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Original Article

The Efficacy of a Combination of *Cinnamomum zeylanicum, Tribulus terrestris, Silybum marianum*, and *Trigonella foenum-graecum* as the Treatment of Type II Diabetes Mellitus: A Double-Blinded, Randomized Clinical Trial

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Abstract

Introduction: The best oral medication for type II diabetes mellitus (T2DM), metformin, and other T2DM medications have noticeable side effects. However, herbal medications are potential emerging treatments. Thus, this clinical study evaluated the efficacy of a combination of *Cinnamomum zeylanicum*, *Tribulus terrestris*, *Silybum marianum*, and *Trigonella foenum-graecum* in treating T2DM.

Methods: This randomized clinical trial was performed on 50 T2DM patients with hemoglobin A1c (HbA1c) ≥ 6.5% and fasting blood sugar (FBS) ≥ 126 mg/dL who only used metformin as T2DM medication in Imam-Reza Hospital, Mashhad, Iran, in 2017. They were randomly divided into intervention (n = 25) and control (n = 25) groups. Sealed envelopes were used to blind patients and researchers. Patients were requested to take one capsule twice a day before lunch and dinner for a period of two months. Then, serum HbA1c, FBS, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride (TG), aspartate transaminase (AST), alanine transaminase (ALT), blood urea nitrogen (BUN), and creatinine were examined at the beginning of the study and two months later.

Results: Seven subjects in the control group were lost during the follow-up. Eventually, 43 patients were evaluated. Twenty-five (58.10%) participants were women, and the mean age of the study population was 57.56 ± 10.51 years old. In the intervention group, FBS was 175.04 ± 34.42 mg/dL before treatment and reached 138.40 ± 26.17 mg/dL after two months ($P = 0.00$). Similarly, HbA1c, cholesterol, LDL, TG, AST, ALT, and BUN were significantly decreased after the intervention, while HDL increased ($P = 0.00$). Creatinine, however, demonstrated no significant change. None of the other measured parameters showed a significant difference in the control group after two months ($P > 0.05$).

Conclusion: The suggested herbs could successfully control the glycemic and lipid profiles of T2DM.

Keywords: Type 2 diabetes mellitus, *Cinnamomum zeylanicum*, *Tribulus terrestris*, *Silybum marianum*, *Trigonella foenum-graecum*

Introduction

Diabetes mellitus (DM) is one of the most serious health problems worldwide. It is defined as a group of metabolic disorders in the regulation of blood sugar. This disorder has two main types. T1DM is due to insulin secretion defects, and T2DM is associated with progressive insulin resistance in the liver and surrounding tissues, decreased beta cell mass, and insulin secretion defects. According to the International Diabetes Federation in 2017, 425 million people worldwide had DM, and this number will reach 629 million by 2045. Population aging, economic development, urbanization, and unhealthy diets are some of the reasons for this upsurge.[1] Moreover, DM leads to macrovascular (e.g., coronary heart disease and stroke) and microvascular (e.g., end-stage renal disease, retinopathy, neuropathy, and lower limb amputation)

complications. With timely treatment, acute and chronic complications of DM are to some extent preventable, and the impact of DM on the healthcare system and patients' quality of life can be reduced.[2] Currently, metformin is the most widely used and probably the best oral medication for T2DM. It improves the body's metabolic control by lowering the amount of glucose produced in the liver while increasing the sensitivity of muscle cells to insulin, consequently reducing the microvascular and macrovascular effects of diabetes. In addition to the benefits of metformin, it has several side effects, such as digestive problems (e.g., diarrhea, nausea, and indigestion), a feeling of metallic taste in the mouth, and reduced absorption of vitamin B12 and folic acid if taken for a long time.[3] Other medications for DM have similar side effects. Furthermore, different medications for DM decrease blood sugar with a variety of mechanisms, which become less effective over time. However, herbal medications for DM are potential treatments with fewer side effects, more acceptability among patients, and new mechanisms of lowering blood sugar.[4] Approximately 800 medicinal plants have been reported as anti-hyperglycemic, but the efficiency and safety of a small number of them have been proven.[5] In this regard, *Cinnamomum zeylanicum*,[6,7] *Tribulus terrestris*, *Silybum marianum*, and *Trigonella foenum-graecum*[8] are among the most investigated herbs.

Additionally, it has been shown that the combination of two herbs, such as *C. zeylanicum* and *T. foenum-graecum*, improves hyperglycemia, and the combination of several plants, including *T. foenum-graecum*, *T. terrestris*, *Terminalia chebula*, and *Terminalia bellerica*, can synergistically reduce fasting blood sugar (FBS) and hemoglobin A1c (HbA1c) while improving hyperglycemia.[9]

Therefore, this double-blinded, randomized clinical trial study aims to investigate the effect of the combination of four well-known herbal medications for the treatment of T2DM, namely, *C. zeylanicum*, *T. terrestris*, *S. marianum*, and *T. foenum-graecum*.

