ijlpr 2021; doi 10.22376/ijpbs/lpr.2021.11.4.P42-48

International Journal of Life science and Pharma Research

ISSN 2250 - 0480

Research Article

Chemistry for New drug discovery

Interactive Effect of Seeds of *Coriandrum Sativum L.* With Glimepiride in Streptozotocin-Induced Diabetic Rats

Uppuluri Spandana*[1,2], Adikay Sreedevi[1] and Kaveripakam Sai Sruthi[1]

1 Institute of Pharmaceutical Technology, Sri Padmavati Mahila Visvavidyalayam, Tirupati, A.P, India.
[2]Department of Pharmaceutical Chemistry, Nirmala College of Pharmacy, Atmakur, A.P, India.

Abstract: Diabetes mellitus is a serious and most prevailing glycemic disorder mainly managed by using allopathic medicines. Due to various side effects of allopathic drugs, till today medicinal plants were widely used in treating diabetes. Among them, spices like C*oriander sativum* L. play a prominent role in managing diabetes. Type-2 diabetic patients use oral hypoglycemic drugs and also follow herbal remedies. There is a probability of interactions when herb interferes with the drug action in the body. The aim of the present study was to assess the interaction of aqueous extract of seeds of *Coriandrum sativum* with oral hypoglycemic drug glimepiride in streptozotocin-induced diabetic rats. In the present study, animals were grouped into seven of six each. Group-I, Group-II, Group-III, Group-IV, Group-V, Group-VI, and Group-VII included normal control, glimepiride, *Coriandrum sativum*, diabetic control, diabetic animals treated with glimepiride, diabetic animals treated with *Coriandrum sativum, and* diabetic animals treated with glimepiride and *Coriandrum sativum, respectively*. Pharmacokinetic and pharmacodynamic interactions were studied. The animals treated with both *Coriandrum sativum* and glimepiride showed significant activity in pharmacokinetic parameters by increasing the levels of the maximum serum concentration (Cmax), Time taken to reach maximum serum concentration (Tmax) and Volume of distribution (Vd). Further pharmacodynamic studies showed promising hypoglycemic effects by decreasing blood glucose levels and ameliorating lipid profile compared with monotherapy of glimepiride or *Coriandrum sativum* treated in diabetes rats. The observations revealed that a significant herb-drug interaction occurred between *Coriandrum sativum* and glimepiride. In conclusion, *Coriandrum sativum* can elevate the bioavailability of glimepiride which seems to be beneficial in diabetic patients receiving glimepiride.

Keywords: *Coriandrum Sativum*, Glimepiride, Hypoglycemic Activity, Herb-Drug Interaction, HPLC

***Corresponding Author**

Uppuluri Spandana , Institute of Pharmaceutical Technology, Sri Padmavati Mahila Visvavidyalayam, Tirupati, A.P, India.

Recieved On 28 April 2021
Revised On 08 July 2021
Accepted On 10 July 2021
Published On 19 July 2021

Funding This research did not receive any specific grant from any funding agencies in the public, commercial or not for profit sectors

Citation Uppuluri Spandana, Adikay Sreedevi and Kaveripakam Sai Sruthi , Interactive Effect of Seeds of Coriandrum Sativum L. With Glimepiride in Streptozotocin-Induced Diabetic Rats.(2021).Int. J. Life Sci. Pharma Res.11(4), 42-48 http://dx.doi.org/10.22376/ijpbs/lpr.2021.11.4.P42-48

