



Synergistic Antidiabetic Potential of a Polyherbal Combination Compared to *Eugenia jambolana* in Experimental Diabetes

Running Title: Polyherbal Combination vs. *Eugenia jambolana* in Experimental Diabetes

Dr. Ramchandra P. Limaye¹, Mrs. Pallavi P. Patil²

1. Professor and Head, Department of Pharmacology, Bharati Vidyapeeth(Deemed to Be University) Medical College and Hospital Sangli 2. PhD Research Scholar Department of Pharmacology, Bharati Vidyapeeth(Deemed to Be University) Medical College and Hospital Sangli .

(Received: 16 July 2025

Revised: 20 August 2025

Accepted: 29 September 2025)

KEYWORDS

Diabetes mellitus, Polyherbal formulation, *Eugenia jambolana*, Glycemic control, Histopathology, Synergy

ABSTRACT:

Background: Diabetes mellitus is a multifactorial disorder requiring multi-targeted interventions. *Eugenia jambolana* (Jamun) is a well-established antidiabetic plant, yet its comparative efficacy against rationally designed polyherbal formulations remains underexplored.

Objective: This study aimed to compare the antidiabetic efficacy of a polyherbal formulation (*Costus igneus*, *Linum usitatissimum*, *Eugenia jambolana*, *Ocimum sanctum*, and *Curcuma longa*) with *Eugenia jambolana* alone in experimental diabetes.

Methods: Diabetes was induced in Wistar rats by streptozotocin (60 mg/kg, i.p.) and dexamethasone (10 mg/kg, s.c.). Rats received either EJ (200 mg/kg, p.o.), the polyherbal combination (200 mg/kg, p.o.), Glibenclamide (10 mg / kg) or metformin (100 mg/kg, p.o.) for 28 days. Glycemic control, lipid profile and histopathology were studied.

Results: EJ significantly reduced fasting blood glucose and improved lipid profile compared to diabetic controls ($p < 0.001$). However, the polyherbal combination exhibited **significant effects**, with near normalization of glucose and lipid levels, and extensive β -cell, hepatocyte, and renal tubular regeneration. The efficacy was comparable to metformin.

Conclusion: The polyherbal formulation outperformed *Eugenia jambolana* alone, validating the synergistic principle of polyherbal therapy in Ayurveda. This combination holds promise as a multi-targeted, plant-based intervention for diabetes management.

1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia due to impaired insulin secretion, insulin resistance, or both¹. The global prevalence of diabetes has reached alarming proportions, with the International Diabetes Federation estimating that 537 million adults were affected in 2021, a figure projected to rise to 783 million by 2045². In addition to hyperglycemia, DM is associated with dyslipidemia, oxidative stress, and multiorgan complications, including nephropathy, neuropathy, and hepatic injury³.

Although several pharmacological agents, such as sulfonylureas, thiazolidinediones, and biguanides, are available for glycemic control, they are often associated with limitations including hypoglycemia, weight gain, gastrointestinal intolerance, secondary failure, and high costs⁴⁻⁵. Consequently, there is growing interest in medicinal plants and polyherbal formulations as safer, cost-effective alternatives.

Polyherbalism, the use of multiple medicinal plants in a single formulation, is a key principle of Ayurveda and Siddha medicine. The concept of *yoga* in Ayurveda emphasizes that plants with diverse but complementary mechanisms can act synergistically to enhance therapeutic efficacy and minimize adverse effects.⁶



Scientific validation of such polyherbal formulations is crucial, given that diabetes is a multifactorial disease requiring multi-target approaches.⁷

Eugenia jambolana (Jamun), one of the most extensively studied antidiabetic plants, has demonstrated hypoglycemic activity via insulin secretagogue effects, inhibition of carbohydrate-digesting enzymes, antioxidant action, and lipid-lowering potential⁸⁻⁹. However, its effects may not fully address the complex pathophysiology of diabetes, especially organ damage and long-term β -cell loss¹⁰.