Material and Methods

Preparing Herbal Compound

The *C. zeylanicum* roots, *Tribulus Terrestris* fruit, *S. marianum* seeds, and *T. foenum-graecum* seeds were purchased from Zojaj Darman Toos Company (Mashhad, Iran) and identified by Mohammad Sadegh Amiri (Department of Biology, Payame Noor University, Tehran, Iran). Overall, 300 mg of tribulus fruit, 300 mg of fenugreek seeds, 300 mg of cinnamomum roots, and 200 mg of silybum seeds were used in this study. These herbal materials were separately powdered and then equally mixed to prepare 250 mg capsules.

Standardizing the Herbal Compound

The increasing interest in herbal drugs requires strict quality control and safety assessments. The disintegration test was performed based on the < 701 > method in USP 40.

Other tests were performed on a diabetes capsules, such as Loss on drying, which is a common method to determine the amount of volatile matter inside a chemical substance, and the validated reversed-phase high-performance liquid chromatography test, which is the method to quantify trigonellin, the bioactive compound of *T. foenum-graecum*.

Appendices 1 and 2 show the high-performance liquid chromatogram of the sample after 3 and 6 months, detected by a photodiode array detector. In addition, microbial examinations based on USP 43 were evaluated for diabetes capsules.

Study Design

This double-blind, randomized controlled trial study was registered in the Iranian Registry of Clinical Trials, a primary registry in the World Health Organization registry network (IRCT20090811002330N2).

Ethics Declaration

All patients filled out written informed consent forms. It should be noted that patients were not charged for the capsules, visits, and laboratory tests. Further, this study was approved by the Ethics Committee of Mashhad University of Medical Sciences [ethical code IR.MUMS.REC.1396.230].

Participants

A total of 50 patients with diagnosed T2DM referred to Imam Reza Hospital of Mashhad, Iran, were enrolled in our study. The criteria for diagnosing diabetes were HbA1c ≥ 6.5% and FBS ≥ 126 mg/dL. Only patients treated with metformin as a diabetes medication were included in the investigation. There were no exclusion criteria, except for allergic reactions to herbal compounds.

The participants were randomly divided into intervention and control groups using computer-generated random numbers. Both groups received metformin, while the intervention group received a herbal compound in addition to metformin. Moreover, sealed envelopes with assigned codes were used to blind the patients and researchers.

Interventions

Patients were instructed to take one capsule twice a day, one hour before lunch and dinner for two months. The capsules in the intervention group contained 250 mg of the dried and several powdered herbs, including *C. zeylanicum*, *T. terrestris*, *S. marianum*, and *T. foenum-graecum*. The control group took placebo capsules in the same manner. The placebo capsules looked identical but contained cellulose powder. Both capsules were provided by Exir Gol Sorkh Company, Mashhad, Iran. Seven subjects in the control group did not return for the second evaluation. Thus, 43 patients were ultimately evaluated in this study.

Outcomes

Blood samples were obtained at the baseline and two months after starting the intervention. Next, HbA1c, FBS, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride (TG), aspartate transaminase (AST), alanine transaminase (ALT), blood urea nitrogen (BUN), and creatinine were examined.

Statistical Analysis

The data were analyzed using SPSS software, version 20 (SPSS Inc., Chicago, IL). The Wilcoxon test, Mann-Whitney U test, and paired T-test were utilized for analysis, and P-values < 0.05 were considered statistically significant.

Results

Fifty subjects were enrolled in our study. Seven subjects in the control group were lost during the follow-up and were excluded accordingly. Eventually, 43 patients underwent investigation. There was no significant difference in the case of demographic characteristics between the two groups ($P > 0.05$, Table 1). Twenty-five (58.10%) participants were women. In addition, the mean age of the study population and the mean body mass index of patients were 57.56 ± 10.51 years old and 28.81 ± 2.44, respectively. Furthermore, fourteen participants (32.56%) reported a positive family history of DM.

Table 1. Demographic Characteristics of Participants

	Intervention	Control	Total
Gender			
Male	12	6	18 (41.86)
Female	13	12	25 (58.14)
Family history			
Yes	7	7	14 (32.56)
No	18	11	29 (67.44)
Age (year) (mean)	58.64	56.06	57.56
Weight (kg) (mean)	78.80	77.72	78.53
BMI (kg/m^2) (mean)	29.00	28.56	28.81
Duration of disease (year) (mean)	3.88	4.16	4.04

Note. BMI: Body mass index.

