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A Study of Therapeutic Strategies in the Management of Diabetes Mellitus (DM) in India

Vikas Yadav[1]* Dr. Chagi Venkatesh[2]

[1] Research Scholar, Sunrise University, Alwar, Rajasthan

[2] Professor, Sunrise University, Alwar, Rajasthan

Abstract – Most new chemical entities are poorly solubilized in water; solubility has been a major issue for many decades, resulting to high intrasubject/intersubject variability in dosing, dosage inconsistency, and eventually low bioavailability. Solubility remains a major concern for formulation scientists despite several techniques such as solid dispersions and complexation with cyclodextrin, nanoparticles and permeation enhancers. As evidenced by various exploratory findings reported in literature, lipid formulations have emerged in recent years as a promising aid in improving the solubility of several lipophilic drugs. These findings show that lipid formulations can enhance absorption by facilitating the solubilized phases while decreasing the inherent restrictions of slow and curtailed drug dissolve rates in aqueous solutions. The self microemulsifying based drug delivery system (SMEDDS) has shown significant improvement in resolving solubility difficulties among lipid-based formulations. The oil, surfactant, cosurfactant, and drug constituents of SMEDDS produce an oil-in-water microemulsion when gently agitated in the stomach and intestine in vivo. SMEDDS are isotropic and thermodynamically stable solutions. SMEDDS has a greater interfacial surface area because of its small droplet size, which results in better release and absorption qualities. If you've ever taken a SMEDDS pill, you'll know that there are a few downsides, such as chemical and physical incompatibilities, drug outflow from the capsule shell, precipitation and ageing issues that can occur. Solid dosage forms don't have these kinds of difficulties, hence solidifying liquid SMEDDS via absorption into solid carriers is a viable option. Many studies have shown that changing liquid SMEDDS into solids and then into dosage forms like tablets, pellets, etc., is a viable option.

Key Words – Therapeutic Strategies, Diabetes Mellitus (DM), India, Self Micro emulsifying Based Drug Delivery System (SMEDDS)

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INTRODUCTION

DIABETES

Stats & Current Scenario: India & World

Worldwide, diabetes prevalence is anticipated to rise to 4.4% by 2030, according to the World Health Organization According to current projections, the global population of urban areas is expected to double from 2010 to 2030, rising from 169 million people in the year 2000 to 354 million in the year 2030 in emerging nation states (Wild et al., 2004). Diabetes's toll is the outcome of a number of interrelated events. Diabetes is on the rise because of a combination of genetic predisposition, lifestyle changes, urbanisation, and globalisation. Based on an estimated 40 million diabetics in India, there are at least seven million individuals with eye disease, 0.6 million people with renal disease, 9.2 million people with brain disease, 7.9 million people with heart disease (CHF), and 1.9 million people with peripheral vascular disease (PVD). As a result of the large population of diabetics in India, the burden of dealing with the disease's complexities is heavy. To be fair, these numbers are conservative; yet, it's possible that people living in rural areas have more discomfort as a result of poorer diabetes management and fewer options for medical care.

Diabetes care in India (key findings)

1. Type I diabetes affects 86% of people in Southeast Asia's 883 million-strong adult population.

2. The economic burden of diabetes in India necessitates attention to economic measures of diabetes, such as prescreening, planned metabolic control, risk factor management, and monitoring, among others.

3. The use of lifestyle modifications such as regular exercise, yoga practise and stress management, as well as pharmacological treatment, is essential in the fight against type 2 diabetes.

4. In order to combat the diabetes epidemic that is currently threatening the lives of millions of Indians, medical professionals must be kept abreast of the most recent discoveries in the field of diabetes care (Joshi, 2015).