1. INTRODUCTION

The world population (approximately 70%) has been using medicinal herbs for chronic diseases, because of its active constituents. These herbs are becoming popular as alternative or complementary medicines worldwide. [1] Herb-drug interactions are a current topic of debate. [2] Herb- drug interaction studies have been described as a double-edged sword presenting both risks and benefits via unchanged therapeutic effect or reduced systemic exposure of the drug, resulting in lower side effects. Various herb-drug interaction studies have been carried out regarding antidiabetic activity. [3]Diabetes mellitus (DM) is a serious lifelong condition, characterized by hyperglycemia resulting directly from insulin resistance, inadequate insulin secretion, or excessive glucagon secretion. [4] Individuals with type 2 diabetes mellitus are helpless in the face of a variety of short- and long-term challenges, which can lead to death. [5] Diabetes mellitus is managed by using anti-hyperglycemic agents. [6]Glimepiride is a sulfonylurea agent; it stimulates release of insulin from pancreatic β-cells and may act via extra pancreatic mechanisms. It is administered to patients with type-2 Diabetes Mellitus in cases where glycemia is uncontrolled by diet and exercise alone, and used in combination with insulin in patients with secondary sulfonylurea failure[7]. The global use of complementary and alternative medicine for the management of diseases such as diabetes has rapidly increased day by day. Many reports revealed that up to 72.8% of people with diabetes used herbal medicines and dietary supplements (add reference). A large number of medicinal plants are believed to possess antidiabetic properties and have been utilized to manage diabetes. However, the concomitant usage of antidiabetic herbs and pharmaceutical medicines have raised safety concerns.[2] Unlike pharmaceutical medicines, where the ingredients are well defined and characterized, herbal medicine contains multiple bioactive components for which there is a lack of understanding of how these components interact with each other and with pharmaceutical medicines when taken in combination. There is a marked possibility of herbal components beneficially in enhancing or facilitating the action of antidiabetic pharmaceutical agents. Positive interactions between herbs and drugs may lead to enhanced effectiveness of the antidiabetic agents through additive or synergistic actions. [3]Coriander (Coriandrum *sativum L.*) is an Indian traditional herb belonging to the Umbelliferous/Apiaceous family. It was one of the earliest spices used by mankind. All parts of this herb are used as flavoring agents and/or as traditional remedies for the treatment of different disorders in the folk medicine systems The plant is a potential source of a multitude of bio-actives; a wide array of pharmacological activities has been ascribed to different parts of this herb. The seeds of *C. sativum* were reported for various pharmacological activities i.e., antioxidant activity, anticonvulsant activity, diuretic activity, cholesterol-lowering activity, anticancer activity, hepatoprotective activity, antimicrobial activity and antidiabetic activity. [8,9] Co-administration of *Coriandrum sativum* either intentionally or unintentionally with diabetic drugs may have possible interactions in diabetic conditions. Hence the present study is aimed to assess the pharmacokinetics (pk) and pharmacodynamic interactions (PD) of aqueous extract of *C. sativum* seeds with co-administration of glimepiride an oral hypoglycemic drug in streptozotocin (STZ) induced diabetic rats.

2. MATERIALS AND METHODS

2.1 Plant material

The *C. sativum* seeds were obtained from the local market of Mangalagiri, Guntur District, and authentication of Dr. P. Satyanarayana Raju, Department of Botany and Microbiology, Acharya Nagarjuna University.

2.2 Preparation of extract

C. sativum seeds were washed with water to remove the dust, after that these seeds were shade dried and were powdered using a mechanical grinder. The powder was subjected to aqueous extract by using the Soxhlet extraction method[10]

2.3 Phytochemical screening

The phytochemicals present in the aqueous extract of *C. sativum* were screened using standard qualitative tests. [11]

2.4 Animals

Sprague Dawley (SD) rats weighing 150 to 200g were purchased from Mahaveer Enterprises, Hyderabad, India, and used for the studies after obtaining permission from the Institutional animal ethical committee (CPCSEA Reg.No.018/IAEC/2017). The animals were housed in standard polypropylene cages and maintained under standard laboratory conditions (12h light/dark cycle; at an ambient temperature of 25 ± 5°C. The animals were fed with a standard rat pellet diet and water *ad libitum*.

2.5 Treatment protocol

Animals were divided into seven groups (n=6). Group-I, II and III were normal rats and Group-IV, V, VI and VII were served as diabetic rats. Diabetes was induced in these groups by a single intraperitoneal injection of freshly prepared streptozotocin (60mg/kg b.w.) dissolved in 0.1 M citrate buffer (pH 4.5). After 72 h, blood glucose level >250 mg/dL was considered as diabetic and used for further study. To study the herb-drug interactions, the following treatment protocols were followed:

Group-I: Normal control
Group-II: Administered with Glimepiride (1 mg/k.b.w.)
Group-III: Administered with Aqueous extract of seeds of *C. sativum* (400mg/k. b. w)
Group-IV: Diabetic control
Group-V: Diabetic rats treated with Glimepiride (1mg/k. b. w)
Group-VI: Diabetic rats treated with *C. sativum* dose (400mg/k. b. w)
Group-VII: Diabetic rats treated with *C. sativum* (400mg/k.b. w) + Glimepiride (1mg/k. b. w)

2.6 Pharmacokinetic studies

HPLC-UV (cyber lab-Rx1600) system was used for the investigation of pharmacokinetic study for this study, the time intervals were selected with commonly used strategies. Blood samples were collected from the retro-orbital vein using heparinized capillary tubes at time intervals of 0,0.25,0.5,1,2,3.,4.,6,8, 12, 24 hours after dose administration. Blood samples were centrifuged at 7500 rpm. These samples were analyzed using HPLC -UV method (analytical column C18 section (250x4.6mm id, 5µ). The flow rate was kept

constant at 1.5 ml/min, the run time was 7 mins, and the temperature was maintained at 50 ^{0}C. A mixer of phosphate buffer: acetonitrile: methanol (40:40:20) was used as the mobile phase with UV detection at 368 nm to detect glimepiride concentration. All concentrations were calculated from a standard curve of glimepiride.

