

Synthetic Implant Rather to Oral and Humulin using Sensors

Sujitha M^{*}, Swetha P^{**}
 Bio Medical Engineering,
 Dhanalakshmi Srinivasan Institute of Technology,
 Affiliated to Anna University
 Chennai

Abstract-The most life threatening disease which is killing all kind of people of all ages is Diabetes Mellitus, commonly referred to as diabetes, is a group of metabolic disorders in which there are high blood sugar levels over a prolonged period. Symptoms of high blood sugar include frequent urination, increased thirst, and increased hunger. If left untreated, diabetes can cause many complications. Serious long-term complications include cardiovascular disease, stroke, chronic kidney disease, foot ulcers, and damage to the eyes and even death. Diabetes is due to either the pancreas not producing enough insulin or the cells of the body not responding properly to the insulin produced. There are lot of treatments which temporarily cure diabetes, but there is no hopeful and permanent solution for this disease, though there are lot of developments in medical science. In today's trend, a plan of developing an invasive implant with sensors, which can detect insulin abnormalities and an internal stimulation can be driven to destroy the disease from totally inside. Micro controllers will be playing the important role in controlling the whole process from outside environment.

key words- Micro Contollers, Insulin Stimulation, Invasive, Implanted Sensor

I. INTRODUCTION

Type 1 Diabetes

Type 1 diabetes mellitus is characterized by loss of the insulin-producing beta cells of the pancreatic islets, leading to insulin deficiency. This type can be further classified as immune-mediated or idiopathic. The majority of type 1 diabetes is of the immune-mediated nature, in which a T cell-mediated autoimmune attack leads to the loss of beta cells and thus insulin. Type 1 diabetes can affect children or adults, but was traditionally termed "juvenile diabetes" because a majority of these diabetes cases were in children

Type 2 Diabetes

Type 2 DM is characterized by insulin resistance, which may be combined with relatively reduced insulin secretion. The defective responsiveness of body tissues to insulin is believed to involve the insulin receptor. However, the specific defects are not known. Diabetes mellitus cases due to a known defect are classified separately. Type 2 DM is the most common type of diabetes mellitus. In the early stage of type 2, the predominant abnormality is reduced insulin sensitivity. At this stage, high blood sugar can be reversed by a variety of measures and medications that improve insulin sensitivity or reduce the liver's glucose production. Type 2 DM is primarily due to lifestyle factors and genetics. Obesity (defined by a body mass index of greater than 30), lack of physical activity, poor diet, stress, and urbanization leads to type 2. Excess body fat is associated with 30% of cases in those of Chinese and Japanese descent, 60–80% of cases in those of European and African descent, and 100% of Pima Indians and Pacific Islanders. Even those who are not obese often have a high waist–hip ratio. Yet now oral medicines and humulin are not satisfied, and diabetes being an emerging disease now a days, could be driven completely down by bio compactable device instead of surgeries, transplants and continuous insulin injection constitutes our research. This paper is about the synthetic device which can monitor glucose and insulin levels and provides cure from inside of the body.

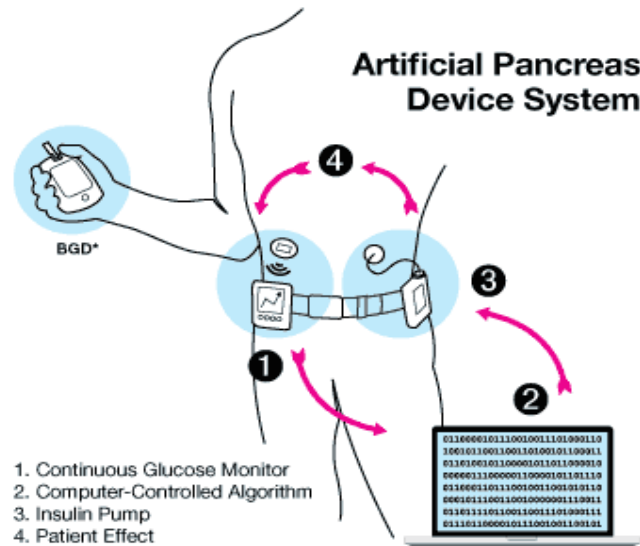
WORKS CARRIED OUT TILL NOW TO CURE DIABETES

Oral medications

Regular insulin injections

Islet cell transplant

Artificial drug delivering system



But all these solutions may end up with one or more discomforts or side effects.

