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DUAL ROLE OF HIGH-FAT DIET IN THE DEVELOPMENT OF DIABETES: REVIEW

Sowmya Shree S[1*], Vindya N S[2], Dharmendra Kumar Sharma[3], Ahmed Jafar Talukdar[4], Durga Priya[5], Md Fayazuddin[6], Ramakanth Malli[7], Yojana khatiwara[8] , Tasmiya khanum[9]

Department of Pharmacology, Al-Ameen College of Pharmacy, Bangalore

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Abstract

A chronic metabolic disease that significantly affects people's health around the world is diabetes mellitus. High chronic fat intake is commonly associated with the development of insulin resistance, and hyperglycemia significantly alters the metabolism of lipids and carbohydrates. The objective of this review is to discuss the function of high-fat diet-induced diabetes mellitus, the mechanism at play, the various types of fats, and their impact on diabetes. DNA methylation, histone modifications, and an increase in the production of non-coding RNAs are some of the factors that might cause insulin resistance and lower the transcriptional activity of crucial genes for beta-cells. This meal pattern has been shown to improve insulin sensitivity and glycaemic control in persons with type 2 diabetes. High-fat diets have been related to better outcomes, but they can also increase insulin resistance and the beginning of type 2 diabetes.

Keywords: Diabetes Mellitus, High-Fat Diet, Insulin Resistance, Insulin Sensitivity, T2D.

***Corresponding Author**
Sowmya Shree S

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Introduction

Diabetes mellitus is now one of the world's top health concerns. Diabetes is a chronic metabolic condition that causes elevated blood glucose levels, which can harm the heart, blood vessels, eyes, kidneys, and nerves over time. Type 2 diabetes is the most common type and is caused by either insufficient or resistant insulin production by the body. According to the World Health Organization, diabetes causes 1.5 million deaths per year, affecting 422 million people worldwide, the majority of whom live in low- and middle-income countries. Diabetes incidence and prevalence have been steadily increasing over the last few decades.[1]There are three types of diabetes based on their etiology and clinical characteristics. These are gestational diabetes(GDM), type 1 diabetes (T1DM), and type 2 diabetes (T2DM).[2]

High Fat Diets are high in calories and bad fats, which can cause insulin resistance and disrupt glucose metabolism. This may eventually lead to the development of diabetes. HFDs can also cause weight gain, which is a significant risk factor for the development of DM. High-fat diets (HFD) have been linked to the development of diabetes.[3]This review article will provide an overview of the current state of knowledge regarding the role of high-fat diets in the onset of diabetes. This article will also look at the effect of high-fat diets on glucose metabolism, insulin resistance, and other metabolic pathways that are known to contribute to the onset of DM. The primary goals of this review are to provide a thorough understanding of how high-fat diets contribute to the onset of diabetes mellitus and suggest potential future research directions.

The Role of HFD-Induced Diets in the Development of Diabetes

It is important to note that not all fats are created equal, and some, such as unsaturated fats, can aid in the prevention of T2D. Overall, high-fat diets significantly impact T2D development, and a balanced diet with moderate fat intake is recommended for lowering T2D risk and maintaining overall health.High-fat diets contribute to the development of diabetic mellitus (DM), particularly type 2 diabetes (T2D), through a complex and multifaceted mechanism.[4]

Mechanism of HFD-Induced Diabetes

The following are some of the key mechanisms by which high-fat diets can cause T2D:

- ✓ Insulin Resistance: Excessive fat accumulation, particularly in the liver and skeletal muscle, leads to insulin resistance, a hallmark of T2D. This happens when cells become less sensitive to insulin, resulting in high blood glucose levels.[5,6]
- ✓ Pancreatic Beta Cell Dysfunction: High-fat diets can also cause changes in the pancreas, resulting in decreased insulin secretion and a decline in the function of beta cells, the cells responsible for producing insulin.[6,7]

- ✓ Free Fatty Acids: High-fat diets can raise blood levels of free fatty acids, interfering with glucose metabolism and contributing to insulin resistance.[8]
- ✓ Inflammation: An excessive intake of unhealthy fats can result in chronic low-grade inflammation, which has been linked to the development of T2D.[9]
- ✓ Adipokines: Adipose tissue, or fat, can produce hormones known as adipokines, which influence insulin sensitivity and glucose metabolism.[10,11]

