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The Effect of Spice and Herbs Mixture on Electrolytes and Liver and Renal Function in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Background: Diabetes has a prevalent nature and still presents a significant public health challenge. This study investigated the effect of spice and herbs on serum biochemical parameters in type 2 diabetes mellitus (T2DM).

Methods: The spice and herbs procured from local market were processed by cleaning, washing, crushing, freeze-drying, formulating, and encapsulating in doses of 2, 4, and 6 grams. Thirty patients with T2DM were assigned to 3 equal groups to receive each mentioned dose fed for 30 days. On day 1 and 31, fasting blood samples were collected and analyzed for electrolytes (Na, K and Cl), urea, creatinine, liver enzymes (AST: aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: alkaline phosphatase), fasting blood glucose (FBG), and lipid profile. The data were further statistically analyzed.

Results: The electrolytes, urea, creatinine, and liver enzymes remained within the normal ranges after the consumption of spices and herbs. There was a reducing trend for HbA1c level after intake of spices and herbs. Total cholesterol and low-density lipoprotein cholesterol (LDL-C) decreased by -10.08-7.36% and high-density lipoprotein cholesterol (HDL-C) increased in 2 and 6 gram consuming groups; whereas it decreased in the 3 gram consuming group. The concentration of triglycerides (TG) decreased notably with increasing doses of spices and herbs.

Conclusion: Consumption of spices and herbs mixture was demonstrated to have beneficial effects on kidney and liver function, blood glucose level and lipid profile in T2DM patients. These findings suggest the potential therapeutic value of incorporating spices and herbs into the management of T2DM.

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Introduction

Type 2 Diabetes Mellitus (T2DM) stands as an established metabolic illness and is characterized by an increased blood sugar due to insulin resistance or a low production (1). Its prevalent nature presents a significant public health challenge, often managed through conventional approaches like medication and lifestyle changes (1). However, exploring the potential efficacy of natural substances in managing T2DM offers a promising chance for complementary therapies (2). Spices and herbs namely cloves, ginger, onion, lemon grass, coriander, curry leaves, holy basil, and bunching onion have been studied and reported in the published literature on diabetes. Cloves and ginger are reported to be effective in T2DM and also help control hyperleptinaemia (3). The water extract from cloves has been reported to be rich in antioxidants that lower pre- and post-prandial blood glucose levels in healthy and prediabetic volunteers (4). Researchers have found that extracts from cloves boost muscle glycolysis and spare respiratory capacity in mitochondria. It has also been shown that clove extract has the potential to enhance muscle glycolysis and improve mitochondrial function by activating both the AMP-activated protein kinase (AMPK) and NAD + -dependent deacetylase (SIRT1) pathways (5).

Ginger boosts potent anti-inflammatory properties (6), aiding in alleviating nausea (7), soothing digestive issues (8), and potentially reducing muscle soreness (9). It is rich in antioxidants that may boost the immune system and contribute to overall health, while its warming effect can promote circulation and help in managing cold symptoms (10). Onions contain compounds that may help regulate blood sugar level, and potentially lower the risk of spikes and enhancing insulin sensitivity (11). The antioxidants in onions aid in reduction of oxidative stress and prevent cell damage (12). On the other hand, lemongrass contains combinations that help control blood sugar concentration (13), and potentially aid in managing diabetes possibly by improvement in insulin resistance. Its antioxidants contribute to the reduction of cholesterol concentration and prevent the oxidation of low-density lipoprotein cholesterol (LDL-C). Therefore, it potentially can lower the risk of cardiovascular diseases (14).

