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Effect of Nutrition Intervention on Gene Expression Profile in Diabetic Individual (Diabetic Animal Model): A Mini Review

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ABSTRACT:
Diabetes mellitus (DM) is a chronic metabolic disorder with multisystem complications, traditionally addressed through treatment and prevention strategies. Recently, growing attention has focused on *nutrigenomics* as a promising approach for diabetes management. *Nutrigenomics* explores how nutrition influences gene expression and metabolic pathways, offering potential for targeted dietary interventions. This mini-review systematically examined literature from Google Scholar, PubMed, and the Cochrane Library using keywords such as "nutrigenomics," "diabetes," "gene expression," "intervention," and "experimental study." Eligible studies included original research articles in English involving diabetic models, while exclusions covered inaccessible full texts, non-English publications, reviews, duplicates, and studies limited to human clinical trials. Findings highlight that dietary interventions significantly influence gene expression related to glucose metabolism, lipid regulation, and oxidative stress in diabetes. Astaxanthin supplementation demonstrated improvements in biochemical markers and insulin sensitivity through the modulation of adiponectin, *AdipoR1/AdipoR2*, and *PPARγ*. Anthocyanin-rich extracts and germinated brown rice (GBR) were found to beneficially regulate transcription factors associated with gluconeogenesis and antioxidant defenses. Additionally, oil tea exhibited the ability to suppress *PCK1* gene expression, suggesting improved glucose homeostasis. Collectively, these interventions underscore the therapeutic potential of bioactive compounds in reprogramming metabolic pathways. In conclusion, evidence from *nutrigenomic* studies indicates that compounds such as astaxanthin, anthocyanins, GBR, and oil tea may serve as effective modulators of gene expression in type 2 diabetes. These findings provide a foundation for developing innovative, nutrition-based strategies aimed at enhancing glycemic control, reducing oxidative stress, and ultimately improving diabetes management and prevention.

Keywords: nutrigenomics, diabetes, gene expression, intervention, experimental study.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder with severe complications affecting the body from head to toe. It increases the risk of stroke, causes diabetic retinopathy, and contributes to cardiovascular diseases such as myocardial infarction (Ordovás & Corella, 2020). Renal involvement often leads to chronic kidney disease, while peripheral neuropathy impairs nerve function (Meng, Chen, Liu, & Zhang, 2023). In men, it commonly results in erectile dysfunction. At the lower limbs, poor circulation and nerve damage increase the risk of foot ulcers, often leading to infection and amputation (Chen, Wang, Zhang, Liu, & Li, 2024).

Considering the extensive complications associated with diabetes, it is unsurprising that the World Health Organization (WHO) has projected diabetes mellitus to become the 7th primary cause of fatality worldwide. For decades, research has primarily focused on treatment and prevention strategies. However, in recent years, attention has shifted toward exploring the potential applications of nutrigenomics in the management and prevention of diabetes (Chen, Liu, Wang, & Zhang, 2025).

Nutrigenomics is the study of how diets influence the expression of genetic information in an individual, as well as how a person's genetic makeup affects how their body processes nutrients and other bioactive ingredients in food (Corella & Ordovás, 2014). Building on the understanding of how nutrition, genes, and diseases are linked through nutrigenomics, several studies have provided evidence supporting this relationship (Guasch-Ferré & Clish, 2021). In light of these advancements, synthesizing preclinical evidence on how specific nutrigenomic dietary interventions influence gene expression and metabolic pathways in diabetes models becomes crucial (López-Miranda et al., 2024). Understanding the mechanisms through which nutrigenomics impacts diabetes may reveal promising targets for clinical application, offering new avenues for the management and prevention of this widespread condition (Konstantinova & Koeva, 2024).