Serologic Parameters

Table 2 presents the serologic parameters at the beginning and after 2 months of treatment. In the intervention group, the mean FBS was 175.04 ± 34.42 mg/dL before treatment and reached 138.40 ± 26.17 mg/dL after two months, which is significantly different ($P = 0.00$). Similarly, Hba1c, cholesterol, LDL, TG, AST, ALT, and BUN were significantly decreased after the intervention while HDL represented an increase ($P = 0.00$). Creatinine, however, demonstrated no significant change. In comparison, in the control group, FBS was 185.28 ± 70.67 mg/dL before treatment and reached 184.33 ± 65.198 mg/dL after two months of treatment ($P > 0.05$). Likewise, none of the other measured parameters showed a significant difference in the control group after two months ($P > 0.05$). Additionally, the Mann-Whitney test revealed that changes in FBS and Hba1c in the intervention group were significantly different compared to the control group ($P = 0.00$).

Analysis Report

The laboratory analysis report (Figure 1) focuses on a new diabetes capsule that has shown hopeful results in disintegration tests and has been proven to be free of bacterial contamination.

Side Effects

No severe adverse events (e.g., hospitalization) were reported, though minor side effects (e.g., gastrointestinal discomfort) were not systematically tracked.

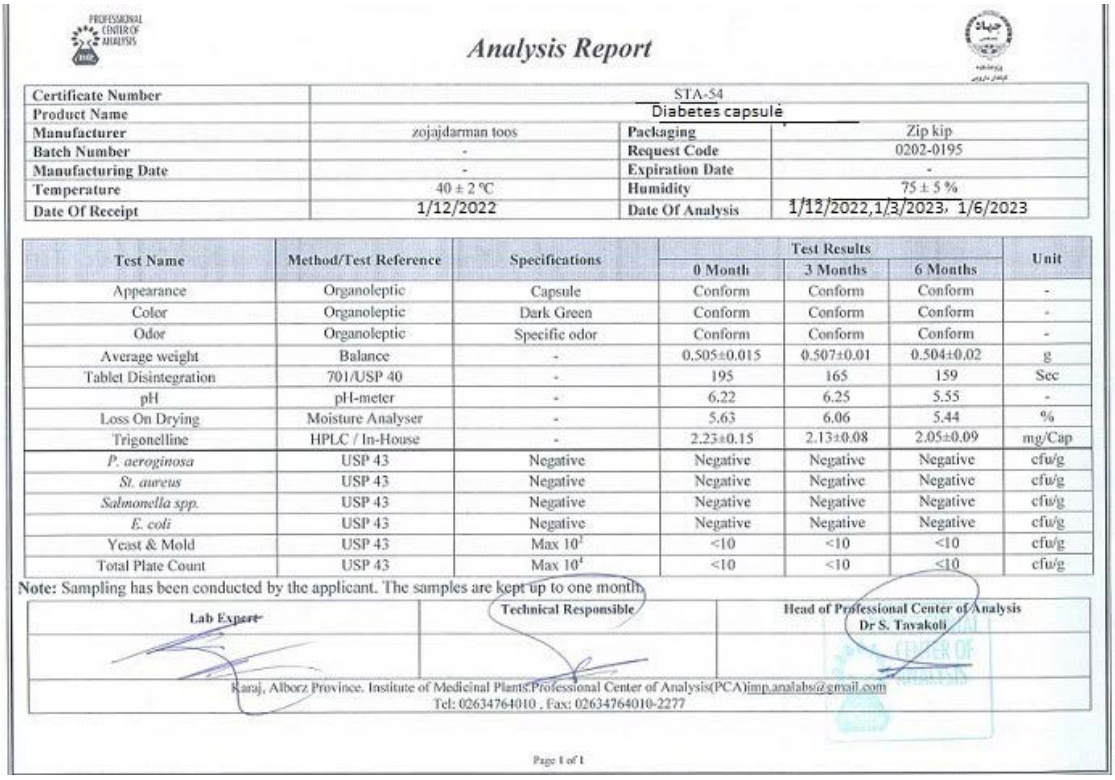
Discussion

Our findings revealed that a combination of *C. zeylanicum*, *T. terrestris*, *S. marianum*, and *T. foenum-graecum* could successfully lower FBS and HbA1c of T2DM patients. It also controlled the lipid profile and BUN and lowered the

Table 2. The Serologic Parameters at the Beginning and After 2 Months of the Study