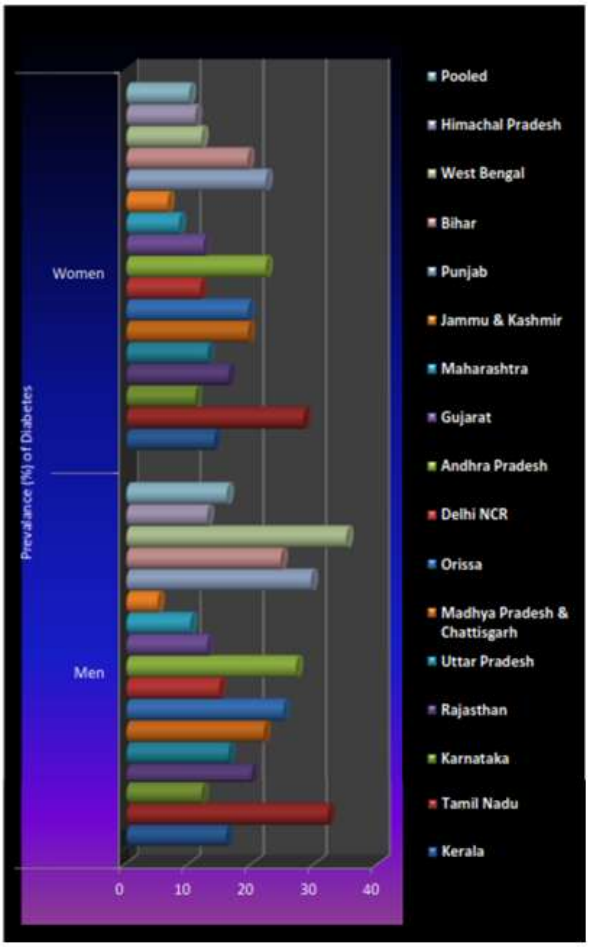

Figure 1. Diabetes stats in India (Age wise)

LITERATURE REVIEW

Wild S, Bchir MB, Roglic G, Green A, Sciree R, King H. (2014): For self-emulsifying systems, it was stated how much oil and surfactants should be used. A liquid crystalline phase emerges between the oil/surfactant and water phases, which effectively swells, thereby allowing 'Spontaneous' creation of an interface between the oil droplets and water. This may explain why self-emulsification requires such a precise ratio of oil and surfactant.

Joshi S. (2015) For the first time, a report was made about the stability of microemulsions based on the components used in them. Researchers found that the manner in which components are combined for microemulsion formation is extremely important. Other clear oil-water dispersions are unstable because they occur only when the concentration gradient is strong enough to allow the passage of amphipathic elements across the oil/water interface. The authors measured the film pressure versus area functions of duplex films for microemulsions that had been created. The results showed that the surfactant monolayer was penetrated. For the same reason, the film strength of 1-Pentanol is increased while remaining elastic. Coalescence of microemulsion droplets is prevented by this concept.

Ahmed AM. (2015) For the development of self microemulsifying drug delivery systems, we investigated the possibility of using conventional non-ionic surfactants and vegetable oils. To create the submicron droplets, they used glycerol tri-oleate ethoxylated with Miglyol 812 and medium chain triglyceride to create the emulsion. A correlation between the good emulsion properties of these excipients and their results was found.

Patlak M. (2015) Studying the role of intestinal lymphatic transport in the absorption of penclomedine, as well as comparing it to that of two other comparable substances, such as DDT and hexacetylene, was done. To test the lymphatic transport of penclomedine in anaesthetized rats, we administered it intraduodenally in the form of a 10 percent o/w penclomedine-based emulsion, a 10 percent o/w penclomedine-based emulsion, or a 10 percent o/w penclomedine-based suspension. Soybean oil and triolein emulsions both carried about 3% of the absorbed dose lymphatically after bioavailability was taken into account. After delivery in the other vehicles, less than 0.75 percent of the absorbed dose was transferred. Penclomedine's lower partition coefficient and higher plasma protein and red blood cell binding may account for its lower lymphatic absorption rate when compared to DDT, while hexachlorobenzene's lower lymphatic absorption rate may be attributable to its lower water and lipid solubility and higher plasma protein and red blood cell binding. In the dynamics of intestinal lymph vs portal blood transfer, it is predicted that a high degree of plasma protein and red blood cell binding will compete with chylomicron affinity.

Dielectric spectroscopy and self-emulsification have been linked, according to Maitra A and Abbas AK. (2015). Imwitor 742 and Tween 80 were used in a series of combinations that were characterised for visual examination and particle size distribution at various temperatures. Dielectric spectroscopy on pure components and binary systems with water added to construct 50% v/v mixes produced results suggesting a significant drop in mean particle size with an increase in temperature. At concentrations that have been proved to be effective self-emulsifying systems,

evidence suggests that liquid crystalline phases can be formed.

Chen L, Magliano DJ, Zimmet PZ. (2016) PGGs with different fatty acid and polyethylene glycol chain lengths were tested for their potential to self-emulsify oil in water. Polyglycolyzed glycerides appear to be effective emulsifiers for SEDDS, according to the data. In order for SEDDS to work well, droplet particle sizes and droplet polarity must match in the emulsion. These qualities can be evaluated using the PC of the medication from these SEDDS. An SEDDS lipophilic drug's solubility and absorption capabilities are compared to those of other dosage forms.

