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The Various Therapeutic Approaches for the Treatment of Diabetes

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Review Article

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ABSTRACT

Diabetes is of the emerging diseases in the world, Day by day the number of patients with type 2 diabetes is rapidly increasing in both developed and developing countries around the world. Many researchers have developed newer generation of drugs like sulphonylureas, thiazolidinedione's, biguanides and α-glucosidase inhibitors with high efficacy for decreasing the hyperglycaemia. Recently new approaches are done in the drug discovery for the treatment and management of diabetes like Incretin mimetics, Stem Cell Technology, Amylin analogues, Nanotechnology approach, Statins Therapy, GIP analogues, Gene Therapy, Herbal Therapy, Nutrition Therapy, Peroxisome proliferator activated receptors, and dipeptidyl peptidase-4 inhibitor. This Review focuses and discusses on the new approaches available for the treatment of high blood glucose levels.

INTRODUCTION

Approximately 10 millions of people are affected by diabetes, even people with 20 years of age is affected with this disease. The current therapy for treating diabetes is not enough to cure the disease completely and the symptoms will return back. Therefore, the started undergoing research on new approaches to treat type 2 diabetes. Normally it includes several allopathic treatments, namely, sulfonylureas and repaglinide acts by enhancing the insulin secretion, whereas the troglitazone acts by increasing the insulin action in fat and muscle, metformin acts by promoting insulin action in liver tissue, and miglitol and acarbose there are alpha glucosidase inhibitors they enact by delaying the carbohydrate absorption from food intake and other carbohydrate source [1-5]. The drugs which we generally used for treating the type 2 diabetes have significant side effects. The other way of treatment constitutes combinational therapy of insulin with other drugs like sulfonylureas which reduced the daily requirement of insulin intake [6,7] and the other combination which is approved by FDA is insulin and metformin combination; and the combination troglitazone-insulin acts efficiently reducing the insulin requirement and improves the glycaemic control [8-10].

However, by considering both the disease together with its multiple complications the researchers puts forward for the immediate requirement for the treating and wellbeing of the people. The main aim was to achieve complete glycaemic regulation, and to minimise the possible side effects and complications [11-15]. The new generation drugs like sulphonylureas or insulin and even Thiazolidinedione not only induce hypoglycaemia but also results in weight gain [16-19] whereas the biguanide like metformin causes gastrointestinal effects such as diarrhoea and nausea and, sometimes it results in lactic acidosis. Recent generation drugs like incretin mimetics shows the side effects like diarrhoea, nausea, vomiting. The drugs are given in combination they were showing the potential synergetic action in curing the diabetes when compared to single administration.

The present people are following the natural products and their analogues for treating the diabetes. Finally by considering the advantages and limitations of the current therapy the all the clinical diabetology, researchers discussed regarding the advantages as well as the limitations of the commercially available therapeutics [20,21]. The present aim is to introduce the new approaches like nanotechnology, stem cell technology, statins, and the natural products and their analogues for the treatment and management of the diabetes.

NEW THERAPIES FOR DIABETES

Thiazolidinedione's (TZDs)

TZDs are a relatively new class of drugs they act by reducing the insulin resistance in order to increase glucose uptake by the muscles and the liver. Rosiglitazone and pioglitazone are the two drugs available which can be used as monotheraphy or in combinations. Rosiglitazone is used in combination with metformin and sulfonylurea whereas Pioglitazone combination with insulin, metformin, or sulfonylurea [22-25].

Incretin Mimetic Drugs

Incretin mimetic drugs like LAF237, Sitagliptin, Exenatide, they act by blocking the action of dipeptidyl peptidase IV (DPP IV). DPP IV is an enzyme which involves in inactivation of glucagon-like-peptide-1 (GLP-1) as GLP-1 shows antidiabetogenic properties [26-30].

PPAR Agonist Drugs

Peroxisome proliferator-activated receptor agonist (PPAR) is another new class of drugs associated with type 2 diabetes treatment. They not only treat the glucose and lipid abnormalities but also reduce the triglycerides, raise HDL levels, and improve insulin resistance [31-34].

Nanotechnology and Diabetes: A New Novel Therapeutic Approach

The impact and usage of nanotechnology in medical field is on-going now days. The use of nanotechnology in case of the diabetes management has been found to be one of the new approaches. Researchers have done demonstration on the advantages of glucose sensors and closed-loop insulin delivery approaches in the management and treatment of diabetes in order to make it beneficial in both forms of diabetes [35-40]. A nanomedical device is a microcapsule size and contains pores which involves in drug delivery approach. These pores are considerably large enough for the passage of small molecules such as glucose, insulin and oxygen, but they do not allow the larger immune system molecules such as graft-borne virus particles and immunoglobulin's. These Microcapsules contain islets of Langerhans cells which are extracted from pigs and they are implanted beneath the skin of diabetes patients [41-45]. The management and treatment of diabetes by means of nanoparticle targeted drug delivery approach has shown enormous benefits due to its improved bioavailability and target specific action on tissues and organs [46-50].

