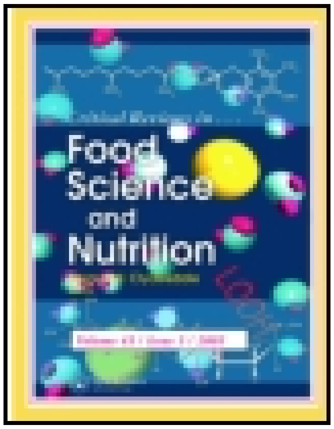

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Therapeutic Effect of Cereal Grains: A Review

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Therapeutic effect of cereal grains: A review

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Abstract

Over the last few decades life style changes have resulted in drastic increase in the incidence of diabetes all over the world especially in the developing countries. Oral hypoglycemic agents and insulin form the main stay in controlling diabetes but they have prominent side effects and fail to significantly alter the course of diabetic complications. Appropriate diet and exercise programs that form a part of lifestyle modifications have proven to be greatly effective in the management of this disease. Dietary therapy is showing a bright future in the prevention & treatment of diabetes. Cereal grains which form the staple diet for humans in most of the countries are increasingly being used to treat diabetes and other associated disorders in view of their antidiabetic and antilipidemic potential. Given this background, this paper reviews the possible mechanisms of lowering blood sugar and cholesterol levels possessed by various commonly consumed cereal grains. It is concluded that cereal grains are

not only the potential sources of energy but also possess the therapeutic role in preventing the metabolic disorders and decreasing the risk factors for cardiovascular and renal disease.

Keywords: diabetes, cereal grains, therapeutic

Abbreviation used:

Non Insulin Dependent Diabetes Mellitus ï NIDDM, Insulin Dependent Diabetes Mellitus ï IDDM, Area Under Curve ï AUC, Diabetes mellitus ï DM, Type 2 diabetes mellitus - T2DM

Article outline

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1.0 Introduction:

Diabetes mellitus (DM), a global public health problem, is now emerging as an epidemic world over. According to a widely accepted estimation, the prevalence of diabetes for all age-groups was 2.8% in 2000 and the number of diabetic patients is expected to reach 4.4% i.e. 366 million by the year 2030 [Wild et al, 2004]. The situation is particularly grim in developing countries like India which has the worldὂs largest diabetic population, encompassing an estimate of 35 million people out of an overall population of 1 billion. Another 79 million people have impaired glucose tolerance. In just over 20 years (i.e. 2025) the country will have almost 200 million people (approximately 15% of the population) affected by diabetes or its precursor [Kaushik et al, 2010].

1.1 Forms, complications and preventive measures for DM

Diabetes is a metabolic disease which affects not only the glucose metabolism but also lipid and protein metabolism. There are mainly two types of diabetesï ð Type 1 and Type 2. In Type 1 or Insulin Dependent diabetes, the hormone insulin is not produced in the absence of pancreatic ß-cells while Type 2 diabetes mellitus (T2DM) is characterized by a progressive impairment of insulin secretion by pancreatic ß-cells and by a relative decreased sensitivity of target tissues to the action of this hormone (Burcelin et al, 1999). DM is a major worldwide health problem predisposing to markedly increased cardiovascular mortality (Savage, 1996). Other serious morbidities and mortalities are related to development of nephropathy (kidney damage), neuropathy (nerve damage), and retinopathy (blindness) due to diabetes [Clark and Lee, 1995; Nathan 1993]. Increased oxidative stress has been implicated in the pathogenesis of DM. Hyperglycemia induced protein glycation generates superoxide free radicals [Memisogullari et al 2003; Cunningham, 1995; Lipinski, 2001]. The generation of active oxygen species may lead to lipid peroxidation and formation of reactive products, which may be involved in severe damage of cell molecules and structures. As a result of these the chances of cardiovascular and cerebral morbidities become manifold.

DM in youth has been recognized to be frequent in populations of native North Americans. Among Japanese school children, T2DM is seven times more common than type 1, and its incidence has increased more than 30-fold over the past 20 years, concomitant with changing food patterns and increasing obesity rates (Rosenbloom et al, 1999). As the prevalence of T2DM continues to increase worldwide, there is an enhanced need for effective disease management. T2DM is managed through a stepwise program of intensive therapy that consists of lifestyle modification including appropriate diet and exercise programs and sequential addition of oral antihyperglycemic agents like (OHAs) and insulin. Improvement in blood glucose through a combination of lifestyle modifications and oral modifications may slow the rate of progression of this disease and enhance the quality of life for people with T2DM (Warren, 2004).

About one third of Type II diabetic patients are treated with oral hypoglycemic agents to stimulate insulin secretion. These drugs however risk inducing hypoglycemia and, over time, lose their efficacy (Burcelin et al, 1999). Although, oral hypoglycemic agents/insulin are the mainstay of treatment of diabetes and are effective in controlling hyperglycemia, they have prominent side effects and fail to significantly alter the course of diabetic complications. The

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common side effects associated with the main classes of drugs used for the treatment of T2DM are hypoglycemia, weight gain, gastrointestinal disorders, peripheral edema and liver disease (Mallare et al, 2005).

The overall management of diabetes not only enthrusts upon achieving normoglycemic and lipid states. While the pharmacological therapies are in use for management, the diabetes prevention trials in China (Pan et al, 1997; Tuomilehto et al 2001; Anonymous 2002] remind us that nutrition and lifestyle approaches can be more effective in delaying the onset of this disease.

1.2 Dietary therapy for DM management

The use of low-glycemic index (GI) diets (comprising of whole grain cereals and legumes) in the management of diabetes has been recommended around the world (Wolever et al, 1992; Brand-Miller et al, 2003). Physical exercise along with diet forms an effective combination for the prevention of DM (Eriksson and Lindgiirde, 1991). Since diet forms the mainstay in the management of diabetes mellitus, there is an urgent need to exploit plant food materials possessing hypoglycemic activity for a possible beneficial use. Cereals form an important part of our diet on account of their nutritive value. Several studies implicate cereal grains in the prevention and treatment of DM. Hence in this background this paper reviews the therapeutic effect of different commonly consumed cereal grains around the globe.