Chamnan P, Simmons RK, Forouhi NG, Luben R. Khaw Ky, (2010) Self-emulsification and low frequency dielectric spectroscopy have been linked to the creation of liquid crystals. They used a visual evaluation method to examine the self-emulsifying capabilities of a series of combinations containing Imwitor 742 and Tween 80. At 25°C, 37°C in water, and 37°C in 0.1 M HC1, the particle size distributions of these emulsions were examined. As the temperature rises, the mean particle size of Imwitor 742/Tween 80 combinations drops significantly, with the majority of compositions also seeing a fall in the average sized particle.

Zimmet P, Alberti KG, Shaw J. (2017) A comparison of the efficacy of distinct fatty acid (C8-C18) chain length co-emulsifiers (surfactants) and lipophilic vehicles (oils) containing different C8-C18 chain length glycerides (co-emulsifiers) was undertaken in manufacturing self-emulsifying systems. HLB in the range of 10-15 and monoglyceride of medium chain fatty acids (C8-C10) were found to produce the best self-emulsifying systems, according to the results of the study.

Patel, J. C. et al. (2017) An extremely small particle size (5-30 nm) microemulsion including an oil, a low and high HLB surfactant blend, and an aqueous phase was developed. In order to select the optimum method for their development, developed formulations were evaluated against each other on several parameters such as viscosity, refractive index, zeta potential, and so on. According to the study's findings, excipients such as Captex 355/Capmul MCM/Tween 80/saline should be used for commercial purposes.

DIABETES MELLITUS (DM)

Diabetes mellitus (DM) is a condition that has plagued humans for as long as anybody can remember. Around 3000 years ago, it was first mentioned in Egyptian writings (Ahmed, 2002). Sort 1 DM and sort 2 DM were clearly separated in 1936. (science.jrank.org). In the early 1980s, Type 2 Diabetes Mellitus (DM) was initially categorised as a metabolic disorder (Patlak, 2002). Insulin-dependent diabetes mellitus (IDM) is the most widely recognised type of DM, characterised by high blood glucose levels, insulin resistance, and insulin inadequacy (Maitra & Abbas, 2005). For Type 2 diabetes, the most vulnerable risk factors are genetic, environmental, and behavioural (Chen et a; nature.com, niddk.nih.gov). People with type 2 diabetes mellitus are more prone to both minor and significant health complications, which frequently lead to their untimely demise. There is a tendency to expand grimness, as well as transience, in people with type 2 DM because of the constancy of this type of DM, its deceiving onset, and its late acknowledgment, particularly in poor countries like Africa (Chamnan et al., 2016).

Epidemiology

As of 2011, it was estimated that 355 million people worldwide have diabetes mellitus; by 2029, that number could reach 552 million (Chamnan et al., 2016). People in low- and middle-income nations make up 80% of those with diabetes mellitus worldwide, according to a new study. In 2010, DM was blamed for the deaths of approximately 3.8 million people. Diabetes mellitus is expected to affect 398 million people by the year 2025, according to the World Health Organization. Type 2 diabetes mellitus rates vary widely by topographical region, depending on natural and human-made hazards (Zimmet et al., 2001). By the middle of the twentieth century, the dominance of DM in India had not been recognised. As recently as early 1960s exploratory data indicated that this condition was prevalent (Patel et al., 1963; KEM Hos grp., 1966; Berry et al., 1966; Gour, 1966; Rao et al., 1966; Vishwanathan & Krishnamoorthy, 1966). Following this, a slew of institutions performing studies on diabetes mellitus control in various parts of the country were introduced. Despite the fact that these publications have used shifting processes, examining systems, and suggestive criteria, their results show a decent increase in the prevalence of diabetes mellitus. The ICMR opened India's first multispecialty centre dedicated to diabetes mellitus research in 1971. This study examined the extent to which DM had spread over six urban areas and towns in India. The illness was found to be 2.6 percent prevalent in urban areas and 1.7 percent prevalent in rural areas (Ahuja, 1979). The nationwide city Diabetes research has now examined patients from six notable Indian cities, with the prevalence ranging from 8.9% in Mumbai to 15.8% in Hyderabad more than two decades later (Ramachandran, 2001). At the same time, the pervasiveness of Diabetes in India was measured by looking at the prevalence of DM in India's residential communities and major cities, respectively. Global Diabetes Federation (GDF) pervasiveness estimates for DM in India in 2010 relied on the results of these and other smaller studies (Anjana et al; 2011). Regardless, none of these assessments can be considered an accurate depiction of India as a whole. Diabetes in India is not concentrated in large cities, as is the case with