	Intervention			Control		
	Baseline	After 2 Months	*P* Value	Baseline	After 2 Months	*P* Value
FBS (mg/dL)	175.04	138.40	0.00	185.28	184.33	0.95
Cholesterol (mg/dL)	246.72	201.20	0.00	189.39	194.94	0.50
LDL (mg/dL)	151.84	130.60	0.00	115.28	122.11	0.33
HDL (mg/dL)	50.20	55.64	0.00	45.72	47.22	0.50
Triglyceride (mg/dL)	292.76	237.40	0.00	181.44	165.61	0.44
ALT (U/L)	23.44	19.60	0.00	17.72	19.39	0.15
HbA1c (%)	8.00	7.00	0.00	8.00	8.100	0.39
AST (U/L)	23.00	20.00	0.00	18.50	20.00	0.93
BUN	20.00	19.00	0.01	16.50	16.65	0.33
Creatinine	0.96	0.96	0.70	0.92	0.92	0.78

Note. Significance for FBS, cholesterol, LDL, HDL, triglyceride, and ALT (normally distributed variables) was calculated using a paired t-test, and data are presented as means. Significance for HbA1c, AST, BUN, and creatinine (not normally distributed variables) was computed using the Wilcoxon test, and the data are provided as medians.



Analysis Report

Certificate Number	STA-54		
Product Name	Diabetes capsule		
Manufacturer	zojajdarman toos	Packaging	Zip kip
Batch Number	-	Request Code	0202-0195
Manufacturing Date	-	Expiration Date	-
Temperature	40 ± 2 ℃	Humidity	75 ± 5 %
Date Of Receipt	1/12/2022	Date Of Analysis	1/12/2022,1/3/2023, 1/6/2023

Test Name	Method/Test Reference	Specifications	Test Results			Unit
			0 Month	3 Months	6 Months	
Appearance	Organoleptic	Capsule	Conform	Conform	Conform	-
Color	Organoleptic	Dark Green	Conform	Conform	Conform	-
Odor	Organoleptic	Specific odor	Conform	Conform	Conform	-
Average weight	Balance	-	0.505±0.015	0.507±0.01	0.504±0.02	g
Tablet Disintegration	701/USP 40	-	195	165	159	Sec
pH	pH-meter	-	6.22	6.25	5.55	-
Loss On Drying	Moisture Analyser	-	5.63	6.06	5.44	%
Trigonelline	HPLC / In-House	-	2.23±0.15	2.13±0.08	2.05±0.09	mg/Cap
P. aeroginosa	USP 43	Negative	Negative	Negative	Negative	cfu/g
St. aureus	USP 43	Negative	Negative	Negative	Negative	cfu/g
Salmonella spp.	USP 43	Negative	Negative	Negative	Negative	cfu/g
E. coli	USP 43	Negative	Negative	Negative	Negative	cfu/g
Yeast & Mold	USP 43	Max 10^2	<10	<10	<10	cfu/g
Total Plate Count	USP 43	Max 10^4	<10	<10	<10	cfu/g

Note: Sampling has been conducted by the applicant. The samples are kept up to one month.

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Page 1 of 1

Figure 1. Laboratory Analysis Reports of Diabetes Capsule

liver enzymes, AST and ALT.

Whether *C. zeylanicum* is effective in controlling the glycemic and lipid profiles of diabetic patients has been studied for many years. In general, most randomized controlled trials [7,10,11] and animal studies [12] have confirmed the positive effect of this plant. The effect of cinnamon on the lipid profile is not consistent in studies, and some studies have shown no positive effect of *C. zeylanicum* on lipid profile.[10] One clinical trial by Blevins et al demonstrated no difference in glycemic and lipid profiles after three months of using *C. zeylanicum* in non–insulin-dependent type 2 diabetes.[13] In this study, the baseline glycemic profile was lower than in our study and other similar studies .

Some molecular pathways of the effect of *C. zeylanicum* on glycemic control have been investigated. Anderson et al observed the insulin-like activity of cinnamon in vitro.[14] In this study, procyanidin type-A polymers were isolated from *C. zeylanicum* and characterized by nuclear magnetic resonance and mass spectroscopy. These water-soluble polymers increased the insulin-dependent breakdown of radiolabeled glucose to carbon dioxide by 20-fold. Another study by Qin et al found an enhanced insulin-signaling pathway in the skeletal muscle of rats treated with *C. zeylanicum*.[15]

In the study by Johnson et al, *S. marianum* displayed antioxidant properties in diabetic Wistar rats.[16] They reported a statistically significant decrease in blood glucose *in S. marianum*-treated rats as well as in the combined treatment of *S. marianum* and vitamin C. In the combined treatment of *S. marianum* and vitamin C, the activity of catalase, superoxide dismutase, and malonaldehyde enzymes significantly decreased compared with controls.

