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Full Length Review Paper

Prophylaxis and treatment of types 1 and 2 diabetes mellitus

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The aim of this study is to review literature on diabetes mellitus disease in the light of recent advances in research made on the prevention and treatment of types 1 and 2 diabetes mellitus. Drinking a barley extract–enriched beverage, physical exercise, and dietary intake of rich sources of calcium, increased insulin secretion and reduced insulin resistance. Insulin analogs e.g insulin lispro, insulin glargine and insulin aspart, improved the therapeutic properties of insulin, without an increase in hypoglycemic events. Self activation of the islets of Langerhan stem cell and stem cell transplantation was effective in curing diabetes. A compound labeled, CP-316819, binds at a regulatory inhibitor site pocket, of the less-active b form of glycogen phosphorylase, so preventing its transformation to the more active a form of the enzyme, and thus serving as a chemotherapy of hyperglycemia in type 2 diabetic patients. Cinnamon has blood sugar-lowering properties, Grape seed extracts have a therapeutic role in decreasing cardiovascular risk in type 2 diabetic human subjects. Metformin causes a reduction in cellular cAMP levels and decreased protein kinase A (PKA) activation and target phosphorylation, thus suppressing glucose production by the liver. The diet most often recommended for diabetic patients is high in soluble dietary fiber, low in saturated fat, moderate in some essential fatty acids (EFAs), low in sugar, with low glycemic Index. A vegan diet is effective in managing type 2 diabetes.

Key words: Hypoglycemic, Islets of Langerhan, Glycogen phosphorylase, Chemotherapy, Insulin.

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic disorders characterized by a chronic hyperglycemic condition resulting from defects in insulin secretion, insulin action or both. Permanent neonatal diabetes is caused by glucokinase deficiency, and is an inborn error of the glucose-insulin signaling pathway (Njolstad *et al*., 2003). Experts project that the incidence of diabetes is set to soar by 64% by 2025, meaning that a staggering 53.1 million citizens may be affected by the disease (Rowley and Bezold, 2012).

There are two main types of diabetes mellitus: i. Type 1 diabetes, also called insulin dependent diabetes mellitus (IDDM), is caused by lack of insulin secretion by beta cells of the pancreas. ii. Type 2 diabetes, also called non-insulin dependent diabetes mellitus (NIDDM), is caused by decreased sensitivity of target tissues to insulin (Ozougwu et al., 2013). The basic effect of insulin lack or insulin resistance on glucose metabolism is to prevent the efficient uptake and utilization of glucose by most cells of the body, except those of the brain. As a result of this, blood glucose concentration increases, cell utilization of glucose falls increasingly lower and utilization of fats and proteins increases. (Guyton and Hall, 2006a).

Type 1 diabetes mellitus is a chronic autoimmune disease associated with selective destruction of insulin-

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producing pancreatic β-cells (Al Homsi and Lukic, 1992). In addition to the loss of insulin secretion, the function of pancreatic α-cells is also abnormal and there is excessive secretion of glucagons in IDDM patients. Deficiency in insulin leads to uncontrolled lipolysis and elevated levels of free fatty acids in the plasma, which suppresses glucose metabolism in peripheral tissues such as skeletal muscle (Raju and Raju, 2010).

Type 2 diabetes is the predominant form of diabetes and accounts for at least 90% of all cases of diabetes mellitus (Gonzalez et al., 2009). The two main pathological defects in type 2 diabetes are impaired insulin secretion through a dysfunction of the pancreatic β-cell, and impaired insulin action through insulin resistance (Holt, 2004). Type 2 diabetes mellitus has a greater genetic association than type 1 DM, the pathogenesis of type 2 diabetes mellitus is characterized by impaired insulin secretion and insulin resistance. Pancreatic abnormalities in islet secretory cells in type 2 diabetes mellitus are noted in beta, alpha and delta cells of the islets.

