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Comparing the Effects of Traditional Chinese Medicine (Diosgenin and Formononetin) and Low-Carbohydrate Diets on Glycemic Control in Type 2 Diabetes

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Abstract: Type 2 diabetes is a worldwide health issue. It's especially prevalent in China, where swift lifestyle changes have increased the disease's prevalence. Extensive evidence also supports their use for improvement of glycemic control (lowered targeted HbA1c plus reduction of fasting blood glucose levels), such as by low-carbohydrate diets and other conventional approaches. Traditional Chinese Medicine (TCM) provides an alternative approach with agents like Diosgenin and Formononetin. Various compounds of the aforementioned medicinal plants are found to mediate insulin sensitivity, ameliorate oxidative stress, and normalize glycolipid metabolism. Higher TGF-β serum levels are associated with greater responsiveness to exercise and diet-induced weight loss in young T2D patients, and TGF-β blockade studies suggest the potential for modification of early glycemic control in young T2D patients by moderate changes in lifestyle. The progressive and multi-target characteristics of TCM treatment address the metabolic and inflammatory mechanisms that underlie type 2 diabetes, while the low-carb diet rapidly reduces blood glucose. Both are promising approaches, and further exploration is needed to understand how they may complement each other in delivering the optimal long-term care for T2D.

Keywords: Type 2 Diabetes, low-carbohydrate diet, Traditional Chinese Medicine, Diosgenin, Formononetin, glycemic control, fasting blood glucose, HbA1c, insulin sensitive

1. Introduction

Type 2 diabetes (T2D), a chronic metabolic disorder, is characterized by chronic hyperglycemia. Symptoms of T2D include insulin resistance and inadequate insulin secretion. Type 2 diabetes is a major public health challenge, affecting more than 537 million people globally as of 2021 [1]. In China, where the prevalence is reported at the highest rate all over the world [2]. In 2021, it has over 141 million people diagnosed with this disease[3] as a result of rapid urbanization and lifestyle transformation in the country. Low-carbohydrate diets, particularly ketogenic diets, are widely recognized and accepted as effective interventions for glycemic control. These diets restrict carbohydrate consumption, forcing the body to utilize fat as an energy source, resulting in better glucose levels in the blood, insulin sensitivity, and decreases in HbA1c [4]. However, the strict dietary restrictions required often lose effectiveness over time. It is hard for most of individuals to maintain the high level of adherence these diets demand in the long term [5]. An alternative or complementary

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approach is provided by traditional Chinese medicine with herbal bioactive compounds for metabolic health. Diosgenin and Formononetin, two significant constituents of TCM, are thought to modulate blood glucose and improve insulin sensitivity, providing novel options to treat T2D [6, 7]. The objective of this review was to compare the efficacy of glycemic control between low-carbohydrate diets and traditional Chinese.

2. Method

A thorough literature search was performed using databases like PubMed, Google Scholar, and Web of Science. Search terms were "Type 2 Diabetes," "low-carbohydrate diet," "Traditional Chinese Medicine," "Diosgenin," "Formononetin," "glycemic control," "fasting blood glucose," "HbA1c," and "insulin sensitive." Filters were applied to the search to narrow down results to articles addressing studies relevant to type 2 diabetes through dietary and TCM interventions. Since clinical trials and meta-analyses published in non-peer-reviewed journals might not maintain a high standard and activity volume, the inclusion criteria only presented features of trials and meta-analyses that had been accepted by the peer-review process (Appendix). Only articles published in the last 10 consecutive years (2014-2024) were included. The review only included intervention studies using low-carb diets and TCM for glycemic control in subjects with type 2 diabetes. Type 1 diabetes, studies without quantitative glycemic data or studies on a dietary or herbal intervention outside of the boundaries defined in the eligibility criteria.