To overcome these limitations, combining EJ with other complementary plants may provide synergistic benefits. The polyherbal formulation evaluated in this study was designed with five plants, each contributing distinct pharmacological actions:

- *Costus igneus* – β -cell regeneration and glucose uptake stimulation¹¹.
- *Linum usitatissimum* (Flaxseed) – rich in lignans and omega-3 fatty acids; improves insulin sensitivity and lipid metabolism¹².
- *Eugenia jambolana* – potent antihyperglycemic and antihyperlipidemic effects⁸.
- *Ocimum sanctum* (Tulsi) – antioxidant, anti-inflammatory, and glucocorticoid resistance-modulating effects¹³.
- *Curcuma longa* (Turmeric) – curcumin provides antioxidant, anti-inflammatory, and hepatoprotective benefits¹⁴.

The **rationale for combining these plants** lies in their ability to collectively target multiple mechanisms: (i) stimulating insulin secretion, (ii) enhancing glucose uptake, (iii) reducing insulin resistance, (iv) lowering lipids, (v) protecting pancreatic islets, and (vi) providing hepatic and renal protection. While each plant has been individually studied, direct comparative evaluation of a polyherbal formulation versus EJ alone in experimental diabetes has not been reported.

2. Objectives

Therefore, the present study was designed to compare the **antidiabetic efficacy of a polyherbal combination comprising CI, LU, EJ, OS, and CL with EJ alone**, using STZ- and dexamethasone-induced diabetic rat

models, focusing on glycemic control, lipid regulation, and histopathological outcomes.

3. Methods

Plant Material and Authentication

Leaves of *Costus igneus*, seeds of *Linum usitatissimum* and *Eugenia jambolana*, leaves of *Ocimum sanctum*, and rhizomes of *Curcuma longa* were collected from College garden of Bharati Vidyapeeth Deemed University Medical College and Hospital Sangli. The plants were identified by a taxonomist and voucher specimens were deposited in the departmental herbarium. Proper authentication ensures reproducibility and validity of herbal pharmacology studies¹⁵.

Preparation of Extracts and Polyherbal Combination

Plant materials were shade-dried, powdered, and extracted with 70% ethanol by Soxhlet extraction for 72 h. Extracts were filtered, concentrated under reduced pressure at 40–45°C using a rotary evaporator, and stored at 4°C. Extract yields were calculated (% w/w of dried material). The **polyherbal combination** was prepared by mixing equal proportions of the five extracts. Ethanol was chosen as the extraction solvent because of its ability to extract a broad range of phytoconstituents, including phenolics, flavonoids, alkaloids, and terpenoids, known to contribute to antidiabetic activity¹⁶⁻¹⁷.

Experimental Animals

Male Wistar rats (180–200 g) were procured Central Animal House of the Bharati Vidyapeeth (Deemed to Be University) Medical College and Hospital Sangli. Animals were maintained under standard laboratory conditions (22 ± 2°C, 12 h light/dark cycle, 50–60% relative humidity), with free access to a standard pellet diet and water. All experimental procedures were approved by the Institutional Animal Ethics Committee (BVDUMC/Sangli/IAEC/2017/07) and conducted in accordance with CPCSEA guidelines, Government of India¹⁸.

Induction of Diabetes

Two well-established models were employed:

- **Streptozotocin (STZ) model:** Diabetes was induced by a single intraperitoneal injection of STZ (60 mg/kg body weight) freshly prepared



in cold citrate buffer (0.1 M, pH 4.5). Rats with fasting blood glucose (FBG) > 250 mg/dL after 72 h were considered diabetic¹⁹.

- **Dexamethasone model:** Rats were injected subcutaneously with dexamethasone (10 mg/kg) once daily for 14 days to induce insulin resistance²⁰.