Stem Cell Technology: A New Novel Therapeutic Approach

Stem cell technology is one of the interested and possible therapeutic ways for diabetes. It is known that both type 1 and type 2 diabetes results from the β cell deficiency of the pancreatic cells, resulting in insufficient insulin secretion [51-55]. The approaches should aim at either enhancing the sensitivity of the body cells to the action of insulin or by removing the defects in pancreatic β cell. Mesenchymal stem cell (MSC) therapy is one of the most developed and favorable therapy in case of type 1 diabetes treatment because of its immunosuppressive nature and has capability and potentiality in differentiating into a number of mesenchymal cell lineages. MSCs have shown immunomodulatory effects in-vitro as well as in in-vivo conditions [56-60]. The hematopoietic stem cells are the multipotent stem cells which results in producing all the cell type in blood and also possess immunomodulatory effect. The transplantation of hematopoietic stem cell has resulted in improved β cell function in newly diagnosed type 1 diabetic patient [61-65].

Statin Therapy: A New Perspective

Statins are the lipid lowering agents and they act by inhibiting the action of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA reductase) [66-70]. The enzyme catalyzes the conversion of HMG-CoA to mevalonic acid which is the rate-limiting step in the formation of cholesterol which results in the decreased levels in the blood. Statins are the main line therapy in reducing cardiovascular risk in the patients who are suffering from type 2 diabetes, which is one of the long term effects of diabetes. Statin therapy shows good efficacy and also effective in decreasing the chances of developing a coronary artery disease by reducing the low density lipoprotein (LDL) cholesterol [71-75].

Medical Nutrition Therapy

The aim of the nutrition therapy in the treatment and management of diabetes is to maintain the low levels of lipids in the blood and to maintain the ideal body weight and normal blood sugar levels in normal. American Diabetes Association in 1994 coined the term "medical nutrition therapy" and it includes 2 phases, one phase mainly involves in adjusting the nutritional requirement of a person and the other phase of the treatment includes the counseling and nutrition therapy [76-80]. Nutrition therapy for diabetes mainly depends on certain factors like patient's age-based nutritive requirements and the type of the food preferences and the main which we have to consider the other medical conditions together with an exercise. The daily calorie requirement for maintaining the

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ideal body weight for moderately to normal active individual is 30-35 kcal/kg/day and for obese people it should be 20-30 kcal/kg/day. The daily nutrition include Low carbohydrate/high protein content which helps in maintaining the body weight and improved glycemic control but it is highly difficult to maintain for longer time periods [81-85].

Natural Products and Diabetes

Herbal medications are used for the treatment of both types of diabetes i.e., insulin dependent and noninsulin dependent diabetes from the ancient period. The traditional way of approaching might be a natural key to unlock diabetic complications [86-92]. Plants possessing antidiabetic active can be used as adjunct to the existing therapies. From ancient period of time, they have used natural products for treating the various disease ailments because of less cost and adverse effects and they will be available easily. Ancient literature revealed that diabetes was a known since Brahmic period [97-100]. Although natural product based medicines has been used traditionally for treating various diseases throughout the world. The new bioactive drugs which are isolated from plants have hypoglycaemic activity and sometimes they show the activity even more potent than known oral hypoglycaemic agent's tolbutamide, and chlorpropamide [92-96]. Several common natural plants like *Withania somnifera*, *Allium sativum*, *Murraya koenigii*, *Gymnema sylvestre*, *Allium cepa*, and *Ferula foetida* which have been found to possess antidiabetic properties and they were assessed by preclinical trials with help of rats as an experimental models [101-102].

CONCLUSION

In the 21st century diabetes is found to be the most challenging health problem throughout the global. Though diabetes is a serious health problem, it can be controlled due to the availability of the medication and advanced approaches for the prevention, detection, and treatment of diabetes is still going on. For the management of type 1 diabetes, patients need to administration insulin about 3-4 times per day throughout their lifetime and their after the blood sugar levels should be monitored regularly in order to avoid serious complications like retinopathy and cardiovascular diseases. For the management of type 2 diabetes, we need to monitor glucose levels regularly along with the medication. Both the oral medicated drugs and insulin are effective in controlling sugar levels but they cannot repair the associated metabolic and glucoregulatory dysfunctions. Though many drugs are available for the treatment and management of diabetes due to their complications and side effects new approaches for treating has been proceeded and still more advanced researches are going on for the management of the diabetes.

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