the National City Diabetes reports, which do not include the country's borders. The ICMR-India Diabetes (ICMR-INDIAB) study, which is currently in progress, aims to fill this knowledge gap by assessing the prevalence of diabetes mellitus (DM) in India using standard testing procedures and indicative criteria in an agent test of people from rural and urban provinces in each of India's twenty-nine states. As a follow-up to stage one of the review, it was found that 59 million Indians had diabetes and 82 million had pre-symptomatic diabetes (i.e., impeded glucose resilience and hindered fasting glucose as indicated by WHO standards) in 2011 as a result of these findings (Anjana et al; 2011). As a result of these findings, the International Development Research Foundation (IDRF) revised their estimates of the number of people with HIV/AIDS in India from 45 million to 56.4 million (IDF, 2011). It's clear that these numbers aren't going to stay the same, and a 2014 data update predicts that 58.6 million Indians will have diabetes mellitus. Table 1.1 provides a detailed breakdown of the prevalence of diabetes mellitus in India.

Table 1. Thirty years of pervasiveness of diabetes mellitus in India (centre studies)

Location	Year	Urban				Rural			
		Subject s (No's)	Age (years)	Methodology (diagnosis)	Pervasiveness (%)	Subject s (No's)	Age (years)	Methodology (diagnosis)	Pervasiveness (%)
North India									
Lucknow	1973	2,190	≥20	BG (R)	2.1	–	–	–	–
Delhi	1974	2,793	≥15	BG (R)	1.6	–	–	–	–
Delhi	1974	2,291	≥20	BG (R)	3.2	–	–	–	–
Delhi	1980	6,878	≥20	DDM	4.4	–	–	–	–
Haryana	1986	–	–	–	–	3,270	≥10	BG (R)	2.9
Varanasi	1987	5,572	≥10	GU	3.7	–	–	–	–
Rewa	1988	–	–	–	–	15,000	–	BG (R)	1.9
Chandigarh	1989	4,348	≥30	GU	4.2	–	–	–	–
Bhopal	1991	5,695	≥20	DDM	3.9	–	–	–	–
Punjab	1994	–	–	–	–	1,100	≥30	DDM, PG	4.6
Srinagar	2000	1,721	≥30	DDM, FS, PG*	5.5	6,132	≥40	–	3.5
Delhi	2001	668	≥18	DDM, FS	9.8	–	–	–	–
Jaipur	2001	1,271	≥20	DDM, FS	11.6	–	–	–	–
Rajasthan	2004	–	–	–	–	885	≥20	–	–
Punjab	2004	988	≥20	DDM, FS	12.1	–	–	–	–
Delhi	2005	2,166	20–59	DDM, FS, PG	14.5	–	–	–	–
Rajasthan	2007	–	–	–	–	2,899	≥20	–	1.7
Nagpur	2007	–	–	–	–	924	≥30	DDM, FS, PG	3.7
Jaipur	2007	1,127	≥20	DDM, FS	20.1	–	–	–	–
Lucknow	2008	1,112	≥30	DDM, FS, PG	21.1	–	–	–	–
Jaipur	2012	739	30	DDM, FS	13.4	–	–	–	–
Haryana	2013	–	–	–	–	4,230	≥18	BG (R)	3.9
Varanasi	2013	5,572	≥10	GU	3.7	–	–	–	–
Rewa	2014	–	–	–	–	17,000	–	BG (R)	2.8
South India									
Trivandrum	1972	722	≥20	BG(R), FS, PG	15.8	–	–	–	–
Hyderabad	1972	–	–	–	–	2122	≥20	US	2.8
Hyderabad	1972	–	–	–	–	1002	≥10	RBG	3.2
Bangalore	1973	24,730	≥5	BG(R)	3.1	–	–	–	–
Chennai	1977	1,555	≥10	BG(R)	4.2	–	–	–	–
Pondicherry	1980	2,694	≥20	GU	1.3	–	–	–	–
Tenali	1984	1048	≥15	RBG	3.8	–	–	–	–
Kudremukh	1988	972	≥20	DDM, FS, PG	4.8	–	–	–	–
Ekaru	1989	6,001	≥0	DDM	2.3	4,807	≥0	DDM	2.3
Gangavati	1990	–	–	–	–	988	≥30	DDM, FS, PG	2.5
Chennai	1992	1000	≥20	DDM, FS, PG	7.8	1335	≥20	DDM, FS, PG	3.2
North Arcot	1994	–	–	–	–	522	≥40	DDM, PG	5.5
Chennai	1997	3,122	≥20	DDM, FS, PG	12.2	–	–	–	–
Chennai	1999	2,555	NA	DDM, FS, PG	8.8	–	–	–	–