2.0 Cereal grains as therapeutic agents

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The major cereal grains include wheat, rice, and maize, with oats, rye, barley, buckwheat, sorghum, and millet as minor grains. About 50% of the calories consumed by the world population originate from three cereals: rice (23%), wheat (17%), and maize (10%) (Khush 2003) They are grown for their highly nutritious edible seeds which are often referred to as grains. They remain the staple food in most diets of several countries. They are composed of starchy endosperm, germ, and bran (including aleurone). Whole grains are important components of the human diet as shown by the inclusion in the Food Guide Pyramid and US Dietary Guidelines (National Research Council, 1989). Cereals are an important source of calories for humans, both by direct intake and as the main feed for livestock. Besides the main energy source, they supply a variety of nutrients and other food components like phytochemicals (Liu, 2007)

Whole grains especially cereal grains have been found to be associated in the prevention of T2DM (Venn and Mann, 2004; Murtaugh et al, 2003), cancer (Jacobs et al, 1998) and other chronic diseases (**Kushi et al, 1999).**

It is in this context an attempt has been made to review the different commonly consumed cereal grains which have been investigated in human and animal trials for their therapeutic role with regard to antidiabetic and antilipidemic potential. Table 1 briefly describes the therapeutic role of below listed cereals.

Table 1: Therapeutic potential of cereal grains

2.1 Rye: Secale cereale

Rye is a commonly used cereal in northern and Eastern Europe. The dietary fiber content of rye is 16.1 g/100 g; the major fiber components are arabinoxylan (60%), cellulose (15%) and b-glucan (9%) (Nilsson et al 1997). Rye is consumed mainly as whole meal bread with a dietary fiber content of approximately 10% (Rastas et al. 1993).

In a number of studies in human subjects and animals intake of rye bran has been associated with improved metabolic status or preventive effects on diabetes (Hallmans et al, 2003). The effect of bread with high rye-bran content was compared in patients with insulin-dependent diabetes was studied by Nygren et al. 1984. When the bread with high rye bran content was included in the diet it was observed that the glucose profile during the day improved or the insulin doses could be reduced. Lower glycaemic indices have also been observed in human subjects when fed traditionally processed rye products. In another study groups of 9-12 (NIDDM) and 5-6 IDDM volunteers were fed test meals containing 50 g carbohydrate portions of four wheat and three rye products. Glycemic indices demonstrated values of 96±5 for wholemeal wheat bread, 89±6 for wholemeal rye bread, 78 ± 3 for pumpernickel bread, 65 ±4 for bulgur, 63 ±6 for whole wheat kernels and 48 ± 5 for whole rye kernels (Jenkins et al, 1986). A high-fibre diet (HFD) containing rye decreased insulin secretion measured as a decreased excretion of C-peptide in urine and as decreased plasma insulin peaks at the end of the day in ileostomy volunteers (Lundin et al, 2004). Protective effects of rye bran on the diabetes syndrome have also been found in rats and mice (Nygren et al. 1981; Lundin et al. 2001b). Diabetic rats fed a high-fibre bread lost less body weight, and exhibited lower blood glucose levels and lower urinary glucose excretion than the animals fed a low-fibre bread.

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Another study found that rye bran slightly lowered blood glucose levels and led to slower weight gain in normal rats and mice and prolonged survival of diabetic mice (Berglund et al. 1982). Rye bread was found to delay gastric emptying of starch when given as suspensions to rats and in standardized breakfast meals to non-insulin-dependent diabetics. In both cases the postprandial glucose response was lower after rye bread than after wheat bread. A larger amount of starch remained in the stomach of the rats 15 min after ingesting rye bread compared to wheat bread (**Hagander et al, 1987).**

Study done on human subjects also showed that when subjects with baseline serum cholesterol concentration of 6.4 ± 0.2 mmol/L consumed rye and wheat breads (20% of daily energy) as part of their usual diet for 4 weeks, serum total cholesterol decreased by 8% in men but was not significantly altered in women during the rye bread period. (Leinonen et al, 2000). Rye crisp bread has been found to reduce total plasma cholesterol concentrations only in rats fed a high cholesterol diet (Lund et al. 1993). Ingestion of rye bread for 9-10 weeks in hypercholesterolaemic pigs resulted in lower plasma total and LDL cholesterol compared to the wheat group. Intestinal viscosity was 7.2 times higher, and organic matter and fat digestibility significantly reduced in the pigs fed rye buns. Also the hepatic expression of the cholesterol 7Ŭ-hydroxylase gene was lowered in rye-fed pigs (Lærke et al, 2008).

2.2 Barley: *Hordeum vulgare*

Barley is used mainly as animal feed but there is a growing interest in it for human food and industrial uses. Starch, dietary ýbre (DF) and protein are the main components of barley

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grain. The starch contents ranged from 53ï 67% starch, the dietary ýbre contents from 14ï 25% and crude protein contents from 9ï 14%. ϐ-glucan present in the grain could be a responsible factor for the serum cholesterol-lowering effect of barley in human and animals (Oscarsson et al, 1996).

Ten women volunteers receiving a standard diet and a barley diet for a period of 4 weeks showed significantly lowered plasma total and low-density lipoprotein cholesterol concentrations, reduced plasma triacylglycerol concentration and increased stool volume with the barley intake. There was no significant difference in glucose tolerance between diet regimens (Li et al, 2003). The glycaemic response to barley was found significantly lower with a low glycaemic index (68.7 in healthy and 53.4 in NIDDM subjects) and a high insulinaemic index (105.2) in NIDDM subjects (Shukla et al, 1991). In another study, barley ϐ-glucans were found to be an economical and palatable ingredient for processed food products to modify glycemic and insulin response. The ϐ-glucan from barley and durum wheat pasta resulted in a lower glycemic response and lower insulin response when consumed by fasting subjects (Yokoyama et al, 1997). Insulin responses for the barley extract consumed by non-diabetic subjects at the rate of 0.33 g/kg of body weight were found to be the lowest (Hallfrisch et al, 2003). In adult diabetic rats, a diet containing barley had a modulating effect on the symptoms of diabetes (blood glucose concentration and water consumption) when compared with a starch or sucrose-based diet. The beneficial effect of barley might be explained by its very high content of chromium (5.69 µg/g) (Mahdi and Naismith, 1991).