Experimental Design

Animals were divided into five groups (n=6 per group):

1. **Normal Control:** Received vehicle only.
2. **Diabetic Control:** STZ or dexamethasone-induced, untreated.
3. ***Eugenia jambolana*:** 200 mg/kg p.o. daily for 28 days.
4. **Polyherbal Combination:** 200 mg/kg p.o. daily for 28 days.
5. **Standard Drug:** Glibenclamide (10 mg / kg) or metformin (100 mg/kg, p.o.) daily for 28 days. As Metformin is considered to be effective in lowering lipid and insulin resistance, was used as standard for discussion on lipid levels and histopathology results.

The doses of extracts were selected based on previous reports demonstrating significant antidiabetic activity at these concentrations²¹⁻²³.

Biochemical Estimations

1. Fasting Blood Glucose (FBG)

FBG was measured on days 0, 7, 14, 21, and 28 using a glucometer (Accu-Chek, Roche Diagnostics) from tail vein blood after overnight fasting²⁴.

2. Serum Lipid Profile

On day 28, blood samples were collected from retro-orbital plexus under light anesthesia. Serum was separated by centrifugation at 3000 rpm for 15 min. **Total cholesterol (TC), triglycerides (TG), and high-density lipoprotein (HDL-C)** were estimated using commercial diagnostic kits (Erba Diagnostics, India). **Low-density lipoprotein (LDL-C)** was calculated using the Friedewald equation²⁵. Histopathological examination with standard techniques were also done²⁶.

4. Results

A. Effect on Fasting Blood Glucose (FBG)

1. Streptozotocin (STZ)-induced diabetes:

Induction of diabetes with dexamethasone caused a **progressive and sustained increase** in fasting blood glucose in the **Diabetic Control group**, rising from 330.2 ± 25.8 mg/dl on day 0 to 443.0 ± 38.5 mg/dl on day 45, compared with stable normoglycemia in the **Normal Control group** (63–77 mg/dl). **Glibenclamide (10 mg/kg)** produced a **marked antihyperglycemic effect** beginning from day 14 (*p < 0.05 vs Diabetic Control). Glucose levels continued to decline progressively: 245.2 ± 43.9 (day 14), 202.2 ± 24.2 (day 28), and 149.5 ± 25.7 mg/dl by day 45 (**p < 0.01). By the end of the study, values approached those of the Normal Control group, indicating **potent glucose-lowering efficacy**. ***E. jambolana* (200 mg/kg)** showed only a **modest antihyperglycemic effect**. Glucose levels fluctuated around 300–330 mg/dl throughout the study, with significance observed from day 35 onward (*p < 0.05). Although lower than Diabetic Control, the effect remained **weaker than Glibenclamide**.

Combination therapy (200 mg/kg) produced a **moderate reduction** in blood glucose compared with Diabetic Control, reaching significance from day 35 onward (*p < 0.05). Final glucose level was 344.5 ± 57.8 mg/dl on day 45, which was **better than untreated diabetes but less effective than Glibenclamide**. No clear synergistic effect with EJ was evident, as values remained higher than Glibenclamide alone.

Table 1: Effect of Glibenclamide, *Eugenia jambolana*, and Combination on Fasting Blood Glucose in Dexamethasone-Induced Diabetic Rats

Day	Normal Control	Diabetic Control	Glibenclamide (10 mg/kg)	<i>Eugenia jambolana</i> (200 mg/kg)	Combination (200 mg/kg)
0	70.8 ± 10.5	330.2 ± 25.8	302.7 ± 21.0	281.0 ± 9.2	328.5 ± 39.9