Trivandrum	2000	888	≥20	DDM, FS, PG	17.5	–	–	–	–
Trivandrum	2000	312	≥19	DDM, PG	15.8	–	–	–	–
Chennai[37]	2000	27,32 2	≥20	K	3.5	–	–	–	–
Chennai	2001	1,323	≥20	DDM, FS, PG	10.2	–	–	–	–
Chennai	2006	3,122	≥20	DDM, FS, PG	13.2	–	–	–	–
Godavari	2000	–	–	–	–	3,122	≥30	FS	14.2
Kochi[37]	2000	4,122	18–80	K, PG*	20.1	–	–	–	–
Hyderabad	2008	–	–	–	–	2,135	≥10	RBG	4.8
Bangalore	2009	25,32 2	≥5	BG(R)	4.2	–	–	–	–
Chennai	2011	1,888	≥10	BG(R)	5.3	–	–	–	–
Pondicherry	2012	5,012	≥20	GU	4.2	–	–	–	–
Tenali	2013	2222	≥15	RBG	5.5	–	–	–	–
Kudremukh	2014	1082	≥20	DDM, FS, PG	5.2	–	–	–	–
Ekaru	2014	7000	≥0	DDM	3.2	5,889	≥0	DDM	3.2
Chennai	2015	2,222	40–64	DDM, FS, PG	40.1	–	–	–	–
East India									
Orisa	1971	–	–	–	–	3,111	≥10	RBG	2.2
Kolkata	1975	3,999	≥20	BG(R)	3.2	–	–	–	–
Guwahati	1998	1,555	≥20	DDM, PG	9.8	–	–	–	–
Manipur	2001	1,722	≥15	DDM, PG	5.1	–	–	–	–
Kolkata	2009	3,111	≥20	DDM, FS	12.2	–	–	–	–
Manipur	2012	1,722	≥20	FS or PG	17.5	–	–	–	–
West Bengal	2013	1,888	20–59	DDM, FS, PG	16.2	–	–	–	–
Arunachal Pradesh[1]	2014	–	–	–	–	1,322	≥20	DDM, PG, FS	20.1
West India									
Mumbai	1963	1,925	≥20	GU	2.3	–	–	–	–
Mumbai	1966	4,222	≥20	BG(R)	3.2	–	–	–	–
Ahmedabad	1978	4,222	≥15	BG(R)	4.5	–	–	–	–
Bhadlan	1986	–	–	–	–	4,586	≥18	BG(R)	4.5
Barshi[37]	1987	–	–	–	–	5,222	All	BG(R)	4.4
Mumbai[37]	2001	655	≥20	DDM, FS, PG	8.5	–	–	–	–
Sindhudurg	2006	–	–	–	–	2,122	≥20	DDM, FS, PG	10.2
Goa	2011	–	–	–	–	2,555	≥30	DDM, FS	11.2

TYPES OF DIABETES MELLITUS

♣ Type one diabetes mellitus

The prevalence of type 1 diabetes mellitus (T1DM) in India is unusually high when compared to western countries. Even so, the rate is higher than in many other Asian countries, including China; measurements showed that every fifth child worldwide had T1DM, compared to every seventh adult with T2DM (kumar et al, 2013). Three new cases of T1DM per one million children aged zero to fourteen years are estimated by the IDF each year. For each one million children, there is a 14.93, 2.2, and 9.2 occurrence rate for each one in Karnataka, Chennai, and Karnal (as well as the region in Haryana), respectively60–62. However, these values are higher than the estimated incidence in China (0.1 per lakh), but they are also lower when compared to European areas, such as Sardinia and Finland (34.9 and 35.8 per 100,000, respectively) (Karvonen etal, 2000). T1DM is referred to as "spontaneous arousal of illnesses" (T1b) diabetes mellitus in India since it is rarely associated with elevated levels of pancreatic autoantibodies (Balasubramanium et al, 2003). Byzantine Indian people have a different link with the human

leukocyte antigen (HLA) and T1DM than white people do. A26-B8-DRB1*03 and Ax-B50-DRB1*03, two genetic chromosomes found in Indian children in the northern region with T1DM, were observed often in this study (identified in twuenty five percent of every single subject). Seven percent of this Asian Indian population was found to have the single type A1-B8-DRB1*03 chromosome that favours autoimmunity in white individuals (Kanga, 2004).