Previous research has demonstrated the promising role of nutrigenomics in managing diabetes mellitus, yet gaps remain in translating molecular evidence into practical dietary strategies (Martinez-Gonzalez, Salas-Salvadó, Estruch, Corella, Fitó, & Ros, 2024). For instance, Ferguson et al. (2016) highlight that nutrigenomics provides critical insight into how nutrients regulate gene expression and metabolic pathways, but most findings remain limited to experimental or preclinical settings without comprehensive integration into patient-centered dietary guidelines. Similarly, Corella and Ordovás (2018) emphasize that although nutrigenomics advances the personalization of nutrition, evidence is still fragmented regarding its direct impact on diabetes-related complications such as cardiovascular disease and neuropathy. Both studies illustrate the potential of nutrigenomics but also underline the lack of synthesis connecting gene–nutrient interactions with specific pathways relevant to diabetes progression and complications.

This study aims to systematically analyze how nutrigenomic dietary interventions influence gene expression and metabolic regulation in diabetes, thereby offering a more integrative understanding that bridges experimental evidence with practical clinical applications. The expected benefits are twofold: theoretically, contributing to the literature on gene–diet interactions in chronic diseases; and practically, providing evidence-based insights that can guide tailored nutritional interventions for diabetes management and prevention.

METHOD

The research methodology employed a systematic literature review approach to meticulously investigate the intricate relationships among nutrigenomics, diabetes, gene expression, and experimental interventions. A comprehensive search strategy was executed across prominent academic databases, specifically Google Scholar, PubMed, and the Cochrane Library. This involved the strategic utilization of various keyword combinations, including "nutrigenomics," "diabetes," "gene expression," "intervention," and "experimental study".

Strict inclusion and exclusion criteria based on PICO framework were applied to ensure the relevance and quality of the selected literature. Only original research articles published in English were considered for inclusion. Conversely, inaccessible full texts, non-English publications, review articles, duplicates, studies lacking clearly defined diabetic models, and those exclusively focused on human clinical trials without an animal model component were systematically excluded. From an initial pool of 161 papers, a rigorous screening process led to the selection of 5 highly relevant studies. These selected papers then underwent critical review, conceptualization, and formed the basis for the final review report.

Table 1. Inclusion and Exclusion Criteria

Category	Inclusion Criteria	Exclusion Criteria
Population/Model	Diabetic animal models (e.g., db/db mice, streptozotocin-treated rats) or in vitro studies.	Non-diabetic models or unclear diabetes status. Only human studies unless combined with animal/in vitro models.
Nutrition Intervention	Defined nutrigenomic compounds or whole foods affecting gene expression (e.g., astaxanthin, fermented maize).	Undefined interventions or broad dietary trends without specific nutrigenomic components.
Comparators	Must include control groups (e.g., healthy controls, untreated diabetic subjects, metformin- treated).	No control group or missing baseline gene expression data.
Nutrigenomic Outcomes	Must measure gene expression related to diabetes (e.g., RNA sequencing, qPCR, DNA methylation).	No gene expression or epigenetic outcomes. Only clinical/metabolic measures without molecular data.
Study Design	Experimental/interventional studies with clear methodology and statistical validation.	Reviews, meta-analyses, case reports, or studies with serious methodological flaws. Must be published in peer-reviewed journals.

RESULTS AND DISCUSSION

The mini review compiles evidence from several studies evaluating the nutrigenomic effects of various dietary interventions, ranging from astaxanthin and anthocyanin-rich black bean extract to germinated brown rice (GBR) and oil tea on diabetic models as showed in Table 1. Despite differences in experimental design, these investigations collectively suggest that nutritional components can modulate key gene expression pathways associated with glucose metabolism, lipid profiles, and oxidative stress. For example, astaxanthin not only improved biochemical markers such as blood glucose and cholesterol but also enhanced the expression of insulin sensitivity genes (e.g., adiponectin, AdipoR1/AdipoR2, and PPARγ) in diabetic rats. Similarly, interventions involving anthocyanin-rich extracts and GBR demonstrated beneficial alterations in transcription factors and genes involved in gluconeogenesis and antioxidant responses, while oil tea was shown to suppress PCK1 gene expression, a potential marker for improved glucose homeostasis. These outcomes support the concept that specific bioactive compounds in foods may act through genomic pathways to exert anti-diabetic effects.

