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Adipsin and Leptin as Therapeutic Targets by Dipeptidyl Peptidase-4 Inhibitors in Type 2 Diabetes Mellitus: Review Article

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Abstract

Type 2 diabetes mellitus (T2DM), one of the most common metabolic diseases, is caused by a mix of insulin-sensitive tissues' inadequate response to insulin and pancreatic β-cells' impaired insulin secretion. Adipsin is involved in preserving the homeostasis of adipose tissues and enhancing insulin secretion in response to glucose. Adipose tissue secretes adipokines, which are cell-signaling proteins that have been connected to various pathologies as well as a low-grade state of inflammation. Although the regulation of energy homeostasis is a well-established function of the obesity hormone leptin, there is increasing evidence that leptin is also essential for glycaemic control. The hormone leptin is a 167-residue peptide produced by the Lep gene. Adipose tissue is the main source of its secretion. Leptin levels in the blood are undetectable when the Lep gene is functionally inactivated. To increase the precision of disease prediction, offer fresh perspectives on pathophysiology, and aid in the prevention of type 2 diabetes in the future, a validated novel biomarker is necessary. Targeting endogenous proteins has led to the development of several more advanced diagnostic techniques, with adipsin being one of the most promising targets. Therefore, the aim of this review study is to assess the effects of DPP-4 inhibitors on adipsin and leptin in T2DM. The function of DPP-4 (DPP4) inhibitors has changed in recent years. DPP-4 inhibitors do not result in hypoglycemia or weight gain, have a good safety profile, an anti-inflammatory profile, and do not need dose escalation. It can also be used with older diabetic patients and patients with certain forms of chronic kidney disease. Adipsin has the potential to become an early novel biomarker in patients with T2DM.

Keywords: Adipsin, Dipeptidyl Peptidase-4, Leptin, Type 2 Diabetes Mellitus.

Introduction

One of the most prevalent metabolic diseases in the world is type 2 diabetes mellitus (T2DM), and its development is primarily brought on by a combination of two main factors: The tissues' incapacity to respond to insulin and the inefficiency of pancreatic β-cells in secreting it [(1)]. For insulin release and action to precisely meet the metabolic demand, the molecular mechanisms underlying insulin synthesis, release, and tissue response must be tightly regulated [(2)]. Therefore, malfunctions in any of the underlying processes could lead to the development of type 2 diabetes and a metabolic imbalance [(3)]. Though both processes occur early in the pathogenesis and contribute to the development of the disease, β-cell dysfunction is usually more severe than insulin resistance (IR). Polonsky *et al* [(4)], indicated that more complex interactions between the environment and various molecular pathways related to cell biology may be the cause of the dysfunction of β-cells in type 2 diabetes.

Hyperglycemia and hyperlipidemia are frequently present in an over nutritional state, resembling obesity and favoring IR and chronic inflammation. IR is used to characterize a decrease in the metabolic response of insulin-responsive cells to insulin or, at the systemic level, a decreased or weakened response of blood glucose levels to insulin that is circulating [(5)]. Both hereditary and environmental factors influence the development of type 2 diabetes, and while their relative contributions vary from case to case, the disease is believed to begin when the combined effects of both factors exceed an established threshold. Combinations of lifestyle factors like obesity, overeating, and inactivity with genetic factors that affect insulin secretion and insulin resistance lead to type 2 diabetes. Based on twin family studies, type 2 diabetic complications have a 40% heritability rate [(6)]. With a body-mass index [BMI] of ≥30 kg/m2, obesity is the greatest risk factor for type 2 diabetes and is linked to metabolic disorders that cause IR [(7)].