Defects involving insulin secretion include relative decrease in basal secretion, decreased first and second phases of insulin response, glucose insensitivity and amino acid hypersensitivity of insulin release (Ozougwu et al., 2013).

Obesity has genetic as well as environmental causes. It has a strong effect on the development of type 2 DM (Bjorntorp, 1992; Haffner et al., 1992). Aging, obesity, insufficient energy consumption, alcohol drinking, smoking, etc are independent risk factors of pathogenesis of type 2 diabetes.

An inability to produce or release antidiuretic hormone (ADH) from the posterior pituitary can be caused by head injuries or infections, or it can be congenital. Because the distal tubular segments cannot reabsorb water in the absence of ADH, this condition, called “central” diabetes insipidus, results in the formation of a large volume of dilute urine, with urine volumes that can exceed 15 L/day (Guyton and Hall, 2006b).

Prophylaxis of Diabetes

Drinking a barley extract–enriched beverage may help to improve insulin sensitivity and prevent type 2 diabetes (Bays et al., 2011). Consuming red meat – especially processed types (such as deli meats, bacon, and sausage), raises a person’s risk of developing type–2 diabetes (Pan et al., 2011).

Dairy milk, cheeses, and yogurts are rich sources of calcium, a mineral that increases insulin secretion and may reduce insulin resistance (Goldman et al., 2013). Men and women who walk briskly for 30 minutes for five days of a week, lower their fat and calorie intake, and achieve a 7% body weight reduction over a three–year period, eliciting a 58% reduction of their risk of developing type 2 diabetes.

Therapeutic Objectives

Diabetes treatment objectives must be adapted to individual-patient factors, such as age, life expectancy, related conditions and learning aptitude. The management of Type 2 diabetes focuses on the prevention of neurovascular complications.

Achieving specific treatment goals in type 2 diabetes can substantially reduce microvascular complications, such as retinopathy, nephropathy and neuropathy. Intensive management has a beneficial effect on cardiovascular disease (Carmen et al., 2010). Correction of hyperglycemia and control of arterial pressure and correction of dyslipidemia play leading roles among therapeutic objectives in type 2 diabetes (Keen, 2000).

The aim of the initial treatment is to reduce insulin resistance and to reduce hepatic glucose production. The next step is to prescribe drugs that stimulate insulin secretion. Exogenous insulin could be administered. In diabetic patients, the target blood pressure should be no higher than 130/80 mmHg. In most cases, a combination of more than one anti-hypertensive drug is required (Hallé, 2001).

Chemotherapy, Genetic Engineering and Stem Cell Technologies-related Diabetes Therapy

Human insulin synthesized by means of plasmid vectors of E coli, cloned with the human insulin, is used in treating diabetes. After more than half a century of treating diabetics with animal insulin, recombinant DNA gene technologies, which is used in producing recombinant insulin recognized by humulin, and advanced protein chemistry, made human insulin preparations available in the late 20th century. In the last decade, insulin analogs (e.g insulin lispro, insulin glargine and insulin aspart), constructed by changing the structure of the native protein, improved the therapeutic properties of insulin, without an increase in hypoglycemic events (Vajo et al., 2001).

Stem cell therapy for diabetes, is a new method. It was developed using molecular biology technology, molecular immunology and cell biology. It is used in treating diabetes from the cell and the gene level and cure diabetes at the clinical stage. It has minor side effects. The merits are the minor side effects and the steadying of the blood sugar levels. Self activation of the islets of Langerhan stem cell and stem cell transplantation is effective in curing diabetes. The types of transplantation cells are embryo stem cells, the insulin type of cells which originate in the embryo and develop into bone mesenchymal stem cells (Chu, 2013).

A major therapeutic strategy for blood glucose control in type 2 diabetes is the regulation of glycogen metabolism. Glycogen phosphorylase catalyzes the first step in the phosphorolysis of glycogen, and for this reason has become a potential key target for controlling hyperglycemia

in type 2 diabetic patients (Oikonomakos and Somsák, 2008). A compound labeled, CP-316819, binds at a regulatory inhibitor site, pocket some 33 Å from the catalytic site (where glucose binds), of the less-active b form of glycogen phosphorylase, so preventing its transformation to the more active a form of the enzyme (Baker et al., 2005).

