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Review

The hypoglycaemic effect of pumpkins as anti-diabetic and functional medicines

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ABSTRACT

Diabetes mellitus is considered as a common, growing, serious, costly, and potentially preventable public health problem. In 2030, the number of people with diabetes is estimated to increase from 117 million in 2000 to 366 million. The prevalence of diabetes has and will continue to have burden on the health and finances of economic climates, which in turn, will impact on individuals, families and nations. There are many different types of insulins available to treat diabetes, but there are still physiological consequences for such use. Alternatives are, therefore, required and this includes herbal preparations as well as dietary plants in the form of *curcubitaceae* (pumpkin).

Pumpkin is widely considered to have active hypoglycaemic properties. Pumpkin is a plant, which has been used frequently as functional food or medicine and belongs to the family Cucubitaceae, and consists of succulent stem with numerous seeds. Based on previous evidence of its fruit pulp, it is reported to have anti-diabetic effects.

This review has focused on the main medicinal properties of pumpkin and how this has been used in animal models, and point out areas for future research to further elucidate mechanisms whereby this compound may reduce disease risk.

Contents

1. Introduction

Cucurbitaceae is a plant family generally considered to consist of melons, cucurbits and pumpkins. Polysaccharides, proteins and peptides, para-aminobenzoic acid, and sterols are biologically active components, which are contained within pumpkins (Appendino, Jakupovic, Belloro, & Marchesini, 1999; Kuhlmann, Koetter, & Theurer, 1999). The leaves of pumpkins contain phytochemicals such as phenolic glycosides, 13-hydroxy-9Z, 11E-octadecatrienoic acid, in addition to proteins from germinated seeds (Bang et al., 2002; Koike, Li, Liu, Hata, & Nikaido, 2005). Much research has been written on the medicinal activities of these polysaccharides and proteins such as: 1) antibacterial (Hammer, Carson, & Riley, 1999); 2) hypocholesterolaemic and anti-oxidant (Kong, 2000); 3) immunomodulatory (Xu, 2000); 4) antimutagenic (Ito, Maeda, & Sugiyama, 1986); 5) anthelmintic (Diaz Obregon, Lloja, Lozano, & Carbajal Zuniga, 2004) and 6) anticancer properties (Xie, 2004). Despite the volume of research published, however, this

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review will only focus on the use of the hypoglycaemic properties of pumpkins for patients, who present with diabetes mellitus.

1.1. The prevalence of DM

In 2004, Wild presented the global prevalence of DM in 2000 and provided estimated projections for 2030 and stated that the number of diabetes patients would increase during the next 30 years (Wild, Roglic, Green, Sicree, & King, 2004). The most dramatic increases would happen in the Middle Eastern Crescent, sub-Saharan Africa, and India. In developed countries such as most areas in Europe, the majority of people with diabetes are older than 65; but in developing countries, most people with diabetes are aged between 45 and 64 years (Cockram, 2000). Wild et al. (2004) estimated that the number of people, who are older than 64 years of age with diabetes, will account for more than 82 million in developing countries by 2030; in developed countries this will be more than 48 million.

As is shown in Table 1, the 10 countries estimated to have the highest numbers of people with diabetes in 2000 and 2030 are listed. In both 2000 and 2030, the top three countries remain the same: India, China and U.S.A., Bangladesh, Brazil, Indonesia, Japan and Pakistan still appear in the top 10 lists from 2000 to 2030. The Russian Federation and Italy are in the list of 2000 but in 2030, it is envisaged that these will be replaced by Philippines and Egypt.

1.2. The burden of DM on health and economy

DM is a metabolic disorder caused by multifarious aetiologies (Alberti, Zimmet, & Shaw, 2006), including disturbances of carbohydrate, fat and protein metabolism (Fowler, 2010). The root cause is the defect in insulin secretion, insulin action, or both. Dysfunction, long-term damage and failure of various organs, especially the eyes, nerves, kidneys, heart, and blood vessels, can be affected by DM (ADA, 2010). People with diabetes are at increased risk of cardiovascular and cerebrovascular disease (CVS/CVD), new cases of end-stage renal disease (ESRD), lower-limb amputations, blindness and even death (ADA, 2007).

Gregg et al. (2000) and associates analyzed data on 6588 individuals (3475 women and 3113 men) with a history of diabetes, and U.S. civilians older than 60 years old (Gregg et al., 2000). The data was concerned with their health status and physical disability, and was carried out by five consecutive cross-sectional national surveys: National Health Examination Survey I (1960–1962), National Health and Nutrition Examination Survey (NHANES) I (1971–1974), NHANES II (1976–1980), NHANES III (1988–1994), and NHANES 1999–2000.

