The Pharma Innovation Journal 2024; 13(3): 268-285

www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277-7695
ISSN (P): 2349-8242
TPI 2024; 13(3): 268-285

www.thepharmajournal.com
Received: 13-01-2024
Accepted: 23-02-2024

Saloni Haldua
Dawley Parade, Dawley Road, Hayes, United Kingdom

Corresponding Author:
Saloni Haldua
Dawley Parade, Dawley Road, Hayes, United Kingdom

Study on the anti-diabetic properties of functional foods: A review

Saloni Haldua

DOI: https://doi.org/10.22271/tpi.2024.v13.i3d.25560

Abstract
The number of diabetic populations is increasing with much higher rate than predicted by various research authorities from various countries. Such drastic peak in diabetic population observed could be to changing lifestyle and unhealthy eating habits of majority of population. Mortality rates concerning with diabetes mellitus are higher in low-income countries due to lack of medical care and infrastructure. Diabetes mellitus is more dangerous when it invites other related complications like organ damage, retina and kidney damage, cardiovascular diseases and lack in the efficiency of nervous system. Various medicines are available which can administer orally or intravenously. These medications are efficient in reducing blood glucose levels of the body but in the same time they send signals to nervous system to stop the production of insulin permanently over a period of time as insulin is available in enough amounts from external sources. People tend to become dependent over medications for life time. In recent times, awareness regarding the clinical benefits of natural foods have been observed among researchers in order to treat diseases like diabetes mellitus and numerous natural foods which are anti-diabetic in nature. These foods inhabit hypoglycaemic compounds which helps in reducing blood glucose levels and trigger the production of insulin naturally. This study focuses on nutritional aspects, *in-vitro* and *in vivo* studies conducted on pumpkin, flaxseeds and oats specifically, in order to prove their hypoglycaemic effect on human body. The exact mechanism and pathways behind this hypoglycaemic effect is difficult to establish, still few researches have predicted the most probable mechanism and pathways which have been discussed.

Keywords: Anti-diabetic foods, diabetes mellitus, flaxseeds, health benefits, hyperglycaemia, hypoglycaemia, *in-vitro*, *in-vitro,* mechanism, oats, pumpkin

Introduction

Diabetes is becoming a global concern as the diabetic population is expanding with higher rate as compared to the rate predicted by researchers previously. Currently, the sum of diabetic people is projected to be 415million. Moreover, diabetes is a serious concern because it brings a greater number of related complications which can be chronic or acute, it decreases eminence of life and increases demand of healthcare funds. (Harding *et al*., 2019). WHO reported in 2022 that there were about 422 million adults living with diabetes in 2014, which was 108 million in 1980. Mortality rates related to diabetes has been increased by 3% between 2000 to 2019. About 2 million deaths have been recorded in the year 2019 due to diabetes and kidney diseases occurred due to diabetes (WHO REPORT, 2022).

According to estimates given by International Diabetic Federation (IDF) in 2018, 8.3% of adults are diagnosed with diabetes, among which 175 million people are undiagnosed population and total estimated number of diabetic people 382 million which was assumed to rise further (Klimova *et al*., 2018) [78]. According to IDF Diabetes Atlas, gestational diabetes is also increasing every year. Gestational diabetes is a type of diabetes mellitus. It is found in females during pregnancy, if not treated on time it may cause prenatal deaths, complications during pregnancy, obesity in infant and increases possibility of diabetes mellitus in mother during later stages of life. The data presented states that globally gestational diabetes mellitus have dominance of about 13.97-14.0% (Wang *et al*., 2022) [140]. In 2021, the global expenditure on diabetes related health products and services is estimated to be 966billion US Dollars, which is possible to increase to 1,054billion US Dollars till 2045 (Sun *et al*., 2021) [134]. Agreeing to the latest informs given by International Diabetes Federation (IDF Diabetes Atlas, 10th edition, 2021), a survey was conducted among the individuals belonging to age group of 20 to 79 and it concluded that about 536.6 million people have diabetes in 2021 which builds 10.5% of total population within this age band. IDF also estimated surge in the diabetic population to be 642.7 million by 2030 and 783.2 million by 2045.

This is a massive distress because these estimates are higher than the prior approximations which were around 578 million by 2030 and 700million by 2045 (Ref: IDF DIABETES ATLAS, Ninth edition, 2019). Thus, we can expect that the real-world estimates can be even worse. The situation is alarming with respect to type2 diabetes because 90% of the total diabetic population is diagnosed with type 2 diabetes exclusively (Hossain *et al*., 2022) [57].

Studies reveals that the prevalence of diabetes in seen more in urban (12.1%) areas than rural (8.3%) areas. The high-income (11.1%) countries were more prone to diabetes as compared to low income (5.5%) countries (Sun *et al*., 2021) [134]. This can be due to difference in the lifestyle of people living in urban and rural areas. Rural population is involved in rigorous physical activities like farming and animal grazing. Few other factors that are responsible for developing diabetes are heredity, obesity and auto-immunity. Genetic factor is most significant factor in the advancement of diabetes after 40 years of age. Risk is higher in people with HLA phenotype B8 and BW. A correlation has been found through experiments between obesity and heredity with onset of diabetes mellitus among elderly population (Setyawati *et al*., 2020) [122]. Type 1 diabetes (insulin dependent) and auto-immune disorder can exist together. It is generally found in children where body itself kills β cells and complete absence of insulin is exhibited by the body. Though recent in recent cases, it is not restricted to children but also observed in adults as well. It is also known as latent autoimmunity diabetes in adults (LADA) (Maddaloni *et al*., 2020) [93]. As the lifestyle and eating habits are changing there has been a tsunami of cases of diabetes around the world. Major population is restricted to their desk and hence no or little activity is possible throughout the day. This means a smaller number of calories are burnt within a day. Due to lack of time people are not indulging in physical activities like exercise, yoga, cycling, etc. BMI (Body Mass Index) below 25 kg/$m2$ is considered an ideal body weight and BMI above 25 kg/$m2$ is considered overweight (Schnurr *et al*., 2020) [120].

In order to deal with this global concern oral and intravenous medications are prescribed by doctors depending upon the severity. In addition to these functional foods can be consumed to maintain normal blood glucose levels, initiation of secretion of insulin naturally and reducing resistance to insulin. Functional foods were first termed in Japan during 1980s. Definition of functional foods can be confused by most people because these foods are not regulated legally in various countries. However, it is defined as foods that have positive effects on human body beyond regular nutrition when consumed regularly in considerable amounts, these foods not only include industrially manufactured foods but also fresh foods (Granato *et al*., 2020) [51]. Foods needs to undergo several clinical control trials in order to prove their health efficacy in order to claim health benefits and to be termed as functional foods (Assmann *et al*., 2014) [15]. Functional foods can also be defined as foods, if taken as integral part of diet, can provide additional health benefits associated with nutrients and bioactive compounds (Boggia *et al*., 2020) [20]. A food can also be said as functional food, if it provides protective, preventive and/or curative benefits in order to manage any disease in addition to basic nutrition (Kazeem *et al*., 2016) [75]. Considering foods that helps to manage diabetes or have anti-diabetic properties are classified into three types: insulin secreting foods, insulin sensitizing foods and insulin mimetic foods. Insulin secreting foods trigger β cells to produce insulin naturally, these include black cumin, field mushroom, soybean, cinnamon, mulberry, etc. Insulin sensitizing foods enhance the ability of insulin to convert glucose to glycogen, these include pineapple, green tea, buckwheat, sweet potato, flaxseed, etc. Insulin mimetic foods or some components of such foods behave like insulin, they include turmeric, pummelo, pumpkin, etc. (Venkatakrishnan *et al*., 2019) [139]. Pumpkin (*Cucurbita pepo*) belonging to Cucurbitaceae family is considered efficient in reducing blood glucose levels naturally. It contains several bioactive compounds which helps in reducing blood glucose level such as quercetin, chlorogenic acid, pumpkin polysaccharides and puerarin. Pumpkin polysaccharides and puerarin provide a synergistic effect and reduce insulin resistance (Chen *et al*., 2019) [27]. Similarly, flaxseeds (*Linum usitatissium*) belonging to Linaceae family contains α-linoleic acid and polyphenols and oats (*Avena sativa*) contain β -D glucan as anti-diabetic bioactive compound (Mechchate *et al*., 2021) [99] & (USDA, 2020). Flaxseeds and oats are found to be responsible for limiting the process of gluconeogenesis inside liver. Gluconeogenesis is basically development of new glucose molecules using non-carbohydrate components. Limiting this process ultimately helps in maintaining blood glucose levels (Mechchate *et al*., 2021) [99]. Similar effects are observed when Cuminum cyminum or cumin seeds are ingested regularly in a considerable amount. It is possible because it contains cuminaldehyde and cuminol as antidiabetic compounds (Allaq *et al*., 2020) [8].

From an industrial point of view, these bioactive compounds can be formulated in various food products in order to increase the health benefits of foods that are consumed daily such as omega-3 enriched oil, flour or bread fortified with folic acid and omega-3 fatty acid, yoghurt fortified with probiotic bacteria. Currently, market is flooded with such products which have been fortified and developed recently, these are acquiring attention among masses gradually. Considering, anti-diabetic food products, various drinks and tea are available have been developed using natural ingredients and bioactive compounds isolated from ayurvedic herbs such as senna leaves, guduchi, haritaki, bitter melon, *Cajanus cajan* and *Syzygium cumini*. Functional foods provide food industries a new area for research, production and development of new food products. Each type of food industries is at major advantage because of the growing demand of functional foods as functional food products are not industry specific and can be developed in any sector including dairy, bakery, beverage, meat and poultry, grain, oil, sugar and even water industries. Functional food sector is new branch in food market which needs to be nurtured in order to provide healthier options to consumers. (Altaf *et al*., 2022; Nataraj *et al*., 2020; Fatima *et al*., 2018) [10, 102, 47]

Concept of diabetes mellitus

Diabetes mellitus is considered as a long-standing disease which is progressive in nature which means that it becomes severe with time if not managed properly. Elevated levels of blood glucose are the main cause of the diabetes mellitus. The condition is known as hyperglycaemia. Diabetes mellitus is defined as, “a chronic disease due primarily to a disorder of carbohydrate metabolism, cause of which is deficiency or diminished effectiveness of insulin, resulting in hyperglycaemia and glycosuria.” (American Diabetes

Association *et al.*, 2020) [12].

In a healthy body, glucose metabolism cycle is initiated when food is digested in the stomach and blood vessels uptake glucose from stomach linings, this result in increase of blood glucose levels. This condition in healthy body triggers β islet cells in pancreas to release insulin. Insulin can work in two ways, it may stimulate glucose uptake from blood and provide it to cells to function or it may convert glucose to glycogen which is stored in liver (Chen *et al.*, 2019) [27]. Now considering lower concentration of glucose in human body, this condition trigger pancreas to release glucagon which stimulates breakdown of glycogen to glucose which increase glucose levels of blood as shown in figure 1. These glucose molecules are provided to the cells to perform their metabolic functions by the action of insulin.

This cycle is disturbed in diabetic condition as β cells of pancreas either stop reacting to the blood glucose levels or body stop responding to the insulin released (Evans *et al.*, 2019) [45].

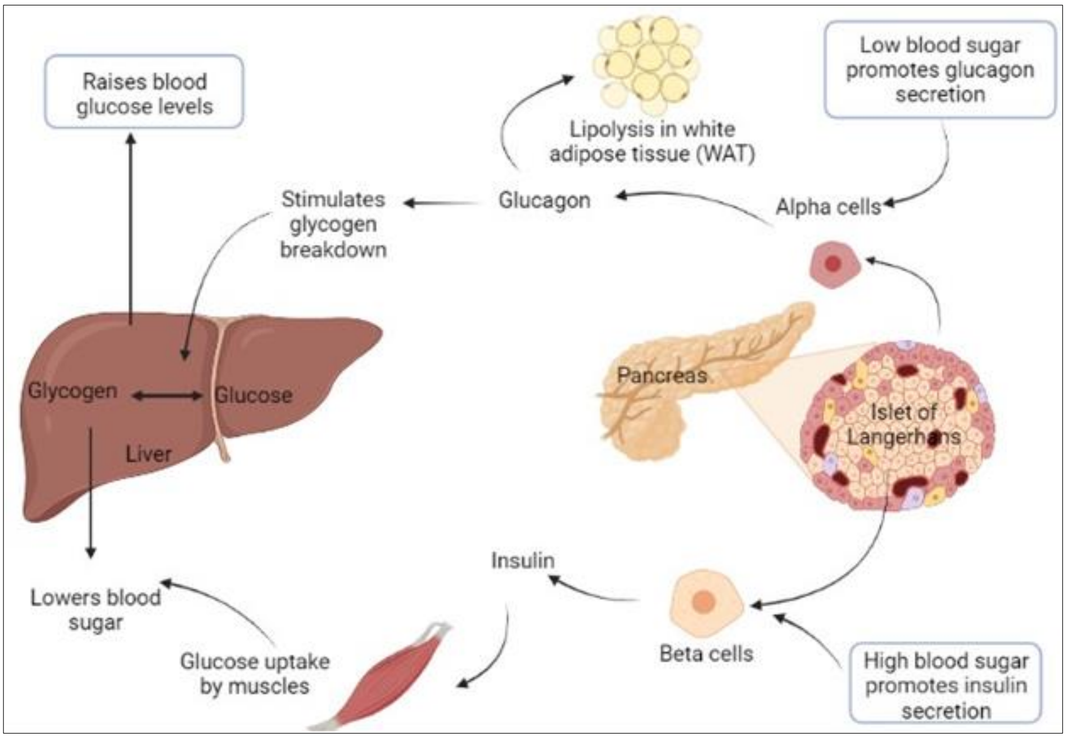


Fig 1: Regulation of glucose in blood in human body

Diabetes mellitus is generally categorized into two types, Type 1 and Type 2 Diabetes mellitus. Type 1 diabetes mellitus is generally found in young children and Type 2 diabetes mellitus is found in elderly population. In severe cases patients can experience complete organ damage, damage to retina, kidney, cardiovascular system, nervous system and severe joint pain. In severe cases, the blood glucose levels need to sustain between 7.8-10mmol/L with the help of medicines or intravenous insulin. (Codo *et al.*, 2020) [30] Recent developments have shown that a new problem is rising rapidly among diabetic population. It is known as hyperinsulinemia; it occurs due to high consumption of insulin or related products. It is a condition in which body become resistant to insulin administered orally or intravenously.

