Innovations

Streptozocin Induced Anti-diabetic Comparitive Study of Ximenia Americana and Lindera Communis

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Abstract:

Finding non-pharmacological therapy for diabetes is important given its rising incidence and the negative side effects of chemical medications. In this work, we compared the anti-diabetic effects of leaf extract of Ximena americana and Lindera communis in streptozocin-induced diabetic rats. The genera Ximenia americana and Lindera communis are members of the Olacaceae and Lauraceae families. The plants Ximenia americana and Lindera are widely used in traditional medicine. The leaves, fruits, and roots of Lindera plants as well as the fruit of Ximenia americana contain particularly noteworthy compounds. A chronic study of 28days was done in streptozocin induced diabetic rats with gains Lindera and Ximenia extract and the results of blood glucose levels and effect of streptozocin and extract in different combination on blood glucose variables in albino rats. Blood glucose levels on day zero showed no significant intra group variation. Administration of streptozocin (60mg/kg, i.p.) showed a significant increase in fasting blood glucose levels. After 28 days, diabetic control rats exhibited significantly higher blood glucose levels (313.8 ± 5.12 mg/dl) as compared to the normal control rats (84.9 ± 1.25).

Key words: *Ximenia americana, Lindera communis, streptozocin, the anti-diabetic activity.*

Introduction:

As an increasingly prevalent traditional medical treatment, current study is focused on enhanced, secure, and natural anti-diabetic and antioxidative plant items. Herbs typically have minimal to no toxicity when taken orally over an extended period of time and are generally accessible on a large scale, especially for cultures that use them traditionally. This encourages the adoption of species with chemopreventive properties because they are more affordable and have less adverse side effects.[2] Ximenia americana[1] belongs to Olacaceae family. The most common disorders treated with Ximenia americana are inflammatory[2,3] and infectious conditions[4, 5]. It is a medicinal bushy, prickly shrub or small tree. Numerous illnesses, including measles, malaria, skin infections, STDs, diarrhoea, muscle cramps, and lung abscesses, have reportedly been treated using Ximenia americana. The twigs and leaves are also used as a mouthwash to prevent toothaches and throat infections, as laxatives, as an eye ointment, and as a cure for colds and fevers[4].The core genus Lindera[5-8], which belongs to the Lauraceae family and has more than 100 species, is a member of the Litseeae tribe. In particular, the tropical, subtropical, and temperate regions of Asia

and North America are home to many plants of the Lindera genus. Because of its exquisite scent, plants from the genus Lindera are regarded as a rich source of essential oils[9] and are frequently utilized in the manufacture of aromatic cosmetic items like soap and lubricants. Most notably, numerous Lindera plants have historically been employed in traditional medicine[10-13] for their capacity to treat a variety of health-related issues[14-17], including pain, colds, urinary tract problems, rheumatoid arthritis, gastric ulcers, abdominal pain, cholera, and beriberi. The results of blood glucose levels and the impact of extract and streptozocin in various combinations on blood glucose variables in albino rats were examined in a chronic trial of 28 days in streptozocin-induced diabetic rats. On the first day, there was no discernible intragroup variance in blood glucose levels. The amount of streptozocin (60 mg/kg, i.p.) administered caused fasting blood sugar levels to significantly rise. After 28 days, diabetic control rats had blood glucose levels that were noticeably higher than normal control rats (84.9 1.25 vs. 313.8 5.12 mg/dl).

Materials and Methods:

Extraction:

Preparation of methanolic extract of Lindera communis

Dried powdered material was refluxed with 500 ml of 95% methanol for 3 h. The extracts were then filtered through filter paper. The filtrates (methanol extract) were concentrated at 50ºC under reduce pressure using rotary evaporator The extract transferred to a closed container for further use and protection.

Preparation of Methanolic extract of X. americana

The leaves of X. americana were dried in an oven for 2 days at 40°C, crushed in an electrical grinder and then powdered. Extraction was performed by taking 25-g powder in 250 ml of distilled water for 18 h in a soxhlet apparatus. The extract was dried at reduced pressure and transferred to a closed container for further use and protection.

Experimental animals: Adult Wistar rats (180±10g) of either sex were obtained from animal house. The animals were housed in large, spacious polyacrylic cages at an ambient room temperature with 12h light/12h dark cycle. Rats had free access to water and rodent pellets diet. The study was approved by the Institute Animal Ethics Committee and all the animal experiments were carried out according to the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines.