It is apparent that people with diabetes are more likely to have fair or poor health, cardiovascular diseases, and visual impairment compared to patients without diabetes. Diabetes mellitus also places a financial burden on the family as well as the nation. For people with diabetes, it influences the quality of life (QoL) and forces lifestyle changes such as the monitoring of blood glucose on a daily basis (Smyth & Heron, 2005). The total estimated cost of diabetes in the U.S. in 2007 was $ 174 billion, including $ 116 billion in excess medical expenditure and $58 billion in reduced national productivity (ADA, 2008). For a low-income country, for example Mexico, in 2005 the cost for diabetes was $ 317 million and the direct and indirect costs were approximately $140 and $177 million, respectively (Arredondo & Zuniga, 2004).

Table 1
List of countries with the highest numbers of estimated cases of diabetes for 2000 and 2030 (Wild et al., 2004).

Ranking	2000		2030	
	Country	People with diabetes (millions)	Country	People with diabetes (millions)
1	India	31.7	India	79.4
2	China	20.8	China	42.3
3	U.S.	17.7	U.S.	30.3
4	Indonesia	8.4	Indonesia	21.3
5	Japan	6.8	Pakistan	13.9
6	Pakistan	5.2	Brazil	11.3
7	Russian Federation	4.6	Bangladesh	11.1
8	Brazil	4.6	Japan	8.9
9	Italy	4.3	Philippines	7.8
10	Bangladesh	3.2	Egypt	6.7

Table 2
Diagnostic thresholds for diabetes and lesser degrees of impaired glucose regulation (Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 2003).

Category	Test	
	FPG	2-h PG
Normal	<100 mg/dl (<5.6 mmol/l)	<140 mg/dl (<7.8 mmol/l)
IFG	100–125 mg/dl (5.6–6.9 mmol/l)	–
IGT	–	140–199 mg/dl (7.8–11.0 mmol/l)
Diabetes	≥126 mg/dl (≥7.0 mmol/l)	≥200 mg/dl (≥11.1 mmol/l)

1.3. Diagnosis and classification of diabetes

After a series of deliberations, the new diagnostic criteria for diabetes including impaired glucose tolerance (IGT) and impaired fasting glycaemia (IFG) are recommended by the Expert Committee (Gavin et al., 1997). The range of fasting plasma glucose FPG levels between normal and diabetes was called "IFG", and that range for 2-h PG was named "IGF". IGF is between 100 and 125 mg/dl of FPG, and IGF is 140–199 mg/dl of 2-h PG (Table 2). As is shown in Table 2, normal fasting plasma glucose (FPG) is less than 110 mg/dl (5.6 mmol/L), and the cut-off point to separate diabetes and non-diabetes is an FPG ≥ 126 mg/dl (7.0 mmol/L) or a 2-hour post-load plasma glucose (2-h PG) ≥ 200 mg/dl (11.1 mmol/L). During the diagnosis of a patient with diabetes, it is important to distinguish a person presenting with gross hyperglycaemia and severe symptoms (Table 3) from an asymptomatic person more than one result is required to confirm the lower diabetic range (ADA, 2010).

1.4. Classification

1.4.1. Type 1 diabetes mellitus (T1DM)

T1DM is caused by β-cell destruction, and leads to absolute insulin deficiency (Cryer, Davis, & Shamoon, 2003), and this type of diabetes only accounts for 5–10% of those with diabetes (ADA, 2010). Because T1DM patients develop an absolute deficiency, they must depend on exogenous insulin (Atkinson & Eisenbarth, 2001). T1DM can be classified as immune-mediated diabetes (type 1A) and idiopathic diabetes (type 1B), and only a minority of patients with T1DM belong

Table 3
Criteria for the diagnosis of the diagnosis of diabetes (American Diabetes ADA, 2010).

1. A1C ≥ 6.5%. The test should be performed in a laboratory using a method that is certified by the National Glycohaemoglobin Standardization Program (NGSP) and standardized to the DCCT assay.

OR

2. FPG ≥ 126 mg/dl (7.0 mmol/l). Fasting is defined as on caloric intake for least 8 h.

OR

3. 2-h plasma glucose ≥ 200 mg/dl (11.1 mmol/l) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous dissolved in water.

OR

4. In a patient with classic symptoms of hyperglycaemia or hyperglycaemic crisis, a random plasma glucose ≥ 200 mg/dl (11.1 mmol/l).

to the latter one (Imagawa, Hanafusa, Miyagawa, & Matsuzawa, 2000). Although these two forms of T1DM usually happen in childhood, it can occur at any time in life, even in the 8th and 9th decades during the life (Fowler, 2010).