Overall, the mechanisms by which high-fat diets contribute to the development of T2D are complex and interconnected, but insulin resistance and changes in pancreatic beta cell function are important factors in T2D development.[13]

Types of Fat and their effects on Diabetes

Not all fats are created equal, and the type of fat in your diet can affect your risk of developing diabetes in different ways. Some of the most common types of fats and their effects on diabetes are as follows:

- ❖ Saturated Fats: These are solid at room temperature and commonly found in animal products such as meat, dairy, and butter. Because they contribute to insulin resistance and inflammation, saturated fats have been linked to an increased risk of developing type 2 diabetes (T2D).Trans fats are partially hydrogenated oils that are commonly found in processed and fried foods. Trans fats, which contribute to insulin resistance and inflammation, are known to increase the risk of T2D and should be avoided.[14]
- ❖ Monounsaturated Fats: These are fats that are liquid at room temperature and are found in olive oil, avocados, and nuts.Monounsaturated fats have been shown to protect against T2D by increasing insulin sensitivity and decreasing inflammation.[15]

It is important to note that a balanced diet rich in healthy fats is recommended for lowering the risk of T2D and improving overall health. Unhealthy fats should be limited or avoided, whereas healthy fats should be consumed in moderation.[16]

High-fat diets have been the subject of much debate and research in recent years, particularly about their effects on diabetes.[17]Diabetes is a chronic metabolic disorder characterized by high blood sugar levels that are primarily caused by lifestyle factors such as diet and physical activity.[1] While some studies have shown that high-fat diets can increase insulin resistance and the development of type 2 diabetes, others have found that those who follow high-fat diets have better outcomes.[18]

One of the most well-known high-fat diets for diabetics is the ketogenic diet. The ketogenic diet is a low-carb, high-fat diet that encourages the consumption of healthy fats and restricts the intake of carbohydrates. This dietary pattern has been shown to improve glycaemic control and insulin sensitivity in individuals with type 2 diabetes. In addition, research has shown that following a ketogenic diet can result in significant reductions in hemoglobin A1c, a marker of long-term blood sugar control.[19]

Another popular high-fat diet for diabetics is the Palaeolithic diet, which emphasizes the consumption of whole, unprocessed foods and allows for moderate amounts of fat from animal sources. This diet has been shown to have positive effects on weight loss, glycaemic control, and insulin sensitivity in individuals with type 2 diabetes. Additionally, the Palaeolithic diet encourages the consumption of fiber-rich foods and reduces the intake of processed and refined foods, which can improve gut health and lower the risk of chronic diseases.[20]

The Atkins diet, another popular high-fat diet, restricts carbohydrates and encourages the consumption of protein and fat to induce weight loss. While this diet is effective for weight loss, it may not be suitable for all individuals with diabetes. This is because a high-protein, high-fat diet can increase insulin resistance, which can be detrimental to those with diabetes.[21]

The Bulletproof diet, a type of keto diet which emphasizes the consumption of healthy fats and moderate amounts of protein, and encourages the consumption of foods that are high in nutrients and low in toxins, has also been studied in the context of though research on the Bulletproof diet is limited, some studies have suggested that this dietary pattern may help improve insulin sensitivity and glycaemic control in individuals with type 2 diabetes.[22]

Table 1: List of high-fat diet-induced diabetes with a mechanism

Sl.no	Types of study and model used	Type of diet models	Functions	Mechanism	Implication of diabetes	Reference
1.	*In vivo*-rats	High-fat Diet	Obesity and anti-hepatorenal	The extract of salvia officinalis has been shown to reduce body weight and fat mass in obese rats. This is thought to be due totheir ability to modulate the expression of genes involved in fat metabolism and inhibit the absorption of fat in the gut	Insulin sensitivity	23
2.	*In vivo*-mice	High-fat Diet	Obesity	The proliferation of adipocytes increases the mitochondrial number. This enhances the burning of excess fat within the adipose tissue by fatty acid β-oxidation which in turn increases the oxidative stress by generating ROS and	Insulin resistance	24

