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# A Review on Emergent Therapy for Diabetes Mellitus-Teneligliptin

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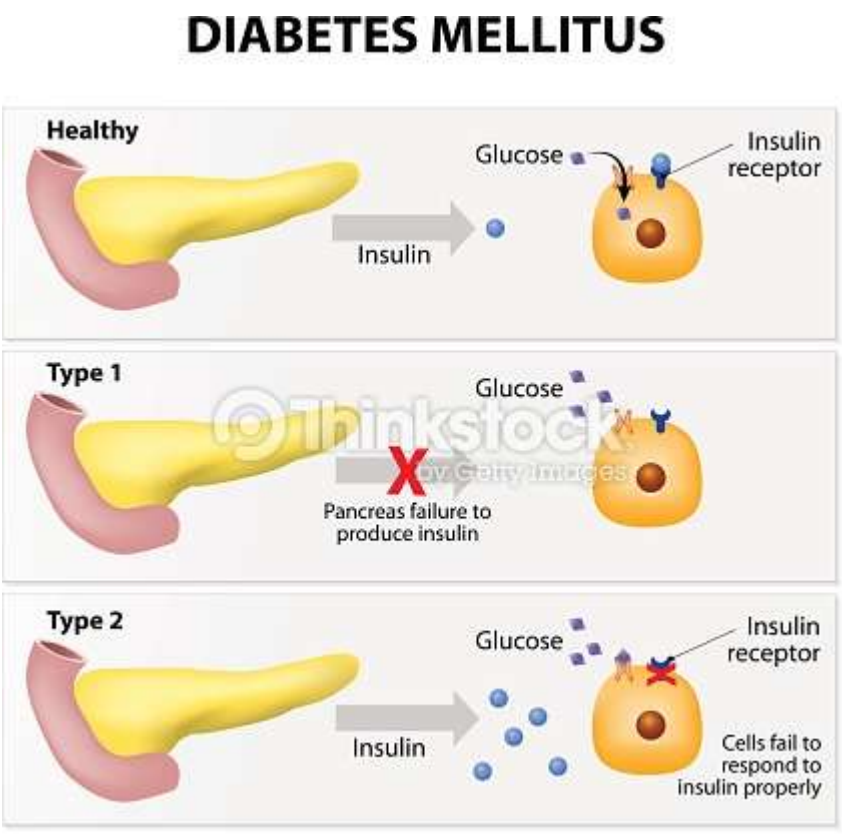
**ABSTRACT**
Chronic metabolic disorder diabetes mellitus is a fast growing global problem with huge social, health and economic consequences. Teneligliptin is one of the most emerging oral hypoglycaemic agent that can be used in the effective treatment of diabetes mellitus. teneligliptin characterized bytwo T-shaped structure formed by five consecutive rings ,is novel Di-peptidyl peptidase 4[ppp iv] inhibitor for the treatment of type 2 diabetes . this article reviews the pharmacology ,therapeutic efficacy and tolerability of teneligliptin in the treatment of adults with type 2 diabetes mellitus .

**KEYWORDS:** Type 2 diabetes mellitus, Di peptidyl peptidase 4-inhibitorTeneligliptin

## I. INTRODUCTION

Diabetes mellitus (DM)is also known as diabetes, is a metabolic disorder which is characterized by high blood sugar levels over a prolonged period of time and is characterized by hyperglycemia, glycosuria, hyperlipidemia, negative nitrogen balance and sometimes ketonaemia. Diabetes is mainly due to either the pancreas not producing enough insulin or the cells in the body not responding properly to the insulin produced by pancrease.



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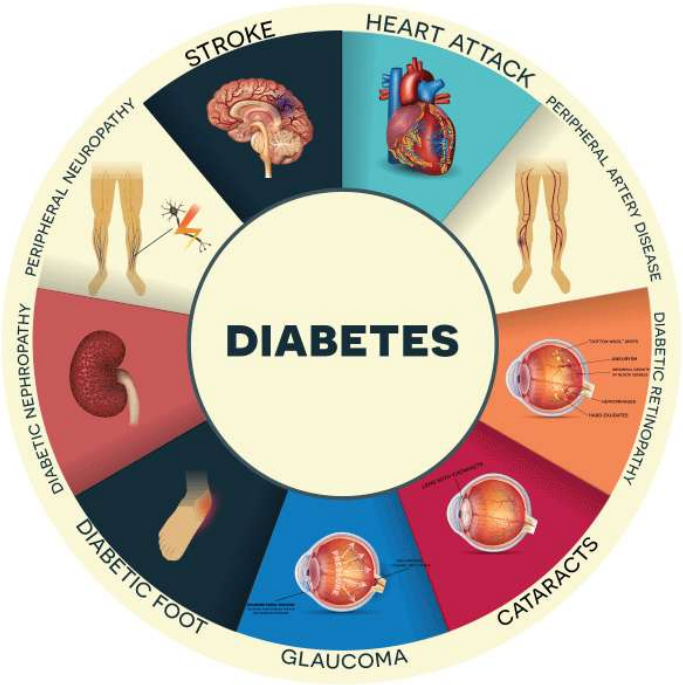
There are three main types of diabetes mellitus:

- Type 1 DM is due to the pancreas's failure to produce enough insulin and is also known as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes". The cause of this is still not known.

- Type 2 DM is due to insulin resistance, is a condition in which cells fail to respond to insulin properly.A lack of insulin may also develop as the disease progresses and is also known "noninsulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes". The main cause is excessive body weight and insufficient exercise.

- Gestational diabetes is the third main form, and associated with pregnant women without a previous history of diabetes develops high blood sugar levels.




Diabetes mellitus is reaching potentially epidemic proportions in India. The level of morbidity and mortality due to diabetes and its potential complications are enormous, and pose significant healthcare burdens on both families and society. Worryingly, diabetes is now being shown to be associated with a spectrum of complications and to be occurring at a relatively younger age within the country. In India, the steady migration of people from rural to urban areas, the economic boom, and corresponding change in life-style are all affecting the level of diabetes. Yet despite the increase in diabetes there remains a paucity of studies investigating the precise status of the disease because of the geographical, socio-economic, and ethnic nature of such a large and diverse country. Given the disease is now highly visible across all sections of society within India, there is now the demand for urgent research and intervention - at regional and national levels - to try to mitigate the potentially catastrophic increase in diabetes that is predicted for the upcoming years.

Diabetes is fast gaining the status of a potential epidemic in India with more than 62 million diabetic individuals currently diagnosed with the disease.In 2000, India (31.7 million) topped the world with the highest number of people with diabetes mellitus followed by China (20.8 million) with the United States (17.7 million) in second and third place respectively. According to, Wild et al.the prevalence of diabetes is predicted to double globally from 171 million in 2000 to 366 million in 2030 with a maximum increase in India. It is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India, while China (42.3 million) and the United States (30.3 million) will also see significant increases in those affected by the disease.India currently faces an uncertain future in relation to the potential burden

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that diabetes may impose upon the country. Many influences affect the prevalence of disease throughout a country, and identification of those factors is necessary to facilitate change when facing health challenges.

The various patterns of diabetes incidence are related to the geographical distribution of diabetes in India. Rough estimates show that the prevalence of diabetes in rural populations is one-quarter that of urban population for India and other Indian sub-continent countries such as Bangladesh, Nepal, Bhutan, and Sri Lanka.Preliminary results from a large community study conducted by the Indian Council of Medical research (ICMR) revealed that a lower proportion of the population is affected in states of Northern India (Chandigarh 0.12 million, Jharkhand 0.96 million) as compared to Maharashtra (9.2 million) and Tamil Nadu (4.8 million). The National Urban Survey conducted across the metropolitan cities of India reported similar trend: 11.7 per cent in Kolkata (Eastern India), 6.1 per cent in Kashmir Valley (Northern India),11.6 per cent in New Delhi (Northern India), and 9.3 per cent in West India (Mumbai) compared with (13.5 per cent in Chennai (South India), 16.6 per cent in Hyderabad (south India), and 12.4 per cent Bangalore (South India).A suggested explanation for this difference is that the north Indians are migrant Asian populations and south Indians are the host populations, however this possible cause-and-effect has not been corroborated through further research. Similar ethnographic disparities have been observed in indigenous and non-indigenous populations in countries colonized by the Great Britain: indigenous people from New Zealand and Australia have been shown to suffer from diabetes and cardio-metabolic disorders more than the non-indigenous people.Further studies are required in India to highlight cultural and ethnic trends and provide a more complete understanding of the differences in diabetes etiology between Indian and other ethnic groups within India.

According to the Diabetes Atlas 2010, India had 51 million diabetics in 2010 compared to 7 million in Pakistan, 6 million in Bangladesh, 27 million in the US and 43 million in China. The epidemic of diabetes is projected to continue unabated. By 2030 this is projected to increase to 87 million in India, 14 million in Pakistan, 10 million in Bangladesh, 36 million in the US and 63 million in China.Thus, India is projected to maintain its dubious distinction of having the highest number of diabetics in the world.However there is a4-fold difference in prevalence within each country with lower rates in the rural areas and higher rates in urban areas.