Types of diabetes mellitus

Considering the cause behind elevated blood glucose levels, the disease is classified as:

1. **Type 1 Diabetes:** It is an autoimmune disorder in which β islet cells in pancreas stop producing insulin naturally. The immune system damages and destroys β islet cells completely. It can occur at any age and immediate insulin treatment is necessary. It is generally observed in young children and teenage children. It should be detected and treated on time (American Diabetes Association 2020) [12]. Type 1 diabetes mellitus occur due to lack of insulin production body (Evans *et al.*, 2019) [45]. Its aetiology is not determined completely. Still, it is observed that glutamic acid decarboxylase, insulinoma-associated protein 2 and zinc transporter 8 are the antibodies present in β cells of islet of Langerhans in pancreas that are found responsible for the development of type 1 diabetes mellitus. These antibodies target β islet cell and destroy them, making them inefficient to release insulin. These antibodies are present much before the appearing symptoms of type 1 diabetes mellitus. Such patients tend to depend over insulin injections for lifetime as this disease does not have any cure.
2. **Type 2 Diabetes:** It is not an auto immune disorder in which body cells become resistant to the insulin produced by the pancreas. It is related to lifestyle and food habits and hence develops gradually with age. It is observed in old people and may occur due to environmental and genetic factors. There is no immediate requirement of insulin but can be dangerous in severe conditions. 90-95% of diabetic population suffer with type 2 diabetes (American Diabetes Association Professional Practice Committee, 2022) [11]. Insulin receptor (IR) contains two subunits alpha and β, insulin combines with alpha subunit and activates tyrosine kinase in β subunit. As soon as tyrosine kinase is effective, auto phosphorylation of β

subunit is increased. The phosphorylation result into protein substrates called protein kinase B (PKB) and a type of protein kinase C (PKC). This PKB produced is responsible for initiating glycogenesis and decrease in the production of glucose from hepatic system (Engin *et al*., 2021) [44]. An experiment was conduct on mice in 2010 to analyse the effect of PKB on blood glucose levels. A group of mice were impaired by disabling PKB and the other group was kept as control. When glucose were infused within both the groups, the control group exhibited normal metabolism of glucose and after a while the blood glucose levels were normalized. Whereas in other group with impaired PKB, the glucose levels increased and exhibited resistance towards insulin. This study depicted that the condition of insulin resistance is connected with the signalling effect of PKB (Engin *et al*., 2021) [44].

3. **Gestational Diabetes:** This is a disorder in which high blood glucose levels are observed during pregnancy. If not, regulated then it may cause complications during pregnancy. This can also increase chances of obesity in infant and Type 2 Diabetes (T_2) in mother (American Diabetes Association Professional Practice Committee, 2022) [11]. Gestational Diabetes generally occur during second and third trimester of pregnancy. During later stages of pregnancy, a decrease of 56% of insulin sensitivity is observed along with 30% of increased glucose production to meet the demand of glucose by the foetus and mother body. In case of normal pregnancy, the body replenish the increased requirements of insulin within few days. In contrast to this, during gestational diabetes the β cells of pancreas remain resistive to insulin demands (Johns *et al*., 2018) [67]. In addition to these, there are two more categories of intolerance of glucose. These are Impaired Fasting Glucose (IFG) and Impaired Fasting Glycemia. Such condition occurs between normal and diabetic. It increases the risk of cardiovascular diseases (American Diabetes Association, 2020) [12].

Management of diabetes mellitus

Diabetes mellitus is generally not suspected during early stage known as pre-diabetic stage. Pre- diabetes if recognized, can be treated and the complications can be reversed following measures mentioned below. Symptoms of diabetes mellitus are comparatively robust during later stages. Symptoms may include polydipsia, polyuria and polyphagia. Polydipsia is increase in thirst whereas polyuria and polyphagia are increase in urination and hunger, respectively. Diabetes mellitus becomes serious concerns when it brings related complications in the picture. These include cardiovascular diseases, loss of vision, problems related to nervous system, yeast infections, etc. (WHO REPORT, 2022). In order to avoid these complications few measures can save diabetics falling into fatal conditions which are discussed below:

Maintaining ideal body weight: The most reliable prevention technique is to maintain ideal body weight by performing physical activities and following a healthy diet. After implying the above prevention technique, Type 1 Diabetes is still inevitable, but the severity of the disease can be reduced. Calculating body mass index (BMI) is the easiest method to categorise on the basis of body weight and height of a person. A person having BMI below 25 kg/$m2$ is considered normal weight, between 25-30 kg/$m2$ is considered to be overweight whereas BMI above 30 kg/$m2$ is considered obese (Schnurr *et al.*, 2020) [120].

Eliminating sugar: The foremost task on detecting high blood glucose levels is to minimise or complete removal of table sugar from the diet. Although nutrition is most important factor effecting metabolism of a person. Proper nutrition from birth including enough calorie intake along with enough protein in diet helps body to sustain a normal weight and better metabolism which further helps in maintaining diabetes (Kaspar *et al.*, 2020) [68].

Including anti-diabetic functional foods in diet: Along with the pharmaceuticals there are various foods that have anti-diabetic properties. They must be incorporated in diet to maintain the blood glucose levels naturally. There are various food products that increase the production of insulin naturally without any side effects. Foods like pumpkin seeds, flaxseeds, oats, *Syzygium cumini,* etc. have anti-diabetic compounds which helps in reducing blood glucose levels and boost the production of insulin naturally. This prevents the person to be completely dependent over pharmaceuticals (Allaq *et al.,* 2020) [8].

Anti-diabetic functional foods are categorized on the basis of mode of action. The three categories are: insulin secreting foods, insulin sensitizing foods and insulin mimetic foods. Insulin secreting foods trigger β cells to produce insulin naturally, these include black cumin, field mushroom, soybean, cinnamon, mulberry, etc. Insulin sensitizing foods enhance the ability of insulin to convert glucose to glycogen, these include pineapple, green tea, buckwheat, sweet potato, flaxseed, etc. Insulin mimetic foods or some components of such foods behave like insulin, they include turmeric, pummelo, pumpkin, etc. (Venkatakrishnan *et al.,* 2019) [139].

Bitter gourd or *Momordica charantia* is one of the insulin secreting foods. It is a well-known remedy for treating diabetes mellitus. Within eight weeks of regular consumption can result in decreasing the symptoms of diabetes mellitus like polydipsia, polyuria, and polyphagia (Lu *et al.,* 2020) [89]. According to a study, an experiment was conducted on diabetic mice. Two groups of diabetic mice were observed for 28 days. One group was kept as control whereas the other group was administered with 400mg/kg body weight of bitter gourd pulp. After 28 days, the blood glucose levels were tested. Group 2 showed decrease in blood glucose levels as compared to group 1 which was kept as control. The insulin secretion was found to be increased in group 2 by 53%. The study further states that the two triterpenes (3β,25-dihydroxy-7β-methoxycucurbita-5,23(E)- diene and 3β,7β,25-trihydroxycucurbita-5, 23(E)-dien- 19-al) are the bioactive compounds which are responsible for increasing the phosphorylation of insulin receptor (IR) substrate (Venkatakrishnan *et al.,* 2019) [139]. Such foods along with their bioactive compounds are mentioned below in table 1.

Functional foods having anti-diabetic bioactive compounds

Various natural foods function as health foods or can be termed as functional foods because of the presence of components that provide additional benefits other than basic nutrition. These components may include polyphenolic compounds, flavonoids, anti-oxidant and nutrient dense foods.

They have anti-inflammatory, anti-carcinogenic, hypoglycaemic, immunity boosting and anti-oxidative effect on human body. Some of these foods are listed below in table 1 along with anti-diabetic components incorporated within them.

Table 1: List of Functional Foods with Anti-Diabetic Properties

S.no.	Health Foods	RDA	Anti-diabetic component	References
1.	Pumpkin	50g/day	Quercetin	Buzigi *et al.*, (2022) [23] Chen *et al.*, (2019) [27] Eid *et al.*, (2017) [90].
			Chlorogenic acid	Santana *et al.*, (2017)
			Pumpkin polysaccharides and Puerarin	Ji *et al.*, (2021) [66]
2.	Flaxseeds	20-30g/day	α linoleic acid	Mechchate *et al.*, (2021) [99]
			Polyphenols	Cheng *et al.*, (2019) [27]
3.	Oats	81g/day	β -D glucan	USDA, (2020)
4.	*Syzygium cumini* (Jamun)	NR	Cinnamaldehyde (cis/ trans), citric acid and oleanolic acid	Amin *et al.*, (2020) [13]
5.	*Cajanus cajan* (Pigeon Pea)	NR	Carotenoids, Vitamin C, Vitamin E, flavonoids, and tannins	Yang *et al.*, (2020) [150]
6.	*Trigonella foenumgraecum* (Fenugreek Seeds)	3-6g/day	Trigonelline	Idris *et al.*, (2021) [61]
7.	*Allium cepa* (Onion)	NR	*S*-methylcysteine and quercetin	Augustine *et al.*, (2021) [16]
8.	*Cuminum cyminum* (Cumin Seeds)	300-600 mg/day	cuminaldehyde and cuminol	Allaq *et al.*, (2020) [8]
9.	*Zingiber officinale* (Ginger)	4g/day	2-(4-hydroxy-3-methoxyphenyl) ethanol	Modi *et al.*, (2022)
	Brassica nigra (Mustard)	6g/day	Amino acids Fatty acids Vitamins and Minerals	De Zoyza *et al.*, (2021)
	Quinoa seeds	40g/day	Flavonoids, 20-Hydroxyecdysone (20HE), and phytoecdysteroids	Valenzuela Zamudio *et al.*, (2022) [138]
	Cranberry	300-900 ml juice/day	Polyphenols like Quercetin and p-coumaric acid	Dhalaria *et al.*, (2022) [34]
	Mulberry	40g/day	Anthocyanin and polysaccharides	Chen *et al.*, (2018) [26]
	Blueberry	74g/day	Anthocyanins and flavonoids	Spinola *et al.*, (2019)
	Pomegranate	1½-2 cup/day	Polyphenols like anthocyanins and ellagitannins	Makino-Wakagi *et al.*, (2019) [94]
	Citrus fruits	1-2 medium sized oranges (75-90mg of vitamin C/day)	Flavonoids like naringin	Ula *et al.*, (2018)
	Strawberry	NA	Polyphenols	Petersen *et al.*, (2019) [108]
	Grapes	NA	Flavonoids and Anthocyanins	Saratale *et al.*, (2020) [119]
	Guava	NA	Polysaccharides	Jiao *et al.*, (2018)
	Lycium barbarum	20-30g/day	Polysaccharides	Masci *et al.*, (2018) [98]
	Blackcurrent	NA	Polyphenols and antioxidants	Staszowska-Karkut *et al.*, (2020) [128]
	Lichi	200-400g/day	Oligonol	Zhao *et al.*, (2020) [154]
23.	Apple	200-250g/day	Quercetin, phloretin, phlorizin and procyanidins	Oliveria Raphaelli *et al.*, (2019) [32]
24.	Fermented soymilk with Rhodiola crenulata extracts	-	Phenolic compounds, antioxidants, and GABA (γ-aminobutyric acid)	Sivamaruthi *et al.*, (2018) [126]
25.	Ethanol extract of fermented rice bran and soybean	-	Phenolic compounds, antioxidants, and GABA (γ-aminobutyric acid)	Sivamaruthi *et al.*, (2018) [126]
26.	Rice wine made with Laminaria japonica J.E. Areschoug	-	Phenolic compounds, antioxidants, and GABA (γ-aminobutyric acid)	Sivamaruthi *et al.*, (2018) [126]
27.	Fermented papaya	-	Phenolic compounds, antioxidants, and GABA (γ-aminobutyric acid)	Sivamaruthi *et al.*, (2018) [126]
28.	LAB-mediated fermented Camu-camu and soymilk	-	Phenolic compounds, antioxidants, and GABA (γ-aminobutyric acid)	Sivamaruthi *et al.*, (2018) [126]
29.	Merlot grape pomace extract (MGPE)	-	Peonidin-3-O-acetylglucoside quercetin-3-O-glucuronide and isorhamnetin-3-O-glucoside Catechin	Kato-Schwartz *et al.*, (2020) [71]
30.	Moringa oleifera	-	polyphenols, carotenoids, alkaloids, terpenoids, and sulphur containing compounds	Ma *et al.*, (2020)
31.	Allium sativum	600-1200 mg/day	Allicin	Yee *et al.*, (2019) [152]
32.	Rice bran	-	Oryzanols, tocopherols, tocotrienols, phytosterols, β glucan and pectin	Saikiran *et al.*, (2019) [82]