Treatment of Diabetes using Natural Products

A number of medicinal plants have been studied for the treatment of diabetes. Cinnamon has blood sugar-lowering properties (Yeh et al., 2003). Extracts from Australian Sandalwood and Indian Kino tree slow down two key enzymes in carbohydrate metabolism, essential to cure of diabetes. Isoorientin is the main hypoglycemic component in Gentiana olivieri (Sezik et al.. 2005). Vitamin E supplements help diabetic men and women who have the 2-2 form of haptoglobin to reduce their risk of heart attacks and dying from diabetes-related heart disease. Thiamine may prevent some diabetic complications (Thornalley, 2005), and chromium supplements, improve glucose metabolism in individuals with diabetes (Balk et al., 2007).

Grape seed extracts have a therapeutic role in decreasing cardiovascular risk, in type 2 diabetic human subjects, because they significantly improved markers of inflammation, glycaemia and oxidative stress in obese Type 2 diabetic subjects at high risk of cardiovascular events over a 4-week period (Kar et al., 2009). Biochemical and histological analysis of diabetic rat kidneys treated with licorice extract revealed that licorice has a potential therapeutic effect for diabetes due to its antioxidant and hyperglycemic properties (Kataya et al., 2011).

Cranberry supplements reduced significantly, atherosclerotic cholesterol profiles (LDL cholesterol, total cholesterol levels, and HDL cholesterol ratio, but have a neutral effect on glycaemic control in Type 2 diabetic subjects taking oral glucose-lowering agents (Lee et al., 2008). The cinnamon extract has a moderate effect in reducing fasting plasma glucose concentrations in diabetic patients with poor glycaemic control (Mang et al., 2006). Hypoglycemic effect of Sorghum extract was related to hepatic gluconeogenesis, and the effect was similar to an anti-diabetic medication.

Coccinia indica, a herb growing abundantly in India, has been used in traditional treatment of diabetes. Significant decrease in the fasting, postprandial blood glucose and glycosylated hemoglobin were recorded of human subjects suffering from type 2 diabetes administered with alcoholic extracts of *Coccinia indica,* suggesting that the extracts have a potential hypoglycemic action in patients with mild diabetes (Kuriyan et al., 2008).

In Asia, type 2 diabetes is treated with mulberry leaf. Mulberry leaf reduced blood glucose in normal rats (Miyahara et al., 2004), and rats with diabetes, induced by streptozotocin (Chen et al., 1995) or alloxan, (Ye et al., 2002), and also reduced fasting blood glucose in type 2 diabetes human subjects, reflecting the ability of mulberry leaf supplements to inhibit intestinal sucrase and induce sucrose malabsorption (Mudra et al., 2007).

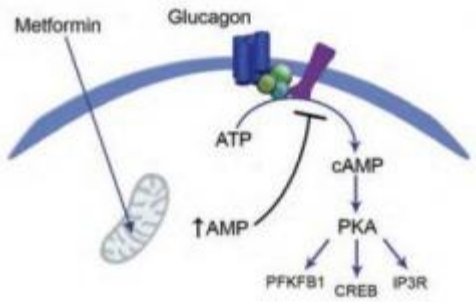
Neem (*Azadirachta indica* A. Juss) leaf extracts, seed oil and nimbidin exert hypoglycaemic/ antihyperglycaemic effects, and are widely prescribed by contemporary Ayurvedic physicians for the treatment of diabetes mellitus (Van Der Nat, 1991). Maitake mushroom (*Grifola frondosa*) lowers blood sugar because it naturally acts as an alpha glucosidase inhibitor and may be beneficial for the management of diabetes [Kubo et al. (1994), Horio and Ohtsuru (2001), Konno et al. (2001), Manohar et al. (2002), Hong et al. (2007), Lo et al. (2008), Matrur et al. (2002)].