1.4.2. Type 2 diabetes (T2DM)

T2DM patients have relative rather than absolute (type 1 diabetes) insulin deficiency, or insulin secretory defect (Kahn, 2003), and constitutes more than 80% of all cases of diabetes (Raslova, 2010) . The relative insulin deficiency will at least present initially, and often throughout the lifetime of patients (Kahn, 2003). Frequently this form of diabetes remains undiagnosed for many years, because the hyperglycaemia is often not severe enough to be noticed with classic symptoms of diabetes and it develops gradually. Although there are many causes of this form of diabetes, the specific aetiologies until now are not known (ADA, 2010). The clinically obese state is usually seen in the majority of patients with T2DM, and obesity can cause insulin resistance in some degree. Thus, exercise, weight loss and health lifestyle can make improvements in the disease state and for some patients reduce clinical symptoms (Simpson, Shaw, & Zimmet, 2003). Unlike T1DM, certain type 2 pharmacotherapies are useful in boosting insulin sensitivity as well as increasing production of β-cell insulin (Rendell & Kirchain, 2000).

1.5. Pumpkins as anti-diabetic functional medicines

Pumpkin is a plant that has been used frequently as functional food or medicine. Pumpkin belongs to the family Cucubitaceae, and consists of succulent stem with numerous seeds (Saganuwan, 2009). The active hypoglycaemic properties which can be recovered from pumpkins are shown in Fig. 1 (Fu, Shi, & Li, 2006). The use of herbal preparations and dietary plants to replace Western medicine for the prevention and treatment of DM has attracted worldwide attention (Hunt, Arar, & Akana, 2000). In Mexico, DM is treated with herbal extracts, which are said to provide considerable benefit during the early stages of DM, and in records, 306 species of herbs can be used in the treatment of this syndrome (Adolfo & Michael, 2005). Chinese herbal drugs are estimated that more than 200 species of plants, including pumpkin and many other common plants, exhibit hypoglycaemic properties (Jia, Gao, & Tang, 2003). Many other countries, such as the former Yugoslav republics, Argentina, India, Brazil and America also use pumpkins traditionally as medicine for diabetes (Fu et al., 2006).

The active hypoglycaemic properties of pumpkins are shown to be active in the fruit pulp and seeds in normal animals, such as alloxan-induced diabetic rats and rabbits (Fu et al., 2006), and in humans, who are T1DM (Riccardi et al., 1999) and T2DM (Shi, Xiong, Cao, & Kang, 2003) patients. Pumpkin powder with sugar-removed and common pumpkin powder both showed a significant increase in plasma insulin and reduction in blood glucose (Ju & Chang, 2001). It has been demonstrated that water-extracted pumpkin polysaccharides possess superior hypoglycaemic properties compared to glibenclamide in alloxan-induced diabetic rats (Zhang, 2004). Additionally, pumpkin is rich in pectin, a type of dietary fibre (Fissore, Ponce, Stortz, Rojas, & Gerschenson, 2007), which when consumed is purported to control glycaemic levels and reduce the need for insulin when fibre-rich foods are consumed by patients with diabetes (Guillon & Champ, 2000).

1.6. Non-pectin polysaccharides

Preliminary investigations have proven that a pumpkin-rich diet has pharmacological activity in reducing blood glucose (Xiong & Cao, 2001; Zhang & Yao, 2002; Zhang, Wang, & Yao, 2002; Cai, Li, Yan, & Li, 2003). The protein-bound polysaccharides from pumpkin can be developed as new agents to anti-diabetic, because it can improve the tolerance of glucose, reduce the blood glucose levels and increase the levels of serum tolerance of glucose (Li, Fu, Rui, Hu, & Cai, 2005).

Xiong and Cao (2001) carried out experiments in alloxan-induced diabetic rats to prove that polysaccharide from pumpkins has this hypoglycaemic action. Alloxan is a specific β-cell toxic agent, which can selectively destroy the β-cells of many animals and cause experimental diabetes, so alloxan-induced diabetic rats are chosen as common animal models for studying the effectiveness of diabetic drugs (Bonner-Weir & Weir, 2005).

Fresh dutch pumpkin, *Cucumis moschata*, was taken and the protocol was followed according to yielding both polysaccharide (A) and polysaccharide (B). In order to set up diabetic rat model groups, 70 Wistar rats were provided: 10 of which were randomly taken as a control group, and the remaining 60 were injected with 1260 mg/dl (70 mmol/L) alloxan which lead to the glycaemic levels rising to above 324 mg/dl (18 mmol/L). Of the 60 rats, 50 diabetic rats were randomly