33.	Wheat bran	-	Fibre, vitamin B6, thiamine, folate and vitamin E, sterols, alkyl resorcinol, ferulic acid, flavonoids, carotenoids, and lignans	Budhwar *et al.*, (2020) [21]
34.	Caulerpa racemosa	-	Phenolic compounds and flavonoids	Aroyehun *et al.*, (2020) [14]

Pumpkin as anti-diabetic

Pumpkin or *Cucurbita pepo* belongs to *Cucurbitaceae* family. It is grown once a year. It is cultivated in varied altitudes ranging from sea level to high altitudes. Most of the plant part have great medicinal value including edible seeds, greens, and fruits. It is well known for its edible seeds because it contains high amount of minerals, vitamins, antioxidants, phenolic compounds proteins, carotenoids, and essential oils. Pumpkin is considered as healthiest of all fruits because it is low in fat and high in protein content, especially the seeds. Seeds also contain high oleic acid content (Ceclu *et al.*, 2020) [20]. Pumpkin contains hypoglycaemic agents which includes biguanides, sulfonylureas and thiazolidinediones which can control hyperglycaemia. Pumpkin has active components like flavonoids, alkaloids, polysaccharides and polyphenols which are beneficial in diabetes mellitus by protecting from oxidative stress damage or increasing sensitivity for insulin and the combination gives better results than individual application (Chen *et al.*, 2019) [27].

***In-vitro* studies of pumpkin**

A series of experiment was conducted in which nutritional constituents of pumpkin peel, pumpkin fruit, and pumpkin seeds were analyzed. Pumpkin contains few components which helps in treating diabetes such as fibre, Vitamin B6, Vitamin C, Vitamin E, Mn, Mg, Zn, chlorogenic acid and quercetin. Pumpkin as whole is considered helpful in diabetes, but pumpkin seeds are most valuable because it contains aforesaid components in considerable amount. Mineral composition was compared which are beneficial in diabetes available in pumpkin peel, pumpkin fruit and pumpkin seeds. Manganese content is estimated to be 0.360 (mg/100g), 0.125 (mg/100g) and 1.47 (mg/100g) in pumpkin peel, fruit and seed, respectively. Magnesium content is estimated to be 3.353 (mg/100g), 12 (mg/100g) and 190.92 (mg/100g) in pumpkin peel, fruit and seed, respectively. Zinc content is estimated to be 0.150 (mg/100g), 0.32 (mg/100g) and 2.52 (mg/100g) in pumpkin peel, fruit and seed, respectively. Further vitamin concentrations were compared between pumpkin peel, pumpkin fruit and pumpkin seeds. Vitamins which can assist in reduction of blood glucose are vitamin B6, vitamin C and tocopherol. Vitamin B6 content is estimated to be 0.061 (mg/100g), 0.037 (mg/100g) and 0.155 (mg/100g) in pumpkin peel, fruit and seeds respectively. Vitamin C content is estimated to be 9.0 (mg/100g), 0.3 (mg/100g) and 1.89 (mg/100g) in pumpkin peel, fruit, and seed respectively. Vitamin E content is estimated to be 1.06 (mg/100g), not reported and 0.00714 (mg/100g) in pumpkin peel, fruit and seed respectively. Analysing the data, we can conclude that vitamin B6 and vitamin C is highest in pumpkin seeds whereas vitamin E content is highest in pumpkin peel. He also discussed anti-diabetic compounds in pumpkin as shown in table 3. These compounds include chlorogenic acid and quercetin. Chlorogenic acid have high ability to treat metabolic syndrome. It is highly anti- inflammatory and have anti-hypertensive activities as shown in table 2. (Santana *et al.*, 2017) Quercetin has high anti-diabetic capacity as mentioned in table 2 (Eid *et al.*, 2017) [90].

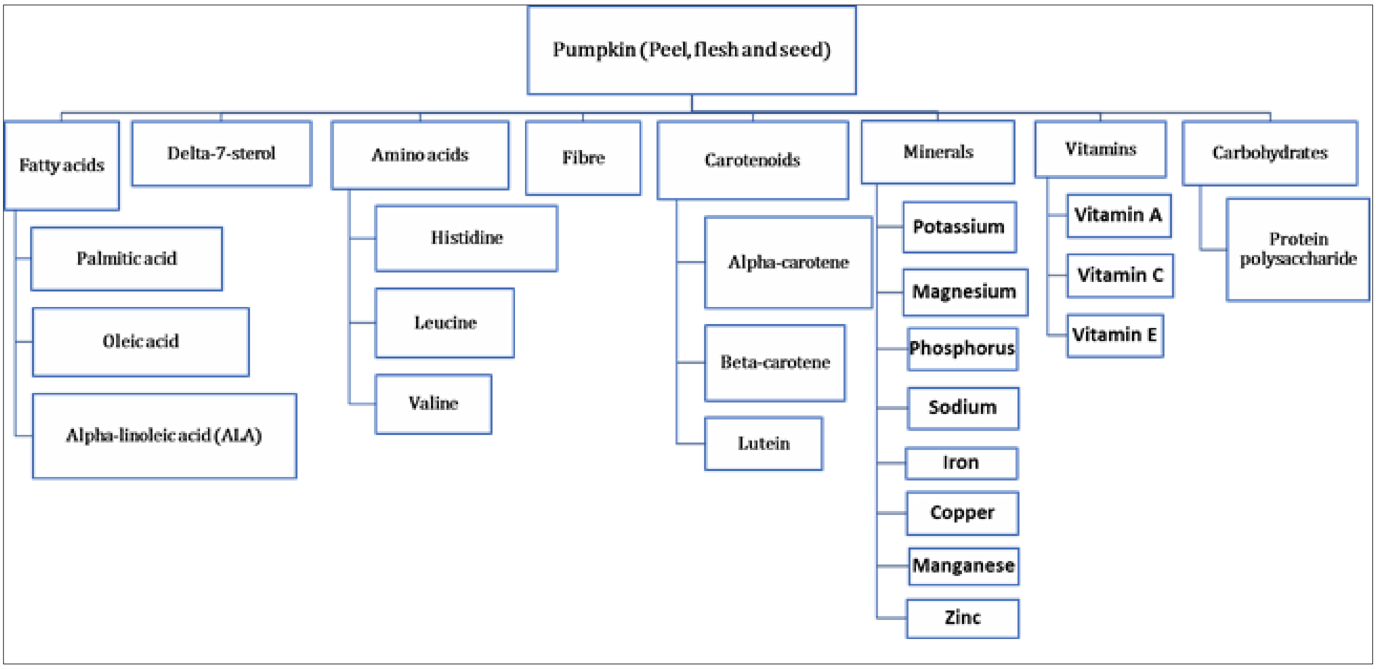
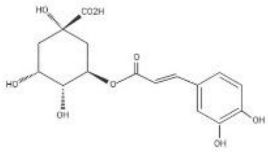
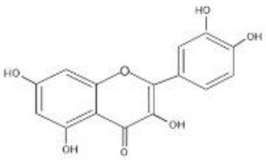
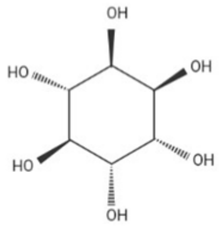
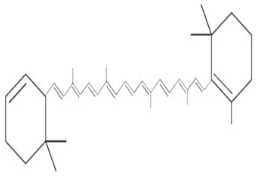
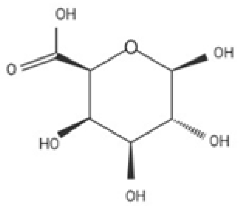
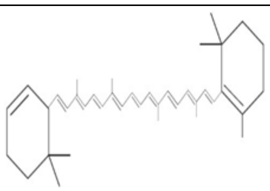
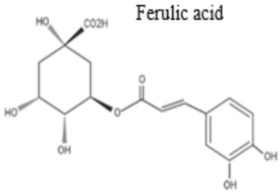
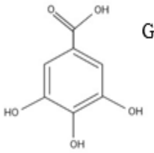
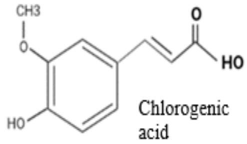
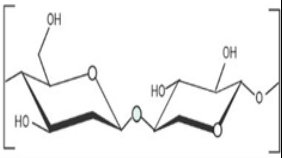


Fig 2: Constituents in Pumpkin Seeds, Peel, and Flesh

Table 2: List of Anti-Diabetic and Bioactive Compounds in Pumpkin, flaxseeds, and oats.

S. no.	Foods		Anti-diabetic compounds	Molecular Formula	Molecular structure	Molecular Weight (g/mol)	Health Effects	References
1	Pumpkin	Flees	Chlorogenic acid	C16H18O9		354.31	Used as a Management for metabolic syndrome, including antioxidant, anti- inflammator, antihypertensive activities	Santana *et al*., (2017)
			Quercetin	C15H10O 7		302.23	Great anti-diabetic potential	Eid *et al*., (2017) [90]
			D-chiro-inositol	C6H12O6		180.15	Increases β cell mass and insulin secretion.	Dowidar *et al*., (2020) [39]
			Phenolic phytochemicals	C6H5OH	-	200kDa to 3500kDa	Reduction in α amylase and α glucosidase activity	Kaur *et al*., (2020) [73]
			Protein bound polysaccharide	(C6H10O 5)n	-	NR	Increases the level of insulin and glucose acceptance.	Ji *et al*., (2021) [66]
			Carotenoids and minerals	C40H56	 (Alpha carotene)	536.9g/mol	Certain minerals which helps in reducing blood glucose levels are Manganese, Magnesium, Zinc, etc. are present abundantly in pumpkin fruit.	Hussain *et al*., (2022) [58]
		Peel	Pectin and fibre	C6H10O7		194.14	Interfere in the absorption of carbohydrates and fats	
		Seeds	Essential oils, proteins, phenols and minerals.	-	 Alpha linoleic acid	-	Certain minerals which helps in reducing blood glucose levels are Manganese, Magnesium, Zinc, etc. are present abundantly in pumpkin fruit.	Hussain *et al*., (2022) [58]
2.	Flaxseeds		Alpha linoleic acid	C18H30O2	 (Alpha carotene)	536.9g/mol	Certain minerals which helps in reducing blood glucose levels are Manganese, Magnesium, Zinc, etc. are present abundantly in pumpkin fruit.	Hussain *et al*., (2022) [58]

			Phenolic compounds (Ferulic acid, Gallic acid, chlorogenic acid etc.)	C10H10O 4 C7H6O5 C16H18O 9	 Ferulic acid  Gallic acid  Chlorogenic acid	194.12 g/mol 170.18 g/mol 354.30 g/mol	Lower blood glucose levels	Bekhit *et al.*, (2018) [19] Mechchate *et al.*, (2021) [99]
3.	Oats		β D-glucan	C18H32O 18		21-1100* 103g/mol (in rye)	Increase glucose and insulin response	Du *et al.*, (2019)

A similar study was conducted which estimated mineral content in pumpkin seeds. Magnesium content in pumpkin seeds is estimated to be 5,690 (mg/100 g), zinc content is estimated to be 113 (mg/100 g), and calcium content is estimated to be 346 (mg/100 g) as per dry weight The studies have illustrated the nutritional content of pumpkin seeds broadly. They have specified that pumpkin seeds are high rich in macronutrients and micronutrients. It has high content of P, Mg, Mn, Ca, Cu and Zn. The nutrient rich seeds have medicinal properties. It helps with anti-inflammation, anti-carcinogenic, antioxidant activity, anti-angiogenesis, anti-hyperglycaemic and antilipogenic effect. These medicinal benefits are possible due to presence of phytochemicals, such as tocopherol, triterpenes and carotenoids Fruit of pumpkin contain least quantity of fat 2.3 (g/100 g) as compared to other fruits, good amount of protein 3 (g/100 g), high content of carbohydrates 66 (g/100 g), and high levels of carotenoid quantity 171.9 (mg/g) as per dry weight basis matter analysis (Kaur *et al.*, 2019) [74].

