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Phytochemical Components of Some Minor Cereals Associated with Diabetes Prevention and Management

Rabia Begum Panhwar[1], Ali Akbar[1], Muhammad Faizer Ali[2], Qinghua Yang[1], Baili Feng[1*]

[1]State Key Laboratory of Crop Stress Biology in Arid Areas/Northwest A&F University, Yangling, China
[2]Environmental Engineering & Management, Mehran University of Engineering & Technology, Jamshoro, Pakistan
Email: Rabiapanhwar@yahoo.com, aliakbarqau@yahoo.com, fyzer_ali@yahoo.com, 1661650143@qq.com, *fengbaili@nwsuaf.edu.cn

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Abstract

Diabetes is a metabolic disorder by a chronic hyperglycemic condition because of defects in insulin secretion and insulin action or both. Minor cereals are often drought tolerant and fertilizer efficient. In this review we focus the content and bioavailability of phytochemicals in some minor cereals on the basis evidence for increasing plasma phytochemical concentrations and reducing oxidative stress as well as inflammation in humans. Phenolics and Flavanoids are major phytochemicals and may be available with high concentration in minor cereals but as tightly attached with cell wall, their bioavailability is mostly limited. Clinical trials concluded that vitamin E and other common antioxidants were not helpful for managing diabetic complications. Vicious cycles can cause type 1 DM, where as hypoglycemia can forward to down and regulate neuroendocrine. Increased phytochemical bioavailability may be achieved through bio processing of grains but the improvements might be small and have not yet led to changes in clinical associated with reduced risk of T2D. Furthermore, the effects of minor cereals against oxidative stress in healthy individuals can be very low or not occurred but systemic inflammation can be reduced in people after huge intake. More than 300 Indian medicinal plants have antidiabetic property but exact mechanisms for hypoglycemic action of many plants are still unknown. Further studies are required to pay attention toward direct role of minor cereal phytochemicals on alarming diseases diabetes.

Keywords

Minor Cereal, Phytochemical, Diabetes, Hypoglycemia Cycle, Prevention

1. Introduction

Diabetes mellitus (DM) and type 2 diabetes (T2D) both are current health problems which affect millions of individuals worldwide and increase dangerously, but among the total population of diabetic patients more than 90% suffer from Type 2 Diabetes (T2D). Death and disability, due to type-2 diabetes are increasing day by day [1] [2] [3]. The cause of Diabetes mellitus (DM) is metabolic disorder of multiple physiology by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism consequently defects in insulin secretion and insulin action, or both. "Type 2 diabetes" can be caused by different factors also includes both genetic as well as environmental factors that affect β-cell function and tissue of pancreas, muscles and liver [4].

Minor cereals including oat (*Avena sativa* L.), barley (*Hordeumvulgare* L.) and common millet (*Panicummiliaceum* L.) have contributed greatly to agriculture [5]. Recently, cultivation of minor cereals has been increasing because of drought resistant, fertilizer efficient, environment friendly and can cultivate under high temperature conditions [6]. Phytochemicals are the bioactive compound of plants having many biological properties such as antioxidant, anti-inflammatory, antidiabetic, anticancer, modulation of detoxification enzymes, stimulation of the immune system and others [7]. Mostly phytochemicals functions as a antioxidants *in vitro* and have the potential to moderate oxidative stress and inflammation which can cause pathogenesis of T2D [8]. Consumption of cereals and balanced dietary patterns have been shown to lower risk of diabetes and better results for diabetes individuals. By the changing life style and intake can overcome this diseases and more effective than different huge medicines. Minor cereals intake can reduce the risk of T2D [9] [10] [11].

Various studies demonstrated that frequent intake of minor cereal foods improves metabolic homeostasis and delays or prevents the development of T2D and its complications in a variety of associates, but in mostly of European pedigree [12]-[18]. If minor cereals food added in daily serves about 2 to 3 times then it can reduced the risk of T2D about 20% - 30% as compared to 1 serve in whole week. There are many different experimental studies provide evidences between minor cereal intake and diabetes prevention [15] [18].