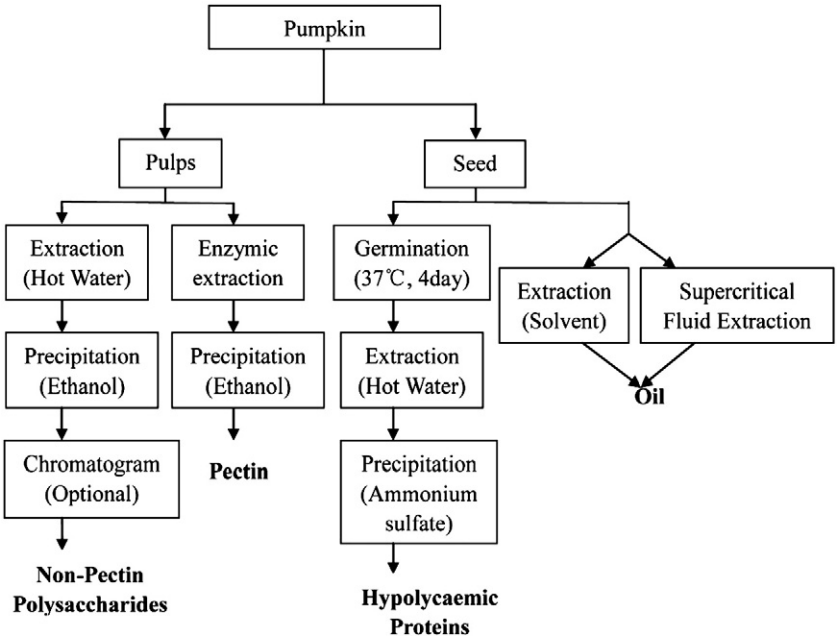

Fig. 1. Recovery for pumpkin anti-diabetic materials (Fu et al., 2006).

Table 4
The glycaemic levels of diabetic rats in response to different levels of purified pumpkin polysaccharide (Xiong & Cao, 2001).

Group	Dosage (g/kg)	Animal (No)	Mean value of glycaemia (mmol/L) (X ± S)
Control (NS)	50 ml	10	8.24 ± 2.99
Model (NS)	0.07	10	18.3 ± 2.72
Xiaoke	0.57	10	17.01 ± 3.14
Polysaccharide (B)	3.8	10	10.25 ± 3.10
Non-polysaccharide	6.88	10	11.06 ± 2.07
Polysaccharide (A)	6.88	10	10.34 ± 4.21

selected and divided into 5 groups: (1) model diabetic group without any treatment; (2) Xiaoke (Chinese medicine to relieve thirst of diabetic patients) to be a positive control group; (3) polysaccharide (A) group; (4) non-polysaccharide and (5) polysaccharide (B). Each group was given normal saline (NS), Xiaoke suspension, pumpkin polysaccharide extract (polysaccharide (A)), pumpkin polysaccharide (B) and pumpkin non-polysaccharide powder.

All drugs were given to fasting rats, twice a day for 21 days. After a fast of 12 h, (day 22), the glycaemic levels in response to different levels of purified pumpkin polysaccharides was tested (Table 4) and the general conditions observed every day: animals' hair, ingestion, drinking, quantity of urine production, body weight, breath and movements of limbs (Xiong & Cao, 2001).

The results indicated the mean value of glycaemia in the model and Xiaoke groups remained high. The 3 groups treated with drugs declined and showed significant differences, but there were no remarkable differences in comparison between the polysaccharide and pumpkin non-polysaccharide groups.

A study carried out by Gu and Li (2008) showed, besides polysaccharides, inositol and zinc (Zn), chromium (Cr), cobalt (Co), oil in ungerminated pumpkin seeds, and proteins from germinated pumpkin seeds also had a hypoglycaemic effect (Gu & Li, 2008). Additionally, Trigonelline (TRG) and nicotinic acid (NA) found in pumpkins also have anti-diabetic properties (Yoshinari, Sato, & Igarashi, 2009) but this is reported separately. Moreover, in observations of general conditions in diabetic rats, on the 2nd day after alloxan was injected, the symptoms of diabetes began to appear, including polyuria and polydipsia. However, improvements occurred in the groups of pumpkin non-polysaccharide and pumpkin polysaccharide: hair was bright and smooth, and water intake and micturition was reduced. The model group, at the same time, had rough hair covering, appeared lethargic and had noticeably increased urine production (Xiong & Cao, 2001).

Protein-bound polysaccharides (PBPP) can also be isolated from water soluble substances of pumpkin fruits by activity-guided isolation (Fu, Cai, Liu, & Li, 2007), and identified to consist of approximately 41.21% polysaccharides and 10.13% protein (Shan, Ren, & Tian, 2009). In 2005, Li carried out an experiment to test the exposure of PPBP in 5 groups. 1) Group 1, 10 normal rats; 2) Group 2, 12 diabetic untreated rats; 3) Group 3, 12 fed with 1000 mg/kg of PPBP; 4) Group 4, 12 fed with 500 mg/kg of PBPP and 5) Group 5, fed with 20 mg/kg of glibenclamide (Li et al., 2005).

Table 6
The comparison of treatment and control group though FPG test (Shi et al., 2003).

Group	Un-treatment (mmol/L) (X ± S)	Post-treatment (mmol/L) (X ± S)	The value of decline (mmol/L) (X ± S)
Treatment group	11.745 ± 3.486	8.781 ± 2.667	2.983 ± 2.783
Control group	10.964 ± 3.645	8.739 ± 2.779	2.324 ± 3.443

Table 7
The comparison of treatment and control group though 2 h-PG test (Shi et al., 2003).