In vivo studies of pumpkin seeds

A study was conducted using mild diabetic or having hyperglycaemic condition for small period but not in severely diabetic animals. It compared the activity of pumpkin with the standard drug known as tolbutamide. The pumpkin extract administered animals showed a similar change in the blood glucose levels as tolbutamide did over a period of time. The study states that this could be possible because of increase in the production of pancreatic insulin from β cells. In *Cucurbita ficifolia* the compound identified as insulin mediator is d-chiro-Inositol but the detailed explanation of the mechanism behind such result is left to be explained (Moya-Hernández *et al.*, 2020) [101]. Another study was conducted to analyse the properties of pumpkin and concluded that pumpkin have anti-diabetic properties and can be included in diabetic human diets. The mechanism and therapeutic side of pumpkin seeds are still left to be explored. (Rahayu *et al.*, 2020) [111].

Mechanism of anti-diabetic effect of pumpkin seeds

A study specified that epithelial cells of small intestine contain α-glucosidase. It acts on complex carbohydrates and break them into simpler sugars. Alpha-glucosidase act by cleaving glycosidic bonds present in complex carbohydrates. As a result, it increases blood glucose level (Patil *et al.*, 2020) [107]. Pumpkin is capable of lowering α-glucosidase activity. It is also oxygen species (ROS) and may perform angiotensin-converting stated that pumpkin can scavenge reactive enzyme (ACE) inhibiting activities. Further studies are yet to be performed in future to understand the effects of pumpkin on α amylase (Elam *et al.*, 2021) [42]. A study used rats as tools to study anti-diabetic effect of any therapeutic agent. Alloxan is the toxic compounds used to make rat diabetic by affecting β cells in pancreas and reducing insulin secretion. According to *in vivo* study conducted in 2019, on both pumpkin polysaccharide (PPe) and pumpkin polysaccharide hydrolysate (PPe-H) concluded that both facilitate in decreasing oxidative stress and stimulates GLP-1 secretion endogenously as shown in figure 3 (Chen *et al.*, 2019) [27].

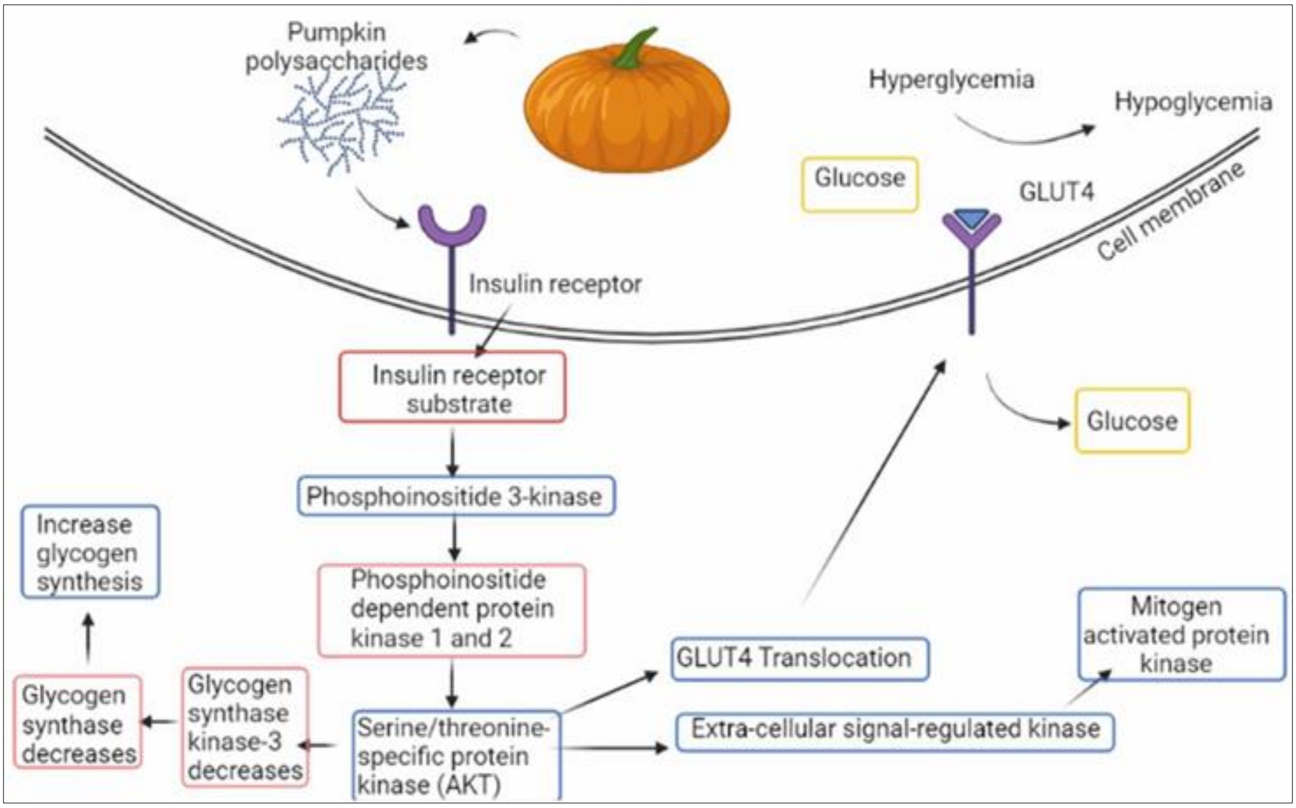


Fig 3: Mechanism of Pumpkin Polysaccharide Hydrolysate in the Treatment of Diabetes Mellitus Type-2. (Adapted from: Chen *et al.*, 2019; Ganesan *et al.*, 2019) [27].

Pumpkin exhibits hypoglycaemic properties in diabetic mice by increasing the insulin levels in plasma and providing a protective function to islet cells from streptozotocin (STZ) injuries by increasing the levels of SOD or superoxide dismutase (Wang *et al.*, 2017) [141]. Puerarin is an iso flavonoid. It is extracted from roots of Pueraria lobata. According to previous studies, it exhibits biological actions against diseases like cardiovascular diseases, gynaecological disease and osteoporosis. It is used as medicine traditionally (Dong *et al.*, 2018) [38], (Wang *et al.*, 2017) [141] and (Li *et al.*, 2017) [87]. Pumpkin polysaccharide with puerarin ease out the resistance against insulin hormone. Further P13k/AKT pathway goes on and the upregulation of Nrf2/ Ho-1 takes place.

A clinical study was performed in order to find the efficacy of pumpkin in treatment and control of Diabetes Mellitus. In a same manner pumpkin polysaccharides (PP) granules are proved to decrease postprandial sugar level through clinical study. (Ji *et al.*, 2023) [65].

Flaxseeds as anti-diabetic

Flaxseed or *Linum usitatissium* belongs to *Linaceae* family with blue flowers. It is a functional food with high Ω-3 fatty acid, high content of antioxidants, α-linolenic acid, dietary fibres (including cellulose, lignin, gums, mucilages) and lignan secoisolariciresinol-di-glucoside. Flaxseeds can range from light yellow to reddish-brown. It can be consumed in various forms like flaxseed oil, ground powder and whole seed (Sachan *et al.*, 2021) [116]. The bioactive compound in flaxseeds helps in anti- inflammatory action, lipid modulation properties and anti-oxidative activities. Flax milk is also an alternative of cow or soy milk or almond milk for people who are lactose intolerant or allergic to soy, gluten, and nuts. Moreover, it is observed that flax seeds contain higher nutritional value than almond milk (Parikh *et al.*, 2019) [104].

In-vitro studies of flaxseeds

The most important nutritional factor come into play when we talk of flaxseed is high content of α- linoleic acid (ALA) and no cholesterol or lactose. The total mass of flaxseed contains 32-45% of oil and 50-55% of α -linolenic acid. With all these benefits, there is less or limited talk of flaxseed products in market. The reasons can be the high omega-3 fatty acid content which goes under oxidation easily and produces rancid flavour, decreasing shelf life of the products. Flaxseeds have a characteristic bitter taste that makes it difficult to popularise flaxseed products in public hence the demand is less. Still 5-28% of the flaxseed products are incorporated in the bakery industry (Yang *et al.*, 2020) [150]. Research conducted in Fayoum University in 2022 concluded that total bioactive compounds in defatted flaxseeds contain 51.15% of flavonoids and 28.42% of total phenolic content (Fahmy *et al.*, 2022) [46]. Flaxseeds are identified as functional food with high content of omega 3 fatty acid, antioxidant content and preferably low carbohydrate content. It is comprised of 41% fat, 28% dietary fibre, 20% protein, 7.7% moisture content and 4% ash content. The active components of flaxseeds are the dietary fibre (including cellulose, gums, mucilage and lignin), omega 3 fatty acid and phytochemicals (Zarzycki *et al.*, 2020) [153]. Few phenolic compounds are available in flaxseeds which are beneficial in treating diabetes. The most important phenolic compounds are ferulic acid (313mg/100g of defatted flaxseeds), gallic acid (17mg/100g of defatted flaxseeds) and chlorogenic acid (1435 mg/100g of defatted flaxseeds) which are responsible for lowering blood glucose levels. These phenolic compounds are present in abundance in flaxseed extract. Analysing data presented by Bekhit in his study, we can say that defatted sample increases extraction for most of the phenolic acids from the sample as mentioned in table 2 (Bekhit *et al*., 2018) [19]. A quantitative analysis of polyphenols available in flaxseeds were analysed using a method liquid chromatography with mass spectrometry (LC-MS/MS). They found that there are 18 number of polyphenols present in flaxseeds as unbound polar fraction. Some of these polyphenols have proven anti-diabetic in nature. Polyphenolic extract was prepared using flaxseeds by washing, sun drying and grinding into fine powder. Before extraction the powder is defatted as it contains high amount oil by taking 10g of flaxseed powder at a time and washing in hexane (30mL x 3). This continued till the clear solution is obtained. Followed by the extraction process. The extraction was carried out using ultrasonic assisted extraction apparatus for 40 minutes at 35kHz frequency, 10g of defatted powder was mixed with methanol having strength of 70%. Using Whatman filter paper No. 5 the extract was filtered out. It further concentrated till it becomes dry. Again, it was extracted with 1-butanol (x2) after adding distilled water. This gave the polyphenolic fraction (PLU). It was stored at 4-degree Celsius (Mechchate *et al*., 2021). Subsequently, *in-vitro* α-amylase inhibitory activity was examined using spectrophotometer. For positive control, acarbose was used which is a α- amylase inhibitor. Each experiment was conducted three times to confirm the results. To determine the α amylase inhibitory activity the sample absorbance is subtracted from control absorbance, divided by control absorbance and multiplied by hundred. Values for inhibiting 50% of amylase activity for acarbose solution and flaxseed solution were determined. The results showed that enzyme inhibition is depending on the dose given each time, as the quantity of flaxseed extract or polyphenolic fraction (PLU) affected the extent of amylase inhibition. The ability of flaxseed extract or polyphenolic fraction (PLU) to inhibit amylase. The positive control value came out to be 0.717 ± 0.054 mg/ml whereas values for PLU was 0.351 ± 0.164 mg/ml. Thus, PLU lowers the blood glucose levels (Mechchate *et al*., 2021) [99].

***In vivo* studies of flaxseeds:** Various *in vivo* research has been conducted to analyse the anti-diabetic properties of flaxseeds. Some of the studies are discussed below:

In an experiment, hyperglycaemic rats were used for determining the effect of flaxseeds in order to tackle diabetes. They were given 10g of flaxseed powder. When diabetic rats were examined, it was found that their overall biochemical profile illustrated improved results. The biochemical profile includes lowering of HDL-C levels and increase of VLDL, TG and small and dense LDL-C levels. Improvement in glucose homeostasis was also observed which improve β cell function present in the pancreas and increase the secretion of insulin and improving sensitivity as well. They concluded that flaxseed supplementation helps in controlling hyperglycaemia, improving lipid profiles and hence decreasing secondary complications associated with diabetes as well (Noureddin Soltanian *et al.,* 2018). An *in vivo* study analysed the effect of flaxseed extract (PLU extract) on diabetic mice. Alloxan induced diabetic mice were given different doses of the extract and the decrease in the blood glucose levels of mice varied along with it. Moreover, a substantial decline in body weight of mice were also observed. When they administered 25mg/kg body weight dose for 1 week the reduction in blood glucose level came out to be 64% whereas when they administered the extract at the rate of 50mg/kg body weight reduction in blood glucose levels was observed to be 45%. Hence, this experiment also shows that flaxseeds are capable of decreasing blood glucose levels (Mechchate *et al*., 2021) [99]. Also, in a study conducted on diabetic mice stated that the antioxidant activity is also improved when effective dose of 30mg/kg body weight of flaxseeds were given (Ebrahimi *et al*., 2021) [41]. Another study conducted on pre- diabetic; overweight individuals for 14 weeks concluded that supplementation of flaxseed oil has another benefit i.e., weight loss and improvement in BMI indices of individuals (Hajiahmadi *et al*., 2020) [53].