In addition, minor cereal foods can improve the index of diabetes risk, including glycemic control, fasting plasma insulin, glucose, and insulin sensitivity, as well as include in the management of those individuals with or at high risk of developing T2D [13] [19] [20] [21]. One of the primary pathogenic factors is oxidative stress which leading to insulin resistance, β-cell dysfunction, impaired glucose tolerance and ultimately T2D [22] [23]. Moreover, a study of human clinical trials concluded that vitamin E and other common antioxidants were not helpful for managing diabetic complications. But cereal fiber can play important role to reduce the diabetes risk associated with minor cereal consumption [24].

1.1. Phytochemical Component of Some Minor Cereals

Barley

Epidemiological studies have proved that regular consumption of barley can reduces the risk of developing chronic diseases and can prevent common nutrition related diseases including diabetes and obesity because of β-glucan in barley fiber. The phytochemicals of barley have antioxidant, antiproliferative, and cholesterol lowering abilities, which can reduce the risk of certain diseases [25] [26] [27]. Phenolics, tocols and folate are the major phytochemicals of barley [25]. Recently a new variety of barley has developed that has a wide range of nutritional and health benefits [28] [29]. Sterols and tocols are major components of plant oils that can provide benefits like protection against toxins, neurological diseases such as Alzheimer's disease and diabetes [30] [31]. Barley has unique phytochemical properties like the presence of all eight tocolvitamers which are mostly not complete in some other cereals [32]. Some phytochemicals of barley have different constituents as shown in **Table 1**.

Rye

Rye has more alkylresorcinols than the other major cereal varieties. The concentration of alkylresorcinol in rye is depending on the high level of folate in the grain. Some varieties of rye also have very high levels of total phenolics but the free phenolics content are very low. Other phytochemicals, such astocols, polyphenols and ferulic acid are also found at low levels in rye [33]. Researcher and reviewers focused on phytochemicals of oat and barley mostly but did not explain rye very well and data is not enough to include in this review article.

Oats

Tocopherols and tocotrienols, phenolic acids, sterols, selenium and avenanthramides are the major phytochemicals of oats [34]. To differ greatly (5 to 48 μg/g) as compare to rice and rye (4 to 9 μg/g) and also to the higher levels present in wheat and barley (23 to 80 μg/g). The range in the total phenolic levels of oats is also similar to those in wheat and rye, but oats have up to 10-fold higher levels of free and conjugated phenolics. Other phytochemicals, including folate, polyphenols, ferulic acid and flavonoids are found at low levels in oats. Some phytochemicals of oat have different components as shown in **Table 1**.

Phytochemicals constituents availability in minor cereals (oat and barley) Develaraja S, *et al.* (2016) [35].

1.2. Type I and Type II Diabetes

Diabetes is a metabolic disorder by a chronic hyperglycemic condition because of defects in insulin secretion and insulin action or both [36] [37]. The incidence of diabetes is increasing rapidly worldwide and WHO & International Diabetes Federation. [38] predicted that the number of adult diabetes can be double in the coming time as from 177 million in 2000 to 370 million in 2030 [39]. During Type I disease different pathogenic processes can be happens from autoimmune destruction of pancreatic β-cell proteins to create complete insulin deficiency

Table 1. Some minor cereal and their approximate phytochemical constituents.

Common Names	Barley	Oat
Scientific Name	*Hordeum vulgare* L.	*Avena sativa* L.
Energy (kJ/100gm)	1481	1628
Protein (gm/100gm)	12.48	16.89
Fat (gm/100gm)	2.3	6.9
Carbohydrates (gm/100gm)	73.48	66.27
Fiber (gm/100gm)	17.3	10.6
Calcium (mg/100gm)	33	54
Iron (mg/100gm)	3.6	4.72
Magnisium (mg/100gm)	133	177
Phosphorus (mg/100gm)	264	523
Potassium (mg/100gm)	452	429
Sodium (mg/100gm)	12	2
Zinc (mg/100gm)	2.77	3.97
Selenium (mg/100gm)	37.7	*NR
Thaimin (mg/100gm)	0.646	0.763
Ribiflavin (mg/100gm)	0.285	0.139
Niacin (mg/100gm)	4.604	0.961
Folate, total (mcg/100gm)	19	56
beta-Carotene	13	*NR
alpha-Carotene	0	*NR
Vitamin A (IU)	22	0