Group	Un-treatment (mmol/L) (X ± S)	Post-treatment (mmol/L) (X ± S)	The value of decline (mmol/L) (X ± S)
Treatment group	16.415 ± 4.899	11.799 ± 3.280	4.516 ± 3.870
Control group	16.044 ± 4.584	11.888 ± 3.429	3.306 ± 4.199

Table 8
The comparison of treatment and control group through 24 h-urination test (Shi et al., 2003).

Group	Un-treatment (mmol/L) (X ± S)	Post-treatment (mmol/L) (X ± S)	The value of decline (mmol/L) (X ± S)
Treatment group	23.016 ± 33.409	14.543 ± 24.376	8.478 ± 16.455
Control group	20.619 ± 18.142	17.217 ± 13.432	6.402 ± 12.574

In Table 5, the data of the serum insulin, blood glucose and tolerance of Group 1 is significantly higher than Group 2, and the significant difference can prove the alloxan-induced diabetic rat models were valid. Group 3 and Group 4 which were treated with different doses of PBPP, and the fasting blood glucose levels were both significantly lower than those untreated diabetic rats (Group 2) as well as glibenclamide rats (Group 5). In addition, Group 3 (1000 mg/kg) showed excellent hypoglycaemic results compared to Group 4, where the rats were subjected to small doses of PBPP group. Based on these results, it suggests that the dose of PBPP can influence the effect of hypoglycaemia and possesses the possibility for PBPP to be developed into new anti-diabetic agents.

In clinical research, diabetic patients were observed in the treatment group with pumpkin polysaccharide granules and the control group with Xiaoke pills (Shi et al., 2003). During the therapeutic process, there were 30 T2DM patients with 17 males and 13 females in a treatment group, and 20 T2DM patients (9 males, 11 females) in control group. The age, course of disease and condition in both groups were similar, so the results of this clinical experiment were comparable. After treatment course 1, which lasted for 4 weeks, the plasma test of FPG (Table 6) and 2-h PG (Table 7), and urination for 24 h (Table 8) were compared. In comparing these groups, there is a reduction in both plasma glucose (including FPG (Table 8) and 2 h-PG (Table 9)) and urination (Table 8) in the treatment group. This showed that the pumpkin polysaccharide granules cannot only control glycaemia in T2DM but also have an effect compared to Xiaoke pills.

Table 5
The effect of PBPP on rats' blood glucose and tolerance of glucose and levels of serum insulin (Li et al., 2005).

Group	Dose (mg/kg)	Insulin (uIU/ml)	Blood glucose and tolerance at different hours after the treatment (mmol/l)			
			0	0.5	1	2
Group 1		109.2 ± 19.00	3.95 ± 1.15	7.30 ± 0.66	5.90 ± 0.72	6.02 ± 1.114
Group 2		62.5 ± 21.18	23.65 ± 11.17	27.33 ± 9.82	22.11 ± 10.33	20.14 ± 9.85
Group 3	1000	100.4 ± 33.89	12.64 ± 10.81	19.43 ± 10.90	14.81 ± 9.69	12.03 ± 9.46
Group 4	500	105.3 ± 30.21	13.23 ± 6.73	21.10 ± 9.76	15.28 ± 9.40	12.79 ± 9.18
Group 5	20	103.4 ± 38.73	13.84 ± 6.42	23.11 ± 9.27	18.13 ± 9.01	14.00 ± 8.56

Table 9
The results of two kinds of pumpkins' polysaccharides to affect blood glucose of diabetic rats (Zhang & Yao, 2002).

Group	Time (h)		
	0	7	11
	(mmol/L)	(mmol/L)	(mmol/L)
	(X ± S)	(X ± S)	(X ± S)
Untreated control group	5.24 ± 1.09	5.50 ± 0.71	5.22 ± 0.28
LCTPP group	15.33 ± 4.38	5.77 ± 1.46	5.80 ± 0.84
HCTPP group	14.70 ± 3.98	8.19 ± 2.54	9.23 ± 2.26
Negative control group	10.85 ± 0.92	13.15 ± 1.59	12.35 ± 1.85

Zhang and Yao (2002) carried out an experiment to show that different kinds of pumpkin polysaccharides have different hypoglycaemic effects and this was exemplified using alloxan-induced diabetic rats. Zhang's justification for this was that pumpkins contain varying levels of carbohydrates: high carbohydrate type pumpkin (HCTP) and low carbohydrate type pumpkin (LCTP). Firstly 10 normal rats were left as the untreated control group and 30 rats were injected with alloxan. The 30 diabetic rats were randomly divided into three groups: (1) LCTP group; (2) HCTP group and (3) negative control group untreated. Timeline plasma glucose measurements were taken: 1) pre-treatment; 2) 7 h post-treatment and 3) 11 h post-treatment. The results indicated that in the LCTP Group, plasma glucose levels declined from 15.33 ± 4.38 to 5.77 ± 1.46 (7 days) and 5.80 ± 0.84 (11 days). The HCTP Group showed a similar trend (Table 9). Despite these results, however, researchers need to bear in mind that the polysaccharide-nutrient components change during fruit development in pumpkin (Li, Fan, Liu, Yang, & Shen, 2006) and this change can be seen in Li's work, where the content of polysaccharide increases as a function of time. Whether this change was considered by Zhang in his work remains inconclusive.