In a randomized controlled trial by Husseini et al, 200 mg silymarin (an active ingredient of *S. marianum*) tablet administrated 3 times a day significantly decreased HbA1c, FBS, total cholesterol, LDL, TG, AST, and ALT compared to placebo.[17]

Many animal studies have investigated the effect of *T. terrestris* extracts on complications of diabetes, especially sexual disorders, all confirming the glucose-lowering effect of these extracts.[18] For instance, in a study performed by Ghanbari et al on diabetic male Wistar rats, *T. terrestris*-treated rats, showed reduced blood glucose and increased sperm motility and sperm count. Seminiferous tubule diameter, percentage of sperms with normal morphology, level of testosterone, and final body weight, compared with the control diabetic group.[19] Similarly, Tag et al reported reduced oxidative stress levels and improved histological features in the testis of diabetic male Wistar rats treated with *T. terrestris* compared to those treated with metformin. In addition, they observed improved serum lipid profiles in these rats.[20] Likewise, Amin et al focused on the antioxidant properties of *T. terrestris*. In their study on diabetic male Wistar rats, *T. terrestris* extract significantly decreased the levels of serum ALT and creatinine. It further lowered the malondialdehyde but increased glutathione in the liver. Moreover, a significant recovery of the liver was observed in histopathological examinations.[21]

T. foenum-graecum is another well-investigated herb, and many studies have shown its anti-oxidative and anti-hyperglycemic effects. A study by Devi et al assessed the effect of supplementation of fenugreek leaves in

diabetic rats. Fenugreek showed a significant effect on hyperglycemia, hyperinsulinemia, and glycosylated hemoglobin. Their results revealed improved body weight and liver glycogen but a significant decrease in glucose 6-phosphatase, fructose-1,6-bisphosphatase, and hexokinase in the liver and kidney of diabetic rats. t at a dose of 1.0 g/kg was similar to that of glibenclamide.[22]

In another similar study, fenugreek leaves lowered serum glucose and the lipid profile in diabetic rats.[23]

In this regard, Gupta et al conducted small randomized clinical trials on 25 diabetic patients. Based on their findings, fenugreek extract decreased FBS and LDL but increased HDL in the fenugreek extract group compared to placebo.[8]

As discussed earlier, a strong body of evidence supports the favorable effects of studied herbs for diabetic patients. However, these effects are mainly through lowering blood sugar, subsequently leading to the normalization of lipid profile and liver and kidney functions. Some studies suggest that these herbs might be directly involved in the improvement of lipid profile and decreasing oxidative stress . Further studies are needed to elucidate the exact mechanisms of the active ingredients of these herbs.

It should be noted that our findings may be subject to some limitations, most importantly the small sample size of the study. In addition, this study did not evaluate the use of each herb alone and relied on previous evaluations of those herbs. Unlike most other studies, this study used dried herb powders rather than their extracts. Our patients only used metformin, thereby minimizing the effect of using different drugs on the results and limiting the study's generalizability. Thus, future studies can address this issue.

Nonetheless, the studied herbs successfully controlled the glycemic and lipid profile of T2DM. These results further support the idea of using the studied herbs in the treatment of diabetic patients. These herbs have shown remarkable functions in controlling the complications of diabetes in addition to their anti-hyperglycemic effects, and this is while no significant side effect was observed in our study and all studies discussed here.

Although the results are promising, further studies with larger sample sizes should investigate whether this compound can be used as an independent treatment of T2DM.

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Not applicable.

Authors' Contribution
Conceptualization: Seyed Abbas Zojaji.
Data curation: Seyed Abbas Zojaji, Mohammad Reza Tabasiyan.
Formal analysis: Seyed Ali Ebrahimi, Mohammad Reza Tabasiyan.
Funding acquisition: Mokhtar Ahmadi, Seyed Hadi Mousavi, Ali Nakhaei.
Investigation: Mokhtar Ahmadi, Seyed Hadi Mousavi, Mahta Mirshojaiyan.
Methodology: Faegheh Zojaji, Mahta Mirshojaiyan.
Project administration: Faegheh Zojaji.
Resources: Seyed Ali Ebrahimi.
Software: Seyed Ali Ebrahimi, Sajjad Samieefar, Ali Nakhaei.
Supervision: Seyed Abbas Zojaji.
Validation: Elahe Karazhian and Ali Nakhaei.
Visualization: Elahe Karazhian and Mohammad Reza Tabasiyan.
Writing–original draft: Seyed Abbas Zojaji.
Writing–review & editing: Seyed Abbas Zojaji.