COMPLICATIONS AND CAUSES

All forms of diabetes increase the risk of long-term complications. These typically develop after many years (10–20) but may be the first symptom in those who have otherwise not received a diagnosis before that time. The major long-term complications relate to damage to blood vessels. Diabetes doubles the risk of cardiovascular disease and about 75% of deaths in diabetics are due to coronary artery disease. Other "macrovascular" diseases are stroke, and peripheral artery disease. The primary complications of diabetes due to damage in small blood vessels include damage to the eyes, kidneys, and nerves. Damage to the eyes, known as diabetic retinopathy, is caused by damage to the blood vessels in the retina of the eye, and can result in gradual vision loss and blindness. Damage to the kidneys, known as diabetic nephropathy, can lead to tissue scarring, urine protein loss, and eventually chronic kidney disease, sometimes requiring dialysis or kidney transplantation. Damage to the nerves of the body, known as diabetic neuropathy, is the most common complication of diabetes. The symptoms can include numbness, tingling, pain, and altered pain sensation, which can lead to damage to the skin. Diabetes-related foot problems (such as diabetic foot ulcers) may occur, and can be difficult to treat, occasionally requiring amputation. Additionally, proximal diabetic neuropathy causes painful muscle atrophy and weakness. There is a link between cognitive deficit and diabetes function. Being diabetic, especially when on insulin, increases the risk of falls in older people. The cause of insulin resistance has been one of the most pressing questions in diabetes research. There's one clear link: being overweight or obese. And there's an even clearer culprit: a large belly. Actually, a specific type of belly fat, called visceral or intra-abdominal fat, is to blame. This is fat in and around the liver and other organs inside the abdomen, and it differs from subcutaneous fat -- fat under the skin. Liposuction can't reduce visceral fat because the procedure removes only subcutaneous fat.

Subcutaneous fat does not seem to cause insulin resistance or the other problems that are part of the metabolic syndrome. visceral fat is toxic because it appears that visceral fat cells manufacture chemicals that prevent other cells from responding to insulin as they should. These chemicals also trigger inflammation. Inflammation is one of the body's ways of responding to injury, but it can also cause injury to tissues and promotes the development of atherosclerosis in blood vessels.

IMPROVED CASE STUDY

Insulin-specific T follicular helper cells (TFH) appear in the lymph nodes, among other organs, and initiate attacks of the immune system by promoting the production of antibodies by B cells. In the search for the causes of the increase in TFH cells during autoimmune activation, the scientists discovered a previously unknown signaling pathway, analyses showed that a molecule called miRNA92a** triggers a chain of molecular events, which ultimately leads to the increase in these immune cells. "In particular, during this process, miRNA92a interferes with the formation of important signaling proteins such as KLF2 and PTEN." For therapeutic intervention, antagomir, which specifically binds to miRNA92a molecules and blocks their effect. In an experimental model of type 1 diabetes and in the humanized model, this treatment resulted in a significantly lower autoimmune response. "The targeted inhibition of miRNA92a or the downstream signaling pathway could open up new possibilities for the prevention of type 1 diabetes." "Furthermore, the insulin-specific TFH cells could serve as biomarkers to determine the treatment success of the insulin vaccinations we perform."

Further Information

* In type 1 diabetes, the insulin-producing cells in the Langerhans islets of the pancreas are destroyed because they are attacked by the body's immune system (formation of islet autoantibodies against structures of the beta cells). As a result, the body can no longer be adequately supplied with insulin. If the destruction of the beta cells exceeds a certain

degree, the disease becomes manifest and blood glucose levels rise due to insulin deficiency.

** microRNAs (miRNAs) are noncoding RNAs which play an important role in gene regulation and in particular in the inactivation of genes. In general, they have a size of 21 to 23 nucleotides, so they are very short -- hence the name.

NOTABLE DIAGNOSIS AND CURE

GAD short for glutamic acid decarboxylase. This is an enzyme that is needed to make a neurotransmitter. Neurotransmitters are involved in nerve messaging. The neurotransmitter is gamma-aminobutyric acid (GABA), an amino acid that has the effect of reducing nerve transmission. GAD inhibits nerve messages. It relaxes muscles, for example. Lack of GAD is involved in a disease known as stiff-person syndrome. GAD is found in the brain and the pancreas. Unfortunately, GAD can also act as an autoantigen. This means that it triggers the immune system to produce antibodies against its own cells. In this case, these GAD autoantibodies mark out cells in the pancreas for attack. These pancreas cells produce insulin. Diabetes is the result of the immune system attacking these cells as if they were foreign material that must be destroyed. Autoimmunity is the cause of type 1 diabetes, and other diabetes-related autoantibodies are also involved aside from GAD autoantibodies. Finding GAD antibodies is a way to diagnose type 1 diabetes when doctors are not sure. This may be when people show signs in later life that start to resemble type 1 diabetes, whereas type 1 usually develops at younger ages.