Mechanism of anti-diabetic effect of flaxseeds

Gluconeogenesis is a process of development of new glucose molecules using non-carbohydrate compounds. After administration of flaxseed polyphenolic extract, gluconeogenesis process diminishes inside liver as phosphoenolpyruvate carboxykinase (PEPCK) gene becomes inefficient for coding for rate-limiting enzyme which is accountable for gluconeogenesis in liver. (Yari *et al.,* 2021) [151]

Oats as anti-diabetic

Oat is one of the cereals hence comes under *Poaceae* family. Its scientific name is *Avena sativa.* It is considered different from other cereals because it has multifunctional properties and vast nutritional profile. Recently many research and developments have been made to reveal the health benefits and nutritional value of oats. It contains high fibre content specifically β-D glucan, minerals and other nutrients which make it beneficial for cardiovascular health and it can be used for treating diabetes (Sun *et al.,* 2021) [134].

***In-vitro* studies of oats:** Oat bran have high amount of vitamin B complex, fat, minerals, proteins and most importantly β glucan which is a soluble fibre. It effects postprandial plasma glucose and insulin response. It also effects excretion of bile salts in lower part of intestine and hence decreases the chances of coeliac disease in human body (Sun *et al*., 2021) [134]. Oats or *Avena sativa* is dual purpose crop because it is used for individual consumption as well as for cattle feed. This increases the commercial value of crop. It contributes about 60% of the total food produced throughout the world. It provides 50% of total requirement of protein and energy in human diets. Comparing to other whole grains, oats contain abundant quantity of zinc, iron, fibre and protein. Oats are unique among other cereals because it is therapeutically active. It helps in diabetes, hypertension, vascular injury, and dyslipidaemia. It is richest and economical option for soluble dietary fibre for customers. Without any clear information about the mechanism, oats are always regarded as healthy and good for lowering cholesterol. Oats contains high amount of starch which is estimated on an average of all the available species to be 60%, protein 13- 20%, crude fat 2-12% and β-D glucan 2.0-7.5% (El-Kholie *et al*., 2020) [43]. Polyphenols present in oats are unique, these are known as avenanthramides which has 10-30 times more antioxidant capacity than other antioxidants available in various cereal grains like ferulic acid and vanillic acid (Algonaiman *et al*., 2022) [6]. Oats contain high amount of dietary fibre (9g per 100g) which helps to control diabetes related complications like cardiovascular diseases. The most important component present in oats is β glucan which is readily available and have multiple bioactive and functional properties. It helps in lowering diabetes, control cardiovascular diseases by reducing absorption of cholesterol (Divya *et al*., 2020) [36].

In vivo studies of oats

There are several studies conducted to understand the effect of oats and oat β-D glucan on streptomycin induced diabetic mice. Some of them are discussed below:

Research was conducted to find mechanism behind the decrease in blood glucose levels when diabetic rats were induced with oat β-D glucan. In this study, they found that there was a significant increase in hepatic insulin resistance when these groups were compared with the negative model group (NM). According to them, some studies have said that the β d glucan is absorbed from the small intestine and enters lymph circulation. They observed that hepatic GK increased and hepatic G-6 pase decreased in the oats β-D glucan group or OBG group which further implies that β-D glucan can transmit more amount of glucose from blood to liver by suppressing the gluconeogenic pathway and glycolytic pathway. They also mentioned in their study that histopathological investigation exposed that administering β-D glucan can restore and improve the functioning of pancreatic islet β-cells (Wang *et al.*, 2023) [145]. They also found that high molecular weight β-D glucan can improve the functioning of pancreatic islet β-cells more effectively in diabetic mice than medium and low molecular weight β-D glucan. Thus, this study demonstrates that β-D glucan has a hypoglycaemic effect on diabetic mice which is streptozotocin-nicotinamide induced and non-obese type (Wang *et al.*, 2023) [145]. Hypoglycaemic effect of oats extract on hyperglycaemic mice were examined. Mice were grouped according to the treatment given to them. Group Am and F11 were orally administered with oat extract (2000mg/kg), Met group given metformin (300mg/kg) and control groups NC and DC were given an equal amount of water. Blood samples from tail vein were collected at regular intervals (0, 30, 60, 90, 120 and 150 min). They found out that after oral administration of glucose, the blood glucose rises to peak value in all the groups and as expected Met group shows decrease in blood glucose levels (−52.48%) after 90 minutes. After repeating same administration for 6 weeks. The oat extract administered group i.e., Am and F11 started showing a decrease in fasting blood sugar readings by −35.57% and −36.25% correspondingly, as compared to drastic increase in the control group DC (64.97%) (Marmouzi *et al.*, 2017) [96]. The data presented in this study shows that the control groups namely NC and DC shows increase in the fasting blood glucose readings over a period of 42 days whereas the group treated with oats extract namely Am and F11 shows a decrease in the fasting blood glucose readings from 215.80 ± 48.83 to 137.57 ± 33.57 after 42 days of time. This shows that oats have anti-diabetic properties (Marmouzi *et al.*, 2017) [96]. A study involved healthy subjects as negative control. About 50g/day of oats were given and serum and insulin levels were investigated. The study concluded that oats administered rats demonstrated enhanced glucose and insulin response (Zu *et al.*, 2020).

Mechanism of anti-diabetic effect of oats

β-D glucan is absorbed from the small intestine and enters lymph circulation. They observed that hepatic glucose kinase was increased and hepatic glucose-6-pase was decreased in oats β-D glucan administered group or OBG group which further implies that β-D glucan can transmit more amount of glucose from blood to liver by suppressing the gluconeogenic pathway and glycolytic pathway. They also mentioned that histopathological analysis disclosed that administering β-D glucan can reform and improve the functioning of pancreatic islet β cells (Wang *et al.*, 2023) [145]. The most predictable pathway is due to its fibre content. It helps in keep stomach full for longer duration of time and maintain pH as well. This favours glucose uptake by skeletal muscles. Another pathway discussed is related to decrease in glucagon activity. Glucagon is responsible for breakdown of complex sugars into simpler ones, so that they are easily available for uptake. Decreasing glucagon naturally helps in maintaining ideal blood glucose levels. Third pathway specified is the increase in P13K/AK activity with the help of various receptors. This increases GLUT-4 expression and further favours transport of blood glucose to cells. Forth and the last pathway discussed is related to the fermentation occurring intestine and produces SCFA which stimulates PPAR-γ which further increases GLUT-A expression as shown in figure 4. This in the similar manner favours transport of blood glucose to cells (Wang *et al.*, 2022) [140].

Toxicity: It is sometimes referred that flaxseed produces hydrogen cyanide in our body after ingestion. Hydrogen cyanide is considered toxic to human body. Hydrogen cyanide toxicity can increase risk to respiratory and nervous system. But it should be considered that, until now no scientific data is shown by anyone regarding this argument. There are two compounds known as cyanogenic glycoside and linatine which are considered toxic. The glycosides are converted into cyanohydrin by intestinal β glycosidase which disintegrates to form hydrogen cyanide. In flaxseeds, this procedure is faster because of the two enzymes which catalyses the whole reaction: linustatinase and linamarase β-glucosidase. The decomposition of cyanohydrin is difficult because it is a highly stable compound. Inspite of the presence of these catalyst there is no increase in the plasma cyanide content when 15-100g of flaxseed is ingested because human body can clean itself up to 100mg/day of cyanide. These many flaxseeds can produce 5- 10mg of cyanide whereas in the direction of acute toxicity, at least 50-60mg of cyanide is required. If the flaxseeds are given any sort of heat treatment, then cyanide is destroyed as it is a heat labile compound. We can conclude that there is no scientific study or data available in order to prove toxicity of flaxseeds or any of the above-mentioned compounds. Four types of cyanogenic glycosides are present in flaxseed: linustatin, neolinustatin, linamarin, and lotaustralin as shown in figure 4 (Parikh *et al.*, 2019) [104].

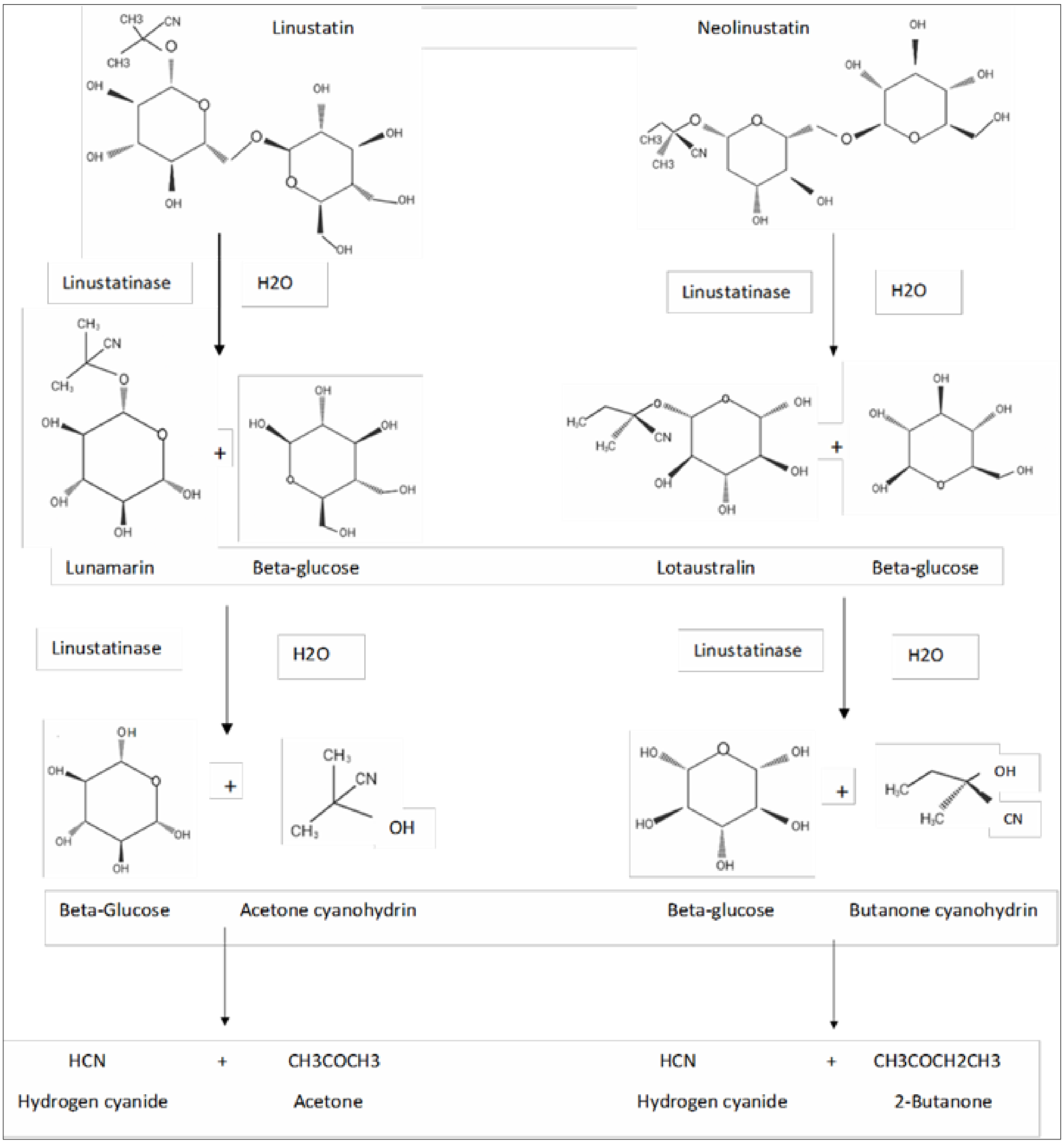


Fig 4: Cyanogenic Glycoside Available in Flaxseeds and their Degradation on the Effect of β Glycosidase. (Bekhit *et al.*, 2018) [19]

Pumpkin is considered one of the healthiest fruits which has multiple health benefits apart from basic nutrition. Thus, it is available is various forms in market for human consumption such as dried pumpkin whole fruit powder, pumpkin seeds, pumpkin seed oil, etc. It is hard to establish any harmful effects of pumpkin, even if consumed more than recommended dietary intake. But it may be harmful if the fruit is cultivated using insecticides, pesticides and herbicides. A study has demonstrated an experiment on rats, where pumpkin seed oil is induced in mice at the rate of 4ml/kg. Along with it an insecticide name emamectin benzoate is administered orally in diet at the rate of 75ppm for 8 weeks. It affected liver, kidney and brain functioning of mice but somehow pumpkin seed oil was able to reverse the effects of insecticides to a considerable level. Hence, pumpkin itself is non-toxic in nature but chemicals applied manually while cultivation, processing and transportation can be harmful is some or the other way (Kulczyński *et al.*, 2019; Abou-Zeid *et al.*, 2018) [79, 1].

Similarly, oats have been proved non-toxic among healthy human being, coeliac disease patients, and patients with dermatitis herpetiformis. All the studies and experiments conducted have concluded that oats do not have any adverse effects on long term consumption of oats. It has been a debate over consumption of oats by gluten intolerant people. A study conducted on 13 individuals including both men and women with average age of 58 years. These individuals were patients of dermatitis herpetiformis. These individuals were having gluten-free diet from more than a decade. They were provided with oats in their diets for 12 weeks and none of them showed any adverse effect, particularly due to consumption of oats. Another study was conducted to examine toxicity of oats on long-term consumption (6-12 months) among coeliac disease patients. Similar to the previous study, this experiment also concluded that there was no toxic effect of oats on patients (Alakoski *et al.*, 2020) [4].