The prevalence of obesity has exploded globally and is getting out of control. As obesity rates rise, obesity - related conditions like type 2

diabetes are also becoming more prevalent. It becomes especially important to understand the pathophysiological mechanisms linking obesity to type 2 diabetes in order to prevent and treat obesity-related diabetes (8). Obesity raises the risk of type 2 diabetes, particularly when linked to the pathologic expansion of visceral white adipose tissue (vWAT). Over 75–90% of patients with type 2 diabetes are overweight or obese, depending on their race. The term "diabesity" supports the strong correlation between obesity and type 2 diabetes" [9]. Research have shown that adipose tissue secretes a variety of bioactive substances known as adipokines, and that it is an endocrine organ capable of storing fat as well [10, 11]. Adipose tissue was first discovered in 1987 as the primary location for the metabolism of sex steroids [12] and the endocrine factor adipsin [12] which is significantly down-regulated in obese rats. Adipose tissue was firmly established as an endocrine organ in 1994 with the detection and characterization of leptin [13]. Adipokines can be classified as either "anti-inflammatory adipokines" or "proinflammatory adipokines"; the former have a protective and advantageous function, while the later encourage inflammation and insulin resistance [14]. Pathogenic alterations result from an imbalance between pro- and anti-inflammatory adipokines. Patients with obesity and type 2 diabetes, for instance, usually have changed adipokine profiles, which increases metabolic risk and affects insulin sensitivity [9]. White and brown adipocytes are the two primary subtypes of adipocytes. White adipocytes, also known as white adipose tissue, are the most common type of adipocytes in the human body (WAT) ***Figure 1***. Adipose tissue produces several cytokines such as omentin, adipsin, leptin, adiponectin, retinol-binding protein 4 (RBP4), monocyte chemoattractant protein-1 (MCP-1), plasminogen activator inhibitor-1 (PAI-1), resistin, and adiponectin [15-18]. In this review, will focus on two types of adipokines, adipsin and leptin, the effects of DPP-4 inhibitor on these two parameters in type 2 diabetic patients.

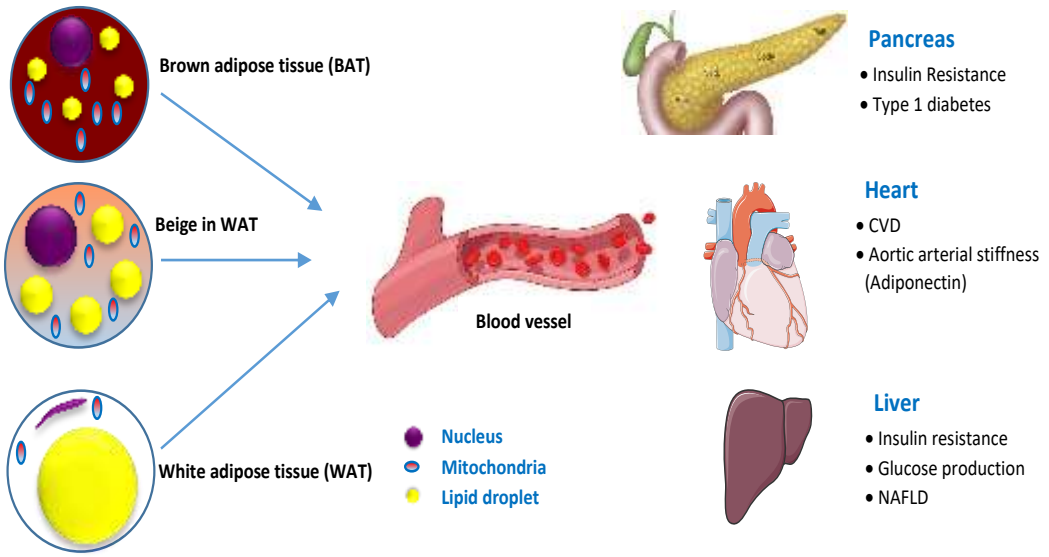

Figure 1. Role of adipose tissue in the pathogenesis of type 2 diabetes mellitus [9].