♣ Fibrocalculous pancreatic diabetes mellitus (FCPD)

Next to pancreatic calcification in non-alcoholics, FCPD is a unique kind of diabetes mellitus that is more common in the young (Zuidema, 1959). abdominal pain that has persisted since childhood, as well as pancreatic calculi linked to pancreatic pipe dilatation and organ fibrosis during puberty (Mohan, 1990). This type of diabetes has a slew of potential labels, including pancreatic diabetes, pancreatogenous diabetes, and steamy pancreatic diabetes. The World Health Organization (WHO) began using the name Fibrocalculus Pancreatic Diabetes (FPD) for this kind of diabetes in the late 1990s. In most cases, patients with FCPD are between the ages of 10 and 40, and many of them have a history of excruciating epigastric pain manifested as a decrease in intensity or an increase in intensity (mohan, 1993). Many reports from Africa and Asia (Shaper, 1960; Nabunnya, 2011) show the start of FCPD in adolescents (Mohan, 2008; Rajasuriya, 1979). At 49 years of age, which is typically the commencement of FCPD, this patient was given FCPD elements without any prior history of such. Many factors are implicated in the pathogenesis of FCPD, including a lack of a healthy diet, the lethal effects of the cyanide obtained from repeated use of cassava, the familial component (which accounts for around 10%), hereditary components (which is proposed as the primary cause), and an increased oxidant concern due to vitamin C and A deficiency. Serine protease inhibitor Kazal sort 1 (SPINK 1) quality has been linked to Tropical calcific pancreatitis by current evidence (Hasan, 2002; Bhatia, 2002). Preventing uncontrolled or incorrect pancreatic compound transport by inhibiting trypsin movement is an essential protease inhibitor. As a result, pancreatitis occurs on an occasional basis.

♣ Gestational diabetes mellitus (GDM)

The prevalence of gestational diabetes mellitus (GDM) varies widely depending on the criteria used and the demographic characteristics of the population. As the obesity pandemic continues, the prevalence is expected to rise (Benharoush, 2003). Risks for both mother and child are elevated in GDM-induced pregnancies, including caesarean and agent vaginal delivery, macrosomia and bear dystocia, newborn hypoglycemia and hyperbilirubinemia (Catalano, 2006). Women with a history of gestational diabetes mellitus (GDM) face an increased risk of developing type 2 diabetes mellitus (T2DM) in the years following their pregnancy, and their children face an increased risk of developing obesity and T2DM earlier in life. Because of this, it is critical to pay close attention to GDM in order to cover a wide range of clinical issues associated with GDM, such as the difficulties of studying disease transmission, symptomatic criteria and screening, the pathophysiology of GDM, the treatment and counteractive action of GDM, and the long and immediate results of GDM for both mother and baby.

♣ Monogenic diabetes mellitus (MDM)

The prevalence of more gynic forms of diabetes mellitus in India is poorly understood. The Tattersall and Fajans medical criterion for greater gynic diabetes of the young (Tattasrsrs, 1975) medical criterion detected nine percent of 96 unconnected participants with HNF1A (formerly known as MODY3) and 3.4 percent of HNF4A (previously known as MODY1) changes (Radha, 2009; Anuradha, 2011). 56 patients with medically confirmed MODY were evaluated in another study, and 11 changes were found, seven of which were new transmutations (Chapla, 2015). Work to explain the experimental appearance of greater female diabetes in India has been thwarted by a lack of meticulous genetic analysis facilities and the associated high expenses.

COMPLICATIONS WITH DIABETES MELLITUS

Retinopathy, nephropathy, and neuropathy are all complications of diabetes mellitus (both fringe and autonomic). People with diabetes mellitus are at an increased risk of developing atherosclerotic vascular disease. Hyperglycemia is associated with a greater risk of microvascular and neuropathic complications, however the increased risk for vascular illness really precedes the start of hyperglycemia to the extent that diabetes mellitus exists. Diabetic retinopathy is the most common cause of vision loss in Western countries, especially among children. Diabetic nephropathy is the primary cause of the need for renal replacement therapy (dialysis or transplantation). Diabetic neuropathy and lower furthest point vascular infection combine to make diabetes the primary cause of nondramatic lower limit removals. Finally, diabetes raises the risk of atherosclerotic vascular infection by a factor of two to five. A patient's ability to be properly managed when dealing with diabetes mellitus is critically dependent on the ability to properly identify, counteract, and administer entanglements (Byron, 2005).