There are two type of drugs are used to treat diabetes- oral hypoglycemic agents and insulin. Oral hypoglycemic agents consist of these main classes of drugs that stimulate insulin secretion (sulphonylureas and rapid-acting secretagogues), reduce hepatic glucose production (biguanides), delay digestion and absorption of intestinal carbohydrate (alpha-glycosidase inhibitors) or improve insulin action (thiazolidinediones). Many forms of insulin treat diabetes. They're grouped by how fast they start to work and how long their effects last.The types of insulin includerapid-acting, shortacting, intermediateacting, long-acting and pre-mixed.Choosing insulin type and dosage/timing should be done by an experienced medical professional working closely with the diabetic patient.

Among these sulphonylureas, meglitinides and insulin will leads to weight gain and hypoglycemia.GI side effects and lactic acidosis are the main drawback of metformin. Acarbose also cause GI side effects along with inability to achieve normal glucose level in the blood. Weight gain, edema, fluid retention and inability to achieve normal glucose level are the major problems associated with thiazolidinediones.

DDP-4 inhibitors are new class of drugs used in the management of diabetes mellitus. The currently available major DPP-4 inhibitors are – Sitagliptin, Vildagliptin, Saxagliptin, and Linagliptin.DPP-4 inhibitors enhance both insulin and incretin secretion. Teneligliptin is the new member of this family which is a novel and potent addition to gliptin category. This drug is approved by Ministry of Health Labor and Welfare (MHLW) and Japanese Pharmaceutical and Medical Devices Agency (JPMDA) in the year of 2012.Teneligliptin have high potency, longer half-life and it is safer in both hepatic as well as renal patients when compared to other gliptins.

**ROLE OF DPP4 INHIBITORS IN DAIBETICS MELLITUS MANAGEMENT**

Incretin hormones are of two types-glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). These

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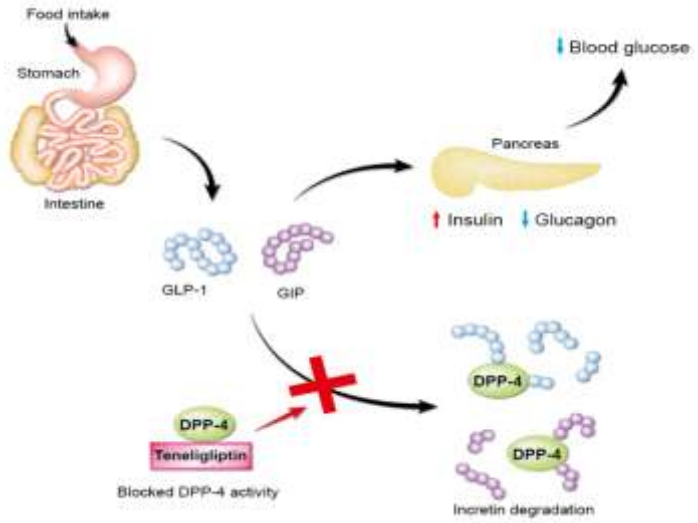
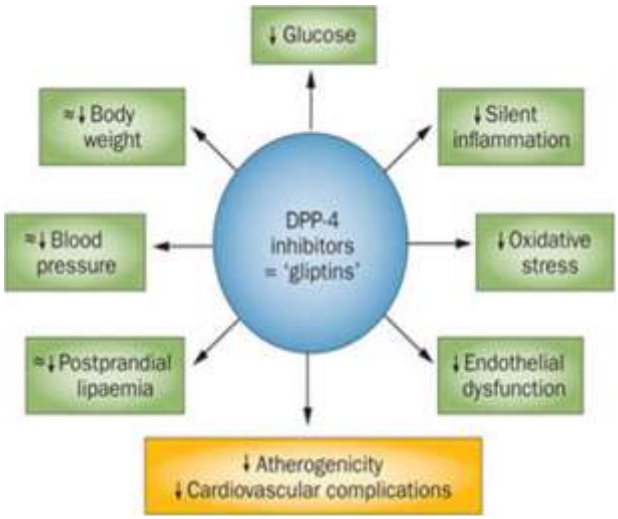
are released from enteroendocrine cells and enhance insulin secretion. Incretion's are rapidly inactivated by the enzyme dipeptidyl peptidase-4 (DPP-4), and thus have a very short half-life ($t_{1/2}$). DPP-4 inhibitors also called as "gliptins" increase the levels of active GLP-1 and GIP by inhibiting DPP-4 enzymatic activity; thus, in diabetic patients, these inhibitors improve hyperglycemia in glucose-dependent manner by increasing serum insulin levels and decreasing serum glucagon levels. Thus, incretin related agents like DPP-4 inhibitors are a new class of antidiabetic agents and that can decrease glucose fluctuations in diabetic patients.