Adipsin

One of the primary proteins that adipocytes express is the adipokine adipsin [19]. It was first identified as complement factor D in 1987 and is an essential component of the complement system [20]. This 28-kilo Dalton protein belongs to the serine protease family and is present in cell lines of mouse embryonic fibroblasts (3T3) [20]. In response to glucose, it increases insulin secretion and protects the homeostasis of adipose tissue since it incorporates into an enzymatic cascade during this process, which releases the anaphylatoxins C3a and C5a as well as the C5–C9 membrane attack complex [21]. The majority of adipsin is produced by adipose tissue (AT) cells and there are correlations between circulating adipsin and measures of obesity and glucose metabolism. The release of complement factor C3a, which is stimulated by adipsin, has been demonstrated to increase the production of insulin in pancreatic ß-cells. Individuals suffering from ß-cell failure and type 2 diabetes (T2D) have lower serum concentrations of adipsin [22]. Moreover, adipsin promotes triglyceride synthesis and glucose absorption in adipocytes [21]. Elevated blood glucose levels resulting from pancreatic β-cell dysfunction and/or insulin resistance are hallmarks of type 2 diabetes mellitus [23]. It has been reported that

adipsin preserves β-cell function, which is critical for increasing insulin secretion [24]. A study by Gómez-Banoy *et al.* 2019, [25] found that restoring adipsin in diabetic mice preserved β-cell mass by enhancing β-cell survival and protecting β-cell transcriptional identity in addition to improving hyperglycemia. Furthermore, a higher adipsin level is linked to a decreased risk of diabetes in individuals. Individuals with T2DM who have recently been diagnosed with diabetes exhibit lower adipsin levels; and there was negative a correlation between homeostatic model assessment for insulin resistance (HOMA-IR) and adipsin. It was determined that the expression of inflammatory cytokines, such as IL-17, in T2DM may be the cause of the negative association [22]. Adipsin's plasma concentrations were discovered to be lower in individuals with type 2 diabetes had impaired glucose tolerance. This condition is linked to glucose metabolism and the pancreatic β-cells' first-phase insulin secretion. Zhou *et al.* 2018, [26], showed that there is a positive correlation between serum adipsin and homeostatic model assessment for insulin resistance-beta (HOMA-β) as shown in Figure ***2***.

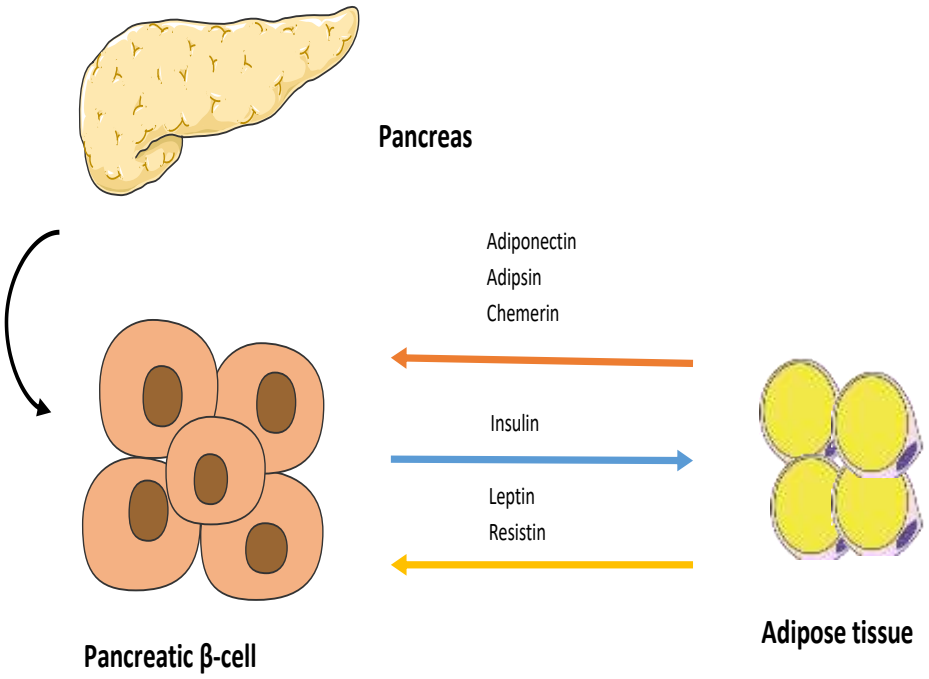

Figure 2. Role of adipsin in type 2 diabetes mellitus [27].