Competing Interests
The author(s) declare no competing interests.

Ethical Approval
This study was performed as a double-blind, randomized controlled trial, which was registered in the Iranian Registry of Clinical Trials, a primary registry in the WHO registry network (IRCT20090811002330N2).

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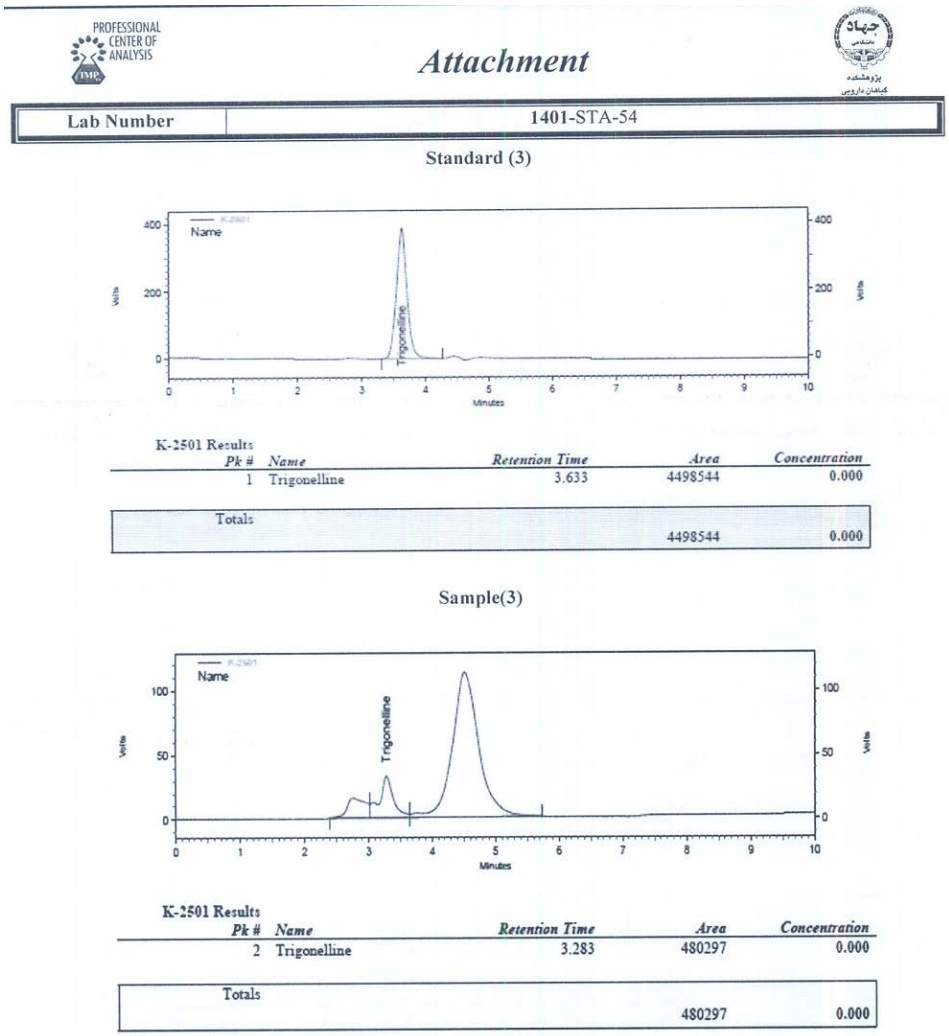
References
1. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol 2018;14(2):88–98. doi:10.1038/nrendo.2017.151
2. Harding JL, Pavkov ME, Magliano DJ, Shaw JE, Gregg EW. Global trends in diabetes complications: a review of current evidence. Diabetologia 2019;62(1):3–16. doi:10.1007/s00125-018-4711-2
3. Bailey CJ. Metformin: effects on micro and macrovascular complications in type 2 diabetes. Cardiovasc Drugs Ther 2008;22(3):215–24. doi:10.1007/s10557-008-6092-0
4. Ghorbani A, Rakhshandeh H. The most effective herbs for diabetes. *Mashhad: Mashhad University of Medical Sciences Publisher*. 2012:21-127 .
5. Sinha D, Dwivedi C, Dewangan M, et al. Anti diabetic potential of herbal plants and polyherbal formulation. *Int J Phytother Res*. 2014;4(3):28-49 .
6. Medagama AB, Bandara R. The use of complementary and alternative medicines (CAMs) in the treatment of diabetes mellitus: is continued use safe and effective? Nutr J 2014;13:102. doi:10.1186/1475-2891-13-102
7. Zare R, Nadjarzadeh A, Zarshenas MM, Shams M, Heydari M. Efficacy of cinnamon in patients with type II diabetes mellitus: A randomized controlled clinical trial. Clin Nutr 2019;38(2):549–56. doi:10.1016/j.clnu.2018.03.003
8. Gupta A, Gupta R, Lal B. Effect of Trigonella foenum-graecum (fenugreek) seeds on glycaemic control and insulin resistance in type 2 diabetes mellitus: a double blind placebo controlled study. J Assoc Physicians India 2001;49:1057–61.
9. Kassaee SM, Goodarzi M, Abbasi E. Antioxidant, antiglycation and anti-hyperlipidemic effects of Trigonella foenum and Cinnamon in type 2 diabetic rats. Jundishapur Journal of Natural Pharmaceutical Products 2018;13(1):e38414. doi:10.5812/jjnpp.38414
10. Akilen R, Tsiami A, Devendra D, Robinson N. Glycated haemoglobin and blood pressure-lowering effect of cinnamon in multi-ethnic Type 2 diabetic patients in the UK: a randomized, placebo-controlled, double-blind clinical trial. Diabetic Medicine 2010;27(10):1159–67. doi:10.1111/j.1464-5491.2010.03079.x
11. Crawford P. Effectiveness of cinnamon for lowering hemoglobin A1C in patients with type 2 diabetes: a randomized, controlled trial. J Am Board Fam Med 2009;22(5):507–12. doi:10.3122/jabfm.2009.05.080093
12. Mahmood S, Talat A, Karim S, Khurshid R, Zia A. EFFECT OF CINNAMON EXTRACT ON BLOOD GLUCOSE LEVEL AND LIPID PROFILE IN ALLOXAN INDUCED DIABETIC RATS.