*NR. Not rated.

whereas in Type II, the multiple abnormalities in which include a combination of genetic factors concerned with impaired insulin secretion, insulin resistance as well as environmental factors such as obesity, overweight, lack of exercise and stress, as well as aging [40]. Whole grain foods and legumes are useful for prevention and management of diabetes [16]. From different observation and various studies on T2D treatment, it is concluded that Pharmacological interference has undesirable side effects but plants and herbal therapy can play important role to overcome or control this serious diseases [7]. Phytochemicals such as catechin, ellagic acid, eugenol, kaempferol, berberin have a unique antidiabetic activity [41]. About 5% world population affected of diabetes but unfortunately modern medical world can not solve this problem without side effects [7]. When the grain structure has been disrupted than the postprandial glycaemic response to grains having whole structure would show to be lower (**Table 2**). While grain structure is the most probably give explanation for the measured differences in glycaemic response, different preparation methods and cooking for example boiling compared with baking might also have had an effect. The size of grains

Table 2. Glycaemic index of grains comparison with disrupted and intact structures.

Reference	Study subjects	Disrupted structure	GI[a]	Intact structure	GI
Jenkins *et al.* [1986] [43]	Diabetics (n = 14)	Whole meal rye bread	89 ± 76	Rye kernels	47 ± 5*
Jenkins *et al.* [1988] [44]	Diabetics (n 1/4 6-8)	Barley flour bread	96 (6)	75% barley kernel bread	39 (7)*
Liljeberg *et al.* [1992] [45]	Non-diabetics	80%Wholemeal barley flour bread	94.9715.1	80% barley kernel bread	57.1710.3
Granfeldt *et al.* [1994] [46]	Non-diabetics (n 1/4 9-10)	Barley flour porridge	6579**	Barley kernels	3578*
Granfeldt *et al.* [1995] [46]	Non-diabetics (n 1/4 9)	Rolled oat porridge	9377	Oat kernel porridge	6077*

GI[a] with reference to white wheat bread (GI 1/4 100); mean7s.d., mean (s.e.). *Significantly different from GI of food with disrupted structure. **Significantly different from white wheat bread. Jenkins *et al.*, (2002) [42]. Researcher did not describe P value in articles.

or their products would show to have a complex relationship with digestion and absorption. During 3 months of study Jenkins observed that just fiber cannot work well because foods has additional fibre and cereal fibre alone into the diet of people with T2DM for 3 months did not improve glycaemic control [42].

1.3. Hypoglycemia Cycle

Hyperglycemia starts obvious excessive excretion of urine (polyuria), thirst (polydipsia), constant hunger (polyphagia), weight loss, vision changes and fatigue mostly in type 1 diabetics [47] (WHO.2015). Chronic hyperglycemia can cause microvascular, macrovascular complications, foot ulcers, renal failure, Charcot joints and disturbances in metabolism [36] [48] [49]. Different studies have explained the role played by antecedent hypoglycemia in producing blunted glucose counter regulatory responses during hypoglycemia. Vicious cycles can cause type 1 DM, where as hypoglycemia or exercise can feed forward to down regulate neuroendocrine and therefore creating further hypoglycemia (**Figure 1**). Exercise can manage diabetes as it aids in glycemic control, weight control, reducing blood pressure and improving life style of patients. Unfortunately, the complexity and difficulties of regulating exogenous insulin in a physiologic manner during different physical activities mostly can cause in hypoglycemia with type 1 diabetes mellitus [50]. Hypoglycemia cycle shown in **Figure 1**.

