as seasonal pollenosis.

More recently, Vazquez-Velasco et al. [108] investigated the effect of high-fat squid-surimi diets enriched in KGM or KGM–spirulina on lipemia, liver glutathione status, antioxidant enzymes, and inflammation biomarkers was determined in Zucker Fa/Fa rats. Groups of eight rats, each received for 7 weeks the squid-surimi control (C), KGMenriched squid-surimi (KG) and KGM–spirulina enriched squid-surimi (KGS). The KGS diet improved superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase (GR) activities and reduced the endothelial (eNOS) and increased the inducible nitric oxide synthase (iNOS) and tumor necrosis factor-alpha (TNF-α) levels. The KGM-enriched and KGM with spirulina-enriched squid-surimi act as functional foods by reducing the oxidative and inflammatory status in Fa/Fa rats. Thus KGM enriched surimi diet induced hypocholesterolemic, antioxidant and proinflammatory effects.

### 4.6. Inflammatory bowel disease (IBD)

Inflammatory bowel disease (IBD) describes a number of multifactorial disorders which occur in the digestive system. The conditions of disease development in IBD are affected by the diet, life style and other susceptible endogenous factors including the gut microflora [109]. It has been suggested in recent years that the human bowel gut microflora produce antigenic factors which initiate the chronic immune inflammation of the bowel mucosa [110]. The chronic immune inflammation and subsequent immune responses cause these intestinal disorders including Crohn's disease (CD) and ulcerative colitis (UC) [111]. Carbohydrates may provide an alternative therapeutic approach for a number of digestive health disorders such as IBD.

Suwannaporn et al. [112] investigated the effect of low and high weight KGM hydrolysates within healthy volunteers and patients suffering from IBD and associated gut conditions. The KGM hydrolysates delivered several biological benefits such as capacity to bind pathogens and arrest them from binding epithelial cells of gut, stimulating topical healing, regulating immune systems, and ability to generate systemic immune responses. Moreover, the KGM hydrolysates act as soluble dietary fiber and as prebiotic.

### 4.7. KGM on absorption of vitamin

It has been suggested that high-fibre diets may be beneficial for diabetics since they reduce the post-prandial blood glucose and serum lipid levels but the exact mechanisms of their actions have not yet been clarified [113]. It is considered, however, that dietary fibres increase the viscosity of the gastrointestinal contents thereby retard the gastric emptying and delaying absorption by the intestinal wall [114]. Therefore, their viscosity appears to be a major factor in suppressing the post-prandial rise in the blood glucose level [115]. The highly viscid fibres such as KGM, guar gum and pectin appear to have the greatest effect on blood glucose and on lipid metabolism. The serum levels of cholesterol and bile acids decrease when the mucilaginous fibres are consumed.

Doi et al. [116] investigated the effect of KGM as dietary fibres. The subjects were given a control test meal, prepared by adding vitamin B12 (mecobalamin) and vitamin E (tocopherol acetate), after a 12 h overnight fast. Then, on the second day in the case of the normal subjects, and on the seventh day in the case of the diabetic

subjects, the subjects received a second test meal with 3.9 g KGM. Venous blood samples were taken immediately before the test meal and again after 1, 3, 5, 8, 12 and 24 h for analysis of vitamins. The absorption rate of vitamin E into the intestine was reduced when KGM was added to the test meals, but that of vitamin B12 was not reduced in normal or diabetic subjects. The results suggested that KGM reduces fat-soluble vitamin (Vit-E) absorption by removing bile acids, but does not reduce fat insoluble vitamin (Vit- B12) absorption in the intestine.

### 4.8. Prebiotic activity

In general, prebiotics can be considered as a 'food' for probiotics. Probiotics can be defined as "live microbial food supplements which benefit the health of consumers by maintaining or improving their intestinal microbial balance when taken in adequate/prescribed quantity" [117].