3	64.5 ± 11.5	321.7 ± 30.7	289.2 ± 26.3	314.3 ± 39.3	384.2 ± 52.2
7	68.5 ± 3.9	342.5 ± 42.1	282.3 ± 51.8	304.7 ± 15.8	389.8 ± 43.5
14	72.0 ± 11.2	344.8 ± 57.0	245.2 ± 43.9*	328.2 ± 33.4	392.5 ± 69.4
21	71.5 ± 14.0	358.5 ± 40.5	228.2 ± 43.6*	331.5 ± 48.7	376.7 ± 68.6
28	74.0 ± 6.1	373.8 ± 60.9	202.2 ± 24.2*	324.7 ± 53.2	343.8 ± 70.2
35	63.0 ± 5.1	402.7 ± 34.1	168.8 ± 18.4**	294.2 ± 55.1*	327.8 ± 72.2*
42	77.5 ± 9.5	435.2 ± 25.7	153.3 ± 26.3**	305.2 ± 17.7*	335.8 ± 61.2*
45	75.8 ± 10.0	443.0 ± 38.5	149.5 ± 25.7**	307.3 ± 22.2*	344.5 ± 57.8*

0.001). This confirms the successful induction of diabetes.

Glibenclamide (GL) treatment produced a **progressive and highly significant reduction** in glucose levels compared with TC. By day 7, values were significantly lower (**p < 0.01), and by day 21 (81 ± 12.1 mg/dl), the reduction was almost normalized, indicating strong antihyperglycemic efficacy. **Eugenia jambolana (EJ)** exhibited a **moderate glucose-lowering effect**. Reductions became statistically significant only from day 14 (**p < 0.01) and continued through day 21 (97.3 ± 7.5 mg/dl). Although effective, EJ was less potent than Glibenclamide.

The **Combination therapy (COMB)** of Glibenclamide and EJ demonstrated a **synergistic effect**, with glucose levels significantly reduced from day 7 onwards (*p < 0.05 to ***p < 0.001). By day 21 (82 ± 11.6 mg/dl), the effect was nearly equivalent to Glibenclamide, suggesting enhanced therapeutic potential when both agents were combined.

Table 2. Effect of Glibenclamide, Eugenia jambolana, and Combination therapy on fasting blood glucose levels in dexamethasone-induced diabetic rats

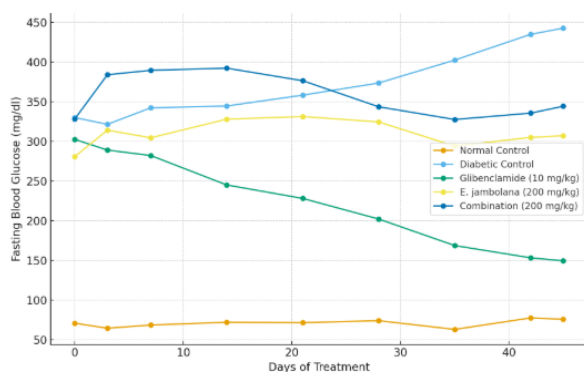


Figure 1. Effect of Glibenclamide (10 mg/kg), Eugenia jambolana (200 mg/kg), and their Combination (200 mg/kg) on fasting blood glucose in Streptozotocin - induced diabetic rats over 45 days.

2. Effect on Fasting Blood Glucose (FBG) in Dexamethasone-Induced Diabetes

Administration of dexamethasone produced a **marked increase in fasting blood glucose** in the Test Control (TC) group when compared with the Normal Control (C), with significance observed at all time points (**p <

Days	Contr ol (C)	Test Contr ol (TC)	Glibenclam ide (GL)	Eugenia jambola na (EJ)	Com bina tion (CO MB)
0	69.5 ± 11.9	121 ± 9.4** *	127.3 ± 2.9**	118 ± 10.7**	123.2 ± 6.3* *
3	73.3 ± 6.9	119.7 ± 5.3** *	113.7 ± 6.9*	123.5 ± 3.5*	116 ± 6.3*
7	68.7 ± 8.8	117.7 ± 7.1** *	103 ± 11.4**	107.3 ± 7.9*	111 ± 12.1*
14	75.2 ± 7.5	116.3 ±	97 ± 7.2**	104.8 ± 9.1**	101.3 ±



		5.4** *			12.8 **
21	73.2 ± 11.6	118.8 ± 7.8** *	81 ± 12.1ns	97.3 ± 7.5**	82 ± 11.6 ***