2.7 *Pharmacodynamic studies*

Pharmacodynamic studies were carried out by collecting the blood samples of animals on the 1, 7, 14, and 21 days followed by estimation of blood glucose levels and body weight. Various other biochemical parameters such as TG, HDL, VLDL levels were also assessed using standard procedures.[12]

3. STATISTICAL ANALYSIS

The data was expressed as mean ± standard error. Mean values between the groups was considered statistically significant p<0.05 after analyzing by one way ANOVA and was compared using Tukey-Kramer multiple comparison tests

4. RESULTS

4.1 *Preliminary phytochemical screening*

The aqueous extract of seeds of *Coriandrum sativum* subjected to Preliminary phytochemical screening, it has disclosed the presence of flavonoids, carbohydrates, proteins, amino acids, fatty acids, alkaloids, tannins, saponins and terpenoids

4.2 *Pharmacokinetic studies*

The aqueous extract of *C. sativum* alters the pharmacokinetic parameters of glimepiride, by a significant increase of its AUC and C_{max}. The plasma GLM concentration versus time curve was plotted for calculation of PK parameters.

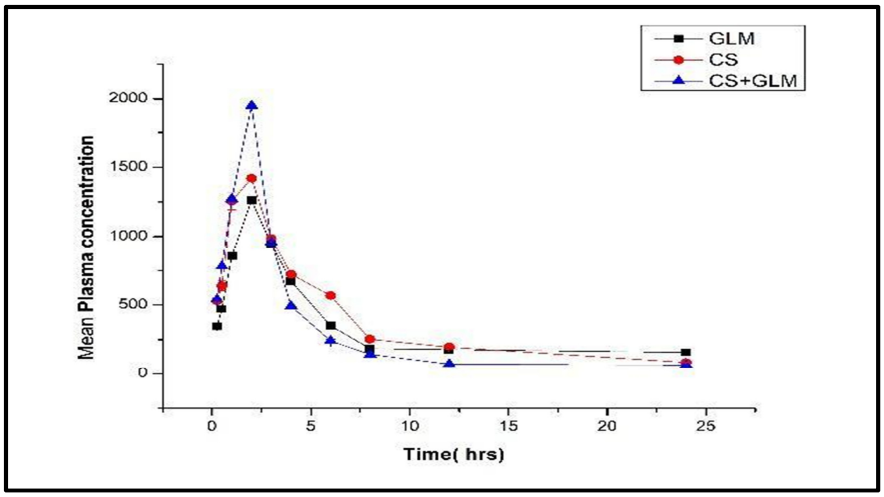


Fig 1: Mean serum concentration-time profile of Glimepiride, *C. sativum* and co-administration of Glimepiride + *C. sativum* in diabetic rats.

All the assessed pharmacokinetic parameters were presented in Table-1.

Table 1: Pharmacokinetic studies of Glimepiride with *C. sativum* in diabetic rats

Parameter	Glimepiride	*C. sativum*	Glimepiride with *C. sativum*
$C_{max(ng/ml)}$	1308.33±1.01	1938.33±0.01	1954.00±0.25*
$T_{max\ (h)}$	2	1	2
AUC $_{0\ to\ n(ng/ml*h)}$	5147.63±0.22	4077.88±1.10	5377.3±0.45*
AUC $_{total\ (ng/ml*h)}$	0.89±0.32	0.947864±0.25	0.654121±0.41*
AUMC	23576.85±0.21	12075.71±0.11	11470.12±0.11*
$t^{1/2}$(h)	2.25±0.21	2.36±1.12	2.98±0.45*
MRT $_{(h)}$	4.07±1.52	2.62±0.02	4.12±0.11*
$V_{d/F(ng/ml)}$	32.48±0.45	25.23±0.45	20.79±0.02*
Cl/F(mg/kg)/(ng/ml)/h	10.2±0.52	8.2±0.96	5.9±0.03*

All values are expressed as mean± SD (n=6)
****p<0.05 considered as significant when compared with Glimepiride***

4.3 *Pharmacodynamic studies*

In this pharmacodynamic study, various biochemical parameters were assessed on the day 1, 7, 14, and 21. Results have shown that, in diabetic control animals body weight was diminished significantly, whereas animals treated with standard and extract have exhibited a prominent increase in body weight. For assessment of diabetes mellitus, estimation of blood glucose levels is an essential parameter. After induction of diabetes by streptozotocin, blood glucose levels were found elevated. In the treatment groups which were administered by glimepiride and *C. sativum* individually and also in combination, the blood glucose levels were found decreased when compared with the diabetic control (Figure

2). HDL levels were significantly increased in treated groups and decreased in diabetic control groups. TG and VLDL were significantly decreased in treatment groups in comparison of diabetic control groups (Figure 3).