Chen et al. [118] conducted the time-course and dose-dependent studies to examine and compare effects of unhydrolyzed KGM with those of acid-hydrolyzed KGM (KGMH) on fecal microflora. In addition, short-chain fatty acid concentration in fecal content was also determined. Seven-week-old mice were fed 5% (w/w) with cellulose and KGM or KGMH diets for 2 or 4 weeks in a time-course study. In a subsequent dose-dependent study, mice were fed with ALN-93 (American Institute of Nutrition-93) fibre-free diets, supplemented with 2.5%, 5%, or 7.5% of KGM or KGMH for 4 weeks. The KGM and KGMH significantly increased fecal anaerobes and bifidobacteria counts at weeks 2 and 4, respectively, compared with the cellulose. In contrast, KGM and KGMH significantly decreased fecal *Clostridium perfringens* counts. In another study, Al-Ghazzewi et al. [119] investigated the potential use of KGMH (derived enzymatically from konjac flour) as a prebiotic for the growth of culture strains of lactobacilli and bifidobacteria grown on De Man, Rogosa and Sharpe (MRS) media or in UHT (Ultra High Temperature) processed milk supplemented with hydrolysates. The KGMH stimulated the growth of lactobacilli. Moreover, the number of colony forming units (CFU) obtained from milk containing the konjac hydrolysates were significantly ($p = 0.01$) higher than those containing inulin. Elamir et al. [120] determined the effects of depolymerized mannans and specifically KGMH on the colonic microflora of mice. In addition, blood glucose and cholesterol were also measured. Twelve-week-old Wister mice were used for a period of 14 weeks and fed with diet containing 5% KGMH. The KGMH promoted the growth of anaerobes and lactobacilli in treated mice, and significant decreased C. *perfringens* and *Escherichia coli* counts in fecal matter. Furthermore, there were increase in average daily feed consumption and weekly body weight in the treated group of mice. In addition, the mean ± SD (mmol/L) of blood glucose and cholesterol was lower in the treated group. Connolly et al. [121] investigated the prebiotic potential of KGMH by fermentation using batch cultures inoculated with human faeces. Bacterial enumeration was carried out using the culture independent technique, Fluorescent In Situ Hybridization (FISH), and short chain fatty acids (SCFA) production was monitored by gas chromatography. The KGMH selectively encouraged the production of beneficial gut microflora (bifidobacteria and lactobacilli). Moreover, the modulation of the microbiota by KGMH and inulin resulted in a propionic rich SCFA profile, which is hypothesized as a possible mechanism to reduce plasma cholesterol concentrations in humans.

Yeh et al. [122] determined the effects of diet containing 5% (w/w) unhydrolyzed KGM, and its acid-hydrolyaste fractions, with degree of polymerization (DP), on the cytotoxicity and DNA damage of fecal water Caco-2 cells. The results indicated that KGM, KGM-acid-hydrolysate fractions (KGMH), and oligofructose (as positive control) diets, showed an increase in the survival rate of fecal water-treated Caco-2 cells as compared to fibre- free diet. Moreover, acid-hydrolyaste fraction of KGM (partially hydrolysed KGM) exerted great positive effects, among KGM-based fibre, on fecal water-induced DNA damage. In addition, the prebiotic effects of partially hydrolyzed KGM were better than that of KGM. It has been concluded that the fecal probiotics may be the major mechanism for the beneficial effects of KGM and its hydrolysates in protecting against fecal water-induced DNA damage in Caco-2 cells. Al-Ghazzewi et al. [123] investigated that the symbiotic combination of lactobacilli with KGMH inhibited the growth of pathogenic bacteria such as *Staphylococcus aureus* and *S. typhinurium*. Growth of *S. aureus* and *S. typhimurium* was assessed individually and when mixed with *Lactobacillus acidophilus* in modified media supplemented with 2% KGMH. The results showed that prebiotic bacteria out grew the pathogenic bacteria in the presence of KGM in mixed cultures. Al-Ghazzewi and Tester [124] further investigated that the efficacy of cellulase and KGM hydrolysates (by β-mannanases) to promote the growth of lactic acid bacteria. Mannanases (β-mannanases) hydrolyse β-(1–4)-linked mannose residues randomly in mannans; whereas, cellualses (β-glucanse) hydrolyse β-(1–4)-linked glucose residues. The lactic acid bacteria growth profiles (expressed in colony forming units, as a function of time) in UHT milk containing KGM hydrolyzed with cellulase were significantly greater than those containing glucose (control) or konjac glucomannan mannanase hydrolysates.