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Waxy hulless barley (β-glucan = -7%) bread products were incorporated in the diet of Type 2 men resulted in lower mean glycemic response area (AUC) and higher insulin response area. Hence incorporation of Barley Bread products (5 g/d β-glucan) into the diet improved glycemic response (Pick et al, 1998). Bread made with enrichment of wheat flour with barley flour with (1Ÿ 3,1Ÿ 4)-β-glucan-enriched fractions, a sieved fraction (SF) and a water-extracted fraction (WF) resulted in 28% lower glycemic index when given to adults (Cavallero et al, 2002). Slow absorption of barley in one of the studies has been shown beneficial for obese and diabetic patients where cooked portion of two kinds of barley Prowashonupana (PW) and standard barley (BZ) when consumed by 10 healthy hydrogen (H2)-producing adults (Lifschitz et al, 2002).

Malted barley extract (MBE) when administered orally to the diabetic mice for 12 weeks at a dose of 62.5 mg/kg of body weight resulted in significantly lower fasting blood glucose, Hemoglobin A1c content, glucose-6-phosphatase activity in kidney as compared with the control. However there was no significant difference in the serum insulin level among groups (Hong et al, 2004).

2.3 Millets: ***Pennisetum*** gambiense

Millet (*Pennisetum* gambiense), which is a variety of the millet family known as pearl, bulrush, spiked orcattail millet, is the staple food consumed in the drier part of tropical Africa, particularly in the arid and semi-arid regions of West Africa. Other varieties are P. typhoides P. americanum and P. spicatum. It may be cooked like rice, or ground into flour

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and made into either a light porridge or gruel, eaten with sugar and milk, or a thick porridge eaten with soup, or stew. It contains 8.8ï 18.2% protein, 3ï 5% fat, 59.3ï 69.5% carbohydrate, 1.2ï 2.8% fibre, 1.5ï 2.7% ash and 2.0ï 2.7% sugar (Baryeh 2002)

There are numerous studies showing the cholesterol and blood glucose lowering effect in animal models but are scarce in human subjects. Rats fed with diet containing Native Starch (NS) and Treated Starch (TS) from barnyard millet had the lowest blood glucose (670.50 mg litre~1 for (NS) and 520.90 mg litre~1for (TS), serum cholesterol (387.1 mg litre~1 for (NS) and 360.3 mg litre~1for (TS) and triglycerides (1502.7 mg/ litre for (NS) and 1303.4 mg /litrefor (TS) as compared to rice (Kumari and Thayumanavan, 1997). In another study feeding food containing 50 g/100 g finger millet (FM) for 4 weeks to diabetic rats controlled the glucose levels and hastened the dermal wound healing process. Skin levels of glutathione (GSH), ascorbic acid and Ŭ-tocopherol in alloxan-induced diabetic rat lowered as compared to non-diabetics. It also improved the impaired production of Nerve Growth Factor (Rajasekaran et al, 2004). Whole grain flour of Finger millet (FM) and kodo millet (KM) when incorporated at 55% by weight in the basal diet fed to alloxan-induced diabetic rats over a period of 28 days showed a greater reduction in blood glucose (42%) and cholesterol (27%) with KM-enriched diet than those fed the finger millet (36% and 13%). The levels of enzymatic, nonenzymatic antioxidants and lipid peroxides significantly reduced in diabetic animals and restored to normal levels in the millet-fed groups. Glycation of tail tendon collagen was only 40% in the finger milletï fed rats and 47% in the KM-fed rats compared to the controls. Diets containing whole grain millet meal flour can thus protect against

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hyperglycemic (Hegde et al, 2005). Effects of methanolic extracts of Finger millet and Kodo millet on glycation and crosslinking of collagen was studied by incubating tail tendons of rats with glucose (50 mM) and 3 mg of methanolic extracts for10 days. Tendon collagen incubated with glucose showed 65% solubility on pepsin treatment; poor resolution of bands in the cyanogen bromide peptide map, and intrinsic viscosity of 0.84 dl/g where as those incubated with Fingermillet and Kodo millet extracts inhibited glycation; showed 89% and 92% solubility in pepsin; good resolution of bands in the cyanogen bromide peptide map and intrinsic viscosity of 0.46 and 0.58 dl/g respectively. The study implicates the potential usefulness of the above millets in protection against glycation and crosslinking of collagen (Hegde et al, 2002). In a recent study rats receiving foxtail millet or proso millet diet showed lower concentrations of serum triglycerides compared to those of the white rice (WR) and sorghum groups (Lee et al, 2010). In another study genetically type 2 diabetic KK-A^y mice fed a normal Korean foxtail millet protein (FMP) diet or a high-fat-high-sucrose diet containing FMP for 3 weeks, showed remarkably increased plasma concentrations of high-density lipoprotein cholesterol (HDL-cholesterol) and adiponectin in comparison with a casein diet group, whereas concentrations of insulin decreased greatly and that of plasma glucose was comparable to that in the casein diet group. Therefore, FMP would serve as another beneficial food component in obesity-related diseases such as type 2 diabetes and cardiovascular diseases (Choi et al, 2005). Porso millet protein has been shown to elevate plasma levels of HDL-cholesterol without the involvement in rising the concentration of low-density lipoprotein cholesterol in different rats and thus would be useful as a new food ingredient which has the function that regulates cholesterol metabolism (Nishizawa et al,