These inhibitors can be administered either as monotherapy or in combination with other drugs. And also, DPP-4 inhibitors have shown favorable results in improving glycemic control with a minimal risk of hypoglycaemia and weight gain.

The currently available DPP-4 inhibitors are:

- Sitagliptin
- Linagliptin
- Vildagliptin
- Saxagliptin



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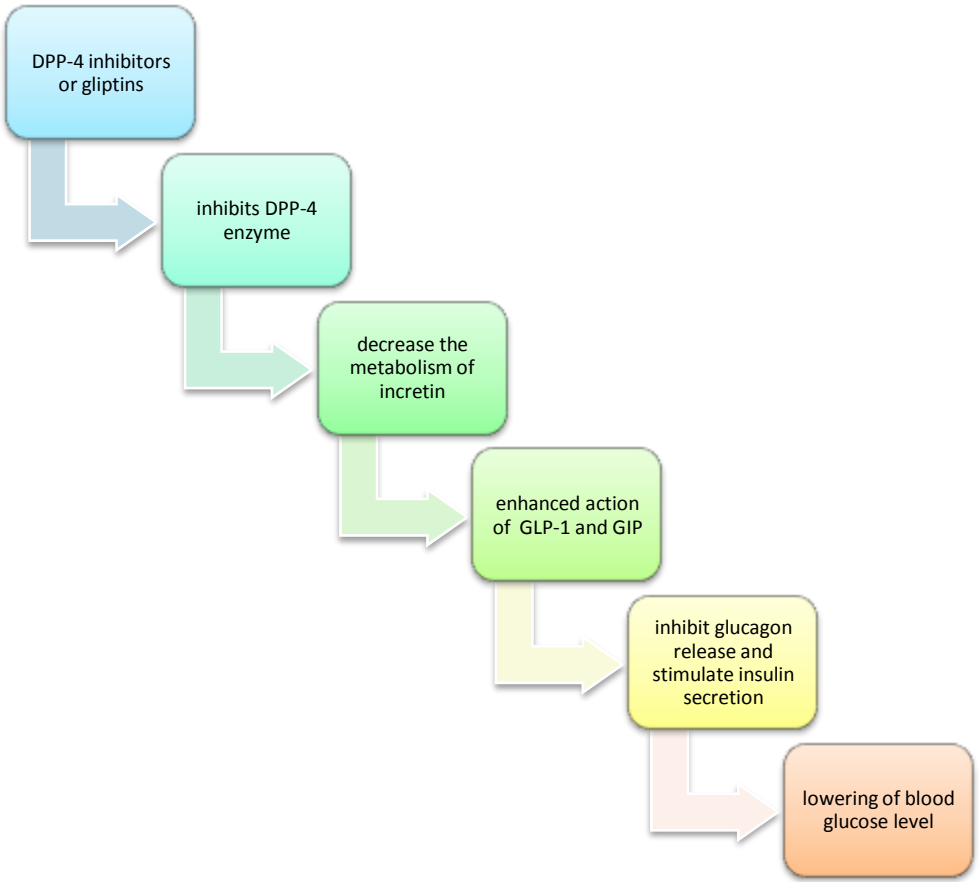
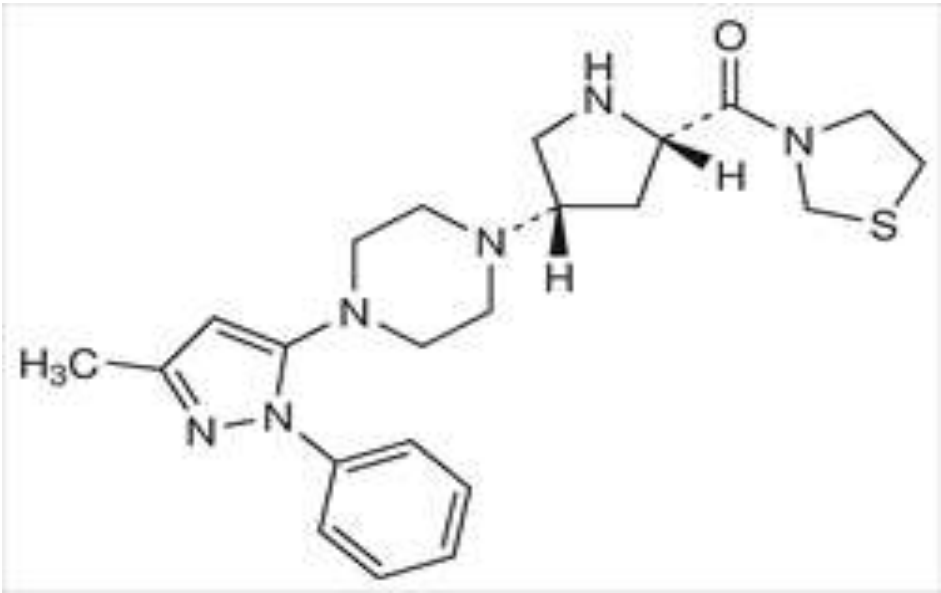