Similarly, coriander oil has the potential to reduce blood glucose concentration and increase insulin secretion, making it beneficial for diabetes (15). Coriander leaves are an excellent source of antioxidants which lower low-density lipoprotein cholesterol (LDL-C) and triglycerides (TG) concentrations, potentially reduce the risk of cardiovascular diseases. The inclusion of coriander leaves in meals or eating it as a supplement may give double benefits for diabetes control and cardiac health (16). Curry leaves have been used to lower blood glucose concentration and insulin activity (17). Furthermore, its antioxidant activities may reduce oxidative stress and inflammation (18). Therefore, incorporating curry leaves into the diet might offer natural support for diabetes and cardiovascular well-being. Holy basil leaves contain antioxidant compounds (19) that might help regulate blood sugar levels, potentially aiding in managing diabetes by improving insulin sensitivity (20).

Furthermore, their antioxidant properties could be useful in reducing inflammation and oxidative stress, potentially benefiting cardiovascular health by lowering the risk of related conditions (19). Bunching onions, also known as green onions, are low in calories and rich in several antioxidants (21), reduce inflammation and oxidative stress (22), and benefit cardiovascular health. It also may regulate blood sugar level and potentially aid in diabetes management. Their sulfur compounds contribute to cardiovascular health by supporting blood vessel function and potentially reducing the risk of heart-related issues (23). As the consumption of bunching onions into meals may offer benefits for both diabetes and cardiovascular well-being, and due to the individual effect of cloves, ginger, onion, lemongrass, coriander, curry leaves, holy basil, and bunching onion, this study aimed to investigate their synergistic effect on T2DM by assessing their impact on kidney and liver functions and electrolyte levels (sodium, potassium and chloride), liver enzymes AST: aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: alkaline phosphatase, blood urea, creatinine, and lipid profiles.

Materials and Methods

The selected spices and herbs namely ginger (Zingiber officinale), onion (*Allium cepa*), cloves (*Syzygium aromaticum*), lemongrass (*Cymbopogon citrates*), coriander leaves (*Coriadrum sativum*), bunch-ing onion (*Allium fistulosum*), curry leaves (*Murraya koenigii*) and holy basil leaves (*Ocimum tenuiflorum*) were procured from local markets and underwent a thorough cleaning, washing, crushing, and freeze-drying. The mixing of spices and herbs were conducted based on the formulation described by Shirazi *et al.*, with a ratio of 12.5% for the eight selected spices and herbs (24). The processed spices and herbs were encapsulated into doses of 2, 4, and 6 grams for daily consumption by T2DM patients. The study protocol was approved by the Kulliyyah Postgraduate and Research Committee (KPGRC) and the IIUM Research Ethics Committee (IREC) and was registered in the National Medical Research Registry Malaysia (NMRR) (Research ID: 17783).

Thirty T2DM patients were recruited from the Medical Outpatient Department of hospitals of Tengku Ampuan Afzan, Kuantan, and Pahang to participate in the study. The subjects were randomly assigned to groups receiving doses of 2, 4, and 6 grams of spices and herbs, with 10 patients in each group. Over 30 days, these patients received the prepared doses of mixed spices and herbs. Participants who met health criteria or had stable health conditions apart from diabetes, they could safely participate in the study. Participants had a confirmed diagnosis of T2DM at age of 18 years or older. Subjects who did not meet the health criteria or had unstable health conditions apart from diabetes and were not safe to participate in the study and those who were not confirmed with T2DM were excluded from the study. The respondents who were on treatments/medications, with comorbidities, or complications related to diabetes were also excluded from the study.

An informed consent was obtained from all the patients on day 1 of the study. The purpose of the study was explained, and they were included in the study only with their willingness. This study adopted a quasi-experimental design by forgoing the inclusion of a control group. It was structured as a self-controlled study during 30 days of an experimental duration. The absence of a control group allowed for a comprehensive focus on the effect of the interventions within the participant group. This design was intended to track and analyse the impact of the spices and herbs on the aforementioned participant's blood parameters.