THERAPEUTIC STRATEGIES IN MANAGEMENT OF DIABETES MELLITUS

Understanding the inherited and natural elements that influence the prevalence of T2DM is critical for formulation scientists who are developing therapeutic methods for this disease. Regular physical activity and a well-balanced diet are essential for managing type 2 diabetes, but making lifestyle adjustments can be difficult for some people, particularly those who live stressful lives. As a result, due to the dynamic nature of the disease process, these fundamental procedures are doomed to failure. Until recently, only sulfonylurea and metformin were available as oral therapeutic therapy alternatives (Roger, 2002). In light of the progressive nature of T2DM, the likelihood of a rise in diabetic complication is also of great concern. Microvascular and macrovascular problems are more common in people with type 2 diabetes. It's also possible that these severe medical disorders are already existing when a patient is diagnosed with them (Stefano, 2006; Adler, 2000). Patients will have to rely solely on insulin therapy as time goes on and complications worsen. As a result, formulation scientists have attempted to analyse the typical combinational medicines in order to tackle this scenario. In order to deal with the complications of T2DM, sufferers will seek out more effective remedies. There will be a demand for more affordable treatments for this disease, however these pharmaceutical mixes have limitations in their application to patients with delayed phase T2DM. To address this issue, new management methods are being developed. As an example, islet cell replacement and glucagons like peptide 1 (GLP-1) or GLP-1 analogues are used to exchange and extend islet cells. For type 1 diabetics, islet cell transplantation is more effective, whereas GLP-1 or GLP-1 analogues are more appropriate, and it can also promote pancreatic islet cell expansion in diabetic animals. Pharmaceutical scientists must create more treatment options for T2DM in order to address and overcome the challenges outlined above. Table 1.2 provides an overview of some of the recent advances in therapeutics.

Table 1.2. Details of therapeutic strategies in the management of diabetes mellitus

Therapeutic Strategy	Therapeutic agent/entrant	Description	Ref
Oral hypoglycemic agents	Insulin secretagogues (sulfonylureas, repaglinide); biguanides and thiazolidinediones; a-glucosidase inhibitors	Generally these agents are utilized to treat T2DM. They generally work by bringing down the glucose levels in the blood. In this class different types of antidiabetic agents are accessible; their utilization relies on upon the way of the diabetes, age and circumstance of the individual and also different elements.	(Tildsley et al, 2007)
Acetyl-CoA carboxylase 2	malonyl-CoA-ACC1 & malonyl-CoA-ACC2	Allosteric direction, covalent adjustment and incessantly by modifications in protein union and turnover. Citrate and palmitoyl-CoA are the two generally powerful allosteric controllers of ACC action. Citrate invigorates ACC action by advancing the arrangement of a very polymerized frame, while palmitoyl-CoA, the final result of the unsaturated fat synthase complex.	(Abu et al., 2006)
Gene expression profiling	Trigger Orthologue Gene Alignment (TOGA)	It acts in managing T2DM by two strategies first by recognizing those genes that are most suitable with the metabolic alterations in specific tissues of patients with disease, and second by identifying those genes which are presented in contrast to response to drug treatment, in order to specify genes related with clinical efficacy versus side effects or toxicity.	(Ju et al., 2002)
Dipeptidyl	T-cell antigen CD26	This approach is efficacious in boosting of endogenous levels of	(incretins,
peptidase IV inhibitors		glucagon like peptide-1, which presents the output of enhanced glucose tolerance in glucose resistant and diabetic animal models.	2006; Ichiyama et al., 2007)
peptide of glucagon (GLP-1)	-	GLP-1 accelerates insulin biosynthesis and insulin gene expression and to have nutritive effects on the b-cells. The nutritive effects include inhibition of apoptosis and proliferation of existing b-cells, maturation of new cells from duct progenitor cells. GLP-1 exerts antihyperglycemic performance in response to meal ingestion.	(Lynn et al., 2007; arakinoshi & Portha, 2006)
Kappa kinase beta (IKKB)	-	involved in inhibiting the insulin signaling pathway in response to high fat loading or obesity	(Kim et al., 2006)
CSII (insulin pump therapy)	-	The merits of insulin pump therapy (less glycemic variability, reduced HbA1c, least chance of severe hypoglycemia, and more flexible lifestyle with a positive impact on the quality of life) should be similar for patients with type 2 as well as type 1 diabetes	61 (Ahuli, 2006)
Nuclear receptors as drug targets	peroxisome proliferator activated receptors (PPAR), liver x receptors farnesoid x receptor.	PPAR-γ partial agonists, PPAR-α and -γ dual agonists, PPAR-δ agonists and panagonists are at present being examined in clinical trials, and present important merits in reference to glycemic control, lipid profiles and weight gain contrasted with the first generation of thiazolidinediones (TZD) drugs. LXR and FXR agonists also show potential strategy and are predicted to boost	(Peraza et al., 2006)