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1996; Nishizawa and Fudamoto, 1995). Feeding proso-millet protein concentrate (PMPC) for 21 days to rats showed a clear elevation of plasma levels of HDL cholesterol without an increase in low density lipoprotein cholesterol levels and enhancement of lecithin: cholesterol acyltransferase (LCAT) activities ($p<0.06$) as compared with a casein diet (Shimanuki et al, 2006). Protein from porso millet showed the hisgest value of plasma HDL-cholesterol (67.4±2.3C) in the rats among three dietary groups of casein and soy protein Isolate (SPI) (Nishizawa et al, 1990)

Consumption of finger millet based diets by 6 NIDDM subjects resulted in significantly lower plasma glucose levels, mean peak rise, and area under curve. Consumption of whole finger millet dosa resulted in a significantly lower fasting plasma glucose (175.2 mg/dl), 2 hr postprandial plasma glucose (182.8 mg/dl), lesser percent peak rise (81.0 mg/dl) and decreased AUC (867.3) followed by germinated finger millet dosa and rice dosa. This may have been due to the higher fiber content of finger millet (2.7 g/serving) (Kumari and Sumathi, 2002).

2.4 **Sorghum:** Sorghum bicolor

Sorghum is the fifth most important cereal crop in the world after wheat, rice, corn and barley. It is able to grow and produce in the warmer temperatures and tropical regions of the world. Sorghum is the chief cereal grain consumed in Asia and Africa. More than 35% of sorghum is grown directly for human consumption. The rest is used primarily for animal feed and alcohol and industrial products (**Awik and Rooney, 2004**). The protein quality of sorghum grain is poor because of the low content of essential amino acids such as lysine, tryptophan and threonine (Anglani, 1998).

Studies on the antidiabetic potential of sorghum are scarce either on human or animal subjects. In one of the human studies hypoglycemic response of three traditional sorghum (both whole and dehulled) recipes namely Missiroti, Upma and Dhokla were studied on six NIDDM patients. Consumption of whole sorghum recipes resulted in significantly lower plasma glucose levels, lesser per cent peak rise (21.8± 2.6, 15.1 ± 4.8 and 22.1 ± 8.5 for whole sorghum missiroti, upma and dhokla and lesser area under curve (AUC) in diabetic subjects when compared with the consumption of dehulled sorghum and wheat recipes. Least glycemic response was observed with whole sorghum semolina upma (74.6 mg) followed by whole sorghum Missiroti (77.8 mg) and whole sorghum dhokla (84.5 mg) (Lakshmi and Vimala, 1996)

Effect of ethanol extracts of several varieties of sorghum bran on albumin glycation, a non-enzymatic process important in the pathogenesis of diabetic complications was examined. One high phenolic sorghum bran variety (sumac) inhibited protein glycation by approximately 60% and produced a 20% decrease in methylglyoxal mediated albumin glycation suggesting that certain varieties of sorghum bran may serve as nutraceutical agent in diabetes and insulin resistance (Farrar et al, 2008). Ethanol extracts of sorghum cultivars, Mongdang-susu(SS-1), Me-susu(SS-2), Susongsaengi-susu(SS-3) and Sikyung-susu(SS-4) exhibited higher inhibitory activities against Ŭ-glucosidase (IC_{50} = 1.1ï 1.4 ɛ g/ml) and

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strongly inhibited degradation of starch by pancreatic and salivary Ǖ-amylase. These in vitro studies indicate the potential of sorghum in the development of effective anti-diabetic agents (Kim et al , 2010). Investigations done on animal models suggested its cholesterol-lowering properties and health benefits when incorporated into human diets. In a study male hamsters were fed AIN-93M diets supplemented with a hexane-extractable lipid fraction from grain sorghum whole kernels for a period of 4 weeks containing the grain sorghum lipids (GSL) at 0.0, 0.5, 1.0, or 5.0% by weight. Dietary GSL significantly reduced plasma non-HDL cholesterol concentration in a dose-dependent manner with reductions of 18, 36, and 69% in hamsters fed 0.5, 1.0, and 5.0% GSL, respectively, compared with controls. Liver cholesteryl ester concentration significantly reduced where as plasma HDL cholesterol concentration was not altered by dietary treatment. Cholesterol absorption efficiency also significantly reduced indicating that grain sorghum contains beneficial components that could be used as dietary supplements to manage cholesterol levels in humans (Carr et al, 2005). In a similar study sorghum distillers dried grains with solubles (DDGS) comprising 0.0%, 0.5%, 1.0%, and 5.0% diet by weight significantly lowered plasma non-HDL cholesterol and liver esterified cholesterol concentration in hamsters. Faecal neutral sterol (i.e., cholesterol) excretion was significantly higher (66% higher compared to controls) in the 5.0% DDGS lipids group (Hoi et al, 2009)

2.5 Wheat: *Triticum aestivum*

Wheat is a grass, originally from the Fertile Crescent region of the Near East, but now cultivated worldwide. In 2007 world production of wheat was 607 million tons, making it the third most-produced cereal after maize (784 million tons) and rice (651 million tons) (Anonymous, 2007). Wheat grain is a staple food used to make flour for leavened, flat and steamedbreads, biscuits, cookies, cakes, breakfast cereal, pasta, noodles etc. (Cauvain, 2003).