Other mushrooms like Reishi [Zhang and Lin (2004), Yang et al. (2007)], *Agaricus blazei* [Kim et al. (2005), Hsu et al. (2007)], *Agrocybe cylindracea* (Kiho et al., 1994), and Cordyceps [Kiho et al. (1993), Lo et al. (2004)], have a hypoglycemic effect, although the mechanism is currently unknown.

Raised serum insulin levels and regeneration/repair of beta cells of the islets of Langerhan in Type 2 diabetic patients upon Gymnema sylvestre (GS) leaf extract supplementation (400mg/day), suggest the anti-diabetic effect of GS leaf extract (Baskaran et al., 1990). Supplementation with olive leaf polyphenols for 12 weeks significantly improved insulin sensitivity and pancreatic β-cell secretory capacity in overweight middle-aged men at risk of developing the metabolic syndrome (Adams, 2013). Olive leaf extract facilitate the reduction of starch digestion and absorption in humans, and thus represent an effective adjunct therapy that normalizes glucose homeostasis in individuals with diabetes (Wanstein et al., 2012).

The hypoglycemic activity of the flavonoids rich fraction of 70% alcohol extract of the Egyptian Morus alba root bark (MRBF-3) on streptozotocin-induced diabetic rats, revealed that MRBF-3 may protect pancreatic beta cells from degeneration and diminish lipid peroxidation (Singab et al., 2005). Papaya leaf extract supplementation decreased the enzyme levels of ALT and AST (bio-markers of type 2 diabetes) among diabetic patients and improved insulin sensitivity. Papaya leaf extracts are helpful in decreasing the secondary complications of diabetes such as fatty liver, kidney damage and oxidative stress. Delayed wound healing in diabetic patients is reversed by the oral administration of papaya leaf extracts, which enhance the process of wound healing by mechanisms of anti-bacterial and antioxidant action (Marks, 2013).

Oral supplementation of Yacon (*Smallanthus sonchifolius*) root flour, a natural product rich in Fructooligosaccharides (FOS), in the diet of streptozotocin-induced diabetic wistar rats, elicited signifi-



Camp response element binding protein (CREB), phosphofructokinase (PKA), inositol 1,4,5-trisphosphate receptor (IP3R).
Figure 1. Mode of drug action of Metformin.

cant decrease in fasting plasma triacylglycerol and very low-density lipoprotein levels, thus revealing its beneficial effects on diabetes-associated hyperlipidemia (Habib et al., 2011). Liquorice (*Glycyrrhiza*) contains a group of natural substances known as the amorfrutins, in the plant's edible root, which has the anti-diabetic effect of significant reduction of blood glucose concentration in human subjects (Sauer, 2012). Saponin extract from the root of *Garcinia kola* (bitter kola), produced significant reduction (35.98%), of blood glucose concentration, and demonstrated remarkable antidiabetic activity (Alli et al., 2012). The root extract of *Aristolochia indica* (Linn) was found to be hypoglycemic and anti- diabetic in function (Cynthia and Rajeshkumar, 2012).

Drug Therapy of Types I and II Diabetes Mellitus

There are several classes of type 2 diabetes drugs. Each works in different ways to lower blood sugar.

As in the treatment of Type 1 diabetes, insulin therapy should begin with two to four injections per day, according to how aggressive the physician wishes treatment to be and the type of patient. The most frequently used protocol for Type 2 diabetes patients who still have endogenous insulin secretion is a combination of fast-acting and intermediate-acting insulins in the morning and at supper (Hallé, 2001).