In vivo study for assessment of antihyperglycemic activity
(Streptozocin Induced Diabetic Model)

Acute Toxicity Studies

Toxicity is involved in estimation of LD50. LD50 is the dose which has proved to be lethal to 50% of the tested group of animals. The acute toxic effect of ethanolic extract **(***Lindera communis and Ximenia americana*) was determined as per the OECD guidelines 423, where the limit test dose of 3000 mg/kg was used. No treatment related toxic symptom or mortality was observed after oral administration of the tested plant extract at a dose of 500, 1000, 2000 and 3000 mg/kg. Physically no signs of changes in the skin, eye color, digestion, body weight, temperature and food intake, rate of respiration, drowsiness, sedation, diarrhea, general physique, urination and coma were observations in Lindera extract. There was no mortality observed at the tested dose nor was the weight loss in the rats affected. No significant differences were observed in the relative organ weights and average body weights of Lindera extract.

Effect of Extract on Blood glucose levels in diabetic rats

A chronic study of 28days was done in streptozocin induced diabetic rats with gains Lindera and Ximenia Extract and the results of blood glucose levels Effect of streptozocin and Extract in different combination on blood glucose variables in albino rats. Blood glucose levels on day zero showed no significant intra group variation. Administration of streptozocin (60mg/kg, i.p.) showed a significant increase in fasting blood glucose levels. After 28 days, diabetic control rats exhibited significantly higher blood glucose levels (313.8 ± 5.12 mg/dl) as compared to the normal control rats (84.9 ± 1.25).

Effect of Extract on biochemical and lipid profile analysis in diabetic rats

Serum albumin levels were decreased in the diabetic animals, as compared with the normal control animals. Whereas the albumin levels in the diabetic control group is 2.84 ± 1.22 mg/dl, but albumin levels after treatment with the Extract shows an increased the serum albumin levels of extract of Lindera.

Derangements in cholesterol metabolism have been associated with the etiology of most human diseases. The results of the present investigation show that streptozocin induced rats developed hyperlipidemia with an increase in total cholesterol, LDL, VLDL, triglyceride levels and an intergroup comparison decrease in HDL levels as compared to the control rats in Extract of Lindera.

Statistical analysis

All data were expressed as mean ± Standard Deviation. Multiple comparisons were performed using one- way analysis of variance (ANOVA) followed by posthoc Tukey's test. Statistical significance was set at the 0.05 level.

Results:

Table 1: Effect of Lindera Extract on blood glucose levels instreptozocin induced diabetic rats

Treatment group	Blood glucose level (mg/dl)				
	0 day	7th day	14th day	21st day	28th day
Normal Control	81.2 ± 1.29	86.8 ± 1.31	83.6 ± 1.29	85.7±1.42	84.9 ± 1.25
Diabetic control	105.4 ± 1.52	164.9 ± 1.24	228.1±2.32	275.5±3.19	313.8 ± 5.12
60 mg/kg STZ + 500mg/kg extract of*Extract*	94.5 ± 1.24	146.2 ± 1.62	165.5±2.29	147.2±1.36	114.4 ± 1.35
60 mg/kg STZ	94.9 ±1.16	158.5 ± 1.28	182.7±2.12	160.1±1.25	124.5 ± 1.42
60 mg/kg STZ + 50 mg/kg metformin	92.7 ± 1.22	136.5 ± 1.12	143.7±1.36	130.5±1.15	110.5 ± 1.28

Table 2: Effect of Ximena Extract on blood glucose levels instreptozocin induced diabetic rats

Treatment group	Blood glucose level (mg/dl)				
	0 day	7th day	14th day	21st day	28th day
Normal Control	67.2 ± 1.12	74.6 ± 1.21	51.6 ± 1.52	61.7±1.22	84.9 ± 1.13
Diabetic control	95.4 ± 1.41	152.9 ± 1.19	229.1±1.66	262.5±3.02	301.8 ± 5.03
60 mg/kg STZ + 500mg/kg extract of*Extract*	82.5 ± 1.16	134.2 ± 1.55	153.5±2.16	135.2±1.24	104.4 ± 1.35
60 mg/kg STZ	82.9 ±1.04	146.5 ± 1.24	148.5±2.11	160.1±1.25	124.5 ± 1.42
60 mg/kg STZ + 50 mg/kg metformin	56.7 ± 1.41	124.7 ± 1.08	119.3±1.16	130.5±1.15	63.5 ± 1.16