Leptin

Adipose tissue secretes leptin, a 167-residue peptide hormone that is the protein product of the Lep gene. When the Lep gene is functionally inactivated, the amount of leptin in the blood is undetectable [28]. Leptin travels via various pathways to reach its targets in the bloodstream, which includes the hypothalamus after it is released by adipose tissue [29]. It has been documented that leptin enters the brain by saturable transport across the blood-brain barrier and direct transport through circumventricular organs [30] and intake into the choroid plexus and brain parenchyma, though the precise mechanisms are still not entirely clear. When leptin binds to its long- form receptor (LepRb), it triggers a well-studied downstream signaling pathway that controls both energy expenditure and food intake [31]. Leptin regulates energy and glucose homeostasis by targeting the central melanocortin system [32]. In contrast, insulin is kept in granules and released instantly when a suitable stimulus is received. The rate of transcription and translation of the lep gene determines how quickly leptin is released [33].

The adipocyte does not have a traditional "triggered" exocytic pathway; instead, it reacts in an inducible manner, releasing factors after a delay of 15 to 30 minutes at the endoplasmic reticulum level [34]. Conversely, leptin levels in the blood are relatively stable over the short term (from meal to meal) and respond to different metabolic stimuli in hours rather than minutes or seconds (assuming normal

physiological conditions) [35]. In the same way, the daily regulation of food intake by leptin is still unclear. Potent inducers of leptin secretion are elevated levels of insulin and glucocorticoids. Due to its role in adipose tissue inflammation, the hormone leptin derived from adipocytes is also referred to as an adipocytokine [36]. It carries out many functions, the most essential of which is preserving energy balance. This is achieved by increasing energy expenditure and decreasing appetite or energy consumption. It is therefore appropriately called the satiety hormone [37]. It has been found that leptin regulates peripheral tissue sensitivity and insulin secretion. Leptin is a potential biomarker for assessing levels of insulin resistance (IR) because hyperleptinemia, a reflection of leptin resistance, plays a major role in the production of IR in T2DM patients [38]. Moreover, it has been suggested that leptin levels predict the onset of metabolic syndrome and are unrelated to obesity [39]. Activating the sympathetic nervous system in the hypothalamus raises blood pressure in addition to its effects on appetite and obesity [39]. The elevated renal sympathetic tone observed in individuals who are overweight is thought to be caused by elevated levels of circulating leptin [40]. Hypertension, angiogenesis, and atherosclerosis are caused by leptin [41], and thus leptin is useful as a biomarker for early detection and diagnosis of metabolic syndrome [42]. While the exact cause of metabolic syndrome and its constituent parts remains unknown, two known contributing factors are central obesity and insulin resistance [43]. Type 2 diabetes and obesity are characterized by leptin resistance, and there is a positive relationship between leptin levels and body fat mass [44].

Dipeptidyl peptidase 4 (DPP-4) and DPP-4 inhibitors

Dipeptidyl peptidase 4 is a type II transmembrane glycoprotein that is widely expressed in the kidney, liver, pancreas, immune system, and fat cells. It circulates in a soluble form. Also, it is a serine protease and can cleave and render inactive incretin hormones, such as glucagon-like peptide 1 (GLP-1), and glucose-dependent insulinotropic polypeptide (GIP) [45]. Furthermore, it has been demonstrated that DPP-4 directly promotes inflammation in smooth muscle cells, macrophages, and lymphocytes. Although its exact roles in the metabolism of glucose and insulin are still unknown, dipeptidyl peptidase 4 is an important player in these processes [46].

However, DPP-4 is an enzyme that breaks down glucose-dependent insulinotropic polypeptide (GIP) and GLP1, two incretin hormones, which act to regulate postprandially glycaemic levels by promoting pancreatic beta-cell insulin synthesis and secretion and decreasing alfa-cell glucagon secretion [47]. Moreover, GIP/GLP-1 promotes satiety and reduces the need for extra food by delaying stomach emptying and central nervous system modulation. Glycaemic control is enhanced by DPP-4 inhibitor by prolonging the duration of circulating incretin hormone levels postprandially and demonstrated the maintenance of pancreatic beta-cell function by enhancing cell survival, proliferation, differentiation, and stimulation [48]. First published in 1995, the hypothesis that a novel endocrine-based approach involving the inhibition of the enzyme dipeptidyl peptidase-4 [49]. The mechanism of action as reported by Deacon *et al.* 1995 [50] included the selective pharmacological inhibition of the physiological enzymatic degradation of glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide 1 (GLP1) causing the biologically active forms of both hormones to accumulate.