1.4. Phytochemicals in Some Minor Cereals

Minor cereals mostly contain diverse combinations of phytochemicals depending on the type of cereal, location within the grain and grain processed. The outer structures of grains, in specific the pericarp seed coat and aleurone layers, contain much higher levels of phytochemicals *i.e.* phenolic compounds, phytosterols, tocols, betaine and folate, than the germand endosperm [51]. Phenolic compounds are the very different and complex class of phytochemicals in cereal grains [52] [53]. They consist of several derivatives of benzoic and cinnamic acids as well as flavonoids, flavones and flavanols, anthocyanidins, avenanthramides, lignans and alkylresorcinols. In most grains phenolic acids are concentrated in the bran and embryo cell walls and exist mostly in an insoluble bound form, free and soluble-conjugated forms being minor bodies [54] [55]. The

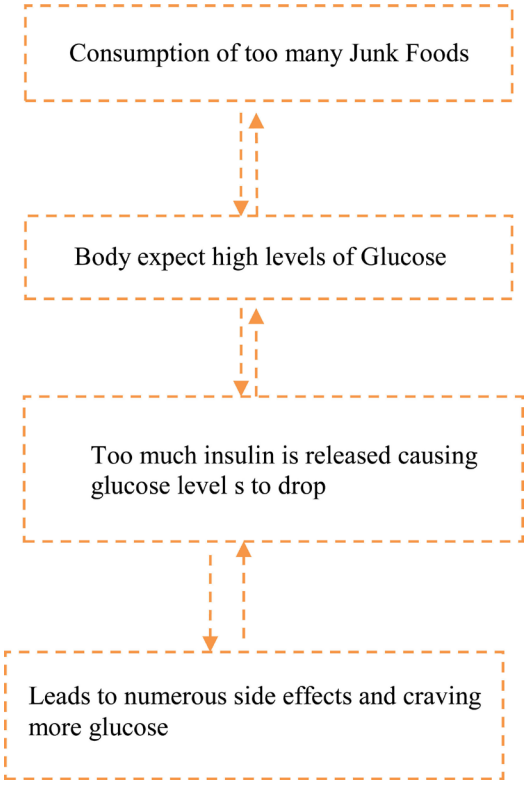

Figure 1. Hypoglycemia cycle.

phenolic acid content of minor cereals is believed as main donor to total antioxidant capacity [54]. Other main phytochemicals that occur in minor cereals which may have a role in protecting against diabetes include a variety of carotenoids, particularly α- and β-carotene, lutein, β-cryptoxanthin and zeaxanthin, all of which are located mostly in the bran and germ fractions [53] Some having provitamin A activity, they all function as antioxidants. Other phytochemicals with strong antioxidant capacities comprise phytate (which chelates prooxidant minerals) and a variety of terpenes and terpenoids (phytosterols and tocols).

If Grains are processed by different method containing milling, grinding and flaking, which make taste and edible grains but these treatments may decreased content of phytochemicals and their bioavailability is increased [56]. Thermal and bioprocessing both can make better phytochemical bioavailability, particularly the latter method, even if the results are not always reliable. Differences among some minor cereals in their contents of different micronutrients and phytochemicals are shown in **Table 3**.

1.5. Metabolic Disease and Prevention Role by Minor Cereals

Diabetes mellitus (DM) can cause by hyperglycemia and metabolic disorder of insulin secretary response [7]. Recently, Type-2 diabetes (T2D) is a big health problem around the world and the incidences are increasing day by day. According to some predictions TD2 can rise from 366 million people to 552 million in the next two decades [1] [57]. It can cause of serious death and disability but

Table 3. Phytochemicals in some minor cereals.