Several classes of type 2 diabetes medicines function to lower blood sugar involving several biochemical mechanisms which include: stimulating the pancreas to produce and release more insulin [e.g Meglitinides (Prandin), and Sulfonylureas (Glucotrol)], inhibiting the production and release of glucose from the liver [e.g Dipeptidy peptidase-4 (DPP-4) inhibitors (Onglyza)], blocking the action of stomach enzymes that break down carbohydrates and improving the sensitivity of cells to insulin[e.g Biguanides (glucophage)] [Verdonck et al. (1981), Rendell (2004), Eurich et al. (2007)]. Two daily injections of delayed-acting insulin like neutral protamine hagedorn (NPH), Levemir® or once daily Lantus® (long-acting insulin analogs) are needed to cover basal, or fasting, insulin needs. Eating, or correcting high blood glucose levels requires a rapid-acting insulin such as Regular or Humalog®, NovoRapid® or Apidra® (rapid insulin analogs). Other injectable medications include: Amylin mimetics e.g symlin, and Incretin mimetics e.g byetta (Howorka and Pumprla, 2010).

Each class of medicine has one or more drugs. Some of these drugs are taken orally, while others must be administered intravenously or intramuscularly. Some type 2 diabetes pills contain a combination of two classes of drugs.

Metformin works by suppressing glucose production by the liver. Metformin directly reduces hepatic glucose production, but slightly increases sensitivity to insulin by reducing hyperglycemia. Metformin enters the cell and acts on the mitochondria, causing increased AMP. Elevated cellular AMP levels inhibit membrane bound adenylyl cyclase, causing a reduction in cellular cAMP levels and decreased protein kinase A (PKA) activation and target phosphorylation (Miller et al., 2013). The mode of drug action of Metformin is shown in figure 1.

Pharmaceutical and biochemical properties of diabetic drugs are shown in Table 1.

Dietary Therapy of Diabetes

A non-pharmacologic approach to the treatment of diabetes begins with a dietician explaining nutritional therapy. The dietician will suggest a balanced diet, which is low in saturated fat, rich in fibre and is designed to bring about progressive weight loss (Hallé, 2001).

The diet most often recommended for diabetic patients is high in dietary fiber, especially soluble fiber, but low in fat (especially saturated fat), but moderate in some essential fatty acids (EFAs), and low in sugar. Recommendations of the fraction of total calories to be

Table 1. Pharmaceutical and biochemical values of diabetic drugs.

Diabetes drugs	Dosage	Mode of drug action	Side Effects/contra-indications	Remarks
Biguanides Metformin (Glucophage) Metformin liquid (Riomet) Metformin extended release (Glucophage XR, Fortamet, Glumetza)	**Metformin:** usually taken twice a day with breakfast and evening meal. **Metformin extended release:** usually taken once a day in the morning.	Decreases amount of glucose released from liver.	Bloating, gas, diarrhea, upset stomach, loss of appetite (usually within the first few weeks of starting). Take with food to minimize symptoms. Metformin is not likely to cause low blood glucose. In rare cases, lactic acidosis may occur in people with abnormal kidney or liver function.	Medication should be discontinued, when patient is having a dye study or surgical procedure.
Sulfonylureas Glimepiride (Amaryl) Glyburide (Diabeta, Micronase) Glipizide (Glucotrol, Glucotrol XL) Micronized glyburide (Glynase)	Take with a meal once or twice a day.	Stimulates the pancreas to release more insulin, both right after a meal and then over several hours	Low blood glucose, occasional skin rash, irritability, upset stomach	Because these medicines can cause low blood glucose, patient should always carry a source of carbohydrate. There might be a need to lower the dose, if patient's blood glucose levels are consistently low or If there is an increase in patient's activity level or reduction in patient's weight or calorie intake,
Meglitinides Repaglinide (Prandin) D-Phenylalanine Derivatives Nateglinide (Starlix)	Both of these medications should be taken with meals. If you skip a meal, skip the dose.	Stimulate the pancreas to release more insulin right after a meal.	Effects diminish quickly and they must be taken with each meal; may cause low blood glucose.	These work quickly when taken with meals to reduce high blood glucose levels. However, they are less likely than sulfonylureas to cause low blood glucose.
Thiazolidinediones Pioglitazone (TZDs) Pioglitazone (Actos)	Usually taken once a day; take at the same time each day.	Makes the body more sensitive to the effects of insulin.	May cause side effects such as swelling (edema) or fluid retention. Do not cause low blood sugar when used alone. Increased risk of congestive heart failure in those at risk.	Increases the amount of glucose taken up by muscle cells and keeps the liver from overproducing glucose; may improve blood fat levels. Patient should consult the services of a health care provider if the following symptoms persist: nausea, vomiting, fatigue, loss of appetite, shortness of breath, severe edema or dark urine.
DPP-4 Inhibitors Sitagliptin (Januvia) Saxagliptin (Onglyza) Linagliptin (Tradjenta)	Take once a day at the same time each day.	Improves insulin level after a meal and lowers the amount of glucose made by your body.	Stomach discomfort, diarrhea, sore throat, stuffy nose, upper respiratory infection. Do not cause low blood glucose.	Can be taken alone or with metformin, a sulfonylurea or Actos. Healthcare provider should be consulted, if patient has any persistent side effects.
Alpha-glucosidase Inhibitors Acarbose (Precose) Miglitol (Glyset)	Take with first bite of the meal; if not eating, do not take.	Slows the absorption of carbohydrate into your bloodstream after eating.	Gas, diarrhea, upset stomach, abdominal pain	Drug should be administered together with meals, to limit the rise of blood glucose that can occur after meals; these do not cause low blood glucose. Side effects should cease after a few weeks, otherwise healthcare provider should be consulted.