(Each value is expressed as Mean ± S.D of five values)

Table 3: Effect of Lindera Extract on serum bilirubin, albumin and protein levels in streptozocin induced diabetic rats -

Group	Treatment group	Bilirubin (mg/dl)	Protein (g/dl)	Albumin (g/dl)
1	Normal Control	0.94 ± 0.29	6.85 ± 1.13	4.75 ± 1.05
2	Diabetic control	2.40 ± 0.52	3.96 ± 1.24	2.84 ± 1.22
3	60 mg/kg STZ + 500 mg/kg of *Extract*	1.05 ± 0.24	6.25 ± 1.02	4.46 ± 1.35
4	60 mg/kg STZ	1.14 ± 0.15	5.96 ± 1.22	4.15 ± 1.42
5	60 mg/kg STZ + 50 mg/kg of metformin	1.07 ± 0.22	6.35 ±0 .12	4.64 ± 1.21

(Each value is expressed as Mean ± S.D of five values)

Group	Treatment group	Phospholipid (mg/dl)	Cholesterol (mg/dl)	Triglyceride (mg/dl)
1	Normal Control	125.51 ± 1.12	76.25 ± 1.22	65.23 ± 1.13
2	Diabetic control	192.24 ± 1.17	130.2 ± 1.92	125.1 ± 1.84
3	60 mg/kg STZ + 500 mg/kg of *Extract*	135.37 ± 1.32	88.64 ± 1.17	77.25 ± 1.33
4	60 mg/kg STZ	147.18 ± 1.41	98.26 ± 1.52	85.14 ± 1.17
5	60 mg/kg STZ + 50 mg/kg metformin	132.64 ± 1.18	90.15 ± 1.24	69.24 ± 1.15

S. No	Treatment group	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
1	Normal Control	26.52 ± 1.25	45.12 ± 1.31	12.25 ± 1.12
2	Diabetic control	16.25 ± 1.15	86.51 ± 1.05	18.53 ± 1.16
3	60 mg/kg STZ + 500 mg/kg extract of *Extract*	24.82 ± 1.22	52.28 ± 1.27	13.19 ± 1.33
4	60 mg/kg STZ	22.75 ± 1.51	60.25 ± 1.15	14.25 ± 1.17
5	60 mg/kg STZ + 50 mg/kg of metformin	24.37 ± 1.33	53.73 ± 1.19	11.94 ± 1.22

Table 4: Effect of Lindera Extract on urea, BUN, creatininelevels in streptozocin induced diabetic rats

S. No	Treatment group	Creatinine (mg/dl)	Urea (mg/dl)	BUN (mg/dl)
1	Normal Control	0.98 ± 1.22	33.15 ± 2.35	23.5 ± 1.15
2	Diabetic control	3.15 ± 1.71	58.12 ± 2.27	48.2 ± 1.23
3	60 mg/kg STZ + 500 mg/kg extract of *Extract*	1.35 ± 1.15	35.85 ± 2.13	32.4 ± 1.12
4	60 mg/kg STZ	1.52 ± 1.21	40.21 ± 2.61	36.9 ± 1.25
5	60 mg/kg STZ + 50 mg/kg of metformin	1.02 ± 1.07	31.51 ± 2.42	28.1 ± 1.38

(Each value is expressed as Mean ± S.D of five values)

Table 5: Effect of Lindera Extract on serum marker enzyme levels in streptozocin induced diabetic rats

S.No	Treatment group	SGOT (IU/L)	SGPT (IU/L)	ALP (IU/L)	ACP (IU/L)	LDH (IU/L)	GGT (IU/L)
1	Normal Control	137 ±1.5	41.5± 2.5	128±1.4	6.8±0.05	280±2.5	4.51±2.3
2	Diabetic control	193 ± 1.2	98.2± 2.1	245±1.3	11±0.26	175±2.9	18.2±2.9
3	60 mg/kg STZ + 500 mg/kg of Extract	143 ± 1.7	64.5± 2.7	154±1.5	7.9±0.22	265±2.1	7.15±2.7

4	60 mg/kg STZ	152 ± 1.1	75.1± 2.2	165±1.7	8.1±0.17	259±2.2	8.51±2.9
5	60 mg/kg STZ + 50 mg/kg metformin	145 ± 1.9	59.1± 2.4	145±1.6	7.4±0.45	274±2.7	6.11±2.8