Currently, T2DM is commonly treated with DPP-4 inhibitors [51]. DPP-4 inhibition was investigated as a possible target for the treatment of type 2 diabetes mellitus because of its ability to prevent GLP-1 from being inactivated (T2DM) [52]. Type 2 diabetes is associated with a persistent, low-grade inflammation brought on by an excess of visceral fat. Peripheral insulin sensitivity and homeostatic glucose regulation are dysregulated as a result of this inflammatory state. The onset and severity of diabetes, obesity, chronic diabetic kidney disease [53], cardiovascular disorders, and atherosclerosis are correlated with dipeptidyl peptidase 4 activity [54].

There is no hypoglycemic effect of dipeptidyl peptidase-4 inhibitor (DPP-4i) by itself. However, their main mechanism of action against hyperglycemia is to modify the amounts of endogenous substrates. Following the inhibition of DPP-4's catalytic activity, these substrates' concentrations alter. The therapeutic effect of DPP-4 inhibitor has been attributed, to this point, to GLP1 [55]. It has been demonstrated that GLP1 is a physiological DPP-4 substrate. Endogenous levels of biologically active, intact peptides rise in vivo upon DPP-4 inhibition and are linked to better glucose homeostasis [56, 57]. Glucose-dependent insulin polypeptide (GIP), commonly referred to as incretin, is another physiological substrate of DPP-4; when DPP-4 activity is inhibited, GIP levels rise [58]. GIP appears to act differently on glucagon secretion, but it increases insulin secretion in pancreatic beta cells in a glucose-dependent manner, identical to GLP-1 [59].

First published in 1995, the theory that type 2 diabetes could be treated with a novel endocrine-based strategy involving the inhibition of the enzyme dipeptidyl peptidase-4 (DPP-4) [50]. Deacon *et al.* 1995 [50], reported that the accumulation of the biologically active forms of both hormones was caused by specific pharmacological inhibition of the physiological, enzymatic breakdown of glucagon-like peptide 1 (GLP1) and glucose-dependent

insulinotropic polypeptide (GIP). The primary goal of the DPP-4 inhibitor concept was to develop a medication with anti-hyperglycemic efficacy and the major benefit of being relatively free from the risk of hypoglycemia due to the incretin hormones' glucose-dependent insulinotropic effect [60]. The majority of adipsin is produced by AT cells. Recent research has revealed correlations between circulating adipsin and measures of glucose metabolism and obesity [61-63]. It has been demonstrated that adipsin stimulates the release of complement factor C3a, which causes pancreatic ß-cells to produce more insulin. Patients with ß-cell failure and type 2 diabetes (T2D) have lower serum concentrations of adipsin [64]. Moreover, adipsin promotes triglyceride synthesis and glucose absorption in adipocytes.