Table 1. Cont.

Bile Acid Sequestrants Colesevelam (Welchol)	Take once or twice a day with a meal and liquid.	Works with other diabetes medications to lower blood glucose.	Constipation, nausea, diarrhea, gas, heartburn, headache (may interact with glyburide, levothyroxine and contraceptives)	Primary effect, when used either alone or with a statin, is to lower LDL cholesterol; has blood glucose-lowering effect when taken in combination with certain diabetes medications. If patient has high triglycerides (blood fats) or stomach problems, then patient should inform healthcare provider before taking this medication. Patient, who is taking thyroid medication or glyburide, should do so, 4 hours before taking Welchol, and should inform healthcare provider if side effects, persist.
Combination Pills Pioglitazone & metformin) (Actoplus Met) Glyburide & metformin (Glucovance) Glipizide & metformin (Metaglip) Sitagliptin & metformin (Janumet) Saxagliptin & metformin (kombiglyze) Repaglinide & metformin (Prandimet) Pioglitazone & glimepiride (Duetact)	Check with your provider; usually taken once a day.	Combines the actions of each pill used in the combination.	Side effects are the same as those of each pill used in the combination. Some combination pills may lead to low blood glucose levels if one of the medications contained in the combination has this effect.	May decrease the number of pills which the patient should take.

Source : King (2014).

obtained from carbohydrate are generally in the range of 40 to 65%, but recommendations can vary as widely as from 16 to 75% (Katsilambros et al., 2006). Diabetics are encouraged to reduce their intake of carbohydrates that have a high glycemic index (GI) (Sievenpiper and Vuksan, 2004). Oleic acid has a slight advantage over linoleic acid in reducing plasma glucose, insulin levels, total cholesterol, low-density lipoproteins (LDLs), and triglycerides (Segal-Isaacson et al., 2001).

Type 1 diabetes mellitus is associated with celiac disease. Supplementation with gluten-free diet (GFD) improved hypoglycemic episodes in patients with type 1 diabetes with subclinical celiac disease (Scaramuzza et al., 1990). In cases of hypoglycemia, diabetics are advised to have food or drink that can raise blood glucose quickly, such as lucozade, followed by a long-acting carbohydrate (such as rye bread) to prevent risk of further hypoglycemia. Some studies have suggested that adding vinegar to food may help to prevent carbohydrates putting up blood sugar too dramatically (White and Johnston, 2007).