Conclusion and future prospects

Diabetes mellitus is a global concern because of unexpected increase in the diabetic population. To facilitate such a huge population, countries have to spend more on health facilities and infrastructure. Underdeveloped countries or poor nations

are unable to do the same, hence they tend to receive higher ratio of deaths as compared to developing and developed countries, particularly due to diabetes mellitus. To solve this problem, people need to understand the importance of healthy lifestyle and maintaining healthy weight. Diabetic population which is completely dependent over pharmaceutical medicines needs to understand the importance of health foods which are not only capable of decreasing blood glucose levels but also boot the secretion of insulin naturally. Incorporation of such foods in regular diets and in required amounts can convert a diabetic person into pre-diabetic and a pre-diabetic person to non- diabetic. The current discussion demonstrates the capability of foods in treating various diseases most specifically type 2 diabetes mellitus. Foods like pumpkin, flaxseeds and oats have high antioxidant activity, anti-inflammatory properties, anti-carcinogenic, hypoglycaemic properties. Presence of required antioxidants, polyphenols, carotenoids, flavonoids, fibre, proteins, minerals, and vitamins in required amounts makes them "functional foods". This is proved through various successful *in vivo* studies and *in-vitro* studies along with their mechanism in human body.
Looking at the growing awareness and demand for functional food, it is not wrong to state that functional food products will acquire its own space in the food market in next decade. Food products like flaxseed induced cookies, anti-diabetic drink made from pigeon pea, cumin seeds, herbs, prebiotic and probiotic yogurt, etc. will become popular among masses. This will provide industries a new area for research, development and production. New opportunities for young minds will result in development of unrealistic foods which will provide therapeutic benefits along with basic nutrition. Food industries are at major advantage because of the popularity gained by functional foods. These foods are not industry specific as they can be developed within all types of food industries like diary, bakery, beverage, fermentation, flour, oil, flavouring and even water. Such products have potential to give an extra wing to each food industry to evolve with the consumer demands.

References

1. Abou-Zeid SM, AbuBakr HO, Mohamed MA, El-Bahrawy A. Ameliorative effect of pumpkin seed oil against emamectin induced toxicity in mice. Biomed Pharmacother. 2018;98(1):242-251.
2. Akash MSH, Rehman K, Chen S. Spice plant Allium cepa: Dietary supplement for treatment of type 2 diabetes mellitus. Nutrition. 2014;30(10):1128-1137.
3. Akter A, Ali E, Islam MMZ, Karim R, Razzaque AHM. Effect of GA3 on growth and yield of mustard. Int J Sustain Crop Prod. 2007;2(2):16-20.
4. Alakoski A, Hervonen K, Mansikka E, Reunala T, Kaukinen K, Kivelä L, Salmi T. The long-term safety and quality of life effects of oats in dermatitis herpetiformis. Nutrients. 2020;12(4):1060.
5. Alam U, Asghar O, Azmi S, Malik RA. General aspects of diabetes mellitus. In: Handbook of clinical neurology. Vol 126. Elsevier; 2014:211-222.
6. Algonaiman R, Alharbi HF, Barakat H. Antidiabetic and hypolipidemic efficiency of Lactobacillus plantarum fermented oat (*Avena sativa*) extract in streptozotocin-induced diabetes in rats. Fermentation. 2022;8(6):267.
7. Alkhalidy H, Moore W, Wang Y, Luo J, McMillan RP, Zhen W, *et al*. The flavonoid kaempferol ameliorates streptozotocin-induced diabetes by suppressing hepatic glucose production. Molecules. 2018;23(9):2338.
8. Allaq AA, Sidik NJ, Abdul-Aziz A, Ahmed IA. Cumin (Cuminum cyminum L.): A review of its ethnopharmacology, phytochemistry. Biomed Res Ther. 2020;7(9):4016-4021.
9. Al-Snafi AE. The pharmacological activities of Cuminum cyminum-A review. IOSR J Pharm. 2016;6(6):46-65.
10. Altaf U, Hussain SZ, Naseer B, Amin T, Bashir O. Nutritional and bioactive components of rice-chickpea based snacks as affected by severe and mild extrusion cooking. J Sci Food Agric. 2022;102(15):7126-7135.
11. American Diabetes Association Professional Practice Committee. Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes—2022. Diabetes Care. 2022;45(1):S17-S38.
12. American Diabetes Association. Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes—2020. Diabetes Care. 2020;43(1):S14-S31.
13. Amin MM. Phyto-medicinal effects of Syzygium cumini on diabetes: A review. Int J Res AYUSH Pharm Sci. 2020;4(3):392-402.
14. Aroyehun AQB, Razak SA, Palaniveloo K, Nagappan T, Rahmah NSN, Jin GW, *et al*. Bioprospecting cultivated tropical green algae, Caulerpa racemosa (Forsskal) J. Agardh: A perspective on nutritional properties, antioxidative capacity and anti-diabetic potential. Foods. 2020;9(9):1313.
15. Assmann G, Buono P, Daniele A, Della Valle E, Farinaro E, Ferns G, *et al*. Functional foods and cardiometabolic diseases: International task force for prevention of cardiometabolic diseases. Nutr Metab Cardiovasc Dis. 2014;24(12):1272-1300.
16. Augustine I. Hypolipidemic and Antidiabetic Potency of Allium cepa (Onions) Bulb in Alloxan-Induced Diabetic Rats. Acta Sci Nutr Health. 2021;4(3):01-08.
17. Bao L, Cai X, Xu M, Li Y. Effect of oat intake on glycaemic control and insulin sensitivity: A meta-analysis of randomised controlled trials. Br J Nutr. 2014;112(1):457–466.
18. Kanwal R, AbdElgawad H, Jaoumi SK, Selim S, Ibrahim SA. Nutritional Value, Phytochemical Potential, and Therapeutic Benefits of Pumpkin (*Cucurbita* sp.). Plants. 2022;11(11):1394.
19. Bekhit AEDA, Shavandi A, Jodjaja T, Birch J, Teh S, Ahmed IAM, *et al*. Flaxseed: Composition, detoxification, utilization, and opportunities. Biocatal Agric Biotechnol. 2018;13(1):129-152.
20. Boggia R, Zunin P, Turrini F. Functional foods and food supplements. Appl Sci. 2020;10(23):8538.
21. Budhwar S, Chakraborty M, Sethi K, Chatterjee A. Antidiabetic properties of rice and wheat bran-A review. J Food Biochem. 2020;44(10):13424.
22. Butt MS, Tahir-Nadeem M, Khan MKI, Shabir R, Butt MS. Oat: unique among the cereals. Eur J Nutr. 2008;47(2):68-79.
23. Buzigi E, Pillay K, Siwela M. Potential of pumpkin to combat vitamin A deficiency during complementary feeding in low- and middle-income countries: variety, provitamin A carotenoid content and retention, and dietary reference intakes. Crit. Rev Food Sci. Nutr. 2022;62(22):6103-6112.
24. Caili FU, Huan S, Quanhong LI. A review on

pharmacological activities and utilization technologies of pumpkin. Plant Foods Hum Nutr. 2006;61(2):70-77.
25. Ceclu L, Mocanu DG, Nistor OV. Pumpkin–health benefits. Diabetes. 2020;26(3):241-246.
26. Chen C, You LJ, Huang Q, Fu X, Zhang B, Liu RH, *et al*. Modulation of gut microbiota by *mulberry fruit polysaccharide* treatment of obese diabetic db/db mice. Food Funct. 2018;9(1):3732–3742.
27. Chen L, Chen XW, Huang X, Song BL, Wang Y, Wang Y. Regulation of glucose and lipid metabolism in health and disease. Sci China Life Sci. 2019;62(1):1420-1458.
28. Chen X, Qian L, Wang B, Liu H, Zhang Y, Liu J. Synergistic hypoglycemic effects of *pumpkin polysaccharides* and *puerarin* on type II diabetes mellitus mice. Molecules. 2019;24(5):955.
29. Cheng C, Yu X, McClements DJ, Huang Q, Tang H, Yu K, *et al*. Effect of *flaxseed polyphenols* on physical stability and oxidative stability of *flaxseed oil-in-water nanoemulsions*. Food Chem. 2019;301:125207.
30. Codo AC, Davanzo GG, de Brito Monteiro L, de Souza GF, Muraro SP, Virgilio-da-Silva JV, *et al*. Elevated glucose levels favor SARS-CoV-2 infection and monocyte response through a HIF-1α/glycolysis-dependent axis. Cell Metab. 2020;32(3):437-446.
31. Colasuonno P, Marcotuli I, Cutillo S, Simeone R, Blanco A, Gadaleta A. Effect of barley chromosomes on the *β-glucan content* of wheat. Genet Resour Crop Evol. 2020;67(1):561-567.
32. de Oliveira Raphaelli C, dos Santos Pereira E, Camargo TM, Vinholes J, Rombaldi CV, Vizzotto M, *et al*. Apple phenolic extracts strongly inhibit α-glucosidase activity. Plant Foods Hum Nutr. 2019;74(1):430–435.
33. De Zoysa HKS, Waisundara VY. Mustard (*Brassica nigra*) seed. In: Oilseeds: Health Attributes and Food Applications. Springer, Singapore; 2021. p. 191-210.
34. Dhalaria R, Verma R, Kumar D, Puri S, Tapwal A, Kumar V, *et al*. Bioactive compounds of edible fruits with their anti-aging properties: A comprehensive review to prolong human life. Antioxidants. 2020;9(11):1123.
35. DiNicolantonio JJ, O'Keefe JH, Wilson WL. Sugar addiction: is it real? A narrative review. Br J Sports Med. 2018;52(14):910-913.
36. Divya M, Karthikeyan S, Ravi C, Govindarajan M, Alharbi NS, Kadaikunnan S, *et al*. Isolation of *β-glucan* from *Eleusine coracana* and its antibiofilm, antidiabetic, antioxidant, and biocompatible activities. Microb Pathog. 2020;140:103955.
37. Dog TL. The use of botanicals during pregnancy and lactation. Altern Ther Health Med. 2009;15(1):54-8.
38. Dong S, Zhang M, Niu H, Jiang K, Jiang J, Ma Y, *et al*. Upregulation of UDP-glucuronosyltransferases 1a1 and 1a7 are involved in altered *puerarin* pharmacokinetics in type II diabetic rats. Molecules. 2018;23(6):1487.
39. Dowidar M, Ahmed A, Mohamed H. The critical nutraceutical role of pumpkin seeds in human and animal health: An updated review. Zagazig Vet J. 2020;48(2):199-212.
40. Du B, Meenu M, Liu H, Xu B. A concise review on the molecular structure and function relationship of *β-glucan*. Int J Mol Sci. 2019;20(16):4032.
41. Ebrahimi B, Nazmara Z, Hassanzadeh N, Yarahmadi A, Ghaffari N, Hassani F, *et al*. Biomedical features of flaxseed against different pathologic situations: A narrative review. Iran J Basic Med Sci. 2021;24(5):551.
42. Elam E, Feng J, Lv YM, Ni ZJ, Sun P, Thakur K, *et al*. Recent advances on bioactive food derived anti-diabetic hydrolysates and peptides from natural resources. J Funct Foods. 2021;86:104674.
43. El-Kholie EM, Khedr SA, Zakiand AN, Gaballah HA. Anti-Diabetic Effect of Oats Flour on Streptozotocin-Induced Diabetic Rats. Dev. 2020;30(4):1-16.
44. Engin AB, Engin A. Protein kinases signaling in pancreatic β-cells death and type 2 diabetes. In: Protein Kinase-mediated Decisions Between Life and Death. 2021. p. 195-227.
45. Evans PL, McMillin SL, Weyrauch LA, Witczak CA. Regulation of skeletal muscle glucose transport and glucose metabolism by exercise training. Nutrients. 2019;11(10):2432.
46. Fahmy TS, Hussein AA, Yousef SM. Antidiabetic Effect of Flaxseed (*Linum usitatissimum L.*) on Hepatic Lipid Metabolism of Alloxan-Induced Diabetic Rats. J Res Fields Spec Educ. 2022;41(1):1187.
47. Fatima T, Bashir O, Gani G, Bhat T, Jan N. Nutritional and health benefits of apricots. Int J Unani Integr Med. 2018;2(2):5-9.
48. Ganesan K, Xu B. Anti-diabetic effects and mechanisms of dietary polysaccharides. Molecules. 2019;24(14):2556.
49. Graf BL, Poulev A, Kuhn P, Grace MH, Lila MA, Raskin I. Quinoa seeds leach phytoecdysteroids and other compounds with anti-diabetic properties. Food Chem. 2014;163:178-185.
50. Graf BL, Rojas-Silva P, Rojo LE, Delatorre-Herrera J, Baldeón ME, Raskin I. Innovations in health value and functional food development of quinoa (*Chenopodium quinoa Willd.*). Compr Rev Food Sci Food Saf. 2015;14(4):431-445.
51. Granato D, Barba FJ, Bursać Kovačević D, Lorenzo JM, Cruz AG, Putnik P. Functional foods: Product development, technological trends, efficacy testing, and safety. Annu Rev Food Sci Technol. 2020;11(1):93-118.
52. Guzmán-Ávila R, Flores-Morales V, Paoli P, Camici G, Ramírez-Espinosa JJ, Cerón- Romero L, Navarrete-Vázquez G, Hidalgo-Figueroa S, Rios MY, Villalobos-Molina R, Estrada-Soto S. Ursolic acid derivatives as potential antidiabetic agents: *In vitro*, *in vivo*, and in silico studies. Drug Dev Res. 2018;79(2):70-80.
53. Hajiahmadi S, Nadjarzadeh A, Gharipour M, Hosseinzadeh M, Fallahzadeh H, Mohsenpour MA. Effect of flaxseed oil on glycemic control and inflammatory markers in overweight adults with pre-diabetes: A double-blind randomized controlled clinical trial. J Herb Med. 2020;24(1):100387.
54. Harding JL, Pavkov ME, Magliano DJ, Shaw JE, Gregg EW. Global trends in diabetes complications: a review of current evidence. Diabetologia. 2019;62(1):3-16.
55. Hardman CM, Garioch JJ, Leonard JN, Thomas HJ, Walker MM, Lortan JE, Fry L. Absence of toxicity of oats in patients with dermatitis herpetiformis. N Engl J Med. 1997;337(26):1884-1887.
56. Hong-Yan ZHU, Guang-Tong CHEN, Guo-Liang MENG, Ji-Liang XU. Characterization of pumpkin polysaccharides and protective effects on streptozotocin-damaged islet cells. Chin J Nat Med. 2015;13(3):199-207.
57. Hossain MM. Diabetes, a Global Threat with the Worse