Comparative experiments on alloxan-induced diabetic mice were also carried out using a water-soluble polysaccharide isolated with hot water from the fruit of *Physalis alkekengi* L., a traditional Chinese medicine herb (Tong, Liang, & Wang, 2008). This was fractionated with different concentrations of ethanol and purified by Sepharose CL-6B gel filtration chromatography.

The structural characterization and hypoglycaemic activity of the purified polysaccharide fraction (designated PPSB) were evaluated. PPSB (Mw = 27 kDa) is an acid heteropolysaccharide consisting of Ara, Gal, Glc and GalA in ratio of 2.6:3.6:2:1 with an □-configuration. It has a backbone composed of (1→5)-linked Ara, (1→6)-linked Gal with three branches attached to O-3 of (1→6)-linked Gal and terminated with either Gal or Gal and Glc, and all of Glc and the majority of GalA are distributed in branches.

Alloxan-induced diabetic mice (mentioned above) were divided into five groups (10 mice per group), and normal mice was used as the control. Group 1: Normal control (NC), normal mice treated with distilled water. Group 2: Diabetic control (DC), diabetic mice treated with distilled water. Group 3: PPSB-L, diabetic mice treated with 50 mg/kg of PPSB. Group 4: PPSB-H, diabetic mice treated with 100 mg/kg of PPSB. Group 5: Diabetic mice treated with 60 mg/kg of Xiangke Pill. All groups were administered orally by gastric intubation once a day. The consumption of diet and water, and body weight were recorded daily. After 7 days treatment with PPSB and Xiaoke Pill, sera from fasting mice were collected to detect blood glucose levels by glucose oxidase–peroxidase enzymatic method. Results showed that PPSB administered orally in alloxan-induced diabetic mice can significantly reduce blood glucose levels and water intake, and increase the body weight of diabetic mice compared with alloxan-induced diabetic control groups. The results suggest PPSB could be considered as a potential candidate for developing a new anti-diabetic agent.

Protein-bound polysaccharides and polysaccharides are the bioactive materials of pumpkin. Despite this, the relationship between the structure and function remain unclear. As a consequence of this, more detailed work is being undertaken in our laboratory in order to examine the relationship between amino acids and hypoglycaemic activity of protein-bound polysaccharides.

1.7. Conclusion

In the contemporary society, diabetes mellitus is considered as a common, growing, serious, costly, and potentially preventable public health problem. It is estimated that the number of people with diabetes will increase from 117 million in 2000 to 366 million in 2030. The prevalence of diabetes will bring a huge burden on the health and finances, which will impact on individuals, families and nations. The symptoms of diabetes itself, if managed in time, are not serious, but other severe pathological and functional changes may occur if the complications of diabetes are not addressed.

The popularity of pumpkin in various systems of traditional medicine has led to many investigators turning their attention to this plant. Considerable evidence from several studies concerning bioactivities have lead to experimentation in a number of animal models, cell culture studies and clinical trials designed to test pumpkin's pharmacological actions.

Pumpkin contains numerous phyto-constituents, which can be categorized into alkaloids, palmitic, oleic, linoleic acids and flavonoids. In addition, the important medicinal properties include acting as an antioxidant, an anti-carcinogenic, and an anti-inflammatory. The purpose of this present article was to also present the hypoglycaemic effect of pumpkins, which have the potential to act as anti-diabetic and functional medicines as well.

References

Adolfo, A. C., & Michael, H. (2005). Mexican plants with hypoglycaemic effect used in the treatment of diabetes. *Journal of Ethnopharmacology*, *99*, 325−348.

Alberti, K. G. M. M., Zimmet, P., & Shaw, J. (2006). Metabolic syndrome—A new world-wide definition. A consensus statement from the International Diabetes Federation. *Diabetes Medicine*, *23*, 469−480.

Appendino, G., Jakupovic, J., Belloro, E., & Marchesini, A. (1999). Multiflorane triterpenoid esters from pumpkin. An unexpected extrafolic source of PABA. *Phytochemistry*, *51*, 1021−1026.

Arredondo, A., & Zuniga, A. (2004). Economic consequences of epidemiological changes in diadetes in middle-income countries. *Diabetes Care*, *27*, 104−109.

AMERCIAN DIABETES ASSOCIATION (ADA) (2007). Diagnosis and classification of diabetes mellitus. *Diabetes Care*, *30*, S42−S47.

AMERCIAN DIABETES ASSOCIATION (ADA) (2008). Economic costs of diabetes in the U.S. in 2007. *Diabetes Care*, *31*, 596−615.