Pakistan Journal of Physiology 2011;7(1):13–6. doi:10.69656/pjp.v7i1.766
13. Blevins SM, Leyva MJ, Brown J, Wright J, Scofield RH, Aston CE. Effect of cinnamon on glucose and lipid levels in non insulin-dependent type 2 diabetes. Diabetes Care 2007;30(9):2236–7. doi:10.2337/dc07-0098
14. Anderson RA, Broadhurst CL, Polansky MM, Schmidt WF, Khan A, Flanagan VP, et al. Isolation and characterization of polyphenol type-A polymers from cinnamon with insulin-like biological activity. J Agric Food Chem 2004;52(1):65–70. doi:10.1021/jf034916b
15. Qin B, Nagasaki M, Ren M, Bajotto G, Oshida Y, Sato Y. Cinnamon extract (traditional herb) potentiates in vivo insulin-regulated glucose utilization via enhancing insulin signaling in rats. Diabetes Res Clin Pract 2003;62(3):139–48. doi:10.1016/s0168-8227(03)00173-6
16. Johnson U, Nwangwa E, Igweh J. Anti-Oxidant Effects of Silybum marianum Extracts on Diabetic Wistar Rats. The Journal of Medical Research 2019;5(4):145–50. doi:10.31254/jmr.2019.5403
17. useini HF, Larijani B, Heshmat R, Fakhrzadeh H, Radjabipour B, Toliat T, et al. The efficacy of Silybum marianum (L.) Gaertn. (silymarin) in the treatment of type II diabetes: a randomized, double-blind, placebo-controlled, clinical trial. Phytotherapy Research 2006;20(12):1036–9. doi:10.1002/ptr.1988
18. Ștefănescu R, Tero-Vescan A, Negroiu A, Aurică E, Vari CE. A Comprehensive Review of the Phytochemical, Pharmacological, and Toxicological Properties of Tribulus terrestris L. Biomolecules 2020;10(5):752. doi:10.3390/biom10050752
19. Ghanbari A, Moradi M, Raoofi A, Falahi M, Seydi S. Tribulus terrestris Hydroalcoholic Extract Administration Effects on Reproductive Parameters and Serum Level of Glucose in Diabetic Male Rats. International Journal of Morphology 2016;34(2):796–803. doi:10.4067/S0717-95022016000200058
20. Tag H, Abdelrazek H, Yasmen S, El-Shenawy N. Efficacy of Tribulus terrestris extract and metformin on fertility indices and oxidative stress of testicular tissue in streptozotocin-induced diabetic male rats. African Journal of Pharmacy and Pharmacology 2015;9(48):1088–98. doi:10.5897/AJPP2015.4450
21. Amin A, Lotfy M, Shafiullah M, Adeghate E. The protective effect of Tribulus terrestris in diabetes. Ann N Y Acad Sci 2006;1084:391–401. doi:10.1196/annals.1372.005
22. Devi BA, Kamalakkannan N, Prince PS. Supplementation of fenugreek leaves to diabetic rats. Effect on carbohydrate metabolic enzymes in diabetic liver and kidney. Phytother Res 2003;17(10):1231–3. doi:10.1002/ptr.1357
23. Annida B, Stanely Mainzen Prince P. Supplementation of fenugreek leaves lower lipid profile in streptozotocin-induced diabetic rats. J Med Food 2004;7(2):153–6. doi:10.1089/1096620041224201