3. Results

3.1. Low-carbohydrate diets' impact on glycemic control

Low-carbohydrate diets, in particular, appear to hold great promise for improving glycemic control, particularly among persons with type 2 diabetes. By reducing carbohydrate consumption, these diets avert postprandial glucose surges and thus promote near-normal blood glucose ranges. This way of eating increases insulin sensitivity and improves glucose handling by lowering dependence on exogenous insulin or medication [8]. Research has furthermore demonstrated that low-carbohydrate diets can induce weight loss, which further assists in refined glycemic regulation [5]. The relatively low carbohydrate intake typically lowers circulating concentrations of HbA1c [9], another principal marker for long-term control of blood sugar. While the level of effect is again dependent on the level of adherence to the diet and the level of difference in metabolic response between individuals, low carbohydrate diets remain a promising intervention for lowering blood glucose levels and controlling the risk of T2D.

The results presented in Table 1 emphasize the potential of low-carb dietary patterns to improve glycemic control and decrease body weight in humans. The range of HbA1c reductions across all interventions was 0.23% to 5.6% with significant differences ($p < 0.05$) in all reported changes. Interestingly, Low-carb 4 (3 months duration) demonstrated considerable mean reductions in HbA1c (-0.23%, 95% CI: -0.32% to -0.14%) and average weight loss (5.9 kg). Low-carb 5 (56 weeks – longest intervention) showed a significant reduction of fasting blood glucose (10.5 mmol/L to 4.9 mmol/) and HbA1c (5.6%), with optimal weight loss (50.9% reduction from baseline). The consistency of significant outcomes across different sample sizes and durations highlights the robust effect of LCDs, particularly in longer interventions. Thus, we conclude that our data indicate that low-carbohydrate diets represent a promising dietary approach to the effective management of type 2 diabetes and other related metabolic factors.

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3.2. Traditional Chinese Medicine's impact on glycemic control

Type 2 diabetes is also a disease that traditional Chinese medicine addresses through a holistic approach to address the root causes of insulin resistance, inflammation, and oxidative stress. While traditional treatments generally address the symptoms, TCM interventions such as herbal formulations, acupuncture, and additional therapies are designed as a whole to restore the general balance in the human body. A study comparing the interactions between different components and proteins showed that certain Chinese herbal formulations containing bioactive compounds, such as diosgenin and formononetin, can significantly improve blood sugar control [10]. These findings highlight the potential of TCM as a valuable complementary therapy for the long-term treatment of T2D and to reduce complications.

3.2.1. Diosgenin

Diosgenin is a type of sapogenin of the steroid group, found in several plants, such as yam, fenugreek, and Dioscorea species [10]. Investigations have examined the antihyperglycaemic effects of diosgenin on the following mechanisms generally involved in T2D pathophysiology: insulin sensitivity, inflammation, and oxidative stress [11]. Diosgenin is reported to regulate blood glucose levels by enhancing peripheral tissues' glucose uptake and increasing insulin receptors [27]. Moreover, based on the data, they suggest that diosgenin can help reduce the production of reactive oxidative stress (ROS), which is involved in beta cell impairment and insulin resistance [12-16]. These features could both reduce the dependence on medication with significant side effects and meet the requirements for improved glycemic control.

3.2.2. Formononetin

Another herbal substance is formononetin, which occurs mainly in red clover and other legumes. Isoflavonoids are potential candidates with anti-inflammatory, antioxidative, and antidiabetic activities [17, 18]. In addition, recent studies have found the beneficial role of formononetin. Its signaling pathways that stimulate insulin secretion and regulate glucose uptake have been identified with a tendency. Additionally, it modulates the immune system by increasing anti-inflammatory pathways and decreasing proinflammatory cytokines. To T2D patients, formononetin has a positive influence on the relative T2D evaluation factors, such as greater insulin sensitivity and lower fasting blood glucose and HbA1c. It also presumably modulates lipid metabolism which provides additional protection from the metabolic sequelae of T2D such as dyslipidemia and atherogenesis.

3.2.3. Other Traditional Chinese Medicine

In addition to Diosgenin and Formononetin, TCM utilizes a vast array of other herbs and compounds that have demonstrated beneficial effects on glycemic control. For example, berberine, a compound found in several TCM herbs including Coptis chinensis, has been shown to enhance insulin sensitivity and reduce blood glucose levels (Table 1) [25]. Similarly, the use of ginseng, bitter melon, and turmeric has been explored for their potential antidiabetic effects, highlighting the rich diversity of natural remedies available in TCM.