AMERCIAN DIABETES ASSOCIATION (ADA) (2010). Diagnosis and classification of diabetes mellitus. *Diabetes Care*, *30*, S62−S69.

Atkinson, M. A., & Eisenbarth, G. S. (2001). Type 1 diabetes: New perspectives on disease pathogenesis and treatment. *Lancet*, *358*, 221−229.

Bang, M. H., Han, J. T., Kim, H. Y., Park, Y. D., Park, C. H., Lee, K. R., et al. (2002). 13-Hydroxy-9Z, 11E, 15E-octadecatrienoic acid from the leaves of *Cucurbita moschata*. *Archives of Pharmacal Research*, *25*(4), 438−440.

Bonner-Weir, S., & Weir, G. C. (2005). New sources of pancreatic β-cells. *Nature Biotechnology*, *23*, 857−861.

Cai, T., Li, Q., Yan, H., & Li, N. (2003). Study on the hypoglycemic action of pumpkin seed protein. *Journal of Chinese Institute of Food Science and Technology*, *3*(1), 7−11.

Cockram, C. (2000). The epidemiology of diabetes mellitus in the Asia-Pacific region. *Hong Kong Medical Journal*, *6*, 43−52.

Cryer, P. E., Davis, S. N., & Shamoon, H. S. (2003). Hypoglycemia in diabetes. *Diabetes Care*, *26*, 1902−1912.

Diaz Obregon, Lloja, D., Lozano, L., & Carbajal Zuniga, V. (2004). Preclinical studies of *Cucurbita maxima* (pumpkin seeds) a traditional intestinal antiparasitic in rural urban areas. *Revista de Gastroenterología del Perú*, *24*(4), 323−327.

Expert Committee on the Diagnosis and Classification of Diabetes Mellitus (2003). Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care*, 26 Suppl 1:S5–20.

Fissore, E. N., Ponce, N. M., Stortz, C. A., Rojas, A. M., & Gerschenson, L. N. (2007). Characterisation of fibre obtained from pumpkin (*Cucumis moschata* duch.) mesocarp through enzymatic treatment. *Food Science and Technology International*, *13*, 141−151.

Fowler, M. J. (2010). Diagnosis, classification, and lifestyle treatment of diabetes. *Clinical Diabetes*, *28*, 79−86.

Fu, C. T. H., Cai, T., Liu, Y., & Li, Q. (2007). Some properties of an acidic protein-bound polysaccharide from the fruit of pumpkin. *Food Chemistry*, *100*, 944−947.

Fu, C., Shi, H., & Li, Q. (2006). A review on pharmacological activites and utilization technologies of pumpkin. *Plant Foods for Human Nutrition*, *61*, 73−80.

Gavin, J. R., III, Alberti, K. G. M. M., Davidson, Mayer, B., DeFronzo, R. A., Drash, A., et al. (1997). Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care*, *20*, 1183−1197.

Gregg, E. W., Beckles, G. L., Williamson, D. F., Leveille, S. G., Langlois, J. A., Engelgau, M. M., et al. (2000). Diabetes and physical disability among older U.S. adults. *Diabetes Care*, *23*, 1272−1277.

Gu, M., & Li, D. (2008). Pumpkin hypoglycaemic active ingredients progress in pharmacological research. *Journal of Medical Research*, *37*(5), 15−16.

Guillon, F., & Champ, M. (2000). Structural and physical properties of dietary fibres, and consequences of processing on human physiology. *Food Research International*, *33*, 233−245.

Hammer, K. A., Carson, C. F., & Riley, T. V. (1999). Antimicrobial activity of essential oils and other plant extracts. *Journal of Applied Microbiology*, *86*(6), 985−990.

Hunt, L. M., Arar, N. H., & Akana, L. L. (2000). Herbs, prayer, and insulin: Use of medical and alternative treatments by a group of Mexican American diabetes patients. *The Journal of Family Practice*, *49*, 216−223.

Imagawa, A., Hanafusa, T., Miyagawa, J., & Matsuzawa, Y. (2000). A novel subtype pf type 1 diabetes mellitus characterized by a rapid onset and an absence of diabetes-related antibodies. *The New England Journal of Medicine*, *342*, 301−307.

Ito, Y., Maeda, S., & Sugiyama, T. (1986). Suppression of 7, 12-dimethylbenz[a]anthracene-induced chromosome aberrations in rat bone marrow cells by vegetable juices. *Mutation Research*, *172*(1), 55−60.

Jia, W., Gao, W., & Tang, L. (2003). Antidabetic herbal drugs officially approved in China. *Phytotherpapy Research*, *17*, 1127−1134.

Ju, L., & Chang, D. (2001). Hypoglycemic effect of pumpkin powder. *Journal of Harbin Medicine*, *21*(1), 5−6.