The participants were allocated a dosage based on a 2, 4 and 6 gram wet weight of the spices and herbs in an encapsulated form that were adjusted to match the dry matter. The defined dose was administered thrice daily, evenly spread over the day to ensure consistent intake. The overall duration of the feeding period was 30 days. Upon obtaining informed consent from the patients, blood samples were collected on days 1 and 31. These samples were promptly processed for further analysis immediately after collection in the hospital laboratory. On day 1 and day 31, fasting blood samples were collected from the participants and subjected to analysis for various parameters, including sodium (Na), potassium (K), chloride (Cl), ALT, AST, ALP, urea, and creatinine concentrations using a clinical analyzer and appropriate kits. The data obtained were compiled and subjected to statistical analysis including descriptive and one-way analysis of variance. The data was expressed as mean±SD and the difference in the means was ascertained at a 95 % confidence interval ($p<0.05$).

Results

The effect of spices and herbs on electrolyte levels (Na, K and Cl), blood urea, creatinine, liver enzymes (ALT, AST and ALP), fasting blood glucose (FBG), and lipid profiles were determined. Table 1 presents the impact of consuming spices and herbs on various biochemical parameters in T2DM. It includes data on electrolytes (Na, K and Cl), urea, creatinine, and liver enzymes (ALT, AST and ALP). The data shows the mean±SD values along with the significance effect and percentage before and after consuming the three different doses of spices and herbs. Additionally, the normal ranges for each parameter were presented in Table 1 and Table 2. Urea level decreased after consuming spices and herbs, with higher doses leading to more reduction. The highest dose showed a substantial decline when compared to the normal range.

Generally, there was a healthier change in the sodium levels after consuming spices and herbs across the three doses. There was a decrease in potassium level after consuming spices and herbs, with higher doses causing a more pronounced

Table 1: Effect of consuming spices and herbs on average and percentage increase or decrease observed in electrolytes, urea, creatinine, and liver enzymes in T2DM patients.

Variable	2 Gram		4 Gram		6 Gram		*P* value	Normal Range
	Before (Mean±SD)	After (Mean±SD)	Before (Mean±SD)	After (Mean±SD)	Before (Mean±SD)	After (Mean±SD)		
Urea	6.02±2.33	4.81±1.37	18.3±42	5.03±1.63	4.16±0.80	3.98±0.68	0.290	36–142 mEq/L
Na	138±5.3	136±4.1	126±2.9	139±3.2	125±43	138±5.4	0.226	3.5–5.0 mEq/L
K	4.36±0.47	4.24±0.62	13.78±0.65	3.93±31	14.0±32	4.27±0.22	0.166	96-106 mEq/L
Cl	101±4.23	101±5.3	97± 17	104±4.0	99±9	102±4.9	0.303	53-97.2 µmol/L
Cr	98±36.8	97±34.1	72± 32.5	91±34	86±22	82±25	0.561	8–23 mg/dL
ALT	22±8.66	26.6±10	28.4±16	27±16	34±17	24±14	0.701	10–40 U/L
AST	22.7±8.25	27±12	29 ± 14	26±9	30±19	25.0±10.9	0.579	10–30 U/L
ALP	87±24	82±27	95± 25	83±1	88±28	82±23	0.298	30–120 IU/L

Na: sodium, K: potassium, Cl: chloride, Cr: creatinine, AST: aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: alkaline phosphatase.

Table 2: Summary of the effect of mixed spices and herbs on kidney and liver function.

Variable	2 Gram/Day	4 Gram/day	6 Gram/day
	% Increase or decrease	% Increase or decrease	% Increase or decrease
Na	-1.09	10.16	10.05
K	-2.66	-71.48	-7071
Cl	0.10	5.20	1.71
Creatinine	-0.20	25.52	-6.69
Urea	-20.08	-72.51	-4.40
ALT	23.53	-5.99	-21.92
AST	19.43	-11.26	-21.52
ALP	-6.07	-11.96	-2.15
FBG	-16.92	5.91	-15.60
2HPP	-20.08	0.80	-17.90
HbA1C	1.29	-1.14	-1306
TL-C	-3.93	-0.08	-10.08
LDL-C	-17.38	4.26	-17.38
HDL_C	22.59	-5.53	11.12
TG	27.36	-27.42	-17.53