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Table 1: Summary of low-carbohydrate diet interventions on glycemic control (HbA1c and fasting blood glucose), weight, and statistical significance [19-23]

Intervention Type	Sample Size	Intervention Duration	HbA1c Initial mean ± SD (%)	HbA1c Final mean ± SD (%)	HbA1c Change (%)	Fasting Blood Glucose Initial mean ± SD (mmol/L)	Fasting Blood Glucose Final mean ± SD (mmol/L)	Fasting Blood Glucose Change (%)	Body Weight Initial mean ± SD (kg)	Body Weight Final mean ± SD (kg)	Body Weight Change (%)	Statistical Significance (p-value)
Low-Carb1	33	6 months	10.9 ± 1.6 (9.0 - 14.4)	7.4 ± 1.4	-3.5 ± 1.6	-	-	-	23.8 ± 3.3 (18.0 - 33.8)	23.5 ± 3.4 (16.8 - 32.8)	-0.3 ± 0.1	< 0.0001
Low-Carb 2	56	6 months	7.43 ± 1.39	6.80 ± 0.83	2.601	8.28 ±1.64	6.87 ± 0.65	4.873	-	-	-	0.016
Low-Carb 3	102	24 weeks	8.2 ± 0.3	7.7 ± 0.1	0.5 ± 0.3	9.0 ± 0.6	6.7 ± 0.6	2.3 ± 0.9	95.71 ± 9.56	89.02 ± 5.97	-7.0	< 0.0001
Low-Carb 4	64	56 weeks	-	-	-	10.5 ± 3.0	4.9 ± 0.6	24.4 ± 6.7%	108.1 ± 21.2	83.5 ± 18.0	50.9 ± 12.5	< 0.0001
Low-Carb 5	150	3 months	-	-	-0.23 % (Cl: -0.32 % to -0.14 %)	-	-	-10.3 (Cl: -15.6 to -4.9)	-		-5.9kg ; (CI: -7.4 to -4.4)	< 0.001

3.3. Effects of low-carbohydrate diets on glycemic control

The mean values of HbA1c Change (%) and Fasting Blood Glucose Change (%) are calculated based on the data in Table 1. Comparison of the effects of TCM and placebo on HbA1c change (%) and fasting blood glucose change (%) in patients (Table 2). Table 2 demonstrates both TCM, namely berberine, and low-carbohydrate diets are effective in enhancing glycemic control. Target reductions were respectively observed for HbA1c and fasting blood glucose substantive to the extent of their intervention duration. There was a highly statistically significant reduction in HbA1c (from 9.0% to 7.4 ± 1.4%) and fasting blood glucose (from 10.5 to 5.3 mmol/L) values over 6 months following low-carbohydrate diets ($p < 0.0001$). Similarly, berberine caused significant reductions in HbA1c (from 7.6 ± 1.1% to 6.7 ± 0.9%) and fasting blood glucose (from 6.9 ± 1.0 to 5.5 ± 0.9 mmol/L) within 14 weeks ($p < 0.0001$). In contrast, the placebo group showed minimal changes in glycemic markers, with non-significant results ($p = 0.111$), highlighting the specific efficacy of the active interventions (Table 2). These findings suggest that both low-carbohydrate diets and berberine-based TCM offer promising, statistically validated approaches to managing type 2 diabetes, with their relative benefits influenced by the intervention type and duration.

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Table 2: Comparison of the effects of low-carbohydrate diets and Traditional Chinese Medicine on glycemic control (HbA1c and fasting blood glucose) [24]

Intervention Type	Sample Size	Intervention Duration	HbA1c Change (%)	Fasting Blood Glucose Change (%)	Statistical Significance (p-value)
Low-Carb Diet	31	6 months	-0.157	5.318	< 0.0001
TCM (Berberine)	60	14 weeks	0.9 ± 2.0	1.4 ± 1.9	< 0.0001
Placebo	60	14 weeks	0.3 ± 2.5	0.6 ± 2.2	0.111