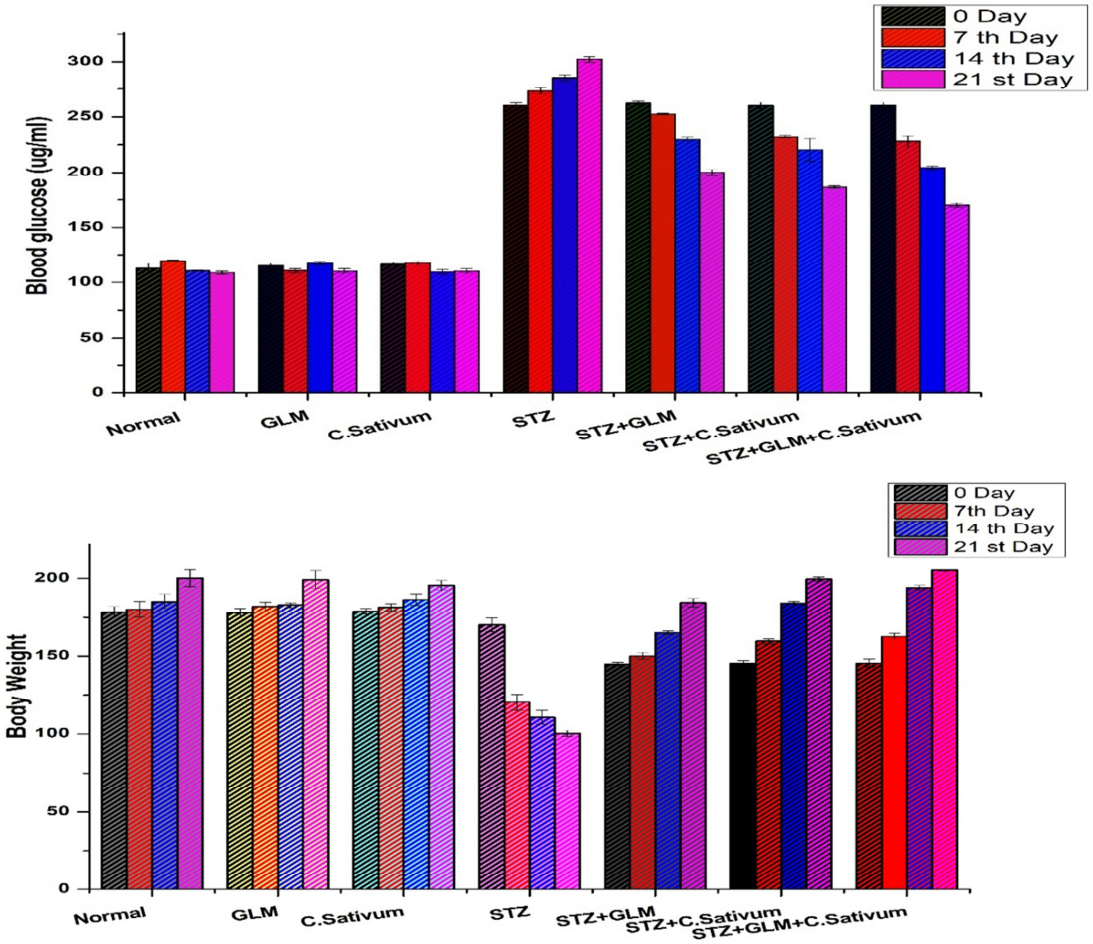
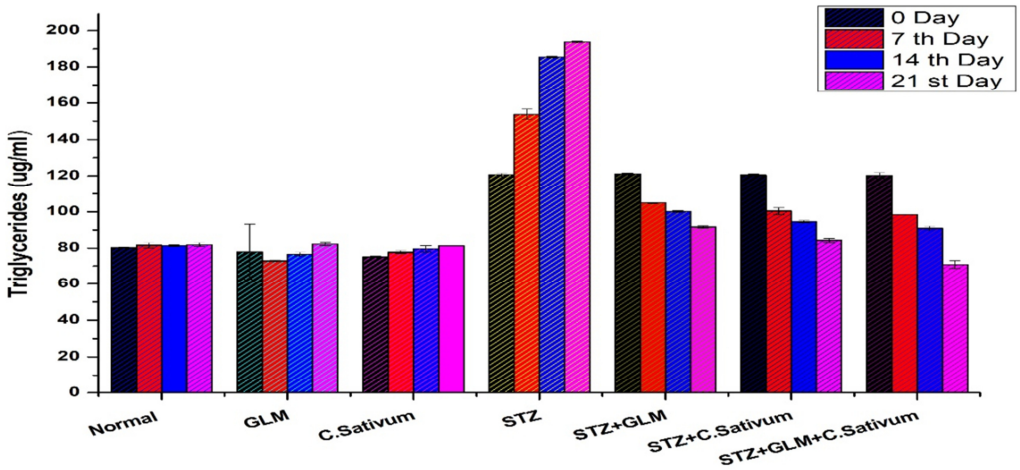