Kahn, S. E. (2003). The relative contributions of insulin resistance and beta-cell dysfunction to the pathophysiology. *Diabeteologia*, *46*, 3−19.

Koike, K., Li, W., Liu, L., Hata, E., & Nikaido, T. (2005). New phenolic glycosides from the seeds of *Cucurbita moschata*. *Chemical & Pharmaceutical Bulletin*, *53*(2), 225−228.

Kong, Q. S. (2000). Studies on extraction and hypolipidemic activity of polysaccharides from pumpkin. *Chin J Biochem Pharmaceu*, *21*(3), 7−11.

Kuhlmann, H., Koetter, U., & Theurer, C. (1999). Sterol contents in medicinal pumpkin (*Cucurbita pepo* convar. citrullinina var. styriaca) depending on genotype and location. *Acta Horticulturae*, *492*, 175−178.

Li, X., Fan, W., Liu, Z., Yang, P., & Shen, J. (2006). The change of major nutrient component during fruit development of pumpkin (Cucurbita spp.). *Journal of Northwest Science Technology University of Agriculture and Forest*, *34*(7), 111−115.

Li, Q., Fu, C., Rui, Y., Hu, G., & Cai, T. (2005). Effects of protein-bound polysaccharide isolated from pumpkin on insulin in diabetic rats. *Plant Foods for Human Nutrition*, *60*, 1−4.

Raslova, K. (2010). An update on the treatment of type 1 and type 2 diabetes mellitus: focus on the insulin detemir, a long-acting human insulin analog. *Vascular Health and Risk Management*, *6*, 399−410.

Rendell, M. S., & Kirchain, W. R. (2000). Pharmacotherapy of type 2 diabetes mellitus. *The Annals of Pharmacotherapy*, *34*(7), 878−895.

Riccardi, G. G. R., Parillo, M., Turco, S., Rivellese, A. A., Ventura, M. R., Contadini, S., et al. (1999). Efficacy and safety of acarbose in the treatment of Type 1 diabetes mellitus: A placebo-controlled, double-blind, multicentre study. *Diabetic Medicine*, *16*, 228−232.

Saganuwan, A. S. (2009). Tropical plants with antihypertensive, antiasthmatic, and antidiabeteic value. *Journal of Herbs, Spices &Medicinal Plants*, *15*, 24−44.

Shan, J., Ren, F., & Tian, G. (2009). Structure characterization and hypoglycemic activity of a glococonjugate from atractylodes macrocephalae koidz. *Functional Plant Science and Biotechnology*, *3*(1), 36−41.

Shi, Y., Xiong, X., Cao, J., & Kang, M. (2003). Effect of pumpkin polysaccharide granules on glycemic control in type 2 diabetes. *Central South Pharmacy*, *1*(5), 275−276.

Simpson, R. W., Shaw, J. E., & Zimmet, P. Z. (2003). The prevention of type 2 diabetes: lifestyle change or pharmacotherapy? A challenge for the 21st century. *Diabetes Research and Clinical Practice*, *59*(3), 165−180.

Smyth, S., & Heron, A. (2005). Diabetes and obesity: The twin epidemics. *Nature Medicine*, *12*, 75−80.

Tong, H., Liang, Z., & Wang, G. (2008). Structural characterization and hypoglycaemic activity of a polysaccharide isolated from the fruit of *Physalis alkekengi* L. *Carbohydrate Polymers*, *71*, 316−323.

Wild, S., Roglic, G., Green, A., Sicree, R., & King, H. (2004). Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. *Diabetes Care*, *27*, 1047−1053.

Xie, J. M. (2004). Induced polarization effect of pumpkin protein on B16 cell. *Fujian Med Univ Acta*, *38*(4), 394−395.

Xiong, X., & Cao, J. (2001). Study of extraction and isolation of effective pumpkin polysaccharide component and its reducing glycemia function. *Chinese J Modern Application Pharmacy*, *18*, 662−664.

Xu, G. H. (2000). A study of the possible antitumour effect and immunocompetence of pumpkin polysaccharide. *J Wuhan Prof Med Coll*, *28*(4), 1−4.

Yoshinari, O., Sato, H., & Igarashi, K. (2009). Anti-diabetic effects of pumpkin and its components, trigonelline and nicotinic acid, on Goto–Kakizaki rats. *Bioscience, Biotechnology, and Biochemistry*, *73*(5), 1033−1041.

Zhang, Y. J. (2004). Study on the hypoglycemic effects and extraction and analysis of pumpkin polysaccharide. *Journal of China Jiliang University*, *15*(3), 0238−0241.

Zhang, Y., Wang, L., & Yao, H. (2002). Study on the biological effects and extraction of blood glucose lowering active component from pumpkin. *Food and Fermentation Industries*, *28*(6), 32−35.

Zhang, Y., & Yao, H. (2002). Study on effect of hypoglycemia of different type pumpkin. *Journal of Chinese Food Science*, *23*, 118−120.