AN ALTERNATE WAY-DEVICE CONSTRUCTION

The device consists of sensor-to detect abnormalities in insulin level. If there is no abnormality, in insulin level the device remains constant as set up. If there is decrease in insulin, the device starts to work as a stimulator ,to stimulate insulin ,to prevent hyperglycemia in case of T1D. In case of T2D, the device exists a thermogenic or ultrasound property, which produces heat to make the visceral fat level to decline or to reduce it and hence, insulin resistance is solved ,therefore type 2 diabetes is possibly cured. If there is not enough insulin for to be stimulated by the device, replacing of 3D designed ,packed beta cell distribution will also be programmed. Beta cells are attacked by auto antibodies released by signaling pathway by miRNA92a, hence if possible interference in the signaling pathway to limit the follicular helper cells could be programmed in future aspects. But there is a bit of difficulty in identification of that signaling way. but it can be come across by developing science in future .All of these can be controlled up using micro controller ,which is trending up today's world. Raspberry pi or beaglebone black could be used for this set of multiple instructions and programming to control this device from outside world. The islets were embedded into three-dimensional scaffolds made from an alginate/gelatin mixture with a cross-linked structure and showed full functionality once extracted, meaning that the scaffolds could function as a potential delivery vehicle in future transplantations. The islet cells were included in the liquid

hydrogel mixture during printing to create the porous three-dimensional scaffold. Bio compactable nano material coatings and polymers can be used for this work. The human body absorbs a significant amount of RF waves that are used for wireless communication. RF transmitters also transmit the signal into the environment in all directions. This is very power inefficient and limits the practical use of this communication technique. RF communication can also be affected by interference from the environment. This leads to security issues because an outside source can receive or affect the transmitted signals. Intra-body communication has proven much better than RF communication because the signal is completely contained inside the body. It provides secure, interference-free, energy-efficient communication. the device would work by conduction property of human body. islet cells were retrieved from the 3D scaffolds in the lab, they were able to produce insulin and respond to glucose in the same way as non-printed islet cells .And this is an implant in which islets are embedded, or encapsulated, from a material that allows for very efficient oxygen and nutrient supply, and quick exchange of glucose and insulin, while keeping the host cells out. L-arginine can stimulate insulin production from islets ,could be used as a stimulator to stimulate insulin from inside body. ultrasonic cavitation anti-cellulite treatment is better than liposuction surgery Because ultrasonic cavitation treatment can get rid of both the superficial fat and visceral fat deposits, while liposuction can only suck the superficial fat tissue. hence piezo electric actuation can be set up in a device to provide ultrasound effect which can reduce visceral fat deposits.

WIRELESS BODY AREA NETWORK(WBAN)

Wearable and implantable body sensor network systems are one tool to achieve this objective, as a prominent application in these areas is the integration of sensing and consumer electronics technologies which would allow people to be monitored during all their everyday activities.

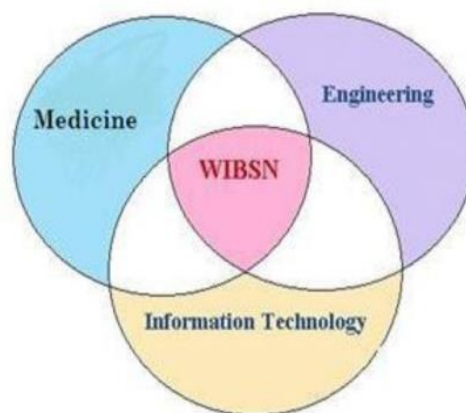
Body sensor network systems can help people by providing healthcare services such as medical monitoring, memory enhancement, control of home appliances, medical data access, and communication in emergency situations. Continuous monitoring with wearable and implantable body sensor networks will increase early detection of emergency conditions and diseases in at risk patients and also provide a wide range of healthcare services for people with various degrees of cognitive and physical disabilities. Not only the elderly and chronically ill, but also the families in which both parents have to work will benefit from these systems to provide high-quality care services for their babies and children.