Table 6: Effect of Ximenia Extract on serum bilirubin, albumin and protein levels in streptozocin induced diabetic rats

Group	Treatment group	Bilirubin (mg/dl)	Protein (g/dl)	Albumin (g/dl)
1	Normal Control	0.82 ± 0.25	5.73 ± 1.07	2.56 ± 0.95
2	Diabetic control	2.01 ± 0.32	2.52 ± 1.13	1.66 ± 0.12
3	60 mg/kg STZ + 500 mg/kg of *Extract*	0.03 ± 0.23	5.21 ± 1.01	2.36 ± 1.22
4	60 mg/kg STZ	1. 2± 0.03	3.85 ± 1.22	2.06 ± 1.36
5	60 mg/kg STZ + 50 mg/kg of metformin	0.06 ± 0.15	4.22 ± 0.08	3.55 ± 1.17

(Each value is expressed as Mean ± S.D of five values)

Group	Treatment group	Phospholipid (mg/dl)	Cholesterol (mg/dl)	Triglyceride (mg/dl)
1	Normal Control	113.49 ± 1.03	56.15 ± 1.09	33.11 ± 1.21
2	Diabetic control	176.21 ± 1.52	100.2 ± 1.32	105.3 ± 1.36
3	60 mg/kg STZ + 500 mg/kg of *Extract*	122.27 ± 1.26	58.64 ± 1.02	44.35 ± 1.66
4	60 mg/kg STZ	113.02 ± 1.23	48.31 ± 1.47	32.23 ± 1.03
5	60 mg/kg STZ + 50 mg/kg metformin	112.32 ± 1.01	60.21 ± 1.36	39.24 ± 1.32

Table 7: Effect of - Ximenia Extract and on urea, BUN, creatinine levels in streptozocin induced diabetic rats

S. No	Treatment group	Creatinine (mg/dl)	Urea (mg/dl)	BUN (mg/dl)
1	Normal Control	0.77 ± 1.03	14.15 ± 1.96	14.5 ± 1.27
2	Diabetic control	1.09 ± 1.55	36.15 ± 2.18	26.2 ± 1.11
3	60 mg/kg STZ + 500 mg/kg of *Extract*	1.21 ± 1.07	15.62 ± 2.03	22.6 ± 1.31
4	60 mg/kg STZ	0.32 ± 1.05	20.03 ± 1.16	16.8 ± 1.21
5	60 mg/kg STZ + 50 mg/kg of metformin	0.07 ± 1.63	22.42 ± 2.54	16.1 ± 1.26

(Each value is expressed as Mean ± S.D of five values)

Table 8: Effect of Ximenia Extract on serum marker enzyme levels in streptozocin induced diabetic rats

S.No	Treatment group	SGOT (IU/L)	SGPT (IU/L)	ALP (IU/L)	ACP (IU/L)	LDH (IU/L)	GGT (IU/L)
1	Normal Control	122 ±1.3	29.5± 2.2	106±1.2	4.8±0.05	223±2.4	2.49±2.1
2	Diabetic control	166 ± 1.1	76.2± 1.2	196±1.1	6±0.15	155±2.6	12.2±2.6
3	60 mg/kg STZ + 500 mg/kg of Extract	126 ± 1.3	64.5± 2.7	131±1.3	5.9±0.22	243±1.3	5.15±2.5
4	60 mg/kg STZ	142 ± 0.9	631± 2.1	144±1.3	6.5±0.12	223±1.8	6.51±2.6
5	60 mg/kg STZ + 50 mg/kg metformin	131± 1.5	37.1± 2.1	122±1.3	5.3±0.32	232±2.6	4.09±2.2

(Each value is expressed as Mean ± S.D of five values)

Conclusion:

The results showed that both extracts of Lindera and Ximenia established their potency against diabetes by reducing hyperglycemia, serum blood glucose level in diabetic animals, with the former extract being found to be more effective than the latter. This scientific information can serve as an important platform for the development of further safe and effective natural medicine. The development of powerful medications derived from plants that can replace clinically hazardous ones might be assisted by the elucidation of the molecular mechanisms at play and the isolation of the bioactive molecules implicated. Therefore, additional research must be done to fully identify and characterize the molecules in charge of the anti-diabetic effects.

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