DPP-4 inhibitors, adipsin and leptin

Insulin resistance and the onset of type 2 diabetes are linked to elevated leptin levels. High levels of leptin have also been linked to microvascular complications, cardiac autonomic dysfunction, and a higher chance of cardiovascular events in those who have type 2 diabetes (T2DM) [65]. In this case, leptin levels were linked to carotid atherosclerosis in T2DM patients, as determined by carotid intima-media thickness (CIMT), as well as the existence and severity of silent MI [66]. Additionally, T2DM patients with elevated leptin levels have higher rates of obesity, hypertension, MetS, and endothelial dysfunction [67]. Notably, it was shown that leptin levels in T2DM patients and healthy individuals decreased after an oral fat tolerance meal. According to Petersen *et al.* 2016 [68], in animal diabetes models, leptin replacement therapy has been demonstrated to decrease liver gluconeogenesis, lipolysis, and fasting hyperglycemia; in lipodystrophy patients, it has also been shown to improve liver and muscle insulin resistance. Data on dipeptidyl peptidase-4 (DPP-4) inhibitors are limited to sitagliptin, which has been demonstrated to lower serum leptin levels in studies involving both humans and animals [69, 70]. Additionally, in the liver of mice, metformin can enhance the expression of leptin receptors and lower leptin concentrations in T2DM patients [71]. All things considered, hyperleptinemia has been linked to insulin resistance, type 2 diabetes, and complications from diabetic vascular disease. Several antidiabetic medications, such as pioglitazone, metformin, sitagliptin, empagliflozin and liraglutide, have been shown to decrease leptin levels; however, it is unclear what clinical consequences, if any, may result from this medication effect [72].

The previously mentioned links between leptin and both cardiometabolic and non-cardiac vascular diseases may be partially accounted for by the pathophysiological mechanisms that leptin influences and predisposes to these conditions, such as insulin resistance, oxidative stress, endothelial dysfunction, vascular inflammation, and cardiac remodeling.

Overall, there is a correlation between leptin levels and the existence, severity, and extent of CHD. As demonstrated in, high leptin levels were also linked to the occurrence, severity, and unfavorable clinical outcomes of both ischemic and hemorrhagic strokes.

Evidence exists to associate leptin levels with CHD, PAD, carotid artery disease, stroke, CKD, and T2DM, as well as their presence, severity, and/or prognosis. Angiogenesis, arteriosclerosis, thrombosis, inflammation, and atherosclerosis are all facilitated by leptin. Their levels may be affected by a number of medications, including antidiabetic and statns, as well as lifestyle changes as shown in

. To determine whether leptin is an acceptable therapeutic target, more investigation is required. In T2DM rats, treatment with metformin, sitagliptin, and liraglutide as a monotherapy resulted in improved blood glucose levels. The mechanism by which these anti-diabetic medications increase insulin sensitivity may involve lipid reduction, adipocytokine serum level correction, and a decrease in retinol-binding protein 4 (RBP-4) serum concentration. Additionally, T2DM patients may benefit from the body mass decreasing effect in the liraglutide-treated group [73]. It's interesting to note that at 20 and 30 mg/kg, sitagliptin considerably improved fatty liver and metabolic syndrome. It enhanced the release of adipokines and reduced inflammation in white adipose tissue. Additionally, it stimulated the phosphorylation of ACC and AMPK in the liver, which enhanced fatty acid metabolism. Stabilization of plasma GLP-1 levels also helped to improve metabolic complications [16, 74].

Additionally, vildagliptin (DPP-4 inhibitor) improves leptin, cholesterol, triglycerides, and other serum parameters in high-fat diet (HFD) mice in addition to glycemic control. Vildagliptin also inhibits high fat and fetuin-A mediated DPP-4 expression, intracellular lipid accumulation and improves insulin secretory defects in pancreatic beta cells. Vildagliptin is known to have an effect on glycemic control by increasing the half-life of GLP-1 and GIP, which are known to enhance pancreatic β-cell insulin secretion and reduce blood glucose, HbA1c, glucagon secretion, and liver glucose production [75]. The improvement in glycemic control brought about by DPP-4 inhibition can account for some of the other effects, such as the decrease in triglycerides, cholesterol, and leptin [76]. DPP-4 inhibitors have been shown in several studies to lower blood triglycerides and cholesterol in both humans and rodents [77-79]. In non-alcoholic fatty liver disease (NAFLD) patients with T2DM, various types of DPP-4 inhibitors, including sitagliptin,

vildagliptin, and alogliptin, have been studied, the beneficial effects of these DPP-4 inhibitors on NAFLD remain controversial despite conflicting results [80, 81]. The pharmacokinetic profile of linagliptin, a different kind of DPP-4 inhibitors, differs from that of the three DPP-4 inhibitors eliminated by the kidneys. It has a high exposure in hepatic tissue and is primarily eliminated unaltered through bile [82]. In animal models of NAFLD and diabetes, linagliptin was shown to have anti-inflammatory and anti-steatotic properties [83, 84]. Unfortunately, there isn't any data on human subjects at this time. Moreover, the improvement in insulin resistance may also be due to modulation of serum concentration of adipocytokines (i.e., increased plasma adiponectin and decreased plasma leptin), which may also be a potential mechanism for the beneficial cardiovascular effects of metformin and sitagliptin [85].