Fig 2: Effect on blood glucose and body weight



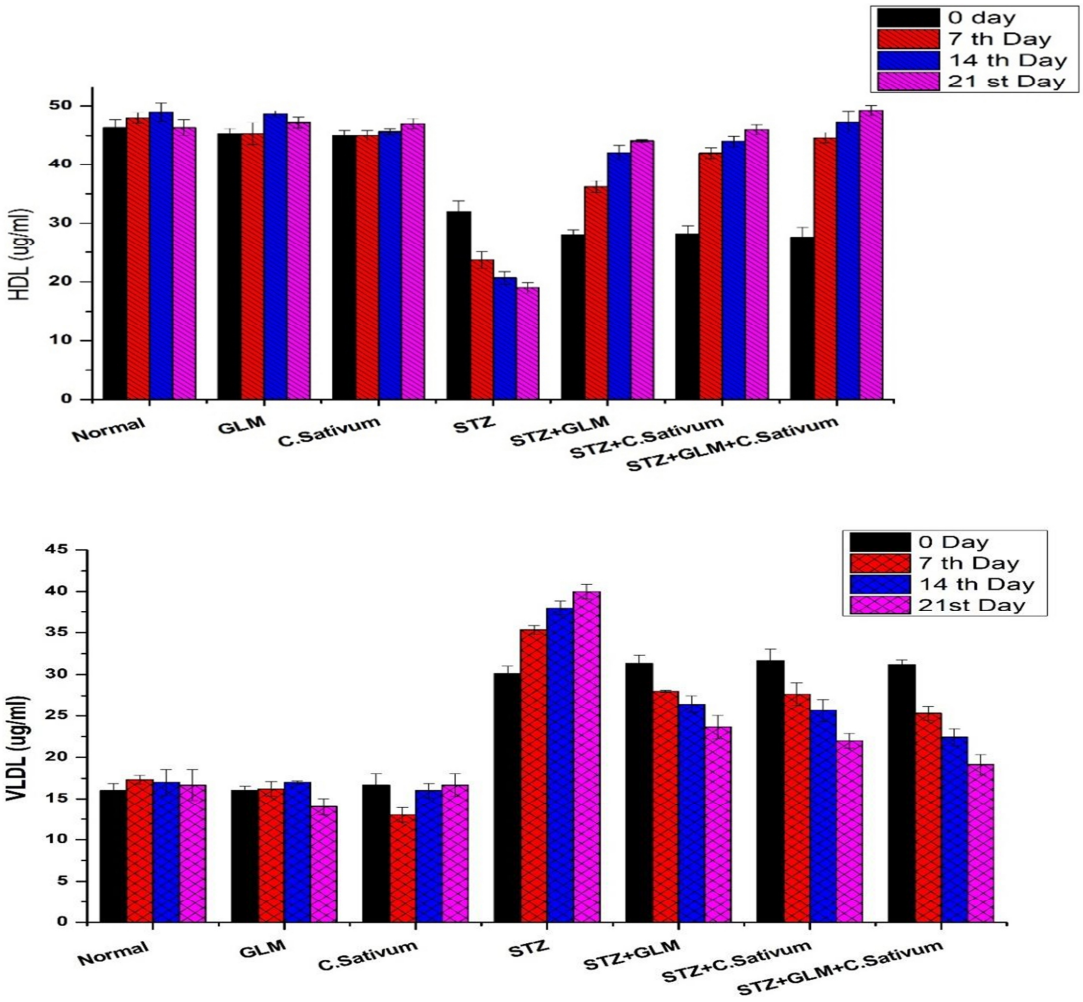


Fig 3: Effect on lipid profile

5. DISCUSSION

Diabetes is a group of metabolic disorders characterized by hyperglycemia resulting from deformities in insulin secretion, insulin action or both, this chronic disease is mainly managed by using oral hypoglycemics drugs.[13] Prolonged use of these oral hypoglycemics leads to some adverse effects and also loss their effectiveness after long term.[14]. Many herbal plants of Indian origin like *Acacia arabica, Aegle marmelo. Allium cepa, Allium sativum, Caesalpinia bonducella, and Coriandrum sativum* have been reported for anti-diabetic activity. [15]Among the wide range of medicinal herbs *Coriandrum sativum* found to possess promising anti-diabetic activity and wide number of patients use the seeds of this plant as a traditional therapy along with oral hypoglycemic drugs like metformin, glibenclamide, glimepiride etc.[16] Hence, there is a need of evidence-based assessment of risk versus benefits when *Coriandrum sativum* is co-administered with conventional oral hypoglycemic drugs. The present study was designed to study the pharmacokinetic and pharmacodynamic interactions of the seeds of *C. sativum* with the selected conventional drug i.e., glimepiride. In Pharmacokinetic study the combined treatment of *C. sativum* and GLM shows a significant improvement in the pharmacokinetic parameters such as Cmax, $AUC_{0\ to\ total}$, $t_{1/2\ and}$ MRT. This may be due to alteration in glimepiride's metabolism either by increasing absorption or inhibition by CYP4502C9 responsible for glimepiride metabolism.[17] The decreased volume of distribution was observed which may be due to the result of metabolic inhibition of glimepiride by *C. sativum*. These findings are in line with the previous reports on pharmacokinetic herb interactions with oral hypoglycemic agents.[18,19]. In compatibility with pharmacokinetic studies further pharmacodynamic interactions of *C. sativum* with GLM were studied in STZ induced diabetic models by assessing various biochemical parameters. STZ was adopted to induce diabetes as it impairs glucose oxidation and leads to a reduction in insulin biosynthesis and secretion.[20] In the current investigation in concordance with prior examinations acceptance of STZ lead to the increase in blood glucose levels. Notably, the beneficial effect on glycemic control was observed for *C. sativum* and GLM combination when compared with treatment alone. This may be due to synergistic effect of use of seeds of coriander with GLM which may be due to additional potential of seeds apart from GLM in recovery of partially destroyed beta cells in the pancreas or displaying insulin-like properties or stimulation of insulin release by the β-cells of the pancreas.[21] During the course of study, it was observed that diabetic rats (had)significantly lost weight as compared to normal ones which might be because of tissue protein breakdown, muscle degeneration and inclined muscle wasting.