Phytochemicals	Barley	Oat	Rye
Methionine (g/100g)	0.03 - 0.08	0.18	0.18
Cystine (g/100g)	0.06 0.2	0.18	0.18
Selenium (mg/100g)	0.002 - 0.030	<0.10 - 3.3	0.00014
Folate (mg/100g)	0.5 - 0.8	0.05 - 0.06	0.55 - 0.80
Choline(mg/100g)	6.9 - 11	2.0 - 2.6	Unknown
Tocopherols + tocotrienols	4.7 - 6.8	0.05 - 4.8	0.4 - 0.7
Carotenoids(total) (mg gallic acid eq./100g)	0.015 - 0.105	0.031	Unknown
Polyphenols(mg/100g)	50 - 196	9 - 34	125 - 255
Phenolic acids (μg/g) Dry weight	100 - 550	350 - 874	200 - 1080
Ferulic acid (total, mg/100g)	110 - 120	2.1 - 2.4	3.9 - 5.0
Flavanoids (total, mg/100g)	12 - 18	5.6 - 8.2	6.7 - 7.5
Other (mg/100g)			
Alkylresorcinols (μg/g)	0 - 150	Not present	570 - 3220
Avenanthramides (mg/100g)	Not present	4.9 - 27.5	Not present
Betaine (mg/100g)	40 - 76	11.3 - 100	Unknown
Phytosterols (mg/100g)	90 - 115	Unknown	Unknown

Damien P Belobrajdic and Anthony R Bird (2013) [8]. Different phytochemicals showed different ratio in oat, barly and Rye.

regular exercise and balance food can overcome this disease than pharmacological interventions. The start and carry of T2D regulated by a complex inter play of multiple lifestyle and heredity chronic metabolic disorders [1] [3] [11]. The decline in β-cell function can create abnormal insulin gene during glucotoxic state and reduce insulin secretion also. Herbal drugs are widely used because of their effectiveness, less side effects and relatively cheap in cost [58]. More than 300 Indian medicinal plants have antidiabetic property but exact mechanism for hypoglycemic action of many plants are still unknown [7]. Phytochemical supplementation will be needed in additional for cardiovascular disease [59]. Different plant derived flavonoids and their common antioxidant activity have been reported to slow down aldose reductase activity and impart beneficial action in diabetic complications (**Figure 2**).

The difference of generation and scavenging of free radicals play specific role in determining tissue damage related with diabetes. There is a hypothesis that if influx of FFAs (free fatty acids) raised into pancreatic β-cell through lipotoxicity mechanism can cause to the loss of their secretory ability and specific sign of type 2 diabetes [60].

1.6. Bioavailability of Minor Cereal Phytochemical

Bioavailability means to take fraction of phytochemical or other food materials

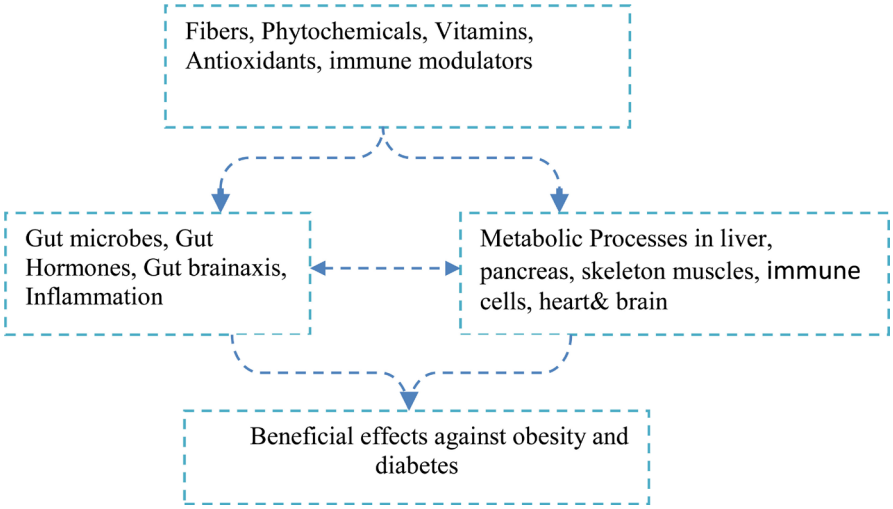

Figure 2. Beneficial minor cereals ingredient against metabolic diseases.