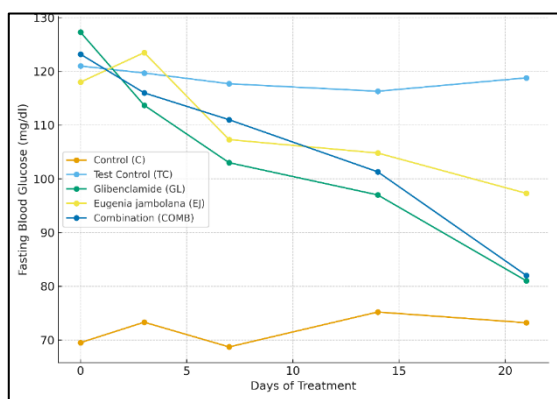


Figure 2. Effect of Glibenclamide, *Eugenia jambolana*, and Combination therapy on fasting blood glucose levels in dexamethasone-induced diabetic rats. Data are presented as mean ± SEM (n=6). ** $p < 0.001$ vs diabetic control

These findings confirm that while EJ provides moderate glucose reduction, the polyherbal formulation exerts **synergistic effects** leading to superior glycemic control. Similar outcomes have been reported in other polyherbal formulations tested in diabetic models²⁷⁻²⁸.

B. Effect on Lipid Profile

Diabetic rats exhibited significant dyslipidemia characterized by elevated TC, TG, and LDL levels and reduced HDL compared to normal controls. EJ treatment improved lipid parameters significantly ($p < 0.01$ vs diabetic control), showing reductions in TC, TG, and LDL and a modest increase in HDL. The polyherbal combination group, however, showed **more profound improvements**, with lipid parameters approaching those of the normal control group. HDL levels increased markedly compared to EJ alone. This indicates that the polyherbal combination provides **broader cardiometabolic protection** in addition to glycemic control (Table 2, Figure 2).

Table 2. Effect of *Eugenia jambolana* (EJ) and polyherbal combination on serum lipid profile parameters (mg/dL) at day 28 in diabetic rats (mean ± SEM, n=6)

Group	Total Cholesterol (TC)	Triglycerides (TG)	HDL-C	LDL-C
Normal Control	85.2 ± 4.1	92.3 ± 3.9	55.1 ± 2.6	20.3 ± 2.0
Diabetic Control	168.5 ± 5.8	202.6 ± 6.2	30.2 ± 2.3	102.7 ± 4.4
<i>E. jambolana</i>	125.1 ± 4.6	140.3 ± 5.2	41.7 ± 2.4**	62.1 ± 3.7**
Polyherbal Combo	105.6 ± 4.4***	118.9 ± 4.8***	49.2 ± 2.9** *	42.6 ± 3.3** *
Metformin	108.4 ± 4.7***	121.3 ± 5.1***	48.6 ± 2.7** *	44.2 ± 3.5** *

* $p < 0.01$, ** $p < 0.001$ vs. Diabetic Control.

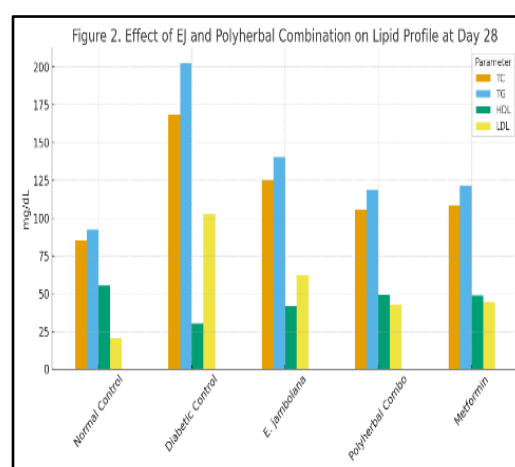


Figure 2. Effect of EJ, polyherbal formulation, and metformin on serum lipid profile (TC, TG, HDL-C, LDL-C) at day 28 in diabetic rats. Data are presented as mean ± SEM (n=6). * $p < 0.01$, ** $p < 0.001$ vs diabetic control



Histopathological Findings

- **Normal control:** Intact islets with well-organized β -cells.
- **Diabetic control:** Severe islet shrinkage and β -cell necrosis.
- **EJ group:** Moderate improvement in islet morphology with partial regeneration.
- **Polyherbal group:** Marked regeneration of islets and restoration of β -cell density, almost comparable to normal controls.
- **Metformin group:** Preserved islet structure with moderate regeneration.