[22] Interestingly the coadministration of GLM + *C. sativum* was found to be more potent in improving body weight than monotherapy with GLM in diabetic rats. This improved body weight in combined therapy may be due to the additional potential of coriander seeds in the activation of AMP-activated protein kinase system, increased GLUT4 transporter protein of muscles and ascended glucose consumption in liver and muscles.[23] It is well known that inadequate control of glucose in diabetes results in disturbance in the serum lipid profile.[24] Under normal conditions, insulin leads to lipoprotein lipase

activation and hydrolyzes lipoprotein bound triglycerides leading to free fatty acids production.[25] In diabetic conditions lipoprotein lipase is not because of insulin inadequacy, resulting in hypertriglyceridemia.[26] The findings of the current study indicated dyslipidemia in STZ induced diabetic rats evidenced by elevated serum Triglycerides (TG), and Very Low Density Lipoproteins (VLDL-C) coupled with reduced level of HDL-C compared to normal rats. These studies are consistent with the studies of earlier researchers which stated that increased level of serum triglycerides, VLDL-C may be attributed to reduced level of blood insulin and cholesterol-mediated downregulation of VLDL receptors respectively.[27] Further the declined levels of HDL may be owed to the inclination of apoA1 clearance from the plasma due to high cholesterol levels. In the current study GLM and *coriandrum,* seeds alone attenuated the changes in lipid profile in diabetic rats which might be related to their ability to reduce glucose levels**.** Interestingly the GLM plus *C. sativum* combination showed a superior effect in regulating serum lipid than individual GLM treatment which is the indicator of stronger antidiabetic role played by the combined therapy. This synergistic effect might be due to accelerated insulin secretion from pancreatic beta-cells that further stimulates fatty acid synthesis and incorporation of fatty acids into triglycerides in the liver and adipose tissues. Many researchers reported that this decline in serum lipids is considered to be beneficial in the long-term prognosis of diabetes.[28] In the present study, the combined therapy has shown improvement in diabetes than that produced by GLM or *C. sativum* alone, this might be due to the additional promising potential of seed extract in ameliorating glucose levels and lipid profile by modulating PPAR-c gene expression and increasing regeneration of pancreatic beta-cells and improved pharmacokinetic aspects like reduced metabolism of GLM. The Seed extract of *C. sativum* contain terpenoids, the terpene and terpenoids are well known for reducing oxidative stress, hyperglycemia, hyper lipidemia, and for secreting insulin. So combination therapy shows significant effect than alone[29]. Moreover, the presence of various bioactive phytoconstituents like flavonoids, saponins and terpenoids may played a wide role in this contribution which comes in consistent with previous findings which stated that these phytochemicals are the potential insulin regenerators by various molecular mechanisms.[30,31.]