Researchers in various interdisciplinary fields such as computing, engineering, and medicine fields are working together in order to ensure that the broad vision of wearable and implantable body sensor networks (WIBSNs) for smart healthcare, as illustrated in following can be fulfilled. There are already several applications and prototypes for this purpose. For example, some of them are considered for continuous monitoring of people suffering from cognitive

disorders like Alzheimer's, Parkinson's or similar diseases. Some papers focus on fall detection, posture detection and location tracking, while others make use of biological and environmental sensors to identify patients' health status. There is also a significant research focus on the development of tiny wireless sensor devices, preferably integrated into fabrics or other wearable substances or implanted in the human body. The range of wearable and implantable biomedical devices will increase significantly in the next years, thanks to the improvements in micro-electro-mechanical systems (MEMS) technology, wireless communications, and digital electronics, achieved in recent years. This paper explores wearable and implantable body sensor network systems which provide rich contextual information and alerting mechanisms for abnormal conditions in continuous monitoring of patients at large. In addition, this paper evaluates the state of the art research activities and present issues that must be addressed to improve the quality of life through wearable and implantable body sensor networks. WBANs provide efficient communication solutions to ubiquitous healthcare systems. Health monitoring, telemedicine, military, interactive entertainment, and portable audio/video systems are some of the applications where WBANs can be used. Khan *et al.* have presented a comprehensive work on the applications of WBANs in smart healthcare applications, including epileptic seizure warning, glucose monitoring, and cancer detection. Mark *et al.* presented BASNs as systems enabling human-centric sensing for a variety of intriguing applications in healthcare, fitness, and entertainment, but such networks must demonstrate enough value for users to overcome inhibitions related to inconvenience, invasiveness, and general discomfort. Wearable technologies that will "silently monitor" heart rhythm, detect irregularities, and alert emergency personnel in the event of a heart attack. This vision, not far removed from current research efforts, illustrates the promise of WBANs in this important area. Embedded electronic systems are widespread or pervasive; from alarm clocks to PDAs, from mobile phones to cars, almost all the devices we use on a daily basis are controlled by embedded or internal

electronics. In relation with the recent advances in technology more than 99% of the microprocessors produced today are used in such embedded systems, and lately the number of embedded systems in use has developed and increased. The concept of ambient intelligence reflects the vision that technology will not only develop but be embedded, invisible, and fully hidden in our natural surroundings, but present whenever we need it, enabled by simple and easy interactions. Ambient intelligence has been defined by the Advisory Group to the EU Information Society Technology Program (ISTAG) as "the convergence of three major key technologies: ubiquitous computing, ubiquitous communication, and interfaces adapting to the user". In the near future ubiquitous computing and communication will attract more interest and arch. A sensor network consists of a large number of sensor nodes, which are deployed either inside the phenomenon to be monitored or very close to it. Sensor networks represent a significant improvement over traditional sensor networks, which are deployed in the following two ways:

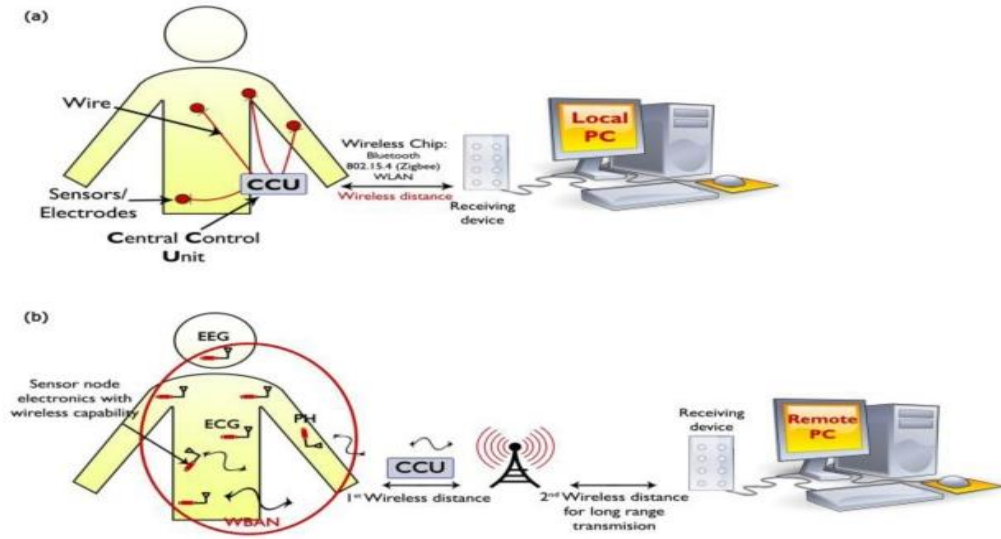
- i. Sensors can be located far from the actual phenomenon to be monitored. With this approach, large sensors that use some complex methods to distinguish the targets from environmental noise are required.
- ii. Several sensors that perform only sensing can be deployed. The positions of the sensors and communications network topology are carefully designed. They transmit time series of data about the phenomenon to central nodes where computations are performed and data are fused. Battery-free sensors could be useful in many areas, including medicine, says Zeke Mejia, chief technology officer of St. Paul-based Digital Angel, an RFID tag maker. They could "check the status and certain conditions in the body" at any moment, Mejia says, from glucose levels in people with diabetes to the pH of blood and other body fluids.