**CHEMISTRY OF TENELIGLIPTINS**



DPP-4 inhibitors are classified into two - peptidomimetic (i.e., sitagliptin, vildagliptin, saxagliptin, and anagliptin) and non-peptidomimetic (i.e., alogliptin and linagliptin). Teneligliptin is a peptidomimetic compound having the molecular formula $C_{22}H_{30}N_6OS$ and molecular

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weight 426.58 g/mol. The melting point is approximately 211 $^0$C.Teneligliptin chemically can be written as, ((2S,4S)-4-(4-(3-methyl-1-phenyl-1H- pyrazol-5-yl)piperazin-1-yl)pyrrolidin-2-yl) (1,3- thiazolidin-3-yl) methanonehemipenta, which exhibits a unique structure and that is characterized by five consecutive rings.Any substitution this basic skeleton will alter the activity.

From an X-ray co-crystal structure of teneligliptin and DPP-4, the key interaction occurs between the phenyl ring on the pyrazole and the S2 extensive subsite of DPP-4 can be confirmed.The S2 extensive subsite ofDPP-4, not only enhances the potency of the drug but also increases its selectivity.DPP-4 enzyme have different binding sites, which are $S_1$,$S_2$,$S_1^I$&$S_2^I$. The interaction of DPP-4 inhibitors with S1 & S2 is considered as the fundamental interaction required for DPP-4 interaction. Additional interaction with S1', S2' & S2 extensive site may further increase the DPP-4 inhibition.

DPP-4 inhibitors are classified according to their interactions with DPP-4 enzymes. DPP-4 inhibitors are classified as Class 1, Class 2 and Class 3 based on their interaction at DPP-4 subsites. Class 1 inhibitors (Vildagliptin&Saxagliptin) bind to S1 & S2 and are considered as fundamental/basic inhibitors. Class 2 (Alogliptin&Linagliptin) bind to additional site of S1, S2 & S1' and may produce more DPP-4 inhibition than Class 1, Linagliptin additionally binds to the S2' subsite. Class 3 inhibitors (Sitagliptin&Teneligliptin) binds to S1, S2 & additional site of S2 extensive and produce more extensive DPP-4 inhibition Teneligliptin consists of a considerably rigid "J-shaped" structure formed by five rings, four of which are directly connected to DPP-4 which provides strongest binding to DPP-4 enzymes as compared to other gliptins. Teneligliptin has 5 fold higher activity than Sitagliptin due to J-shaped anchor-lock domain, strong covalent bonds with DPP-4 & more extensive S2 extensive binding than Sitagliptin. Theantioxidativeproperties of teneligliptin are associated with the sulphur atompresent in the structure.

For Teneligliptin, introduction of the "anchor lock domain", which binds to the S2 extensive subsite, increased the activity by 1500-fold over the corresponding fragment that binds to S1 & S2 only. Although, Teneligliptin&Sitagliptin both fall in Class 3 & both bind to S2 extensive subunit, Teneligliptin has 5-fold higher activity than Sitagliptin for DPP-4 enzymes. Teneligliptin has total contact area of 2.08 nm$^2$ while Sitagliptin has total contact area of 1.90 nm. Teneligliptin may bind more tightly to the S2 extensive subsite as a result of stronger hydro- phobic interactions mediated by the "anchor lock domain". Binding of the anchor lock domain may relate to the residence time of DPP-4 inhibition and the long in vivo duration of action [7]. Inhibition of the DPP-4 substrate by Teneligliptin occurs in a manner that involves formation of a reversible covalent enzyme–inhibitor complex. This complex binds and dissociates from the catalytic site of the DPP-4 substrate very slowly resulting in persistent DPP-4 inhibition even after the drug is inactivated. This means that the catalytic activity remains inhibited even after the free drug has been cleared from the circulation. Binding to the S2 extensive subsite, DPP-4 inhibitors can increase not only their inhibitory activity but also their selectivity towards other DPP enzymes. The J-shape and anchor-lock domain, contributes to the strong inhibitory function and potency of this drug with the lowest IC50 value (0.37 nmol/L). It is extremely selective for DPP-4 as compared to DPP-8 (703 fold) & DPP-9 (1460 fold).