Outcome in COVID–19 Pandemics. Sir Salimullah Med Coll J. 2022;30(1):1-2.
58. Hussain A, Kausar T, Jamil MA, Noreen S, Iftikhar K, Rafique A, Iqbal MA, Majeed MA, Quddoos MY, Aslam J, Ali A. *In vitro* Role of Pumpkin Parts as Pharma-Foods: Antihyperglycemic and Antihyperlipidemic Activities of Pumpkin Peel, Flesh, and Seed Powders, in Alloxan-Induced Diabetic Rats. Int J Food Sci. 2022;2022(1):1-10.
59. Hussain A, Kausar T, Sehar S, Sarwar A, Ashraf AH, Jamil MA, Majeed MA. A Comprehensive review of functional ingredients, especially bioactive compounds present in pumpkin peel, flesh and seeds, and their health benefits. Food Chem Adv. 2022;1(1):100067.
60. Hutchins AM, Brown BD, Cunnane SC, Domitrovich SG, Adams ER, Bobowiec CE. Daily flaxseed consumption improves glycemic control in obese men and women with pre-diabetes: a randomized study. Nutr Res. 2013;33(5):367-375.
61. Idris S, Mishra A, Khushtar M. Recent therapeutic interventions of fenugreek seed: A mechanistic approach. Drug Res. 2021;71(04):180-192.
62. Isutsa DK, Mallowa SO. Increasing leaf harvest intensity enhances edible leaf vegetable yields and decreases mature fruit yields in multi-purpose pumpkin. J Agric Biol Sci. 2013;8(1):610-615.
63. Jaiswal N, Srivastava SP, Bhatia V, Mishra A, Sonkar AK, Narender TS, Srivastava AK, Tamrakar AK. Inhibition of α -Glucosidase by Acacia nilotica Prevents Hyperglycaemia along with Improvement of Diabetic Complications via Aldose Reductase Inhibition. J Diabetes Metab. 2012;6(4):1-7.
64. Janatuinen EK, Kemppainen TA, Julkunen RJK, Kosma VM, Mäki M, Heikkinen M, Uusitupa MIJ. No harm from five-year ingestion of oats in coeliac disease. Gut. 2002;50(3):332-335.
65. Ji X, Guo J, Cao T, Zhang T, Liu Y, Yan Y. Review on mechanisms and structure- activity relationship of hypoglycemic effects of polysaccharides from natural resources. Food Sci Hum Wellness. 2023;12(6):1969-1980.
66. Ji X, Peng B, Ding H, Cui B, Nie H, Yan Y. Purification, structure and biological activity of pumpkin polysaccharides: a review. Food Rev Int. 2021;39(1):307-319.
67. Johns EC, Denison FC, Norman JE, Reynolds RM. Gestational diabetes mellitus: Mechanisms, treatment, and complications. Trends Endocrinol Metab. 2018;29(11):743-754.
68. Kaspar D, Hastreiter S, Irmler M, Hrabé de Angelis M, Beckers J. Nutrition and its role in epigenetic inheritance of obesity and diabetes across generations. Mamm Genome. 2020;31(1):119-133.
69. Katare C, Saxena S, Agrawal S, Prasad GBKS, Bisen PS. Flax seed: a potential medicinal food. J Nutr Food Sci. 2012;2(1):120-7.
70. Kato A, Higuchi Y, Goto H, Kizu H, Okamoto T, Asano N, Hollinshead J, Nash RJ, Adachi I. Inhibitory effects of Zingiber officinale Roscoe derived components on aldose reductase activity *in vitro* and *in vivo*. J Agric Food Chem. 2006;54(18):6640-6644.
71. Kato-Schwartz CG, Corrêa RCG, de Souza Lima D, de Sá-Nakanishi AB, de Almeida Gonçalves G, Seixas FAV, Peralta RM. Potential anti-diabetic properties of *Merlot* grape pomace extract: An *in vitro*, in silico and *in vivo* study of α-amylase and α- glucosidase inhibition. Food Res Int. 2020;137(1):109462.
72. Katsarou A, Gudbjörnsdottir S, Rawshani A, Dabelea D, Bonifacio E, Anderson BJ, Lernmark Å. Type 1 diabetes mellitus. Nat Rev Dis Primers. 2017;3(1):1-17.
73. Kaur S, Panghal A, Garg MK, Mann S, Khatkar SK, Sharma P, Chhikara N. Functional and nutraceutical properties of pumpkin–a review. Nutr Food Sci. 2020;50(2):384-401.
74. Kaur S, Panghal A, Garg MK, Mann S, Khatkar SK, Sharma P, Chhikara N. Functional and nutraceutical properties of pumpkin–a review. Nutr Food Sci. 2019;50(2):384-401.
75. Kazeem MI, Davies TC. Anti-diabetic functional foods as sources of insulin secreting, insulin sensitizing and insulin mimetic agents. J Funct Foods. 2016;20(1):122-138.
76. Kerimi A, Nyambe-Silavwe H, Gauer JS, Tomas-Barberan FA, Williamson G. Pomegranate juice, but not an extract, confers a lower glycemic response on a high-glycemic index food: Randomized, crossover, controlled trials in healthy subjects. Am J Clin Nutr. 2017;106(1):1384–1393.
77. Kim MY, Kim EJ, Kim YN, Choi C, Lee BH. Comparison of the chemical compositions and nutritive values of various pumpkin (*Cucurbitaceae*) species and parts. Nutr Res Pract. 2012;6(1):21-27.
78. Klimova B, Kuca K, Maresova P. Global view on Alzheimer's Disease and Diabetes Mellitus: threats, risks and treatment Alzheimer's Disease and Diabetes Mellitus. Curr Alzheimer Res. 2018;15(14):1277-1282.
79. Kulczyński B, Gramza-Michałowska A. The profile of carotenoids and other bioactive molecules in various pumpkin fruits (*Cucurbita maxima* Duchesne) cultivars. Molecules. 2019;24(18):3212.
80. Kwon YI, Apostolidis E, Kim YC, Shetty K. Health benefits of traditional corn, beans, and pumpkin: *in vitro* studies for hyperglycemia and hypertension management. J Med Food. 2007;10(2):266-275.
81. Kwon YI, Apostolidis E, Kim YC, Shetty K. Health benefits of traditional corn, beans, and pumpkin: *in vitro* studies for hyperglycemia and hypertension management. J Med Food. 2007;10(2):266-275.
82. Lavanya MN, Saikiran KCS, Venkatachalapathy N. Stabilization of rice bran milling fractions using microwave heating and its effect on storage. J Food Sci Technol. 2019;56(2):889–895.
83. Lavelli V, Harsha PSCS, Ferranti P, Scarafoni A, Iametti S. Grape skin phenolics as inhibitors of mammalian α-glucosidase and α-amylase–effect of food matrix and processing on efficacy. Food Funct. 2016;7(1):1655–1663.
84. Lee CJ, Horsley RD, Manthey FA, Schwarz PB. Comparisons of β-glucan content of barley and oat. Cereal Chem. 1997;74(5):571-575.
85. Li PY, Hsu CC, Yin MC, Kuo YH, Tang FY, Chao CY. Protective effects of red guava on inflammation and oxidative stress in streptozotocin-induced diabetic mice. Molecules. 2015;20(1):22341–22350.
86. Li Q, Tian Z, Cai T. Study on the hypoglycemic action of pumpkin extract in diabetic rat. Acta Nutrimenta Sin.

1956;(6).
87. Li X, Cai W, Lee K, Liu B, Deng Y, Chen Y, Zhang X, He JC, Zhong Y, Zhong Y. Puerarin attenuates diabetic kidney injury through the suppression of NOX4 expression in podocytes. Sci Rep. 2017;7(1):1-11.
88. Liu M, Zhang Y, Zhang H, Hu B, Wang L, Qian H, Qi X. The anti-diabetic activity of oat β D-glucan in streptozotocin–nicotinamide induced diabetic mice. Int J Biol Macromol. 2016;91(1):1170-1176.
89. Lu KY, Chen SH, Lin YS, Wu HP, Chao PM. An antidiabetic nutraceutical combination of red yeast rice (*Monascus purpureus*), bitter gourd (*Momordica charantia*), and chromium alleviates dedifferentiation of pancreatic β-cells in db/db mice. Food Sci Nutr. 2020;8(12):6718-6726.
90. M Eid H, S Haddad P. The antidiabetic potential of quercetin: underlying mechanisms. Curr Med Chem. 2017;24(4):355-364.
91. Ma JQ, Ding J, Xiao ZH, Liu CM. Puerarin ameliorates carbon tetrachloride-induced oxidative DNA damage and inflammation in mouse kidney through ERK/Nrf2/ARE pathway. Food Chem Toxicol. 2014;71(1):264-271.
92. Ma ZF, Ahmad J, Zhang H, Khan I, Muhammad S. Evaluation of phytochemical and medicinal properties of Moringa (*Moringa oleifera*) as a potential functional food. S Afr J Bot. 2020;129(1):40-46.
93. Maddaloni E, Moretti C, Mignogna C, Buzzetti R. Adult-onset autoimmune diabetes in 2020: An update. Maturitas. 2020;137(1):37-44.
94. Makino-Wakagi Y, Yoshimura Y, Uzawa Y, Zaima N, Moriyama T, Kawamura Y. Ellagic acid in pomegranate suppresses *resistin* secretion by a novel regulatory mechanism involving the degradation of intracellular *resistin* protein in adipocytes. Biochemical and Biophysical Research Communications. 2019;417(1):880–885.
95. Mani UV, Mani I, Biswas M, Kumar SN. An open-label study on the effect of flax seed powder (*Linum usitatissimum*) supplementation in the management of diabetes mellitus. Journal of Dietary Supplements. 2011;8(3):257-265.
96. Marmouzi I, Karym EM, Saidi N, Meddah B, Kharbach M, Masrar A, Bouadellah M, Chabraoul L, Allali KE, Cherrah Y, Faouzi MEA. *In vitro* and *in vivo* antioxidant and anti-hyperglycemic activities of Moroccan oat cultivars. Antioxidants. 2017;6(4):102.
97. Martha R, Gutierrez P. Medicinal chemistry review of *Cucurbita pepo* (*pumpkin*): its phytochemistry and pharmacology. International Journal of Pharmacology and Phytochemistry Research. 2016;9(9):1190-1194.
98. Masci A, Carradori S, Casadei MA, Paolicelli P, Petralito S, Ragno R, *et al*. *Lycium barbarum* polysaccharides: extraction, purification, structural characterisation and evidence about hypoglycaemic and hypolipidaemic effects. A review. Food Chemistry. 2018;254(1):377–389.
99. Mechchate H, Es-Safi I, Conte R, Hano C, Amaghnouje A, Jawhari FZ, Radouane N, Bencheikh N, Grafov G, Bousta D. *In vivo* and *in vitro* antidiabetic and anti-inflammatory properties of flax (*Linum usitatissimum* L.) seed polyphenols. Nutrients. 2021;13(8):2759.
100. Modi M. Ginger Root. StatPearls - NCBI Bookshelf. 2022 Nov 28. Available from: https://www.ncbi.nlm.nih.gov/books/NBK565886/
101. Moya-Hernández A, Bosquez-Molina E, Verde-Calvo JR, Blancas-Flores G, Trejo-Aguilar GM. Hypoglycemic effect and bioactive compounds associated with the ripening stages of the *Cucurbita ficifolia* Bouché fruit. Journal of the Science of Food and Agriculture. 2020;100(14):5171-5181.
102. Nataraj BH, Ali SA, Behare PV, Yadav H. Postbiotics-parabiotics: The new horizons in microbial biotherapy and functional foods. Microbial Cell Factories. 2020;19(1):1-22.
103. Oomah BD, Mazza G. Flaxseed proteins—a review. Food Chemistry. 1993;48(2):109-114.
104. Parikh M, Maddaford TG, Austria JA, Aliani M, Netticadan T, Pierce GN. Dietary Flaxseed as a Strategy for Improving Human Health. Nutrients. 2019;11(5):1171.
105. Park CH, Lee JY, Kim MY, Shin SH, Roh SS, Choi JS, *et al*. Oligonol, a low-molecular-weight polyphenol derived from lychee fruit, protects the pancreas from apoptosis and proliferation via oxidative stress in streptozotocin-induced diabetic rats. Food & Function. 2016;7(1):3056–3063.
106. Patil SB, Takalikar SS, Joglekar MM, Haldavnekar VS, Arvindekar AU. Insulinotropic and β-cell protective action of cuminaldehyde, cuminol and an inhibitor isolated from *Cuminum cyminum* in streptozotocin-induced diabetic rats. British Journal of Nutrition. 2013;110(8):1434-1443.
107. Patil SP, Goswami A, Kalia K, Kate AS. Plant-derived bioactive peptides: A treatment to cure diabetes. International Journal of Peptide Research and Therapeutics. 2020;26(1):955-968.
108. Petersen C, Wankhade UD, Bharat D, Wong K, Mueller JE, Chintapalli SV, *et al*. Dietary supplementation with strawberry induces marked changes in the composition and functional potential of the gut microbiome in diabetic mice. The Journal of Nutritional Biochemistry. 2019;66(1):63–69.
109. Prasad K, Dhar A. Flaxseed and diabetes. Current Pharmaceutical Design. 2016;22(2):141-144.
110. Quanhong LI, Caili F, Yukui R, Guanghui H, Tongyi C. Effects of protein-bound polysaccharide isolated from pumpkin on insulin in diabetic rats. Plant Foods for Human Nutrition. 2005;60(1):13-16.
111. Rahayu M, Kasiyati M, Martsiningsih A, Setiawan B, Khasanah F. Hypoglycemic and antioxidant activity of yellow pumpkin (*Curcubita moschata*) in diabetic rats. Indian Journal of Public Health Research & Development. 2020;11(1):1300-1304.
112. Ramya S, Neethirajan K, Jayakumararaj R. Profile of bioactive compounds in *Syzygium cumini* - a review. Journal of Pharmacy. 2012;5(8):4548-4553.
113. Regand A, Chowdhury Z, Tosh SM, Wolever TM, Wood P. The molecular weight, solubility and viscosity of oat β-glucan affect human glycemic response by modifying starch digestibility. Food Chemistry. 2011;129(2):297-304.
114. Rehman A, Saeed A, Kanwal R, Ahmad S, Changazi SH. Therapeutic effect of sunflower seeds and flax seeds on diabetes. Cureus. 2021;13(8).
115. Roglic G. WHO Global report on diabetes: A summary. International Journal of Noncommunicable Diseases.