Table 1. Comparison of effects of oral hypoglycemic drugs on leptin.

Study (year)	Oral hypoglycemic agent	Type of study	Therapy regimen	Therapy period (weeks)	Results
Wei *et al* 2021 [86]	DPP-4 inhibitors	Randomized controlled trials	Not specified	Not specified	Did not modify leptin and have no benefit compared to traditional antidiabetic drugs
Komorizono *et al* 2021 [87]	Linagliptin Metformin	Clinical, patients with T2DM and non-alcoholic fatty liver disease	Linagliptin 5 mg/day added to metformin 750 mg/ day. Metformin up to 1500 mg 2-3 times/day	52	There is no enhanced effectiveness of linagliptin on T2DM with NAFLD patients
Awal *et al* 2020 [^^]	Linagliptin Placebo	Clinical, patients with T2DM and chronic kidney disease	Metformin 1-2 g/day and/or Insulin with 5mg/day Linagliptin or placebo	12	Linagliptin improves CD34+ (biomarker of endothelial function), so it may improve renal function compared to a matched placebo
Schiapaccassa *et al* 2019 [89]	Vildagliptin Metformin	Clinical, obese type 2 diabetic women	Metformin 850mg two times/day Vildagliptin 50mg two times/day	4	Vildagliptin decreased C-peptide and LDL, and increased peptide-1 and ADP. Metformin decreased TC, LDL-c, HDL-c, and DPP-4, with increased TNF-α (unexpected).
Takeshita *et al* 2019 [90]	Alogliptin Metfomin	Clinical, type 2 diabetic patients	Alogliptin 25 mg/ day Metformin 1,000 mg, two times/ day	12	Alogliptin increased body weight. Metformin decreased body weight.
Takihata *et al* 2019 [91]	Sitagliptin Luseogliflozin	Clinical, type 2 diabetic patients	Sitagliptin 50 mg for 12 weeks Luseogliflozin for 12 weeks	24	Luseogliflozin was more effective in decreasing HbA1c levels than sitagliptin.
Dore *et al* 2018 [92]	Saxagliptin Placebo	Clinical, type 2 diabetic patients with no known CVD.	Metformin 1-2 g/day with Saxagliptin 5mg/day or placebo	12	Saxagliptin improved the function of CD34+ cells, renal function metabolic parameters, and arterial stiffness compared to placebo
Matsushima *et al* 2016 [93]	Sitagliptin Voglibose	Clinical, type 2 diabetic patients	Sitagliptin 50 mg/day Voglibose 0.6 mg three times/day	12	Sitagliptin exhibits more hypoglycemic effects compared to voglibose
Kato *et al* 2015 [94]	Sitagliptin Glimepiride	Clinical, type 2 diabetic patients with a fatty liver or BMI≥25kg/ m^2	Sitagliptin 50mg/day Glimepiride 1mg/day	24	Both drugs have the same glycemic effect while sitagliptin decreased IHL and total body fat.

Continued table1.

Takeshita *et al* 2015 [95]	Vildagliptin Liraglutide	Clinical, type 2 diabetic patients	Vildagliptin 50mg two times/day Liraglutide 0.9mg /day	12	Liraglutide has a greater effect on decreasing HbA1c and BMI than vildagliptin. Vildagliptin decreased C-peptide and increased ADP.
Takeshita *et al* 2015 [96]	Sitagliptin Mitiglinide	Clinical, type 2 diabetic patients treated with rapid-acting insulin analog	Sitagliptin 50mg/day	16	Both drugs increased HbA1c and decreased C-peptide. Mitiglinide increased FBS while sitagliptin has no effect on it. Sitagliptin decreased HDL-C and ADP while increasing TG.