6. CONCLUSION

In conclusion, these results indicated that combining *Coriandrum sativum* with GLM therapy showed synergistic effect which may be beneficial by providing additional benefits in the form of reduced glucose levels and improvement in lipid profile. Further the findings revealed that *Coriandrum sativum* elevates the bioavailability of Glimepiride which seems to be beneficial in diabetic patients receiving Glimepiride. However, further study is defensible to apprehend the possible mechanism underlying in pharmacokinetic and pharmacodynamic interactions and interpretation of animal data to humans.

7. AUTHORS CONTRIBUTION STATEMENT

The author's confirmed contribution to the paper is as follows: Spandana Uppuluri: Conceptualization, Performed the experiments, analysis and interpretation of results. Adikay Sreedevi: Provided the expertise, timely ideas and suggestions. Kaveripakam Sai Sruthi: Assisted in drafting the final manuscript. All authors read and approved the final manuscript.

8. CONFLICT OF INTEREST

Conflict of interest declared none.

9. REFERENCES

1. Shaikh J, Matsyagandha P. Qualitative tests for preliminary phytochemical screening: An overview. Int J Chem Sci.; 2020 Feb 19; 8(1): 603 -608.
2. Kamble B, Gupta A, Moothedath I, Khatal L, Janrao S, Jadhav A, et al. Effects of *Gymnema sylvestre* extract on the pharmacokinetics and pharmacodynamics of Glimepiride in streptozotocin induced diabetic rats, Chemico-Biological Interactions, 2016 Dec 22; 245: 30-38.
3. Gupta, R.C., Chang, D., Nammi, S., et al. Interactions between antidiabetic drugs and herbs: an overview of mechanisms of action and clinical implications. *Diabetol Metab Syndr*.2017 Jul 26; 9-59.
4. Safa ME, Sean HT, Grace PL, Nicole WT, Naveenya CA, Subrat KB, et al. Type 1 and 2 diabetes mellitus: A review on current treatment approach and gene therapy as potential intervention. *Diabetol Metab Syndr*. 2019 Feb 13(1): 364-372.
5. Abdulfatai B. Olokoba, Olusegun A. Obateru, Lateefat B. Type 2 diabetes Mellitus: A review of current trends; Omen medical journal 2012 Jul; 27 (4) 269-273.
6. Kristina B, Fran SN, Ivan K, Ivana PR. Treatment approach to type 2 diabetes: Past, Present and Future. World J Diabetes. 2018 Dec 15; 2018; 9 (12):209-219.
7. Langtry HD, Balfour JA. Glimepiride. A review of its use in the management of type 2 diabetes mellitus. Drugs. 1998 Apr; 55(4):563-84.
8. Iqbal MJ, Butt MS, Suleria HA. Coriander (*Coriandrum sativum* L.): Bioactive Molecules and Health Effects. In: Mérillon JM., Ramawat K. (eds) Bioactive Molecules in Food. Reference Series in Phytochemistry. Springer, Cham. 2017 Oct; 1-37.
9. Sreelatha S, Inbavalli R. Antioxidant, antihyperglycemic, and antihyperlipidemic effects of Coriandrum sativum leaf and stem in alloxan-induced diabetic rats. J Food Sci.2012 Jul; 77(7):119-23.
10. kamran javed naquvi*, mohd. ali, javed ahamad antidiabetic activity of aqueous extract of coriandrum sativum l. fruits in streptozotocin induced rats International Journal of Pharmacy and Pharmaceutical Sciences 2012; Vol 4, Suppl 1, 239-241.
11. Harbone JP: Phytochemical Methods, A Guide to Modern Techniques of Plant Analysis: London: Chapmann and Hall. 1984: 1-36.
12. Choudhari, VP, Gore KP, Pawar AT. Antidiabetic, antihyperlipidemic activities and herb-drug interaction of a polyherbal formulation in Streptozotocin induced diabetic rats. *J Ayurveda Integr Med*. 2017 Nov 11; 8(4):218-225.