CONCLUSION

A BCS class II medication, repaglinide (RPG) is an orally given benzoic acid derivative that improves pancreatic insulin production in people with type 2 diabetes. Repaglinide, unfortunately, has solubility and bioavailability difficulties. Repaglinide is a key ingredient in our research studies, and we are hoping to take liquid SMEDDS formulation to a new level by developing and refining self-microemulsifying tablets of repaglinide. With 2mg of RPG, the liquid SMEDDS formulation (RS2) with optimised RPG loading contains Labrafil M1944CS, Kolliphor EL, and propylene glycol as the main fat and surfactant/co-surfactant, respectively. Droplet size (72 3.2nm), zeta potential (- 20.4 0.15mV), cloud point (70 + 1.35°C), and viscosity (190.2 + 1.23cps) were all shown to be significant in the drug release measured by RPG for the liquid SMEDDS formulation. For batch-wise preparation of SMET's, the RS2 formulation was used in conjunction with the selective adsorption approach and Aeroperl300pharma as an optimal solid adsorbent carrier, and wet granulation compression was used. There was a 99.2 percent in-vitro release rate for RPG loaded SMETs in batch B1; this was much better than the commercial formulation and pure medication. Although blood glucose levels dropped to 101.2 after eight hours, a significant increase in oral bioavailability was seen (up to two folds) during in-vivo testing. Solubility and availability at the site of action for RPG can be improved by adding liquid SMEDDS to a solid carrier and changing them into tablets, according to our research, which found this strategy to be effective.

REFERENCES

1. Wild S, Bchir MB, Roglic G, Green A, Sciree R, King H. (2014) Global Prevalence of Diabetes. Epidemiology. 27(5): pp. 1047-1053.

2. Joshi S. (2015) Diabetes care in india. Annals of global health.; B1(6): pp. 830-839.

3. Ahmed AM. (2015) History of diabetes mellitus. Saudi Med J;23(4): pp. 373-378.

4. Diabetes mellitus history- from ancient to modern times. Available at http:// science.jrank.org/pages/2044/Diabetes-Mellitus.html. (accessed on 30th Jan, 2016).

5. Patlak M. (2015) New weapons to combat an ancient disease: treating diabetes. FASEB;16(14): pp. 1853.

6. Maitra A, Abbas AK. (2015) Endocrine system. In: Kumar V, Fausto N, Abbas AK (eds). Robbins and Cotran Pathologic basis of disease. Philadelphia, Saunders; pp. 1156-1226.

7. Chen L, Magliano DJ, Zimmet PZ. (2016) The worldwide epidemiology of type 2 diabetes mellitus: present and future perspectives. Nature reviews endocrinology. Available at: www.nature.com/uidfinder.

8. Genetic basis of type 1 and type2 diabetes, obesity, and their complications. Advances and emerging opportunities in diabetes research: a Strategic Planning report of the DMICC. www2.niddk.nih.gov/NR. (Accessed 26th Feb 2016).

9. Chamnan P, Simmons RK, Forouhi NG, Luben R. Khaw Ky, Wareham NJ et al. Incidence of type 2 diabetes using proposed HbA1c diagnostic criteria in the EPICNorflok cohort: Implication for preventive strategies. Diabetes Care. 2017; 4: 950-6. doi: 10.2337/dc09-2326. Epub 2010 Jul 9.

10. Zimmet P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. Nature. 2017; 414: pp. 782-787. doi:10.1038/414782a.

11. Patel, J. C. et al. A sample survey to determine the incidence of diabetes in bombay. J. Indian Med. Assoc. 2017; 41: pp. 448–452.

Corresponding Author

Vikas Yadav*

Research Scholar, Sunrise University, Alwar, Rajasthan