Conclusion

Recent research has revealed correlations between the levels of circulating adipsin and indicators of glucose metabolism and obesity. It has the potential to become an early novel biomarker in patients with T2DM. Although there are no studies available for the effect of DPP-4 inhibitors on adipsin level in type 2 diabetic patients. However, there may be a positive or synergistic or additional effect since both of them increase insulin secretion which aids in treatment of T2DM. In regards to leptin, there is evidence in type 2 diabetes that elevated leptin levels are associated with an increased risk of cardiovascular disease, microvascular complications, and cardiac autonomic dysfunction. Fortunately, one of Dpp-4's effects (sitagliptin, vildagliptin and linagliptin) is a reduction in leptin levels, which helps people with type 2 diabetes. Interestingly, no study available on the effect of (saxagliptin and alogliptin) on leptin level.

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Conflicts of Interest

No conflict of interest was declared by the authors.

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Ethics Statements

Review article. Ethical approval not applicable.

Author Contribution

Study conception and design: M. Sura, F. Zainab.; data collection: M. Sura; analysis and interpretation of results: M. Sura, M. Jehan.; draft manuscript preparation: M. Sura, F. Zainab. All authors reviewed the results and approved the final version of the manuscript.

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الأديبسين والليبتين كأهداف علاجية بواسطة مثبطات DPP-4 في داء السكري من النوع الثاني: مقال مراجعة

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الخلاصة

داء السكري من النوع الثاني (T2DM)، أحد أكثر الأمراض الاستقلابية شيوعًا، عن مزيج من الاستجابة غير الكافية للأنسجة الحساسة للأنسولين وضعف إفراز الأنسولين في خلايا بيتا البنكرياسية. ويشارك الأديبسين في الحفاظ على توازن الأنسجة الدهنية وتعزيز إفراز الأنسولين استجابة للجلوكوز. تفرز الأنسجة الدهنية الأديبوكينات، وهي بروتينات إشارات للخلايا تم ربطها بأمراض مختلفة بالإضافة إلى حالة التهاب منخفضة الدرجة. على الرغم من أن تنظيم توازن الطاقة هو وظيفة راسخة لهرمون السمنة اللبتين، إلا أن هناك أدلة متزايدة على أن الليبتين ضروري أيضًا للتحكم في نسبة السكر في الدم. هرمون اللبتين هو عبارة عن ١٦٧ بقايا من الببتيد ينتجها جين ليب. الأنسجة الدهنية هي المصدر الرئيسي لإفرازها. لا يمكن اكتشاف مستويات اللبتين في الدم عندما يتم تعطيل جين الليبتين وظيفيًا. لزيادة دقة التنبؤ بالمرض، وتقديم وجهات نظر جديدة حول الفيزيولوجيا المرضية، والمساعدة في الوقاية من مرض السكري من النوع ٢ في المستقبل، من الضروري وجود علامة حيوية جديدة تم التحقق من صحتها. أدى استهداف البروتينات الداخلية إلى تطوير العديد من تقنيات التشخيص الأكثر تقدمًا، حيث يعد الأديبسين أحد أكثر الأهداف الواعدة. ولذلك، فإن الهدف من هذه الدراسة المراجعة هو تقييم آثار مثبطات DPP-4 على الأديبسين والليبتين في T2DM. لقد تغيرت وظيفة مثبطات DPP-4 (DPP4) في السنوات الأخيرة. لا تؤدي مثبطات DPP-4 إلى نقص السكر في الدم أو زيادة الوزن، ولديها ملف تعريف أمان جيد، وملف تعريف مضاد للالتهابات، ولا تحتاج إلى تصعيد الجرعة. ويمكن استخدامه أيضًا مع مرضى السكري الأكبر سنًا والمرضى الذين يعانون من أشكال معينة من أمراض الكلى المزمنة. لدى Adipsin القدرة على أن يصبح علامة حيوية جديدة في المرضى الذين يعانون T2DM.

الكلمات المفتاحية: DPP-4 ، أديبسين، ليبتين، داء السكري من النوع ٢.