However, several limitations must be acknowledged. There is considerable heterogeneity in both the nutritional interventions and the gene expression targets assessed. Each study focused on a different set of markers, ranging from insulin sensitivity and lipid metabolism to oxidative stress and gluconeogenesis, complicating direct comparisons and synthesis of results. This raises questions about the translatability of these findings to clinical settings. The overall number of studies included in this review is small, and diverse experimental protocols (variations in dosage, duration, and combinations of diets/interventions) further constrain the ability to draw comprehensive conclusions about the efficacy and mechanisms of these nutritional strategies (Sales, Pelegrini, & Goersch, 2014).

The implications of these findings underscore the potential for nutritional interventions to serve as adjunct strategies in the management of diabetes. By modulating gene expression, whether by upregulating insulin-sensitizing or antioxidant genes, or by downregulating gluconeogenic genes, these dietary components could complement conventional therapies, providing a basis for personalized nutritional recommendations in diabetes care. On the other hand, the review clearly indicates a need for future research using standardized protocols and larger, ideally human, cohorts. Future studies should aim to identify consistent biomarkers that can be reliably influenced by dietary modifications, facilitating the development of targeted nutrigenomic interventions (Pérez-Martínez, García-Ríos, Delgado-Lista, Pérez-Jiménez, & López-Miranda, 2016).

Moreover, enhanced clinical trials incorporating genomic profiling could validate these preclinical observations, ultimately informing guidelines that integrate dietary strategies into personalized medicine for diabetes management (Pinheiro, Cunha, Aguiar, & Saraiva, 2019).

In summary, this review provides promising insights into the role of nutrition in modulating gene expression related to diabetic pathophysiology, it also highlights critical gaps, namely the diverse range of gene targets and interventions, coupled with limited study numbers, that must be addressed to transform these findings into robust clinical applications (Rodriguez-Hernandez, Simental-Mendia, & Rodriguez-Moran, 2024). This review paves the way for integrative studies that blend nutrigenomics with precision medicine, thereby enriching our understanding of how dietary factors influence metabolic health and offering potential new avenues for diabetes therapy (Ramos-Lopez et al., 2017).

Table 2. article review

Study	Study Design	Population/Model	Dietary Intervention	Comparator	Gene Expression Outcomes	Key Findings
Zhuge et al.[4]	Animal study with diabetic rats.	Male Wistar rats (90–100 g). Diabetes was induced by a high-energy diet and a low-dose STZ injection.	Astaxanthin was added to the diet. Three doses were used: 15, 30, and 50 mg/kg for 3 weeks after diabetes induction.	Control group on a basic diet. Another group was given monacolin K (11.8 mg/kg) for comparison.	mRNA levels were measured in adipose tissue, liver, and muscle. Key genes included adiponectin, AdipoR1, AdipoR2, PPARγ, UCP2, and FAS.	Astaxanthin lowered blood glucose and total cholesterol. It raised HDL-C. Astaxanthin treatment increased the expression of insulin sensitivity-related genes (adiponectin, AdipoR2, and PPARγ) in a dose-dependent manner. Monacolin K had similar effects.
Damián-Medina	Animal experimental	Wistar rats induced with	Anthocyanin-rich black	Diabetic untreated	RNAseq analysis of	Black bean extract reduced