Wheat bran supplementation in diabetics for 2 months resulted in reduction in fasting and 2 h postprandial blood sugar levels after one month's bran therapy. No appreciable changes in the serum glycosylated protein levels, glycosylated albumin levels, serum lipids and lipoprotein cholesterol levels were observed during the period of supplementation (Mani & Mani, 1987). Arabinoxylan (AX) rich fiber extracted from wheat-flour when given to healthy subjects resulted in lower glycaemic response. The peak postprandial glucose concentration after meals containing 6 and 12 g AX-rich fiber was significantly lower (6.3 ± 1.3 compared with 7.2 ± 1.0 mmol/L, $P < 0.01$; 5.9 ± 0.9 compared with 7.2 ± 1.0 mmol/L, $P < 0.001$, respectively). The incremental area under the curve (IAUC) for glucose was 20.2% (95% CI: 5.8%, 34.7%; $P < 0.01$) and 41.4% (25.9%, 56.8%; $P < 0.001$) lower, whereas IAUC for insulin was 17.0% (2.0%, 32.1%; $P < 0.05$) and 32.7% (18.8%, 46.6%; $P < 0.001$) lower, respectively (**Lu et al, 2000).** Mean postprandial blood glucose decreased from 12.0 ± 3.8 mmol/l (mean ± SD) to 9.7 ± 2.7 mmol/l (p<0.01) in the bran period and HbA1 decreased from 10.5 ± 2.1% to 9.9 ± 1.2% (not significant) at the end of the bran period when the diet of insulin-dependent diabetics was supplemented with wheat bran at a mean dose of 33g (Vaaler et al, 1986). The comparison of four types of wheat viz. whole grain, cracked grain, coarse and fine wolemeal flour in 10 healthy subjects resulted in glucose responses to whole

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grain of approximately one-third the response of the fine flour. Insulin responses were found to be similar (Behall et al, 2000)

Thirty NIDDM females after a month of control period were fed 125 g of instant wheat meal (45 g in breakfast, 40 g in mid morning, and 40 g in evening) on weekly basis for 2 months. The body weight, BMI, and waist hip ratio reduced significantly but were still higher than the recommended standard after supplementation. Significant decrease in blood pressure of the subject was also recorded after supplementation of instant wheat meal (Anita et al 1963)

2.6 Oats: *Avena sativa*

Like most other grains, oat is used as feed for livestock and pets and food for humans. It is considered to be a nutritious source of protein, carbohydrate, fiber, vitamins and minerals and it contains minor constituents like ϐ-glucan which is known to reduce cholesterol and lower the risk of heart diseases (Peterson, 2004). Oat grain contains 13% protein, 7.5% fat, 10.3% dietary ýber (Butt et al, 2008)

Oat bran muffins were subjected to a controlled range of ϐ-glucan solubility to repeated freeze-thaw temperature cycling. ϐ-Glucan solubility decreased as the number of freeze-thaw cycles increased. Peak blood glucose rise (PBGR) after fresh muffins (8 and 12 g of ϐ-glucan/serving) was significantly lower than that after muffins (8 and 12 g of ϐ-glucan/serving) treated with four freeze-thaw (FT) cycles (1.84 ± 0.2 vs. 2.31 ± 0.1 mmol/L, P = 0.007). Compared with the control whole wheat muffins, the reduction in

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incremental area under the glucose response curve (AUC) after fresh muffins (8 and 12 g of β-glucan/serving) was nearly twice that after 4 FT cycles (43.3 ± 4.4% vs. 27.0 ± 5.4%, P = 0.016) suggesting that reduction of β-glucan solubility in foods lowers postprandial glycemia (Lan-Pidhainy et al, 2007). Four men with NIDDM consumed oat bran concentrate breads containing 22.8% β-glucan and control white breads with a mean total dietary fiber intake of 19 g/day in the white bread period and 34 g/day in the oat bran concentrate period. Mean glycemic and insulin response areas (area under the curve) (PÒ.05 and not significant), mean total plasma cholesterol and low-density lipoprotein cholesterol levels were lower in the oat bran concentrate period than in the white bread period. Also, the mean ratio of low-density lipoprotein cholesterol to high-density lipoprotein cholesterol reduced by 24% (Pick at al, 1996). Fasting control subjects and subjects with Type 2 diabetes were fed porridge meals containing either wheat farina, wheat farina plus oat gum or oat bran. Oat bran and wheat farina plus oat gum meals reduced the postprandial plasma glucose excursions and insulin levels when compared with the control wheat farina meal in both control and Type 2 diabetic subjects. A diet rich in β-glucan may therefore be beneficial in the regulation of postprandial plasma glucose levels in subjects with Type 2 diabetes (Braaten et al, 2009). Corn flakes and ready to eat oat-bran cereal diets (25 g oat bran/d) were fed for 2 weeks to 12 men with undesirably high serum total-cholesterol concentrations. The oat-bran cereal diet lowered serum total-cholesterol and serum LDL-cholesterol concentrations significantly by 5.4% and 8.5% respectively. The study implicated that ready-to-eat oat-bran cereal provides a practical means to incorporate soluble fiber into the diet to lower serum cholesterol (Anderson et al, 1990). When 20 hypercholesterolemic men were given oat bran, there was a decrease in total

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cholesterol by 12.8%, low-density-lipoprotein cholesterol by 12. 1% and apolipoprotein B-100 by 3.7%. Serum triglycerides decreased by 10% (Anderson et al, 1991). Twenty hypercholesterolemic male and female adults consuming the oat gum (2.9 g beta-glucan) twice daily for 4 weeks with a 3 week wash-out between phases showed reduction in total cholesterol and LDL by 9% relative to initial values. There were no significant changes in high density lipoprotein (HDL) cholesterol and triglyceride levels (Braaten et al, 1994). Six normolipidemic males showed lower serum triglyceride response in the presence of oat bran, wheat fiber, or wheat germ (Cara et al, 1992). On oat-bran diets in an alternating sequence to eight men with previously documented hypercholesterolemia, average reductions in serum total cholesterol concentrations were 13% plasma low-density lipoprotein cholesterol concentrations were 14% lower while high-density lipoprotein cholesterol concentrations were not changed. Fasting and postprandial serum glucose, insulin, and triglyceride concentrations were similar on the two diets. Fecal excretion of total bile acids was 54% higher on oat-bran diets than on control diets but neutral steroid excretion was slightly lower while on oat bran (**Kirby et al, 1981)**