Na: sodium, K: potassium, Cl: chloride, AST: aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: alkaline phosphatase, FBG: fasting blood glucose, 2HPP: 2 hours postprandial, HbA1C: HemoglobinA1C, TL-C: total cholesterol, LDL-C: low-density lipoprotein cholesterol, HDL-C: high-density lipoprotein cholesterol, TG: triglycerides

Table 3: Effect of consuming spices and herbs on average and percentage of increases or decreases in FBG, 2HPP blood glucose, and lipid profile in T2DM patients.

Variable	2 Gram		4 Gram		6 Gram		*P* value	Normal range
	Before (Mean±SD)	After (Mean±SD)	Before (Mean±SD)	After (Mean±SD)	Before (Mean±SD)	After (Mean±SD)		
FBG	8.39±5.08	6.97±2.98	7.29±2.43	7.72±3.28	8.40±2.62	7.09±1.73	0.345	<5.60 mmol/L
2HPP	12.90±6.25	10.31±4.93	12.51±4.01	12.61±4.53	11.93±4.16	9.79±4.30	0.233	<7.80 mmol/L
HbA1c	7.46±1.18	7.56±1.12	7.92±1.96	7.83±1.50	8.84±2.18	7.69±1.63	0.418	<5.70%
TL-C	5.09±1.03	4.89±1.23	4.88±0.72	4.88±1.29	4.96±0.85	4.46±0.65	0.370	3.0-6.40 mmol/L
LDL-C	3.16±0.81	2.61±0.64	2.68±0.76	2.79±1.22	2.78±0.58	2.59±0.54	0.365	2.3-4.40 mmol/L
HDL-C	1.14±0.22	1.40±0.24	1.30±0.33	1.23±0.28	1.19±0.37	1.32±0.46	0.258	0.90-1.50 mmol/L
TG	1.85±1.01	2.36±1.96	2.06±0.93	1.50±0.63	2.04±1.06	1.68±0.65	0.065	0.70-1.55 mmol/L

T2DM: Type 2 diabetes mellitus; FBG: Fasting blood glucose; 2HPP: 2 hours postprandial; HbA1C: HemoglobinA1C; TL-C: Total cholesterol; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; TG: Triglycerides.

decrease; but not significantly due to larger intra- and extra-group standard deviations. The decrease was particularly substantial for the higher doses in some of the patients. Chloride level showed similar effects, with some doses causing an increase; while others resulted in a decrease. Overall, the changes were relatively insignificant compared to the normal range. Creatinine level demonstrated normalizing effects with the doses of 2, 4, and 6 gram causing a slight decrease or increase. The 6 gram dose resulted in a notable decrease, but overall, the changes were insignificant compared to the normal ranges which might be clinically significant; but the difference was not statistically significant. The liver enzyme namely of AL, AST and ALP were not affected and were within the normal range (Table 1 and 2). Table 2 presents the average values before and after consuming different doses of spices and herbs, along with the percentage of increases or decreases. Additionally, it provides the normal values for each parameter as reference.

Table 3 summarizes the effect of consuming spices and herbs on various parameters related to blood glucose and lipid profile in the T2DM patients including fasting blood glucose (FBG), 2 hours postprandial (2HPP) blood glucose, and lipid profile indicators such as total cholesterol (TL-C), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG). There was a notable decrease in FBG concentration after consuming spices and herbs, with higher doses leading to more reductions. The percentage of the decrease in FBG level indicated the effectiveness of the treatment. Normal FBG values were given for reference, to achieve concentrations below 5.60 mmol/L for optimal control. Like FBG,

Table 3 presents the mean and SDs for 2HPP blood glucose level before and after consuming spices and herbs. There was a decrease in 2HPP blood glucose concentration after treatment, especially with 6 gram dose of spices and herbs. The percentage of the decrease in 2HPP blood glucose concentration illustrates the effectiveness of the treatment (Table 2 and Table 3). The mean HbA1c concentration before and after treatment with spices and herbs showed a decrease in HbA1c concentration after treatment with higher doses leading to more reductions (Table 2 and Table 3). The reason for the insignificance can be due to larger standard deviations recorded in the individual patients.