Tester et al. [5] reported that KGMH could support the healthy re-colonisation of vaginal microflora post infections. A total of 26 female patients (12 controls and 14 treatments; aged between 18–25) were recruited for the study. The patients were randomly divided into two groups: one group received the antifungal treatment and the other group received a standard antifungal treatment plus pessary capsules containing 200 mg KGMH (twice a week for 30 days). It was observed that counts of *Candida* were diminished completely with antifungal treatment in both the groups. Further, the vaginal health recovery (post antifungal treatment for the *Candida* infection), especially the presence of healthy microflora could be re-established only with the introduction of KGMH in the vagina suggesting the benefits of KGMH in a vaginal health format.

Bateni et al. [125] investigated the prebiotic property and effect of KGMH with respect to improving skin health especially the reduction of infection due to acne vulgaris. Twenty six female volunteers (aged between 18–39 years) with active lesions of acne vulgaris were included for the study. Patients are assigned randomly into two groups to receive either a standard treatment or a spray formulation containing KGMH at a concentration of 5% (w/v). Before and during treatment, the skin was evaluated according to the acne severity index (ASI). The results showed that there was a significant improvement of the skin health at the second (20 days) and third clinical evaluation (40 days) for established (*e.g.* antibiotics) and KGMH treatments. Overall these data indicated that the KGMH could be used as a biotherapeutic agent for the treatment of mild to moderate acne in patients and as an adjuvant treatment for severe acne vulgaris. However, Horvath et al. [126] assessed the impact of KGM as the sole treatment for abdominal pain-related functional gastrointestinal disorders (FGIDs). A total of 89 eligible children, 84 (94%) completed the study and were assigned to receive KGM, at dosage of 2.52 g/d (1 sachet of 1.26 g 2 times a day), or a comparable placebo (maltodextrin) at the same dosage. The result suggested that the KGM was more effective than placebo in receiving therapeutic success in the management of abdominal pain in children.

From the studies discussed above, it envisaged that the unique properties of KGM hydrolysates make it valuable as a prebiotic that can be applied to a wide range of foods, feeds and pharmaceutical products. Therefore, KGM selectively stimulates the production of beneficial gut microflora like probiotics (bifidobacteria and lac-

tobacilli) and proclaims the treatment of abdominal pain-related functional gastrointestinal disorders.

### 4.9. Wound dressing

Few studies have evaluated the use of KGM-based materials in wound dressings applications. However, in recent years, scientists have attempted to apply KGM and KGM based conjugated biomaterials such as chtisoan (CS) as wound dressing materials [127]. These are found to be nontoxic, biocompatible, and provide antimicrobial activities on the wound surface. Moreover, KGM and KGM-based biomaterials can create a moist wound healing environment, absorb excess exudates, allow gaseous exchange, can be removed easily from the wound surface; thus easily acceptable by the consumers [127,128].

Fan et al. [129] prepared a novel wound dressings material from chitosan/KGM (CS/KGM) films embedded with gentamicin-loaded poly (dex-GMA/AAc) nanoparticles (giving GNP-CS/KGM films). The conjugated KGM based films are considered as promising novel biodegradable and biocompatible wound dressings with haemostatic capabilities and antibiotic effects for treatment of external bleeding injuries. To investigate the potential medical application of KGM, Huang et al. [130] treated KGM film with $Ca(OH)_2$ for investigation of its wound dressing potency. The *in vitro* 3-(4,5-dimethylthiazol-2-yl)-2,5- diphenyltetrazolium bromide assay (MTT-assay) was carried out for the biocompatibility of the $Ca(OH)_2$-KGM film with fibroblast and keratinocyte cells. However, an *in vivo* experiment was performed with Male Sprague-Dawley rats (250–400 g). The results indicated that the $Ca(OH)_2$-KGM film inhibited the absorption and activation of platelets, and effectively promoted wound contractility, particularly at an early healing stage. In addition, histological examination revealed markedly secretion and development of collagen and granulation tissue, respectively. The developed tissue further responsible for epithelial coverage (Days 7 and 14) of post surgery victim in wounds treated with $Ca(OH)_2$-KGM film. Shahbuddin et al. [131] synthesized a range of cross-linked KGMs and poly (*N*-vinyl pyrrolidinone) hydrogels for wound healing applications. The cross-linked KGM were found to be cytocompatible and stimulated fibroblast metabolic activity and also enhanced the migration of both fibroblasts and ketatinocytes. Al-Ghazzewi et al. [132] investigated the effects of ingested depolymerised KGM on minor wound healing in mice. The mice were divided into four groups of twenty each, and healing scores were recorded over eight days. The healing scores claimed stimulation of skin regeneration of wounded skin of mice.