				results in insulin resistance.		
3.	*In vivo*-Rats	High-fat Diet	Oxidative stress	The result showed that insulin modulates beta-cell mass expansion indirectly via the Nuclearhormone receptor peroxisome proliferator-activated receptor γ in response to obesity.	Increased islet cell counts and enrichment of hormone secretion	25
4.	*In vivo*-Mice	High-fat Diet	Gut Microbiota	Metabolic endotoxemia leads to an increase in pro-inflammatory cytokines and oxidative stress, impairing insulin signaling and promoting fat accumulation in adipose tissue.	Insulin resistance	26
5.	*In vivo*-mice	High-fat Diet	DNA methylation	HFD has increased DNA methylation levels in specific regions of their DNA. These changes in DNA methylation were associated with changes in gene expression, particularly in genes involved in glucose metabolism .these changes in gene expression were found to contribute to the development of glucose intolerance in the offspring.	Provoke inflammation And insulin resistance	27
6.	*In vivo*-Mice	High-fat Diet	Obesity via a PPARγ-Dependent	downregulation of PPARγ the PPARγ field is that adipose mass increases almost proportionally to PPARγ activity, whereas inhibition or activation of PPARγ sensitizes the body for insulin	Insulin sensitivity	28
7.	*In vivo*-mice	High-fa Diet	Non-coding R (micro RNA	Increased DAG levels, which are produce greater levels of enzyme phosphatidic a phosphate (LPP3) contribute to high-fat d induced cardiac insulin resistance. Wher the cardiomyocyte modulates cardiomyo insulin sensitivity by regulating LPP3 expression and DAG levels.	Insulin resistar	**3**

DISCUSSION:

High-fatdiets have been used for decades to model obesity, diabetes, oxidative stress, dyslipidemia, gut microbiota, cardiovascular diseases, and DNA methylation in rodents. In this study, we have provided a view of high-fat diet-induced diabetes, its role in the development of DM, its types, and its effects.High-fat diet susceptibility,that is, the extent of the metabolic disorder induced by the respective diet, depends more on the specific rodent strain and the dietary regimen employed than on the species itself.[30]Low insulin secretion from pancreatic -cells and peripheral insulin resistance are two characteristics of type 2 diabetes. Increased fat breakdown and raised plasma fatty acids as a result of insulin resistance reduce the amount of glucose that can enter muscle cells and increase hepatic glucose synthesis. Type 2 diabetes can only develop if both insulin resistance and pancreatic beta-cell malfunction occur simultaneously. The HFD altered insulin and beta-cell function, glucose and lipid metabolism, and insulin levels, leading to hyperglycemia, dyslipidemia, hyperinsulinemia, and late pancreatic cell failure, all contributing to T2DM. The multiorgan system was impaired by a high-fat diet. Saturated fat promotes weight gain in adipose tissue by increasing the white adipose tissue (WAT), changing lipid homeostasis, differentiating adipocytes, and extending life span. HFD also causes inflammation, greater tolerance to hepatic insulin, and poor expression of lipogenic genes in the liver. On HFD in skeletal muscles, changes in the expression of numerous insulin signaling genes are found to be a factor in insulin resistance. HFD alters the structural makeup of the vascular and renal systems, leading to hypertension, high glucose levels, and endothelial dysfunction. In response to the altered glucose and lipid metabolism caused by HFD, the activities of metabolic organs like the pancreas, liver, adipose tissue, kidney, and vascular system have largely been damaged.

Adipose tissue is a metabolically active organ that releases a wide range of biologically active substances. It is thought to be involved in the development of numerous metabolic modifications, including oxidative stress, insulin tolerance, low-grade inflammation, mitochondrial dysfunction, cell dysfunction, and others, which can lead

to the development of lifestyle diseases. The HFD's fatty acid content frequently promotes weight gain, altering lipid homeostasis, differentiating adipocytes, and controlling the size and number of fat cells. These modifications subsequently encourage leucocyte infiltration and an inflammatory state in adipose tissue.[3]

Conclusion

In this study, the role of a high-fat diet has shown influence in the development of diabetes mellitus. The literature provides strong evidence that a high-fat diet increases the risk of developing type 2 diabetes.

In conclusion, high-fat diet-induced diabetes is a serious and growing health problem that requires increased attention and research. By making simple lifestyle changes, such as reducing the consumption of fat and increasing physical activity, people can reduce their risk of developing this type of diabetes.

HFDs have been shown to disrupt glucose metabolism and increase the risk of developing DM. The mechanisms behind the relationship between HFDs and T2DM are not fully understood but oxidative stress, lipotoxicity, and changes in the gut microbiome are believed to play a role.

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