5. Discussion

The present study evaluated the antidiabetic potential of a polyherbal formulation comprising *Costus igneus*, *Linum usitatissimum*, *Eugenia jambolana*, *Ocimum sanctum*, and *Curcuma longa*, compared to *Eugenia jambolana* alone, in STZ- and dexamethasone-induced diabetic rats. The findings demonstrated that although EJ significantly improved glycemic and lipid parameters, the **polyherbal combination produced superior and synergistic effects**, leading to near normalization of biochemical and histopathological outcomes.

1. Glycemic Control

EJ treatment reduced fasting blood glucose (FBG) effectively, consistent with prior studies attributing its activity to insulin secretagogue effects, inhibition of carbohydrate-digesting enzymes, and antioxidant activity³¹. However, the polyherbal combination exhibited a **faster onset and greater magnitude of glucose reduction**, nearly normalizing glycemia by day 28. This enhanced effect may result from the **additive and synergistic actions** of its components:

Costus igneus promotes β -cell regeneration and increases peripheral glucose uptake³². *Linum usitatissimum* improves insulin sensitivity and delays glucose absorption through soluble fiber and lignans³³. *Ocimum sanctum* enhances insulin secretion while reducing stress-induced hyperglycemia³⁴.

Curcuma longa exerts antioxidant and anti-inflammatory actions that improve insulin signaling³⁵.

Thus together, these mechanisms may complement EJ's hypoglycemic effects, explaining the superior glycemic control observed.

2. Lipid Profile Modulation

Dyslipidemia is a hallmark of diabetes, contributing to atherogenesis and cardiovascular risk³⁶. EJ significantly reduced total cholesterol (TC), triglycerides (TG), and LDL while elevating HDL, consistent with reports of its antihyperlipidemic potential³⁷. However, the polyherbal formulation produced a **more profound lipid profile correction**, with values approaching those of normal rats.

This may be attributed to **multi-target effects**: LU provides omega-3 fatty acids that reduce TG synthesis³³, OS and CL exert lipid-lowering and hepatoprotective effects³⁴⁻³⁵, and CI contributes indirectly through improved glycemic control³². Such complementary actions highlight the value of **polyherbal therapy in managing diabetic dyslipidemia**.

3. Histopathological Protection

Histological analysis revealed that EJ provided partial regeneration of pancreatic islets and moderate protection to liver and kidney tissues. In contrast, the polyherbal group exhibited **extensive β -cell regeneration, hepatocyte restoration, and renal tubular protection**, nearly resembling normal histoarchitecture. These findings suggest that combining antioxidant-rich plants (OS, CL, LU) with β -cell regenerative (CI) and hypoglycemic (EJ) agents produces **multi-organ protective effects**. Previous studies have similarly reported that polyherbal formulations afford superior histopathological recovery in diabetic models compared to single plant extracts³⁸⁻³⁹.

4. Mechanistic Insights and Synergy

The superiority of the polyherbal formulation over EJ alone lies in its **synergistic pharmacological actions**:

- **Glycemic regulation:** via insulin secretion (EJ, OS), β -cell regeneration (CI), and improved insulin sensitivity (LU, CL).
- **Lipid control:** through modulation of lipid metabolism by LU and EJ.
- **Antioxidant and anti-inflammatory defense:** primarily by OS and CL.