2016;1(1):3-8.
116. Sachan N, Yadav DK, Chandra P. Ethnomedicinal uses, phytochemistry, pharmacological effects, pre-clinical and clinical studies on flaxseed: A spice with culinary herb-based formulations and its constituents. Science of Spices and Culinary Herbs-Latest Laboratory, Pre-clinical, and Clinical Studies. 2021;4(1):28-53.
117. Saini V. Molecular mechanisms of insulin resistance in type 2 *diabetes mellitus*. World J Diabetes. 2010;1(3):68.
118. Sangwan S, Singh R, Tomar SK. Nutritional and functional properties of oats: An update. J Innov Biol. 2014;1(1):3-14.
119. Saratale GD, Saratale RG, Kim DS, Kim DY, Shin HS. Exploiting fruit waste grape pomace for silver nanoparticles synthesis, assessing their antioxidant, antidiabetic potential and antibacterial activity against human pathogens: a novel approach. Nanomaterials. 2020;10(8):1457.
120. Schnurr TM, Jakupović H, Carrasquilla GD, Ängquist L, Grarup N, Sørensen TI, Kilpeläinen TO. Obesity, unfavourable lifestyle and genetic risk of type 2 diabetes: a case-cohort study. Diabetologia. 2020;63(1):1324-1332.
121. Scully T. Diabetes in numbers. Nature. 2012;485(2012):S2-S3.
122. Setyawati AD, Padila P, Andri J. Obesity and Heredity for Diabetes Mellitus among Elderly. J Nurs Health. 2020;1(1):26-31.
123. Shayan M, Kamalian S, Sahebkar A, Tayarani-Najaran Z. Flaxseed for health and disease: Review of clinical trials. Comb Chem High Throughput Screen. 2020;23(8):699-722.
124. Shi Y, Xiong X, Cao J, Kang M. Effect of pumpkin polysaccharide granules on glycemic control in type 2 diabetes. Cent South Pharm. 2003;1(1):275-276.
125. Singh H. Nanotechnology applications in functional foods; opportunities and challenges. Prev Nutr Food Sci. 2016;21(1):1.
126. Sivamaruthi BS, Kesika P, Prasanth MI, Chaiyasut C. A mini review on antidiabetic properties of fermented foods. Nutrients. 2018;10(12):1973.
127. Spínola V, Pinto J, Llorent-Martínez EJ, Tomas H, Castilho PC. Evaluation of *Rubus grandifolius* L. (wild blackberries) activities targeting management of type-2 diabetes and obesity using *in vitro* models. Food Chem Toxicol. 2019;123:443-452.
128. Staszowska-Karkut M, Materska M. Phenolic composition, mineral content, and beneficial bioactivities of leaf extracts from black currant (*Ribes nigrum* L.), raspberry (*Rubus idaeus*), and aronia (*Aronia melanocarpa*). Nutrients. 2020;12(2):463.
129. Steinbrenner H, Duntas LH, Rayman MP. The role of selenium in type-2 diabetes mellitus and its metabolic comorbidities. Redox Biol. 2022;50:102236.
130. Su C, Yang C, Gong M, Ke Y, Yuan P, Wang X, Li M, Zheng X, Feng W. Antidiabetic activity and potential mechanism of amentoflavone in diabetic mice. Molecules. 2019;24(11):2184.
131. Subramanian SP, Prasath GS. Antidiabetic and antidyslipidemic nature of trigonelline, a major alkaloid of fenugreek seeds studied in high-fat-fed and low-dose streptozotocin-induced experimental diabetic rats. Biomed Prev Nutr. 2014;4(4):475-480.
132. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, Magliano DJ, *et al*. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022;183:109-119.
133. Sun J, Liu W, Ma H, Marais JPJ, Khoo C, Dain JA, *et al*. Effect of cranberry (*Vaccinium macrocarpon*) oligosaccharides on the formation of advanced glycation end-products. J Berry Res. 2016;6(2):149–158.
134. Sun T, Li J, Qin Y, Xie J, Xue B, Li X, Shao Z. Rheological and functional properties of oat *β-glucan* with different molecular weight. J Mol Struct. 2021;1209:127944.
135. Tang ZX, Shi LE, Wang XM, Dai GW, Cheng LA, Wan ZX, Huang LH. Whole flaxseed-based products and their health benefits. Food Sci Technol Res. 2020;26(5):561-578.
136. Tiefenbacher KF. The Technology of Wafers and Waffles I: Operational Aspects. Netherlands: Elsevier Science. Academic Press; 2017.
137. Ulla A, Alam MA, Rahman M, Isha Olive Khan DM, Sikder B, Islam M, *et al*. Supplementation of *Citrus maxima* fruits peel powder improves glucose intolerance and prevents oxidative stress in liver of alloxan-induced diabetic rats. Mediterr J Nutr Metab. 2018;12(1):1–12.
138. Valenzuela Zamudio F, Segura Campos MR. Amaranth, quinoa and chia bioactive peptides: a comprehensive review on three ancient grains and their potential role in management and prevention of Type 2 diabetes. Crit Rev Food Sci Nutr. 2022;62(10):2707-2721.
139. Venkatakrishnan K, Chiu HF, Wang CK. Popular functional foods and herbs for the management of type-2-diabetes mellitus: a comprehensive review with special reference to clinical trials and its proposed mechanism. J Funct Foods. 2019;57:425-438.
140. Wang H, Li N, Chivese T, Werfalli M, Sun H, Yuen L, Yang X. IDF diabetes atlas: estimation of global and regional gestational diabetes mellitus prevalence for 2021 by International Association of Diabetes in Pregnancy Study Group's Criteria. Diabetes Res Clin Pract. 2022;183(1):109050.
141. Wang L, Liu F, Wang A, Yu Z, Xu Y, Yang Y. Purification, characterization and bioactivity determination of a novel polysaccharide from pumpkin (*Cucurbita moschata*) seeds. Food Hydrocolloids. 2017;66:357-364.
142. Wang S, Lu A, Zhang LU, Shen M, Xu T, Zhan W, Jin H, Zhang Y, Wang W. Extraction and purification of pumpkin *polysaccharides* and their hypoglycemic effect. Int J Biol Macromol. 2017;98(1):182-187.
143. Wang S, Zhang T, Li J, Zhang J, Swallah MS, Gao J, Yu H. Oat β-glucan and l-arabinose synergistically ameliorate glucose uptake in insulin-resistant HepG2 cells and exert anti-diabetic activity via activation of the PI3K/AKT pathway in db/db mice. Food Funct. 2022;13(19):10158-10170.
144. Wang SY, Huang WC, Liu CC, Wang MF, Ho CS, Huang WP, Hou CC, Chuang HL, Huang CC. Pumpkin (*Cucurbita moschata*) fruit extract improves physical fatigue and exercise performance in mice. Molecules. 2012;17(10):11864-11876.
145. Wang Y, Fan M, Qian H, Ying H, Li Y, Wang L. Whole grains-derived functional ingredients against hyperglycemia: targeting hepatic glucose metabolism.

Crit Rev Food Sci Nutr. 2023:1-22.
146. Webster F. Oats: chemistry and technology. Academic Press; 2016.
147. Wu N, Fu K, Fu YJ, Zu YG, Chang FR, Chen YH, Liu X, Kong Y, Liu W, Gu CB. Antioxidant activities of extracts and main components of pigeon pea (*Cajanus cajan* (L.) Millsp.) leaves. Molecules. 2009;14(3):1032-1043.
148. Xia T, Wang Q. Antihyperglycemic effect of *Cucurbita ficifolia* fruit extract in streptozotocin-induced diabetic rats. Fitoterapia. 2006;77(7):530-533.
149. Yadav M, Jain S, Tomar R, Prasad GBKS, Yadav H. Medicinal and biological potential of pumpkin: an updated review. Nutr Res Rev. 2010;23(2):184-190.
150. Yang SE, Vo TLT, Chen CL, Yang NC, Chen CI, Song TY. Nutritional composition, bioactive compounds and functional evaluation of various parts of *Cajanus cajan* (L.) Millsp. Agriculture. 2020;10(11):558.
151. Yari Z, Cheraghpour M, Hekmatdoost A. Flaxseed and/or hesperidin supplementation in metabolic syndrome: An open-labeled randomized controlled trial. Eur J Nutr. 2021;60(1):287-298.
152. Yee MM. Investigation of chemical composition, antimicrobial and antioxidant activities of *Allium wallichii* Kunth (Garlic) Bulb. Am Sci Res J Eng Technol Sci (ASRJETS). 2019;54(1):30-41.
153. Zarzycki P, Sykut-Domańska E, Sobota A, Teterycz D, Krawęcka A, Blicharz-Kania A, Zdybel B. Flaxseed enriched pasta—chemical composition and cooking quality. Foods. 2020;9(4):404.
154. Zhao L, Wang K, Wang K, Zhu J, Hu Z. Nutrient components, health benefits, and safety of litchi (*Litchi chinensis* Sonn.): A review. Compr Rev Food Sci Food Saf. 2020;19(4):2139-2163.
155. Zhu Y, Dong L, Huang L, Shi Z, Dong J, Yao Y, Shen R. Effects of oat β-glucan, oat resistant starch, and the whole oat flour on insulin resistance, inflammation, and gut microbiota in high-fat-diet-induced type 2 diabetic rats. J Funct Foods. 2020;69(1):103939.
156. Zimmet PZ, Magliano DJ, Herman HW, Shaw JE. Diabetes: a 21st century challenge. Lancet Diabetes Endocrinol. 2014;2(1):56-64.
157. Zuofeng L, Zhaofu W, Jie C, Zuo C. A study on the extraction and purification of pumpkin polysaccharide and the hypoglycaemic effect of its compound oral liquid. Prog Pharm Sci. 2004;28(11):515-518.