KGM being a natural polymer possesses better biodegradability, biocompatibility, and non-toxicity and has remoulded ability than various synthetic materials [133]. It has a three-dimensional polymer network, and when placed in excess water, it readily swells and holds large volume of water without dissolution [134]. Due to this exclusive property, KGM acts as a bioactive reagent and is used in wound dressing application.

### 4.10. Treatment of hyperthyroidism

A limited study has been conducted with KGM on the reduction of serum thyroxin in hyperthyroidism patients. Azezli et al. [134] investigated the activity of KGM in the treatment of hyperthyroidism. A randomized, placebo-controlled, one-blinded study design was used with newly diagnosed 48 hyperthyroid patients (30 patients with Graves' disease and 12 with multinodulary goitre). They were assigned to various treatment groups (such as group I: with methimozole $2 \times 10$ mg, propranolol $2 \times 20$ mg, and KGM $2 \times 1.1.3$ g and group II:methimazole $2 \times 10$ mg, propranolol $2 \times 20$ mg, and placebo powder) daily for two months. It was observed that patients receiving KGM at the of the study had significantly reduce serum T3, T4, FT3 and FT4 levels of thyroxin as compared to patients receiving placebo.

### 4.11. Colorectal cancer

Colorectal cancer is one among the leading causes of cancer mortality (approx. 8.5%) worldwide [135,136]. Intake of dietary fibre as supplements provide protection against colorectal cancer by increasing colonic bulk, reducing transit time [137,138], and promoting the production of short-chain fatty acids, which leads to induce apoptosis, and differentiation of colon cancer cells [139]. Recent studies also suggest that probiotics, such as bifidobacteria and lactobacilli, may reduce the colon carcinogenesis [140,141]. The anti-carcinogenic effect of soluble dietary fibres may be partially mediated by their prebiotic effect [142,143]. Wu and Chen [86] investigated that KGM potentially reduced the high fat-induced risk in colon carcinogenesis. These soluble fibres also reduced the fecal lithocholic acid concentration and enhanced the fecal output of bifidobacteria and lactobacilli.

### 4.12. Effect on immune system

Administration of pulverized KGM prevented the development of allergic rhinitis-like symptoms and the increase of plasma immunoglobulin E (IgE) and G (IgG) levels in mice [5,106]. In this connection, several authors have reported that consuming hydrolysed KGM can help prevent atopic diseases by suppressing IgE production in mice [144]. Lin et al. [145] reported that KGM have immuomodulatory effect on immune organ development, and provide humoral, cellular and mucosal immunity. More recently, Onitake et al. [11] investigated the role of pulverized KGM in intestinal immunity in a mouse model of oxazolone (OXA)-induced colitis.

In conclusion, on consumption of KGM the serum biochemical-haematological values such as albumin, total protein, activity of creatinine, aspirate aminotransderase and alanine aminotransferase levels significantly get affected which enhances the process of biological detoxification in animals [146].

### 4.13. Antioxidant activity

Generally free radicals are produced in large amounts during metabolic disease conditions like atherosclerosis, urolithiasis, ulcers *etc.* [147]. They may cause damage to the organs and ultimately lead to fatal effects. Administration of anti-oxidants has a protective role to play. Several anti-oxidants of plant origin are experimentally proved and used as effective protective agents against oxidative stress. There are various plants which are used to treat the diseases like ulcer, diabetes, epilepsy and cardio vascular diseases [46]. One such plant is *Amorphophallus* spp.