4. Discussion

It is crucial to take into account both the short- and long-term effects on glycemic control, insulin sensitivity, and general metabolic health when evaluating the efficacy of low-carb diets and TCM for the management of T2D. Low-carb diets, especially ketogenic diets, have been demonstrated to significantly decrease blood sugar levels and increase insulin sensitivity. The metabolic state known as ketosis occurs when the body uses fat as fuel rather than carbs [26]. HbA1c and fasting blood glucose levels drop notably is a common response in the short-term. However, we cannot ignore the limitations of strict diets, which is that low-carb lifestyles are difficult to adhere to in the long term. This can result in nutrient shortages, such as a lack of fiber and other micronutrients, as well as possible cardiovascular risks. By contrast, TCM offers a more gradual and holistic approach to managing T2D, focusing on improving insulin sensitivity and reducing inflammation over time. The mechanism by which diosgenin, formononetin, and other compounds are believed to impact sustained glycemic control in the body includes modulation of the activity of insulin receptors as well as antioxidative and anti-inflammatory benefits. While the effects of TCM may take some time to surface, its focus on the body's balance and general well-being may offer a more enduring and longer-term solution.

Biochemically, low-carbohydrate diets primarily function by altering glucose metabolism through the induction of ketosis. In this state, the liver produces ketones from fat, which replace glucose as the primary energy source. This causes more uptake of glucose in the body and thus low blood glucose levels, along with better lipid profile and insulin sensitivity. In contrast, TCM interventions focus on modulating specific pathways such as improving insulin receptor activity, reducing oxidative stress, and regulating inflammatory responses. TCM compounds, such as Diosgenin and Formononetin, target multiple pathways involved in metabolic regulation. This comprehensive approach offers a more sophisticated method of treating the metabolic dysfunctions linked to type 2 diabetes. These different mechanisms suggest that while both interventions are effective, they work through different but complementary approaches.

The effective implementation of diabetes control techniques depends critically on adherence to treatment procedures. We have to admit that low-carb diets are so strict that many patients find it difficult to stick with short-term, successful tactics over the long run. In contrast, people looking for a more natural, holistic method of treating their illness with fewer dietary limitations could find TCM more appealing. However, some patients might be put off by the absence of standardized formulas and lack of access to guidance from systematically educated experts. As a result, patient preference is at the forefront of deciding the correct treatment choice.

However, low-carb diets have their problems of safety. In some specific cases, such as gastrointestinal problems, dietary deficiencies, and the risk of cardiovascular disease due to higher intake of saturated fats. Compared to low-carb diets, on the other hand, although TCM is often safer to practice, it also carries potential risks. Such kinds of risks include not only the quality and purity of herbal supplements used but also potential interactions with other medications or therapies.

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Essentially, some of the herbs are not appropriate for certain health conditions; therefore, it is crucial for patients to consult with healthcare providers before entering new treatments. Both strategies carry their own risks and benefits and should be personalized according to a person's health profile and preferences.

To date, the overall evidence indicates that combined approaches to low-carbohydrate diets with TCM may improve glycemic control in T2D patients. However, data on the combined effects of TCM and low-carbohydrate diets are scarce. Combining TCM herbs like Diosgenin and Formononetin with the well-known metabolic benefits of low-carbohydrate diets may provide a more extensive solution, but further long-term studies, as well as head-to-head trials, are needed. Personalized treatment plans can adjust interventions to factors specific to the individual, such as their age, health, and cultural preferences. While TCM appeals to those seeking natural therapies, low-carbohydrate diets offer a structured approach. It is very critical that the interventions are effective; adherence, cultural acceptance, and accessibility (including costs and availability) are also relevant factors to help increase the likelihood of success and help improve patient outcomes and quality of life.

5. Conclusion

In conclusion, there are significant advantages to both low-carb diets and Traditional Chinese Medicine for the management of type 2 diabetes, which include better glycemic control, weight control, and potential reduction in medication use. However, there are also drawbacks like the lack of large-scale, long-term research and head-to-head trials comparing these two strategies. Although further study is required to further investigate their synergistic benefits and improve treatment procedures, the combination of these therapies may hold hope. In practice, it is essential to adopt individualized approaches that consider factors such as patient preferences, cultural backgrounds, and health status. Continued research into multi-therapy interventions and tailored treatments will be key to optimizing the care of T2D patients.

Authors' contributions

Shengtong Shao designed the study, conducted the research, analyzed the data, and wrote the manuscript. All aspects of the article, including conceptualization, methodology, literature review, and final editing, were carried out by Shengtong.

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