The actual concentration for the blood in Table 3 and the percent changes were presented in Table 2. Table 3 represents the mean concentration of TL-C, LDL-C, HDL-C, and TG before and after treatment with spices and herbs. For TL-C and LDL-C, there were decreases in concentrations after treatment, with higher doses leading to more reductions; but were not statistically significant. HDL-C concentration revealed varying effects, with some doses causing an increase and others resulting in a decrease. TG concentration decreased after treatment, especially with higher doses of spices and herbs.

Percentage changes were exhibited in table 2 displaying the potential beneficial effects of consuming spices and herbs on blood glucose and lipid profile parameters in T2DM patients, with higher doses generally leading to more pronounced improvements (Table 2). However, none of the identified changes were significant due to larger variation among the individual patients. Overall, the consumption of mixed spices and herbs appears to have a beneficial impact on kidney and liver function, as well as blood glucose and lipid profile parameters in T2DM patients, with some variations in the effects observed across different doses.

Discussion

The observed effect of the administered doses of mixed spices and herbs on various blood parameters is noteworthy for the implications. Spices and herbs have been studied for their potential roles in managing blood glucose concentration, particularly in individuals with T2DM. The potential mechanisms by which certain spices and herbs may help in the control of blood glucose in T2DM are complex and may involve multiple pathways. Some of the proposed mechanisms that control blood glucose include improvement in T2DM are (i) insulin sensitivity, (ii) inhibition of carbohydrate digestion and absorption, (iii) anti-inflammatory effects, (iv) antioxidant properties, (v) stimulation of glucose uptake, (vi) regulation of enzymes involved in glucose metabolism, (vii) affecting gut microbiota, and (viii) enhancement of beta-cell function. Improved insulin sensitivity means that cells respond more effectively to insulin, facilitating better glucose uptake and utilization (25).

Some herbs may slow down the digestion and absorption of carbohydrates. This can lead to a more gradual rise in blood glucose concentration after meals, helping to maintain better glycaemic control. This happens possibly by inhibiting key carbohydrate hydrolyzing enzymes (26). Similarly, chronic inflammation is associated with insulin resistance, a key factor in T2DM; while spices contain anti-inflammatory compounds such as curcumin, which may help mitigate inflammation and improve insulin sensitivity (27). The herbs and spices are rich sources of antioxidants, which can neutralize free radicals and reduce oxidative stress (28). Oxidative stress has been linked to an impaired insulin signalling and reduction (29). Therefore, spices and herbs may indirectly contribute to better blood glucose control. Some compounds found in herbs and spices, such as ginger, may stimulate glucose uptake by cells (30). Therefore, it can enhance glucose utilization and reduce its concentration in the bloodstream (31).

Another possibility could be to the effect on enzyme activities involved in glucose metabolism. For example, compounds in garlic have been studied for their potential to modulate enzymes related to insulin function and glucose utilization (32). Some herbs and spices may influence the composition and activity of gut microbiota (33). The gut microbiome plays a role in metabolic health, and changes in its composition could impact glucose metabolism. Compounds in certain herbs may support the health and function of beta cells, promoting insulin secretion and improving overall glucose control (34).