### 4.14. Drug delivery

In recent years, researchers have focused on natural polymers including polysaccharides, cellulose derivatives, and proteins as drug carriers/drug delivery systems. These biomaterials have received considerable attention for their controlled release of drugs and targeted specific delivery sites [148].

Among the natural polymers, KGM is regarded as a potential carrier for site-specific bioactive protein drug delivery system. Xiong et al. [149] designed thermo-sensitive hydrogels drug carriers from KGM copolymerized with *N*-isopropylacrylamide. The influence of several parameters on the swelling properties of hydrogel was determined and *in vitro* release of model drug bovine serum albumin was studied at 20 °C and 30 °C in phosphate buffer solution. The release percentage hydrogel was found nearly 80%

and 30% after 5 h at 20 °C and 30 °C respectively. Yu et al. [150] developed composite hydrogels from KGM as the macromolecular cross-linking agent for chitosan in drug delivery systems. The composite hydrogels claimed effective targeted specific delivery sites. Korkiatithaweechai et al. [151] studied the controlled release of drug, diclofenac sodium from a chitosan-oxidized KGM polymer blended film. The controlled release of test drug showed the slowest release rate and gave the highest percentage of encapsulation efficiency. Nair and Jyothi [152] prepared cassava starch KGM based blend films suitability for the sustained release of a model drug, theophylline. The rate of drug release was positively correlated with the degree of degradation of the blend films. The study showed that the blend films with appropriate composition (cassava starch: $1.5 \times 10^{-3}$ kg and KGM: $1.5 \times 10^{-3}$ kg) was found relevant for the sustained release of the drug.

Colon targeting drug delivery systems allowed the local treatment of colonic diseases and constituted an alternative route for systemic absorption of drugs [153]. Liu et al. [154] prepared a novel pH-sensitive hydrogel by using KGM and poly (aspartic acid) as a suitable polymeric carrier for site-specific drug delivery in the intestine. The release profiles of test hydrogel from a model drug 5-Flurouracil were studied in simulated gastric and intestinal pH media. The results indicated that the hydrogel served as a potential device for the delivery of drugs in upper small intestine. In a further report, Liu et al. [155] prepared a KGM-based capsule for colon-specific drug delivery system. The capsule showed a typical pulsatile release profile with a lag time followed by a rapid release phase. Xu et al. [156] prepared hydrogels from KGM and poly (methacrylic acid) carrier for colon-specific drug delivery. *In vitro* drug release of hydrogels was investigated under different conditions using model drug 5-flurouracil. The results of *in vitro* drug release of hydrogels showed pH sensitive and specific of enzymatic degradation that are desirable in colon-specific drug delivery applications.

The formulated drugs for colon targeting drug delivery system are a highly effective pharmaceutical approach due to potential for specific degradation of excipients by colon enzymes [157]. However, for application KGM as disintegrating and coating material and their characteristics properties have to be assured considering the natural abundant of KGM.

### 4.15. Research on epidemiological study

Recently, several research groups have been carried out systemic review to evaluate the effects of KGM on health and disease conditions in defined populations. Xiang-Qun Liu and Lv [158] evaluated a systemic review of randomized controlled trials for the effects KGM on children with constipation. A meta-analysis was conducted using the random effects model. The result claimed that KGM moderately increases the defecation frequency of children with constipation. However, KGM consumption is not associated with a reduction in stool consistency. Zalewski et al. [159] studied a systemic review of randomized controlled trials to evaluate the effects of KGM on body weight and body mass index in healthy obese children and adults. The data suggested that KGM has the potential to reduce body weight but not body mass index in adults. However, the data in children were too limited to drawn a definite conclusion (Table 2).