Study	Study Design	Population/Model	Dietary Intervention	Comparator	Gene Expression Outcomes	Key Findings
et al. [5]	study	T2DM via Streptozotocin (n = 24, divided into groups)	bean extract (260 mg/kg/day for 31 days)	rats	adipose tissue; 566 differentially expressed genes, including transcription factors (GATA2, IRF3, PPARA)	blood glucose, altered adipose tissue gene expression, and modulated transcription factors involved in metabolic regulation.
Imam & Ismail.6	Animal and in vitro study	Sprague-Dawley rats (n = 30); HEPG2 cell line	Germinated brown rice (GBR) with 50-100% substitution in diet	Standard chow and metformin	Downregulation of gluconeogenic genes (Fbp1, Pck1)	GBR improved glycemic control more effectively than metformin, significantly reducing plasma glucose and downregulating gluconeogenesis-related genes.
Imam et al.7	Animal experimental study	Type 2 diabetic rats induced via high-fat diet and Streptozotocin	White rice, brown rice, and germinated brown rice diets	White rice and metformin groups	Expression of antioxidant genes (SOD2, catalase)	GBR preserved liver and kidney function, upregulated antioxidant genes, and reduced oxidative damage compared to white rice.
Hu et al.8	Animal experiment & case- control study	db/db mice; human population in Guangxi, China	Oil tea intervention for 8 weeks	Saline or metformin controls	Expression of PCK1 gene; SNP association (rs707555, rs2071023)	Oil tea improved glucose homeostasis and suppressed PCK1 gene expression, suggesting PCK1 as a genetic marker for diabetes treatment.

The findings of this mini-review strengthen the evidence that dietary bioactive compounds can modulate gene expression pathways central to diabetes pathophysiology, including glucose metabolism, lipid regulation, oxidative stress, and gluconeogenesis. Interventions such as

astaxanthin supplementation (Zhuge et al., 2020), anthocyanin-rich black bean extract (Damián-Medina et al., 2020), germinated brown rice (Imam & Ismail, 2012; Imam et al., 2014), and oil tea (Hu et al., 2021) consistently demonstrated improvements in biochemical parameters alongside molecular-level changes. These nutrigenomic mechanisms offer a promising adjunctive strategy to conventional therapies, highlighting the potential of diet-based interventions in promoting insulin sensitivity, preserving organ function, and reducing oxidative damage (Simopoulos, 2020).

Despite these encouraging results, several limitations restrict the broader application of these findings. First, heterogeneity across studies—differences in animal models, dietary formulations, dosages, and duration of interventions—limits the ability to compare outcomes directly. Second, most of the evidence is preclinical, with few translational or clinical trials confirming these effects in humans. This raises concerns about the external validity of nutrigenomic interventions, particularly regarding the reproducibility of molecular outcomes across diverse populations and dietary contexts. Additionally, the diversity of gene expression targets, from PCK1 suppression to antioxidant gene upregulation, complicates the establishment of consistent biomarkers for clinical monitoring (Wu, Zhao, Shen, & Zhang, 2020).

The implications of these findings are twofold. On the theoretical level, they underscore the capacity of nutrigenomics to bridge molecular biology and nutrition, advancing precision medicine approaches in diabetes care (Zhang, Li, Wang, Chen, & Liu, 2025). On the practical level, these insights encourage the design of targeted nutritional interventions that could reduce dependence on pharmacological treatments while lowering the risks of long-term complications. However, future research should move beyond isolated animal models and prioritize well-structured clinical trials integrating genomic profiling. This approach would enable the identification of consistent, clinically relevant biomarkers, refine dietary recommendations, and inform public health policies aimed at diabetes prevention and management.

CONCLUSION

The research indicates that bioactive dietary compound, such as astaxanthin, anthocyanin-rich extracts, germinated brown rice, and oil tea hold promising potential for modulating key metabolic genes involved in type 2 diabetes, thereby improving glycemic control and reducing oxidative stress. However, the variability in gene expression responses, diverse nutritional interventions, and the limited number of studies, especially those involving human subjects, suggest that further standardized, large-scale clinical research is essential to validate these findings and translate them into effective, personalized dietary strategies for diabetes management.

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