It is important to note that the evidences supporting the effects of spices and herbs on blood glucose control is still evolving, and not all studies show consistent results. Additionally, individual responses can vary, and these natural remedies should be considered as part of an overall diabetes management plan. While the correlations between the doses and FBS, PPBS, and HbA1c were modest, indicating a trend toward improved glycemic control with higher doses. The negative associations between the doses and TC and LDL-c hold significant promise. As mentioned earlier, higher concentrations of TC and LDL-C are recognized as crucial risk factors for cardiovascular diseases, which commonly accompany T2DM. The pronounced negative correlations between the doses of spices and herbs and these lipid markers suggest a potential role in mitigating cardiovascular risk factors, presenting a multifaceted approach to managing T2DM complications (34).

However, the relatively weaker negative correlation between the doses and TG warrants further exploration. It prompts the need for more extensive research to unravel the varying effects of these spices and herbs on distinct lipid markers and discern the specific components responsible for these observed effects. Certain spices and herbs have been studied for their potential benefits in controlling blood lipids, including cholesterol and TG concentrations (35).

The mechanisms by which these natural compounds may exert lipid-lowering effects are multifaceted and include (i) the inhibition of cholesterol absorption which is brought by the interference with the absorption of cholesterol in the intestine. For example, compounds found in spices and herbs may inhibit the absorption of dietary cholesterol, leading to lower concentrations in the bloodstream (35). (ii) Causing excretion of cholesterol which is brought into effect by enhancing the excretion of cholesterol through bile acids. This can help lower the cholesterol concentration by reducing the amount of cholesterol reabsorbed in the intestine (36). (iii) The antioxidant activity of herbs and spices can neutralize free radicals and reduce oxidative stress, and oxidative stress can contribute to the oxidation of LDL cholesterol, and by reducing it, the compounds in spices and herbs may help prevent the formation of oxidized LDL, which is more harmful to blood vessels (37).

(iv) The mechanism by which these natural compounds may exert lipid-lowering effects can be by modulation of lipid metabolism enzymes and influencing the activity of enzymes involved in lipid metabolism (38), For instance, compounds in ginger have been studied for their potential to regulate enzymes that play a role in lipid synthesis and breakdown (39); (v) the anti-inflammatory effects, for example, chronic inflammation are associated with dyslipidaemia, while certain herbs have anti-inflammatory properties that may help reduce inflammation and improve lipid profiles (40); (vi) enhanced lipid clearance by improving insulin sensitivity, which, in turn, can enhance lipid clearance from the bloodstream, and an improved insulin sensitivity can lead to better utilization of lipids by cells (34, 35); (vii) the modulation of lipoprotein metabolism by the action of some spices and herbs may influence the production and metabolism of lipoproteins, including LDL and HDL. This change in the balance between these lipoproteins can contribute to healthier blood lipid profiles (35, 36); and finally (viii) by the regulation of TG synthesis and breakdown which happens due to the compounds in certain herbs, which may impact the synthesis and breakdown of TGs that help regulate TG concentration in the bloodstream. It is important to note that the effects of spices and herbs on blood lipids can vary among individuals, and more research is needed to establish consistent findings. These results prompt further investigation into the nuanced effects of the administered doses of spices and herbs on different lipid markers and their potential mechanisms of action.

Conclusion

This study sheds light on the potential efficacy of combinations of cloves, ginger, onion, lemongrass, coriander, curry leaves, holy basil, and bunching onion in improving blood glucose concentration and lipid profile among T2DM patients. The observed negative associations between the administered doses of these spices and herbs and various blood parameters emphasize their potential role in complementary or alternative approaches to manage T2DM. Further research is warranted to unravel their mechanisms of action and optimize their clinical utility.

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Authors' Contribution

This research was conducted under the supervision of M.M.A.K.K, who provided intellectual guidance, oversight, and critical insights throughout the project. N.A.M.S was the co-supervisor, offering valuable support and direction in refining the study's design and execution. T.M played a crucial role in data collection, meticulously gathering clinical data from the hospital while ensuring effective patient management. Q.A and M.R contributed significantly to data analysis, the scholarly composition of the manuscript, and its final proofreading.

Conflict of Interest

None declared.

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