**Pharmacokinetics Of Teneligliptin**

Teneligliptin is an oral hypoglycemic agent which is well absorbed from gastro-intestinal tract and is well distributed throughout the body. Teneligliptin is administered once daily at a dose of 20 mg, which can be increased to 40 mg if the response is insufficient. It can be taken either in empty stomach or after food. CYP3A4, a cytochrome $P_{450}$isozyme and flavincontaining monooxygenases (FMO1 and FMO3) play major roles in the metabolism of teneligliptin.Teneligliptin is priorly metabolized by cytochrome $P_{450}$3A4&flavinmonooxygenases (FMO). . In vitro, teneligliptin exhibits a weak inhibitory effect for CYP2D6, CYP3A4, and FMO; however, it demonstrates no inhibitory effect for CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C8/9, CYP2C19, and CYP2E1.And also the teneligliptin does not induce the expression of either of the CYP3A4 or CYP1A2.

Teneligliptin follows dual mode of excretion, i.e. renal and hepatic. About 34.4% of teneligliptin is excreted through the kidney and the remaining 65.6% teneligliptin is metabolized and eliminated via renal and hepatic excretion.Atleast 90% of the radiolabeled dose of Teneligliptin was excreted within 216 h, with 45.4% excreted in the

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urine and 46.5% excreted in the faeces. Teneligliptin is excreted in the urine as unchanged drug approximately 20%. Teneligliptin has long half-life of 26.9 hours which offers convenient once a day administration. The plasma concentrations of teneligliptin after the administration of teneligliptin at dosages of 10 or 20 mg once daily for 4 weeks revealed a median time to maximum concentration ($C_{max}$) of 1.0 hour in both groups and a mean t1/2 of 20.8 and 18.9 hours, respectively.

In case of renal impaired patients, 20 mg of teneligliptin in patients with renal impairment revealed not shown changes at $C_{max}$ and t1/2. Area under curve shown comparatively mild cretinine clearance shown 80 ml/min., moderate renal impairment cretinine clearance shown 50 ml/min. and severe renal impairment cretinine clearance shown 30 ml/min was approximately 1.25 times, 1.68 times, and 1.49 times higher than that of healthy adult subjects, respectively.

In case of hepatic impaired patients,20 mg of teneligliptin in patients with hepatic impairment revealed that the $C_{max}$ of mild hepatic impairment and moderate hepatic impairment was approximately 1.25 times and 1.38 times that of healthy adult subjects, respectively. Compared to healthy adult subjects, the area under curve of teneligliptin shown with mild and moderate hepatic impairments was approximately 1.46**.**

Teneligliptin is administered once daily at a dose of 20 mg, which can be increased to 40 mg if the response is insufficient. Its elimination half-life in plasma is 24.2 and 20.8 h in 20 and 40 mg doses, respectively, with resulting DPP-4 inhibition through the day. Teneligliptin is eliminated via both the liver and kidney, meaning its use can be considered in patients with hepatic or renal impairment. A Phase I mass balance study using a sin- gle oral 20 mg dose of [14C]-teneligliptin showed that, in contrast to other DPP-4 inhibitors, 20 -- 34% of the absorbed teneligliptin was excreted via the kidneys and 66 -- 80% was eliminated via multiple drug metabolic enzymes. In a study of patients with mild, moderate, severe, and end- stage renal impairment, a single 20 mg dose of teneligliptin had no effect on maximum plasma concentration ($C_{max}$) in those with mild, moderate, and severe renal impairment. The area under the concentration--time curve to infinite time (AUC0--INF) was increased in all groups compared with healthy controls, but the degree of increase was no larger than twofold. Overall, the results suggested that teneligliptin was well tolerated in patients with renal impairment, including those with end-stage renal disease. In patients with hepatic impairment, $C_{max}$ and AUC0--INF were increased in patients with mild and moderate hepatic impairment, but were below FDA-recommended thresholds for dose adjustment. Teneligliptin was generally well tolerated in these patients, but caution in its use is needed, particularly in patients with severe hepatic impairment.