A low-carbohydrate diet or low glycemic Index diet may be effective in dietary management of type 2 diabetes, as both approaches prevent blood sugars from spiking after eating (Nielsen and Joensson, 2006). A vegan diet is effective in managing type 2 diabetes (Barnard et al., 2006),

because switching diabetics to a vegan diet lowered hemoglobin A1C and Low Density Lipoproteins levels. Blood filterability is improved by a vegan diet (McCarty, 2002). Vegan diets may lower advanced glycation end products (McCarty, 2005). Foods such as legumes, nuts, fruits, and vegetables are considered particularly beneficial for diabetics due to their high levels of dietary fibre (Henshaw, 2012).

Diabetics who take insulin or tablets such as sulphonylureas should not consume alcohol as alcohol inhibits glycogenesis in the liver and sulphonylureas inhibit hunger symptoms associated with impaired judgment, memory and concentration which result in hypoglycemia.

People who use intensive insulin therapy (those on multiple daily injections) and people who take other types of oral diabetes medications (eg, insulin sensitizers such as metformin) have more flexibility around meal timing. With these regimens, skipping or delaying a meal does not usually increase the risk of low blood sugar. When using rapid acting insulin before a meal, the blood sugar level may become low shortly after eating a high fat meal and then rise hours later.

Many people with type 2 diabetes are overweight. Losing even a small amount of weight (5 to 10 percent of total body weight) can help the body to produce and use insulin more efficiently. There are several strategies that can aid in weight loss, including eating fewer calories, exercise, weight loss medications, and weight loss surgery. Type 2 diabetes patients who want to avoid weight loss should measure their weights on regular basis (e.g, once weekly), and decrease the amount of food consumed, if weight gain exceeds 2 pounds. As blood glucose control improves, it may be necessary to decrease caloric intake by 250 to 300 calories per day to avoid weight gain.

If blood glucose levels are frequently low at a particular time of day, the insulin dose or medication dose, should be reduced rather than add a snack. If the blood sugar level becomes low (2.8 to 3.8 mmol/L) or (less than 2.7 mmol/L), during exercise, diabetic patient should eat 10 to 15 grams of fast-acting carbohydrate (eg, 1/2 cup fruit juice, six to eight hard candies, three to four glucose tablets) or eat 20 to 30 grams of fast-acting carbohydrates, respectively. A retest should be conducted after 15 minutes and treatment repeated, if blood glucose is still too low [Cox et al. (1994); Fanelli et al. (1998); McCulloch (2014)].

CONCLUSION

Diabetes mellitus (DM) is a group of metabolic disorders characterized by a chronic hyperglycemic condition resulting from defects in insulin secretion, insulin action or both. Type 1 diabetes, also called insulin dependent diabetes mellitus (IDDM), is caused by lack of insulin secretion by beta cells of the pancreas. Drinking a barley extract–enriched beverage, physical exercise, and dietary intake of rich sources of calcium, increases insulin secretion and may reduce insulin resistance. Genetic engineering of recombinant gene technology, Stem cell therapy, and chemotherapy using inhibitor anti-metabolites have been employed in the treatment of diabetes mellitus. Natural products which include extracts of cinnamon, sorghum, *Coccinia indica*, mulberry leaf, neem leaf, nimbidin, maitake mushroom, Gymnema sylvestre (GS) leaf, olive leaf, Egyptian Morus alba root bark, Liquorice root, linn root, bitter kola, and yacon root have been implicated as therapeutic agents of diabetes mellitus. Drug therapies of diabetes mellitus include : Meglitinides, Sulfonylureas, Biguanides, Amylin mimetics, and Incretin mimetics. The diet most often recommended for diabetic patients is high in soluble dietary fiber, low in saturated fat, moderate in some essential fatty acids (EFAs), low in sugar, with low glycemic Index. A vegan diet is effective in managing type 2 diabetes.

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