## 5. Other uses of KGM

KGM and its derivatives were also used in many other applications such as in biotechnological and fine chemical fields. KGM can be used as encapsulating membrane which entails the holding of liquid without bursting through a temperature range of about −20 °C to about 90 °C [160]. They can be used in immobilization of cells such as recombinant *E. coli, yeast*, and *Bifidus bacillus* [161]. Moreover, carboxymethyl KGM–chitosan (CKGM–CS) nanocapsules were used for immobilizing enzyme (*e.g.* l-asparaginase) [161]. The immobilized enzyme has better stability and activity in contrast to the native enzyme [162]. KGM can also be used as fish feed binder [163,164].

Moreover, the solution and gelling properties of KGM and its interaction with other hydrocolloids including carrageenan and xanthan have been proved better means for coating and packaging in food applications [165]. Besides the applications in mentioned above, KGM and its derivatives were also used in the pharmaceutical area, such as prosthetic implants, bio-adhesive for healing effects, and recognize mannose receptor in signal transduction pathway [166–170].

## 6. *Konjac* starch and its application

Starch is the major caloric source in a variety of diets of people worldwide. It is an important ingredient in various tuber crops like cassava (*Manihot esculenta* Crantz), sweet potato (*Ipomea batatas* L.) and Elephant foot yams (*Amorphophallus* spp.). Two most important *Amorphophallus* species of economic importance are *A. paeoniifolius* [171] and *A. konjac* [23,172]. The functional properties of *A. paeoniifolius* starch and flour have been recently studied in production of composite flour [173] and food products developed from *A. paeoniifolius* tubers have been reviewed [171]. *Konjac* starch is the second major nutrient in *A. konjac* and only lesser than KGM [174,179]. It has been extracted from *A. konjac* K. Koch, using 0.1% (w/v) sodium metabissulphite solution [175]. The *Konjac* based foods like *Konnyaku* or *Shirataki* noodles are traditionally used in Japanese recipe. In china, the *A. konjac* is also used in many traditional foods such as *Moyu* or *Juruo*, due to its high starch content, light taste and elastic in texture [173,176].

A number of physiological effects have been described by several researchers, which have been proved to have health benefits [177,178]. The foods containing *konjac* starch moderate the rate of digestion, which influence the controlled glucose release profiles associate reduced glycemic response and insulin resistance of diabetes patients [172].

## 7. KGM *versus* other dietary fibre

Dietary fibre polysaccharides are of considerable physiological importance [15]. The fibre comprising plant cell wall polysaccharides and lignin (but not crude fibre) that affects human large bowel function is refereed as “dietary fibre” [180]. The dietary fibre acts in the colon depending on the extent to which they are digested by colonic microflora and water holding capacity of fibres [181–183]. The fibres having less water holding capacity are extensively broken down and unable to provide support for stimulation of colonic microbial growth (*e.g.* cabbage fibre). However, dietary fibre polysaccharide such as KGM and other soluble fibres (wheat, oats, minor millets, guar gum, pectin, and psyllium) remains largely undigested and retains water in gut lumen [184,189].

The KGM flour is used in the production of various types of food such as noodles, rubber jelly, and certain food additives [92,93]. For example, Japanese shirataki noodles, which are very low in calories, are composed of KGM flour [15]. It has been cultivated for centuries in Japan and KGM is known to be used as a food storage polysaccharide. It is well known as a “hunger suppressant” because it produces a feeling of fullness in stomach by forming a viscous solution that prevents absorption of the nutrients in food. The mechanisms by which KGM is regarded as an excellent dietary fibre include its extraordinary high water holding capacity that forms high viscous

**Table 2**
Applications of KGM.

| Applications of KGM | Responses/effects | Reference |
|---|---|---|
| *Local and traditional uses of KGM* | | |
| Food and food additives | 1.Thickening and gelling agent | [190] |
| | 2. Improved texture | [44,49] |
| Health applications | | |
| Blood glucose and cholesterol | Increased cholesterol binding | [102–104] |
| Constipation and diarrhoea | Stimulated gut transit, and controlled bowel movement | [112] |
| Body weight control | Approved body weight loss | [89] |
| Dietary fibre and Prebiotic roles | Regulated gastrointestinal microflora counts | [117] |
| Inflammatory bowel disease (IBD) | Positive effect on IBD | [112] |
| Intestinal micro-biota | Increased beneficial intestinal micro-biota | [120] |
| Immune system | Modulated immune system | [145] |

solution in water [178]. It has been reported that one gram of KGM can absorb up to 200 mL of water and has high viscosity at lowest concentration of any known dietary fibre [179].