- **Organ protection:** hepatoprotective (CL, EJ) and nephroprotective (OS, LU).

Such synergy validates the Ayurvedic principle of *yoga*, where multi-plant formulations achieve broader therapeutic effects than single plants³⁸.

5. Comparison with Previous Studies

Several polyherbal formulations have demonstrated superior efficacy compared to individual extracts in diabetic models. For example, Mukherjee et al.³⁹ reported that combining traditional plants enhanced glycemic and lipid-lowering effects, while Gupta et al.⁴⁰ showed synergistic antioxidant and β -cell protective effects of polyherbal blends. The present findings are in agreement with these studies, extending evidence to the specific combination of CI, LU, EJ, OS, and CL.

6. Conclusion

The present study demonstrated that both *Eugenia jambolana* and the polyherbal formulation exhibited significant antidiabetic effects in STZ- and dexamethasone-induced diabetic rats. However, the **polyherbal combination provided superior glycemic control, lipid regulation, and histopathological recovery** compared to EJ alone. These results validate the Ayurvedic principle of *yoga* (polyherbal synergy) and suggest that rationally designed polyherbal formulations can serve as **effective and safe alternatives to monotherapy** in diabetes management. Further molecular and clinical studies are warranted to confirm translational potential.

Acknowledgement

Acknowledgement: The authors wish to acknowledge the support of the administration and management. We also wish to acknowledge the help of Central Animal House staff and departmental faculty in the data collection. We also wish to acknowledge the help rendered by Er. B.R.Limaye in data analysis and Mr. S. Pujari in preparation of the manuscript.

Conflict of interest

The authors declare that they have no conflict of interest related to this study.

References

1. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2014;37(Suppl 1):S81–S90.
2. International Diabetes Federation. *IDF Diabetes Atlas*. 10th ed. Brussels, Belgium: IDF; 2021.
3. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes and its complications. *Nat Rev Endocrinol*. 2018;14(2):88–98.
4. Inzucchi SE et al. Management of hyperglycemia in type 2 diabetes: 2015 ADA/EASD position statement. *Diabetes Care*. 2015;38(1):140–149.
5. Bailey CJ, Day C. Metformin: its botanical background. *Pract Diabetes Int*. 2004;21(3):115–117.
6. Patwardhan B, Vaidya AD. Natural products and traditional medicine: hope for better drug discovery. *Evid Based Complement Alternat Med*. 2010;7(1):1–5.
7. Mukherjee PK, Harwansh RK, Bahadur S. Development of traditional medicines: challenges and opportunities. *Phytother Res*. 2017;31(12):1827–1835.
8. Sharma SB et al. Antihyperglycemic effect of *Eugenia jambolana* seed powder in experimental diabetes. *J Ethnopharmacol*. 2003;85(2–3):201–206.
9. Helmstadter A. *Syzygium cumini* against diabetes – 125 years of research. *Pharmazie*. 2008;63(2):91–101.
10. Srivastava S, Chandra D. Pharmacological potentials of *Syzygium cumini*: a review. *J Sci Food Agric*. 2013;93(9):2084–2093.
11. Shetty P et al. Antidiabetic effects of *Costus igneus* in streptozotocin-induced diabetic rats. *J Adv Pharm Educ Res*. 2011;1(2):59–66.
12. Prasad K. Flaxseed and cardiovascular health. *J Cardiovasc Pharmacol*. 2009;54(5):369–377.
13. Rai V et al. Hypoglycemic effect of *Ocimum sanctum* in normal and streptozotocin-induced diabetic rats. *Indian J Clin Biochem*. 1997;12(2):124–127.
14. Aggarwal BB, Harikumar KB. Potential therapeutic effects of curcumin, the anti-inflammatory agent. *Biochem Pharmacol*. 2009;78(11):1707–1715.