2.7 Rice: Oryza sativa

Rice is the staple diet in 39 countries but the dependence is much higher in Asian countries (Juliano 1993). It contains 7.5%, 1.9%, 77.4% and 0.9% of protein, fat, carbohydrate and fiber respectively (Charalampopoulos et al, 2002)

Feeding pre-germinated brown rice (PGBR) diet to diabetic rats ameliorated the elevation of blood glucose and PAI-1 concentrations significantly, and tended to decrease the plasma lipid peroxide concentrations in comparison with rats fed a white rice diet (Hagiwara et al, 2004). administration of a modified AIN-76 diet, and an the ethyl acetate fraction (EAE) or ferulic acid fraction from rice bran (FA) orally for 17 days to Type 2 diabetic mice significantly decreased blood glucose levels and increased plasma insulin levels, elevated hepatic glycogen synthesis and glucokinase activity, decreased plasma total cholesterol and low density lipoprotein (LDL) cholesterol concentrations (Jung et al, 2007). After 21 days, plasma cholesterol in hamsters was significantly reduced by rice bran diets containing added unsaponfiable matter compared to the cellulose control diet, while the high density lipoprotein cholesterol-to-low density lipoprotein cholesterol ratio remained unchanged in all treatment groups (Kahlon et al, 1996). Diets containing full-fat rice bran (FFB), defatted rice bran (DFB) oil resulted in significantly lower liver cholesterol levels in hamsters. Cholesterol plasma and liver cholesterol and plasma triglycerides properties of full-fat rice bran (FFB) are present when defatted rice bran (DFB) is recombined with higher in animals fed a diet of 0.3% cholesterol with cellulose (Kahlon et al, 1996). Blending rice bran oil (RBO) with safflower oil at a definite proportion (7:3, wt/wt) magnifies the hypocholesterolemic efficacy in hypercholesterolemic rats in light of the presence of peculiar components such as oryzanol and tocotrienols (**Sugano and Tsuji, 1997)**

Total cholesterol levels decreased 7.0% when subjects consumed rice bran or oat bran two 3-week periods followed by a control diet without bran for 2 weeks. Rice bran was found equally effective as oat bran in lowering blood cholesterol levels (Hegsted et al, 1993). a dose of 100 mg/day of tocotrienol-rich fraction (TRF_{25}) of stabilized and heated rice bran to hypercholesterolemic human subjects produce maximum decreases of 20, 25, 14 ($P<0.05$) and 12%, respectively, in serum total cholesterol, LDL-cholesterol, apolipoprotein B and triglycerides compared with the baseline values (Qureshi et al, 2002a). Fractions of rice bran were found to reduce hyperglycemia and hyperlipidemia in diabetic subjects. Type I subjects fed Stabilized rice bran (SRB), rice bran water soluble (RBWS), and rice bran fiber concentrates (RBFC) plus AHA Step-1 diet reduced glycosylated hemoglobin 1%, 11%, and 10%, respectively and fasting serum glucose levels 9%,29%, and 19% respectively. In Type II subjects RBWS, and RBFC plus AHA Step-1 diet decreased levels of glycosylated hemoglobin (15% and 11%) and fasting glucose (33% and 22%), respectively. Serum total cholesterol, LDL-cholesterol, apolipoprotein B, and triglycerides levels were reduced with ricebran fiber concentrates in the Type I (10, 16, 10, 7%) and Type II groups (12, 15, 10, 8%), respectively (Qureshi et al, 2002b). Serum cholesterol decreased significantly by $8.3 \pm 2.4\%$ and LDL-C decreased by $13.7 \pm 2.8\%$ in the rice bran group in hyperlipidemic humans justifying its inclusion in the prudent diet of individuals with hyperlipidemia (**Gerhardt and Gallo, 1998).** Mean fasting and postprandial serum glucose levels were reduced in diabetic patients whose diet was enriched with 40 g of fiber (30.6% insoluble and 11.7% soluble components) from rice bran (Rodrigues et al, 2005)

2.8 Corn: *Zea mays*

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Maize is one of the most important cereal crops, providing between 50% and 70% of the dietary protein for humans, depending on geographical distribution. It is also one of the major crops used for feeding farm animals, particularly poultry and swine. It contains 8.9%, 3.9%, 72.2% and 2.0% of protein, fat, carbohydrate and fiber respectively (Charalampopoulos et al, 2002).

Long-term supplementation (6 months) with corn bran hemicellulose (CBH) decreased the post OGTT curve and fasting glucose level for patients with impaired mild Type II diabetes. Hemoglobin A1c decreased significantly during CBH supplementation in the obese patients (Hanai et al, 1997). Consumption of 52 g corn bran by type II diabetics decreased very low-density lipoprotein cholesterol, triglycerides, and glycosylated Hb (**Mahalko et al, 1984)**. Macerated decoction extract of Zea mays styles produced consistent hypoglycemic effect in fasting rabbits as compared to crystalline insulin (Menczel and Sulman, 1962). Some Native American corn products such as tortillas (54%) and hominy (57%) have much lower glycemic indices than white bread (Miller 1995). Test beverages containing maize-based fiber ingredients (25g total carbohydrate) fed to 12 healthy volunteers resulted in significantly lower glycemic and insulinemic responses for the incremental area under the curve (iAUC) and at all time points compared with the control **(Kendall et al 2008)**

Zea mays L. saponin (ZMLS) could remarkably decrease the blood glucose and prevent the pancreatic islet beta-cell from the injury induced by Streptozotocin in the diabetic rats (Miao et al, 2008). A recent study by Robertson et al, 2009 found that the consumption of hi-maize-resistant starch (40 g of dietary fiber/day) increased insulin sensitivity in 10 overweight subjects with insulin resistance and metabolic syndrome after 8 weeks. It increased their hepatic insulin sensitivity by 54%, their peripheral (muscle) insulin sensitivity by 24%, and their glucose uptake into forearm muscle by 68%. They also had reduced fasting insulin levels, reduced postprandial insulin responses to a standardized meal, and significantly lower levels of fasting non-esterified fatty acids.