which circulates and reaches at digestive system. Tracer methods present accurately determining bioavailability in which atoms or molecules of the phytochemical within the grain are labelled with an intrinsic radioactive or stable marker but this technique has not been used to measure bioavailability of phytochemicals in cereals. Mostly indirect measures are very common, for example, the balance method (intake minus fecal output), incremental area under the postprandial serum concentration curve and incremental urinary excretion. Many in vitro methods have also been published but not sufficient to understand. Bioavailability of phytochemicals types is quite different from one another. Folate and α-tocopherol are quickly absorbed from the small intestine and their bioavailability is free from dietary fibre content (**Table 4**). Mostly polyphenols are tightly bound to cell walls within the grain matrix thus their bioavailability is limited in the upper gut [61]. If polyphenols even are released from the grain matrix during digestion but they may not be absorbed in the small intestine as they are very hydrophilic to cross the epithelium by passive diffusion [62]. The evidence for minor cereals rich diets improving blood is based on antioxidant defense is during modulation of the glutathione radical scavenging system. This system consumes glutathione peroxidase to metabolise hydrogen peroxide to water by via reduced glutathione as a hydrogen donor [63]. Another supporting evidence is a reduction in pro-inflammatory markers in human intaking higher levels of minor cereals fibre. For example, cereal fibre intakes, although not total fibre were connected with significantly lower plasma cytokine levels in healthy adults [64]. Minor cereals have bioactive phytoconstituents *i.e.* fibers, alkaloids, flavonoids, saponins and other phytochemicals, vitamins, antioxidants and immune modulators with some known health benefits against obesity and diabetes. These bioactive phytochemicals, both in isolation and in combination play important role for improvement of glucose metabolism in different metabolic organs such as liver, pancreas, skeletal muscles, adipose tissue, gastrointestinal tract, immune cells and brain directly or indirectly through effect on gut microbiome,

Table 4. Minor cereal phytochemicals, factors affecting their bioavailability and suggested mechanisms for promoting health.

Phytochemical	Minor cereal Sources	Food & dietary factors affecting bioavailability	Other factors that Enhance bioavailability	Potential mechanisms of action
Phenolics				
Free	Oats	Milk Heme iron	Unknown	Increase plasma total antioxidant capacity to directly mitigate oxidative stress
			Unknown	Indirect through cell signaling
Bound	barley, oats, rye	Grain structure	Bioprocessing of grain	Increase plasma total antioxidant capacity to directly mitigate oxidative stress
			Colonic fermentation (limited evidence)	Indirect through cell signaling
Flavanoids	Barley	Grain structure	Unknown	Increase plasma uric acid levels which has reducing and free radical scavenging activities Improve glutathione radical scavenging system
Selenium	barley oats rye	Not relevant as readily available	Not relevant as readily available	A cofactor for glutathione peroxidase, an enzyme that quenches reactive oxygen species

Damien P Belobrajdic and Anthony R Bird, (2013) [8].

gut hormones, gut-brain axis, inflammatory response, oxidative stress and cholesterol profiles as well.

2. Conclusions

In conclusion, diabetes is a very serious disease but T2D is more dangerous than DM because T2D can cause serious morbidity, disability and mortality in humans, however Hyperglycemia, abnormal lipid metabolism and antioxidant stress are the most common complications in diabetes mellitus.

Minor cereals are sustainable crop as well as environment friendly and their phytochemicals have many useful biological properties against diabetes and other diseases but unfortunately the researches and reviews to focus these unique properties are still negligible. Medical world still can not solve this problem without any side effects. Diabetic patients are taking pharmaceutical drugs to get relief from diabetes complications but side effects creating other problems so in this critical situation, modern science should focus on natural things benefits.

Nowadays researcher getting interest toward colonic micro biota and bio processing used for phytochemical bioavailability but unfortunately it's very limited and insufficient to reduce the risk of diabetes. More studies are required to investigate the direct role of minor cereal phytochemicals and diabetes.

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