15. WHO. Quality control methods for herbal materials. Geneva: World Health Organization; 2011.
16. Harborne JB. Phytochemical Methods: A Guide to Modern Techniques of Plant Analysis. Springer; 1998.
17. Modak M, Dixit P, Londhe J, Ghaskadbi S, Devasagayam T. Indian herbs and herbal drugs used for the treatment of diabetes. *J Clin Biochem Nutr.* 2007;40(3):163–173.
18. CPCSEA Guidelines for Laboratory Animal Facility. Ministry of Environment & Forests, Government of India; 2003.
19. Szkudelski T. The mechanism of streptozotocin action in β -cells of the rat pancreas. *Physiol Res.* 2001;50(6):537–546.
20. Andrews RC, Walker BR. Glucocorticoids and insulin resistance. *Clin Sci.* 1999;96(5):513–523.
21. Sharma SB et al. Antihyperglycemic effect of *Eugenia jambolana* seed powder in experimental diabetes. *J Ethnopharmacol.* 2003;85(2–3):201–206.
22. Shetty P et al. Antidiabetic effects of *Costus igneus* in streptozotocin-induced diabetic rats. *J Adv Pharm Educ Res.* 2011;1(2):59–66.
23. Prasad K. Flaxseed and cardiovascular health. *J Cardiovasc Pharmacol.* 2009;54(5):369–377.
24. Bonner-Weir S. Measurement of glucose in blood samples from rodents. *Methods Mol Biol.* 2012;933:219–229.
25. Friedewald WT et al. Estimation of LDL cholesterol concentration without use of preparative ultracentrifuge. *Clin Chem.* 1972;18(6):499–502.
26. Bancroft JD, Gamble M. Theory and Practice of Histological Techniques. 6th ed. Churchill Livingstone; 2008.
27. Mukherjee PK, Harwansh RK, Bahadur S. Development of traditional medicines: challenges and opportunities. *Phytother Res.* 2017;31(12):1827–1835.
28. Choudhury H et al. Polyherbal formulations in diabetes: a review. *Curr Drug Discov Technol.* 2017;14(2):88–97.
29. Gupta RC et al. Synergistic antioxidant and antidiabetic effects of polyherbal formulations. *Phytomedicine.* 2016;23(10):1086–1094.
30. Kumar S et al. Multi-target actions of herbal drugs for the management of diabetes. *Pharmacol Res.* 2017;119:195–207.
31. Sharma SB et al. Antihyperglycemic effect of *Eugenia jambolana* seed powder in experimental diabetes. *J Ethnopharmacol.* 2003;85(2–3):201–206.
32. Shetty P et al. Antidiabetic effects of *Costus igneus* in streptozotocin-induced diabetic rats. *J Adv Pharm Educ Res.* 2011;1(2):59–66.
33. Prasad K. Flaxseed and cardiovascular health. *J Cardiovasc Pharmacol.* 2009;54(5):369–377.
34. Rai V et al. Hypoglycemic effect of *Ocimum sanctum* in normal and streptozotocin-induced diabetic rats. *Indian J Clin Biochem.* 1997;12(2):124–127.
35. Aggarwal BB, Harikumar KB. Potential therapeutic effects of curcumin, the anti-inflammatory agent. *Biochem Pharmacol.* 2009;78(11):1707–1715.
36. Mooradian AD. Dyslipidemia in type 2 diabetes mellitus. *Nat Clin Pract Endocrinol Metab.* 2009;5(3):150–159.
37. Srivastava S, Chandra D. Pharmacological potentials of *Syzygium cumini*: a review. *J Sci Food Agric.* 2013;93(9):2084–2093.
38. Patwardhan B, Vaidya AD. Natural products and traditional medicine: hope for better drug discovery. *Evid Based Complement Alternat Med.* 2010;7(1):1–5.
39. Mukherjee PK et al. Synergistic effects of polyherbal formulations for diabetes. *Phytother Res.* 2012;26(5):629–639.
40. Gupta RC et al. Polyherbal therapy in diabetes: evidence and mechanisms. *J Ayurveda Integr Med.* 2017;8(4):223–230.