2.9 Sago: *Metroxylin sagu*

Sago (Metroxylin sagu) is one of the main sources of native starch. In Malaysia sago dishes are commonly eaten with sugar. However, other societies use sago as a staple food item instead of rice or potato. The sago palms grow all over Southeast Asia, and are used as staple foods in places where there is insufficient rain to grow wet rice. In India, it is used as ósabudanaô. In Sarawak, Malaysia, sago is widely used to produce sago pearls and ñtabaloiò, a local biscuit delicacy (Hong-Siong et al, 1991)

When three different physical forms of a sago viz., sago porridge (SR), sago paste (SP), sago gel (SG) were supplemented in the diets of 12 male subjects, plasma glucose AUC for white bread (WB) was significantly lower than SG but not significantly different from SR and SP. Plasma insulin AUC for SG was significantly higher than WB and SR. All three sago meals were not significantly different in their glycaemic responses (Ahmad et al, 2009). Rats fed raw and gelatised sago starch showed a statistically significant decrease in the total serum cholesterol and the atherogenic index as compared to tapioca starch. Serum triacylglycerol

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concentrations in the rats fed raw sago starch were significantly lower than raw tapioca starch. These were due to the lower digestibility and higher amylose content of sago starch (Hirao et al 2000)

2.10 Buckwheat: Fagopyrum esculentum

Bitter-buckwheat is not a true cereal and it originates from the southwest of China, which has long history of cultivation. The content of protein, fat and carbohydrate is 11.66%, 2.9% and 64.5%, respectiveIy. Bitter-buckwh also contains 18 kinds of amino acids (Wang et al 1995).

Buckwheat contains relatively high levels of D-chiro-inositol D-CI, a component of an insulin mediator. In fed streptozotocin STZ rats, both doses of the buckwheat concentrate (containing 10 and 20 mg of D-CI/kg of body weight) were found effective in lowering serum glucose concentrations by 12-19% at 90 and 120 min after administration (Kawa et al 2003).

Two week supplementation with buckwheat protein product (BWP) resulted in signiýcantly lowered plasma and liver concentrations of cholesterol in the hamsters (Tomotake et al, 2000). Rats fed a semipurified diet containing buckwheat protein extract (BWPE) for 3 weeks showed lower levels of plasma cholesterol and hepatic cholesterol (Kayashita et al, 1995; Kayashita et al 1997). Study done by the same investigator later on showed significantly lower hepatic triglyceride concentration with BWPE as compared with those fed casein diet. BWPE feeding also caused lower activities of hepatic glucose-6-phosphate

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dehydrogenase and fatty acid synthase, but did not affect the activity of hepatic carnitine palmitoyltransferase (Kayashita et al, 1996). These results suggest that buckwheat protein is one of the dietary factors available for improvement of cholesterol metabolism.

3.0 Conclusion

With increasing development and affluence the changes in lifestyle and dietary habits have resulted in increasing incidences of lifestyle diseases like Type 2 Diabetes Mellitus especially in the developing countries. The disease have enormous burden in terms of diagnosis costs of and treatment lifestyle approaches including diet appropriate and exercise programs are effective in managing this disease. Dietary intervention with a diet incorporating cereal grains seems to be a natural, cost effective, and free from side effects solution for the prevention & treatment of T2DM. It is concluded that cereals which form a part of diet all over the world possess therapeutic properties and help in lowering blood glucose levels and maintain blood cholesterol.

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Table 1: Therapeutic potential of cereal grains

SNo.	Cereal	Part/form administered	Organism	Action	Reference
1.	Rye	Bread	Volunteers	Glycemic indices demonstrated values of 96±5 for wholemeal wheat bread, 89±6 for wholemeal rye bread, 63 ±6 for whole wheat kernels and 48 ± 5 for whole rye kernels.	Jenkins et al, 1986
2.	Rye	High-fibre diet	Volunteers	Decreased insulin secretion	Lundin et al, 2004
3.	Rye	Bread	Diabetic rats	Lower blood glucose levels and lower urinary glucose excretion	Nygren et al. 1981; Lundin et al. 2001b
4.	Rye	Rye bran	Diabetic mice and normal rats	Lowered blood glucose levels and led to slower weight gain in normal rats and mice and prolonged survival of diabetic mice	Berglund et al. 1982
5.	Rye	Bread	NIDDM diabetics	Lower postprandial glucose response and delayed gastric emptying of starch	Hagander et al, 1987
6.	Rye	Bread	Hypercholesterolemic patients	Decrease in serum total cholesterol (8%) in men	Leinonen et al, 2000
7.	Rye	Bread	Hypercholesterolaemic pigs	Lower plasma total and LDL cholesterol	
8.	Barley	Diet	Women volunteers	Lowered plasma total and low-density lipoprotein cholesterol concentrations, reduced plasma triacylglycerol concentration	Li et al, 2003
9.	Barley	β-glucans	Fasting subjects	Lower glycemic and insulin response	Yokoyama et al, 1997
10.	Barley	Diet	Diabetic rats	Modulating effect on the symptoms of diabetes (blood glucose concentration and water consumption)	Mahdi and Naismith, 1991
11.	Barley	Bread products	NIDDM diabetics	Lower mean glycemic response area (AUC) and higher insulin response area.	Pick et al, 1998
12.	Barley and	Bread	Men	28% lower glycemic index	Cavallero et al,