13. Latha S1, Vijayakumar R. The Facts about Diabetes Mellitus- A Review. Galore International Journal of Health Sciences and Research.2019 Jun; 4(2): 64-75.
14. Kooti W, Moradi M, Akbari SA, Sharafi-Ahvazi N, AsadiSamani M, Ashtary-Larky D. Therapeutic and pharmacological potential of *Foeniculum Vulgare* Mill: A Review, J Herb Med Pharmacol. 2015 Jan; 4(1):1-9.
15. Rizvi SI, Mishra N. (2013) Traditional Indian medicines used for the management of diabetes mellitus. J Diabetes Res. 2013 Jun; 712092.
16. Bochra L, Karima K, Mahmoud MH, Taoufik B(2015) Coriander (Coriandrum sativum L.) and its bioactive constituents. Fitoterapia. 2015 Jun; 103: 9-26.
17. Basit A, Riaz M, Fawwad A. Glimepiride: evidence-based facts, trends, and observations (GIFTS). [corrected]. Vasc Health Risk Manag. 2012 Aug; 8:463-72.
18. Han DG, Cho SS, Kwak JH. Medicinal plants and phytochemicals for diabetes mellitus: pharmacokinetic characteristics and herb-drug interactions. J. Pharm. Investig.; 2019 May; 49: 603–612.
19. Sushant S, Kalyan K, Dada P, Sanjay M. (2018). Herb drug interaction of Nisha Amalaki and curcuminoids with metformin in normal and diabetic condition: A disease system approach. Biomed pharmacother. 2018 May; 101: 591-598.
20. Damasceno DC, Netto AO, Lessi IL, Gallego FQ, Corvino SB, Dallaqua B et al. (2014) Streptozotocin-Induced Diabetes Models: Pathophysiological Mechanisms and Fetal Outcomes. BioMed Res Int. 2014 May;2014: 819065.
21. Ahmed I, Lakhani MS, Gillett M, John A, Raza H. Hypotriglyceridemic and hypocholesterolemic effects of anti-diabetic Momordica charantia (karela) fruit extract in streptozotocin-induced diabetic rats. Diabetes Res Clin Pract. 2001 Mar; 51(3): 155-161.
22. Perry BD, Caldow MK, Brennan-Speranza TC. Muscle atrophy in patients with Type 2 Diabetes Mellitus: roles of inflammatory pathways, physical activity and exercise. *Exerc Immunol Rev*. 2016; 22: 94-109.
23. Mohammed E, Amina B, Bachir EB, Haiji LH, Naoufel AZ. Antidiabetic plants improving insulin sensitivity. J Pharm Pharmacol. 2014 Sep; 66(9): 1197-1214.
24. Shah N, Khan M. Antidiabetic effect of *Sida cordata* in alloxan induced diabetic rats Biomed Res. Int. 2014 Jul; 2014: 671294
25. Sears B, Perry M. The role of fatty acids in insulin resistance. Lipids Health Dis. 2015; 14: 121.
26. Hirano T. Pathophysiology of Diabetic Dyslipidemia. J Atheroscler Thromb. 2018 Jul; 25(9) :771-782.
27. Vergès B. Pathophysiology of diabetic dyslipidaemia: where are we? *Diabetologia*. 2015 May; 58: 886-899.
28. Rehab AR, Gamal AS, Abdulaziz SS, Hanan AO, Reham MA, Saleh I. et al. Molecular and biochemical monitoring of the possible herb-drug interaction between Momordica charantia extract and glibenclamide in diabetic rats, Saudi Pharm J. 2019 Sep; 27(6): 803-816.
29. Kajal, A., & Singh, R. (2019). Coriandrum sativum seeds extract mitigate progression of diabetic nephropathy in experimental rats via Age's inhibition. *PloS one*, *14*(3), e0213147
30. Patrick E, Isaac U. Mechanisms of actions of some bioactive anti-diabetic principles from phytochemicals of medicinal plants: A review. Indian J Nat Prod Res.2018 Jun; 9(2): 85-96.
31. Uppuluri Spandana*1,2, Adikay Sreedevi2, Kaveripakam Sai Sruthi2 Synergistic anti-hyperglycemic activity of Coriandrum sativum with Metformin in Streptozotocin-induced Diabetic Rats Bull. Env. Pharmacol. Life Snv. Pharmacol. Life Sci., Vol 10 [3] February 2021: 36-41.