Wireless Body Area Networks (WBANs)

The expansion of WSNs for medical applications is increasingly turning these technologies into body sensor networks (BSNs). The biosensors can record electrocardiograms, electromyographs, measure body temperature and blood pressure, electro-dermal activity, among other healthcare parameters. For example, accelerometers can be used to sense heartbeat rate, movement or even muscular activity. Human health monitoring is emerging as a prominent application of the

embedded sensor networks. A number of tiny wireless sensors are strategically placed on/in a patient's body, to create a WBAN. A WBAN can monitor vital signs, providing real-time feedback to allow many patient diagnostics procedures using continuous monitoring of chronic conditions, or progress of recovery from an illness. Recent technological advances in wireless networking promise a new generation of wireless sensor networks suitable for those on-body/in-body networked systems.



Implantable Wireless Body Area Network (IWBAN)

To measure health parameters, biosensors must be in close contact with the skin, and sometimes even inside the human body. Implantable biosensors are an important class of biosensors based on their ability to continuously measure metabolite levels, without the need for patient intervention and regardless of the patient's physiological state (sleep, rest, etc.). For example, implantable biosensors represent a highly desirable proposition for diabetes management which currently relies on data obtained by using test strips blood from finger pricking, a procedure which is not only painful, but also is incapable of reflecting the overall direction, trends, and patterns associated with daily habits.

This initiated a broad research effort aimed at developing implantable biosensors for continuous monitoring of multiple biologically relevant metabolites, but not wearable sensors. Other classes of implantable devices which have been intensively investigated include sensors for nerve stimulation can ease acute pain sensors to the detecting electric signals in brain and sensors to monitor biological analysis in brain with implanted drug delivery systems for controlled delivery at the site of pain and stress. The range of implantable biomedical devices will increase substantially over the next decade, thanks to improved technology in MicroSystems technology achieved during the last decade. IWBANs are more desirable than WWBAN for many advantages. WWBANs have some disadvantages: they limit the mobility of the patients; in addition, they can cause skin infections, thus contributing poor health conditions. Despite the wireless connection is not an

important requirement for monitoring physiological parameters from implanted sensors. This problem is considered as one of the main motivations for the trend in modern biomedical implanted systems to use wireless technology.

Symbiotic Nodes

The transition from the state of the art, the scientific community is pushing to more aggressively scaled cubic millimeter size devices (called "smart dust", which may support a number of new in-body bio-monitoring applications. The technical problems to be addressed are, first, the implementation of self-powered nodes that can collect energy from the body (temperature gradients, movement, in-body chemical reactions, etc.). Second, the size limitation imposes demanding requirements on the process of integration and microfabrication: wireless communications, electronic data processing, chemical data processing, microfluidic capabilities should all be packed in a few cubic millimeters. Finally, further problems arise in connection with the safety requirements: nodes must be short and long term bio-compatible. We call these nodes symbiotic because they have a true mutual advantage relationship of the target organism.