	wheat flour				2002
13.	Barley	Malted barley extract	Diabetic mice	Lower fasting blood glucose, Hemoglobin A1c content, glucose-6-phosphatase activity in kidney	Hong et al, 2004
14.	Millet	Diet containing Native Starch (NS) and Treated Starch (TS)	Rats	Lowest blood glucose, serum cholesterol and triglycerides	Kumari and Thayumanavan, 1997
15.	Finger millet	Diet containing 50 g/100 g finger millet	Diabetic rats	Lowered levels of glutathione (GSH), ascorbic acid and Ŭ-tocopherol	Rajasekaran et al, 2004
16.	Finger millet	Diet containing finger millet	Diabetic rats	Reduction in blood glucose (36%) and cholesterol (13 %), levels of enzymatic, nonenzymatic antioxidants and lipid peroxides	Hegde et al, 2005
17.	Finger millet	Finger millet based diets	NIDDM diabetics	Lower fasting plasma glucose (175.2 mg/dl), 2 hr postprandial plasma glucose (182.8 mg/dl), lesser percent peak rise (81.0 mg/dl) and decreased AUC (867.3)	Kumari and Sumathi, 2002
18.	Porso millet	Protein concentrate	Rats	Elevation of plasma levels of HDL without an increase in LDL levels	Nishizawa et al, 1996; Nishizawa and Fudamoto, 1995Shimanuki et al, 2006
19.	Korean foxtail millet	Protein diet	Type 2 diabetic KK-A^y mice	Increased levels of HDL, decreased concentrations of insulin	Choi et al, 2005
20.	Sorghum	Whole sorghum recipes	NIDDM patients	Lower plasma glucose levels, lesser per cent peak rise and lesser area under curve (AUC)	Lakshmi and Vimala, 1996
21.	Sorghum	Diets supplemented with a hexane-extractable lipid fraction	Hamsters	Reduced plasma non-HDL cholesterol concentration and cholesterol absorption efficiency also significantly reduced	Carr et al, 2005

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22.	Sorghum	Dried grains in diet	Hamsters	Lowered plasma cholesterol concentration. Faecal neutral sterol excretion was significantly higher	Hoi et al, 2009
23.	Wheat	Bran	NIDDM diabetics	Reduction in fasting and 2 h postprandial blood sugar levels	Mani & Mani, 1987
24.	Wheat	Arabinoxylan rich fiber	Healthy subjects	Lower glycaemic response	Lu et al, 2000
25.	Wheat	Wheat bran	IDDM diabetics	Decreased postprandial blood glucose and HbA1	Vaaler et al, 1986
26.	Wheat	Meal	NIDDM diabetic women	Body weight, BMI, blood pressure and waist hip ratio reduced significantly	Anita et al 1963
27.	Oat	Bran diets	Hypercholesterolemic men	Reductions in serum total cholesterol (13%) and LDL (14%) concentrations. Increased fecal excretion of total bile acids (54%)	Kirby et al, 1981
28.	Oat	Oat gum	Hypercholesterolemic patients	Reduction in total cholesterol and LDL by 9%	Braaten et al, 1994
29.	Oat	Bran	Hypercholesterolemic men	Decrease in total cholesterol by 12.8%, LDL cholesterol by 12% and serum triglycerides by 10%	Anderson et al, 1990; Anderson et al, 1991
30.	Oat	Oat bran concentrate breads	NIDDM diabetic	Lower glycemic and insulin response areas, total plasma cholesterol and LDL cholesterol levels	Pick at al, 1996
31.	Rice	Pre-germinated brown rice	Diabetic rats	Ameliorated the elevation of blood glucose and decreased the plasma lipid peroxide concentrations	Hagiwara et al, 2004
32.	Rice	ferulic acid fraction from rice bran	Type 2 diabetic mice	Decreased blood glucose levels and increased plasma insulin levels, elevated hepatic glycogen synthesis and glucokinase activity, decreased plasma total cholesterol and LDL concentrations	Jung et al, 2007
33.	Rice	Fibre from rice bran	Diabetic patients	Reduced fasting and postprandial serum glucose levels	Rodrigues et al, 2005
34.	Rice	Rice bran fiber concentrates	Type 1 and 2 diabetic patients	Reduce hyperglycemia and hyperlipidemia	Qureshi et al, 2002b

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35.	Rice	tocotrienol-rich fraction (TRF_{25}) of rice bran	Hypercholesterolemic human subjects	Decreases of 20, 25, 14 and 12%, in serum total cholesterol, LDL-cholesterol, apolipoprotein B and triglycerides	Qureshi et al, 2002a
36.	Corn	Bran hemicellulose	Type II diabetics	Decreased the post OGTT curve, Hemoglobin A1c and fasting glucose level	Hanai et al, 1997
37.	Corn	Bran	Type II diabetics	Decreased LDL cholesterol, triglycerides, and glycosylated Hb	Mahalko et al, 1984
38.	Corn	Macerated decoction extract of Zea mays styles	Fasting rabbits	Hypoglycemic effect	Menczel and Sulman, 1962
39.	Corn	Maize-based fiber ingredients	Healthy volunteers	Lower glycemic and insulinemic responses	Kendall et al 2008
40.	Corn	Saponin	Diabetic rats	Decrease the blood glucose and prevent the pancreatic islet beta-cell from the injury induced by Streptozotocin	Miao et al, 2008
41.	Corn	Starch	Overweight subjects with insulin resistance and metabolic syndrome	Increased hepatic insulin sensitivity by 54%, peripheral (muscle) insulin sensitivity by 24%, and their glucose uptake into forearm muscle by 68%. Also reduced fasting insulin levels, postprandial insulin responses to a standardized meal, and significantly lower levels of fasting non-esterified fatty acids	Robertson et al, 2009
42.	Sago	Raw and gelatised sago starch	Rats	Decrease in the total serum cholesterol and the atherogenic index	Hirao et al 2000
43.	Buckwheat	Buckwheat concentrate (containing D-chiro-inositol)	STZ rats	Lowered serum glucose concentrations by 12-19% at 90 and 120 min	Kawa et al 2003
44.	Buckwheat	Protein product	Hamsters	Lowered plasma and liver concentrations of cholesterol	Tomotake et al, 2000

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45.	Buckwheat	Protein product	Rats	Lower levels of plasma cholesterol and hepatic cholesterol	Kayashita et al, 1995; Kayashita et al 1997