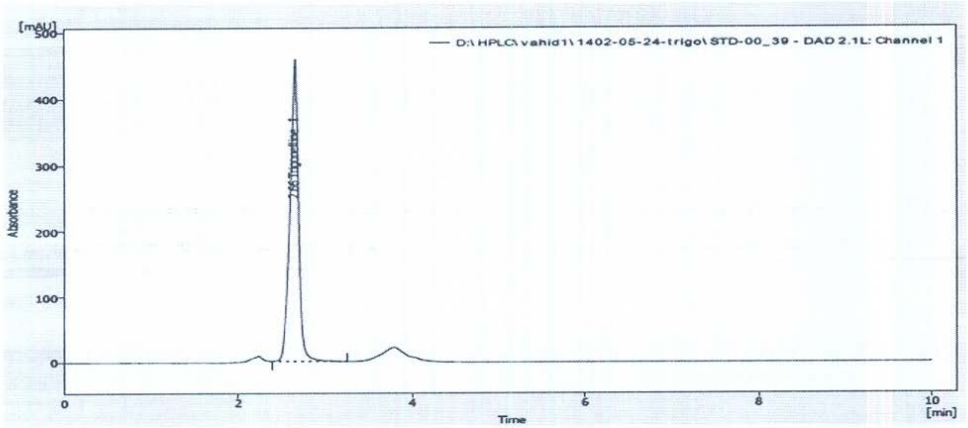
Appendix 1. HPLC Chromatogram of the Sample After 3 Months
Note. HPLC: High-performance liquid chromatography

PROFESSIONAL CENTER OF ANALYSIS

Attachment

Lab Number	1401-STA-54

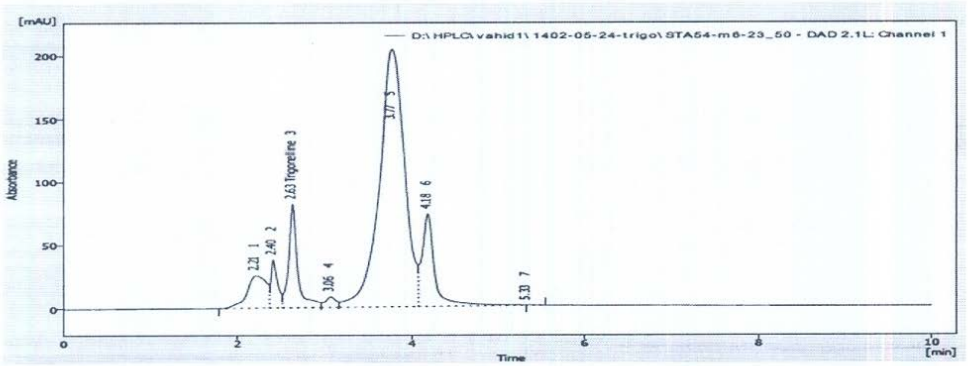
Standard (6)



Result Table (Uncal - D:\HPLC\vahid1\1402-05-24-trigo\STD-00_39 - DAD 2.1L: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	PDA Peak Purity	Compound Name	PDA Best Match
1	2.657	3088.515	457.411	100.0	100.0	0.10	962	Trigoneline	
	Total	3088.515	457.411	100.0	100.0				

Sample(6)



Result Table (Uncal - D:\HPLC\vahid1\1402-05-24-trigo\STA54-m6-23_50 - DAD 2.1L: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	PDA Peak Purity	Compound Name	PDA Best Match
1	2.208	391.446	25.160	6.4	5.9	0.26	957		
2	2.405	204.198	37.750	3.4	8.8	0.09	999		
3	2.628	577.327	81.558	9.5	19.0	0.09	977	Trigoneline	
4	3.065	72.550	8.313	1.2	1.9	0.18	994		
5	3.770	4093.643	203.388	67.2	47.4	0.29	957		
6	4.185	747.559	72.748	12.3	16.9	0.14	950		
7	5.333	2.233	0.356	0.0	0.1	0.14	999		
	Total	6088.956	429.273	100.0	100.0				

Appendix 2. HPLC Chromatogram of the Sample After 6 Months
Note. HPLC: High-performance liquid chromatography