Bio-Inspired Nodes

As the end point of the evolution trends, we envision bio-inspired units (nodes), both from the architecture and technology viewpoint. The physical scale of these devices approaches a few cubic microns (or less), and the interaction

between the target sensor and the sensor itself disappears. Molecular engineering and nanotechnology will make these devices a reality in the near future. Some research efforts showed that some of the features required in the sensor node can be realized by molecular-scale devices, which are often engineered with the use of bio-molecules. These devices operate autonomously, powered by chemical reactions inspired by biological systems. The process of construction and architecture of these devices will also resemble natural processes in biology: bottom-up self-assembly, self-reproduction and self-repair will be necessary in addition to the safety and biocompatibility. Hardware component for medical and biological applications has to consider biocompatibility problems and the high specific properties of the interaction at the molecular and atomic level. This can be achieved through development of technologies, such as: (a) advanced synthetic or non-molecular receptors; (b) innovative three-dimensional membranes for highly-molecular controlled release ; (c) bio-hybrid systems as bio-coated nano particles for a vehicle of drugs or transfection agents inside the cell ; (d) bio-inspired systems to simulate specific features of biological systems as adaptation and self-regulation; (e) smart surfaces for organic transduction electronically specific mechanical or optical stimuli.

STIMULATOR

The mechanism of L-arginine stimulation of glucose-induced insulin secretion from mouse pancreatic islets was studied. At 16.7 mmol/l glucose, L-arginine (10 mmol/l) potentiated both phases 1 and 2 of glucose-induced insulin secretion. This potentiation of glucose-induced insulin secretion was mimicked by the membrane depolarizing agents tetraethylammonium (TEA, 20 mmol/l) and K⁺ (60 mmol/l), which at 16.7 mmol/l glucose obliterated L-arginine (10 mmol/l) modulation of insulin secretion. Thus L-arginine may potentiate glucose-induced insulin secretion by stimulation of membrane depolarization. At 3.3 mmol/l glucose, L-arginine (10 mmol/l) failed to stimulate insulin secretion. In accordance with membrane depolarization by the electrogenic transport of L-arginine, however, L-arginine (10 mmol/l) stimulation of insulin secretion was enabled by the K⁺ channel inhibitor TEA (20 mmol/l), which potentiates membrane depolarization by L-arginine. Furthermore, L-arginine (10 mmol/l) stimulation of insulin secretion was permitted by forskolin (10 micromol/l) or tetradecanoylphorbol 13-acetate (0.16 micromol/l), which, by activation of protein kinases A and C respectively sensitize the exocytotic machinery to L-arginine-induced Ca²⁺ influx. Thus glucose may sensitize L-arginine stimulation of insulin secretion by potentiation of membrane depolarization and by activation of protein kinase A or protein kinase C. Finally, L-arginine stimulation of glucose-induced insulin secretion was mimicked by NG-nitro-L-arginine methyl ester (10 mmol/l), which stimulates membrane depolarization but inhibits nitric oxide synthase, suggesting that L-arginine-derived nitric oxide neither inhibits nor stimulates insulin secretion. In conclusion, it is suggested that L-arginine potentiation of glucose-induced insulin secretion occurs independently of nitric oxide, but is mediated by membrane depolarization, which stimulates

insulin secretion through protein kinase A- and C-sensitive mechanisms.

ULTRASOUND CAVITATION

To produce an ultrasound, a piezoelectric crystal has an alternating current applied across it. The piezoelectric crystal grows and shrinks depending on the voltage run through it. Running an alternating current through it causes it to vibrate at a high speed and to produce an ultrasound. This conversion of electrical energy to mechanical energy is known as the piezoelectric effect. The sound then bounces back off the object under investigation. The sound hits the piezoelectric crystal and then has the reverse effect - causing the mechanical energy produced from the sound vibrating the crystal to be converted into electrical energy. This ultrasound cavitation can result in reduction of visceral fat which consequently cures type 2 diabetes from inside, by placing a piezo bio electric into the device. The device could be designed in a manner that the crystal works by body's natural potential (70 milli volt). Hence these measures planned up might bring a best solution to diabetes.

CONCLUSION

By 2030, Diabetes will be the most dangerous seventh factor causing death in the world according to WHO. Hence prior to that, there must be promising solution to prevent, cure and eradicate Diabetes. Therefore we hope our idea will be a new era in medical field to prevent loss of lives caused by diabetes, since this leads to eradication of the disease totally from outside.

REFERENCES

- [1] <http://onlinelibrary.wiley.com/doi/10.15252/embj.201490685/pdf>
- [2] <https://www.niddk.nih.gov/health-information/diabetes/overview/insulin-medicines-treatments/pancreatic-islet-transplantation>
- [3] <http://longevityfacts.com/pancreas-box-beta-cells-historys-first-stem-cell-transplant-treat-type-1-diabetes-pancreas-in-a-box/>