**Pharmacodynamics Of Teneligliptins**

Teneligliptin is a relatively new drug and is used to control glycaemia. A report by Eto et.al proves that, teneligliptin significantly improved 24-hour blood glucose control in patients with type 2 diabetes.

**Effects on blood sugar level:** The postprandial blood glucose-lowering effects of teneligliptin administered before breakfast are sustained throughout the day and the once-daily administration of teneligliptin before breakfast improved blood glucose control, even at dinnertime.

**Effects on insulin and glucagon level**: Administration of teneligliptin improves the insulin secretion and thus increases level of insulin in the blood. But, the postprandial glucagon secretion is suppressed by the administration of teneligliptin.

**Effect on lipid profile**:Teneligliptin reduce the postprandial triglyceride levels as well as free fatty acid levels in the blood by lipolysis of adipose tissue. This helps in the management of blood cholesterol level.

**Natriuretic & Diuretic Effects of Teneligliptin**: GLP-1R & DPP-4 are expressed in the renal proximal tubular brush border, and they regulate $Na^+$ reabsorption. The drug exist in physical complexes with $Na^+$-$H^+$ exchanger in the brush border membranes of renal proximal tubule cells. This complex exists predominantly in the microvilli of renal tubules. DPP-4 inhibition of teneligliptin reduces the activity and induces natriuresis.In addition to this; GLP-1 activation induces diuresis.

**Combination Of Teneligliptins With Other Oral Hypoglycemic Agents**

Teneligliptin is administrated either as monotherapy or in combination with other antidiabetic agents. Even though teneligliptinand metformin improve glycemic control by different methods, they are complementary to each other, and thus combination therapy of these two agents provides effective and potentially additive glycemic control. From the studies using

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combination therapy of teneligliptinand metformin showed favorable results in glycemic control because of favorable pharmacokinetic characteristics and complementary pharmacodynamics effects, which include enhanced incretin effect, suppressed hepatic glucose production, and improved peripheral insulin sensitivity. As total, the combination of this drug into a single tablet often results in a lower cost of treatment and improves patients' compliance.

The α-glucosidase inhibitors (α-GIs) enhanced GLP-1 responses and reduced the total GIP responses. While considering the different but complementary mechanisms of action by which α-GIs and teneligliptin lower glucose levels and increase GLP-1 action, combination therapy using these agents may provide a valuable means of treating diabetes.

The combination of teneligliptin& sulfonylureas, like glimepiride, glibenclamideetc.shows a significant improvement in glycemic control. Due to the hypoglycemic events may occur with the combination of teneligliptinand sulfonylurea, dose of sulfonylurea should be reduced in order to minimize the risk of hypoglycemia.

The combination of teneligliptin and thiazolidinedione is an attractive and rational approach. This combination mainly helps to reduce the postprandial blood sugar level when compared to thiazolidinedione monotherapy.

The effectiveness of insulin injections has been already established and the increasing the insulin dosage to achieve better glycemic control. But it has been associated with an increased risk of hypoglycemia and weight gain. To resolve these problems, combination therapy with insulin injection and oral antidiabetic agents can be considered. Due to the different mechanisms and complementary effects of DPP-4 inhibitors and insulin, combination of these agents would be a rational treatment option for insulin-treated patients. These combination preparations are exclusively used for decreasing post-meal glucagon excursion in insulinopenic patients with type 1 diabetes. Taken together, these reports encourage further study of the use of incretin-related agents in insulin-treated patients with type 2 or type-1 diabetes. Teneligliptin is not currently approved for co-administration with insulin. And thus, a combination therapy of insulin and teneligliptin is quite promising.

**ADVANTAGES OF TENELIGLIPTIN OVER OTHER GLIPTINS**

Teneligliptin is one of the latest amongst the gliptins. Looks promising, and according to the research, it is easy on the kidneys and it gives you a very good control over your blood sugar levels, without falling into hypoglycemia .

Mainly there are four DPP-4 inhibitor that are currently available and these medications are similar in many ways. They are sitagliptin, vildagliptin, saxagliptin and linagliptin. All these DPP-4 inhibitors are oral agents which are taken once a day. They are simple for patients to take, and they have few side effects. These drugs do not cause hypoglycemia and they do not cause weight gain; they have many good attributes.