## 8. Critical appraisal of KGM as a nutraceutical fibre

The information presented in this review show the potential nutritional and nutraceutical importance of KGM in improvement of health and well beings of human beings. KGM influences the digestion of food in general [15]. Konjac is an affordable source of storage carbohydrates, starch, soluble sugars, protein, minerals, crude fibres, and health promoting fatty acids [3]. Scientific studies have provided substantial evidences to support the actual/potential benefits of KGM in lowering the risks of various chronic diseases particularly in reducing the insulin needs of people with type II diabetes [76], altering lipid digestion [19,102] and cholesterol absorption [93], influencing the bile acid metabolism [23] and protecting against colonic cancer [86]. KGM has been widely considered as a dietry fibre that has also nutraceutical properties [10]. Intake of foods containing high levels of cholesterol harms human health. But, increase in the intake of KGM in diet is likely to mitigate these ill effects [19].

However, information pertaining to the role of KGM in human disease prevention and the mechanism of action are somewhat scanty. This is probably due to the complex nature of disease etiology and multiple factors that have impacts on their occurrence [23].

## 9. Research gaps

The KGM is an attractive dietary fibre that acts as a neutral hydro-colloid having significant health functions [116]. It has been widely used in food industry because of its good gelling, swelling and other properties [185]. In spite of several advantages of KGM, their applications in food industry and pharmaceutical processes limited due to highly perishable nature of fresh tuber. The tubers are prone to many abiotic (physiological disorders and mechanical injuries) and biotic (diseases and pests) stresses [15]. Therefore, there is a need of identifying effective storage methods to extend the shelf life of the tuber.

Moreover, though KGM have been traditionally utilized for so many years, KGM and its derivatives still need to be well investigated compared to other well established polysaccharides such as cellulose, starch, and chitosan. Thus, the challenge of understating its importance is being met an expansion of research in the biomedical arena.

## 10. Conclusions and future perspective

From the ongoing discussion, it is evident that KGM is a very versatile biomaterial and dietary fibre that can have wide applications in pharmaceuticals particularly in treatment of type 2 diabetes (reducing blood glucose), obesity, regulating lipid metabolism, diminution of constipation, treatment of hyperthyroidism, colorectal cancer, wound healing and antioxidant, antibiotics and prebiotic activities.

Over the last few years a number of KGM-based food products, food additives, and functional foods have been designed for human consumption. KGM and their derivatives have gained importance as a new source of dietary fibres and food ingredients. It has desirable physicochemical properties such as bland flavour, swelling, gel formation capacity *etc*. KGM also has beneficial properties such as increase in viscosity and water binding capacity. It can be used also in a wide variety of biomedical applications from wound dressing to restriction of the diffusion of glucose into the blood of diabetic patients. Moreover, number of KGM-based biomedical systems, intended for administration for different purposes have been invented. It is a better candidate for biomedical application as compare with synthetic polymers since it is both biocompatible and biodegradable. KGM-based biomaterials are used for constipation mitigation, control of blood glucose and cholesterol level (in case of diabetes and obesity), as antioxidant, as anti-inflammatory, and bioadhesive supplements and medical implants.

KGM can improve the textural and rheological properties of food products by regulating certain physico-chemical properties such as solubility, viscosity and water holding capacity.Although, KGM and its derivatives have been the focus of biomedical research in the recent years but yet the number of studies are far less as compared to other polysaccharides such as cellulose, starch *etc*. Despite the widespread consumption of konjac derived products in East and South East Asia, there has been limited research on the biology, processing and cultivation of the *A. konjac* species in the western world. Further research on newer product development from KGM-based polysaccharides need to be explored for potential applications in food, beverage, nutritional supplements as well as for biomedical purposes.

## Conflict of interest

None.

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