The first DPP-4 inhibitor on the market was sitagliptin. Sitagliptin is available in 3 dose strengths- 100 mg, 50 mg, and 25 mg. The dose is determined by the estimated glomerular filtration rate (GFR). The dose can be adjusted as the patient's GFR declines.Vildagliptin is the second DPP-4 inhibitor and is available as 50 mg and 100 mg tablets. The next DPP4 inhibitor is saxagliptin and is comes in 2 dose strengths, which are also adjusted based on the estimated GFR. Linagliptin is available in one dose strength and one size fits all in terms of renal function.

Teneligliptin is available as 20 mg tablet which is administrated once daily. Teneligliptin is highly cost effective than other gliptins. And this drug can be used in case of both renal impaired and hepatic impaired patient, since it follows both hepatic as well as renal excretion. Teneligliptin have longer half-life when compared to other gliptin.

**USES OF TENELIGLIPTIN**

a) Teneligliptins are mainly used in the management of diabetes mellitus or type 2 diabetes. This drug helps to improve blood sugar level without the increase in body weight. This drug works based on the amount of sugar in the blood and thus it will not produce hypoglycaemia.
b) The studies shows that teneligliptins can be employed in the management of obesity since it improves metabolic abnormalities and increase energy expenditure.
c) Teneligliptin attenuates hepatic lipogenesis via AMPK activation and thus it can be used in non-alcoholic fatty liver disease.

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d) Treatment with teneligliptin improves left ventricular diastolic function as well as endothelial function.
e) The gliptins also shows an independent anti-atherosclerotic effect.

**TOLERABILITY OF TENELIGLIPTIN**

As mentioned earlier, teneligliptin was well tolerated in various clinical trials. Data from 1,183 patients reported that 118 (10%) patients experienced AEs, and the most common AEs were hypoglycemia (3%) and constipation (0.9%). Hypoglycemia can occur when other antidiabetic drugs are co-administered.Intestinal obstruction may occur with teneligliptin and must be administered cautiously in patients with a history of intestinal obstruction or surgery. This may be because of reduced gastrointestinal motility due to enhanced activity of incretins. Cases of intestinal obstruction were also reported with sitagliptin, vildagliptin, exenatide, and liraglutide.

QT/QTc evaluation was studied for teneligliptin; this may be as a part of regular drug development program. Reported evidence suggests that no QT prolongations were noted with teneligliptin 40 mg daily dose. Nevertheless, mild and transient QTc prolongation can be seen at a supra-clinical dose of 160 mg/day given for a prolonged period. Therefore, caution is exercised if the drug needs to be used for a longer period of time in patients who are prone or have comorbid arrhythmia/ischemic heart disease and along with medications known for QT prolongation.

Cardio protective effects of teneligliptin were studied in a small group (n=29) of patients with T2DM with a high risk of chronic heart failure. Treatment with teneligliptin for 3 months reported improvements in left ventricular systolic and diastolic function, endothelial function, and an increase in circulating adiponectin levels. This evidence supports cardio protective effects of teneligliptin.

**Adverse Drug Reactions Of Teneligliptin**

Teneligliptin cause some unwanted effects too. The commonly occurring side effects are;

- Hypoglycemia (Low blood sugar level) in combination with insulin or sulphonylurea
- Constipation
- Nausea
- Loss of appetite
- Diarrhea
- Abdominal pain
- Abdominal discomfort

**CONTRAINDICATIONS OF TENELILIPTIN**

Here is a set of conditions when Teneligliptin must not be used or consumed

- Hypersensitivity
- If a person is pregnant or is breastfeeding
- If a person is suffering from serious allergies
- Excessive sensitivity to Teneligliptin dosage is a contraindication.

Also, Teneligliptinhydrobromide hydrate ought not to be utilized on the off chance that you have the accompanying conditions:

- Excessive touchiness
- Hypotension
- Liver issue

## II. CONCLUSION

- Teneligliptin is one of the most emerging oral hypoglycemic agent that can be used in the effective treatment of diabetes mellitus type 2.
- This gliptin have an advantage over other gliptins is that, it have both renal as well as hepatic excretion and thus can be employed in the case of renal impaired as well as hepatic impaired patients.
- As its mechanism is depends on the incretin level in the blood, it doesn't cause hypoglycemia if it taken alone. But in combination with other oral hypoglycemic agents it may cause hypoglycemia eventhough the combination improves the therapeutic action.
- Teneligliptin possess cardio protective acion and can be used safely in patients with T2DM with a high risk of chronic heart failure.
- It shows only few side effects as compared to other gliptins and oral hypoglycemic agents.

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