International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 30, Issue 12, December 2024 **ijppr.humanjournals.com** ISSN: 2349-7203

Phytochemical and Pharmacological (Antidiabetic) Activity of *Aegle marmelos* (L.) Corr

Mohan Kashyap*, Dr. Dharmendra Kumar Shrivastava, Dr. Yogendra Singh, Avinash Singh Kushwah, Sunil Singh Narwaria

Shri Ramnath Singh Mahavidyalaya (Pharmacy), Gormi, Bhind (M.P.) – 477660 India.

Received: 2024-12-10 Revised: 2024-12-20 Accepted: 2024-12-27

ABSTRACT

The antidiabetic activity of hydroalcoholic leaf extracts of Aegle marmelos in alloxan induced diabetic rats. Alloxan induced diabetic in rats (n=6) were administered hydroalcoholic leaves extracts of Aegle marmelos (125, 250 & 500 mg/Kg) and standard drug Vildagliptin (0.3mg/kg) for 7 days. On eight day of the treatment, blood samples were collected by puncturing the retro-orbital plexus under mild ether anesthesia and kept aside for ½ h for clotting. Blood glucose levels were determined by glucose oxidase method. Serum was separated by centrifuging the samples for 20 mins and stored in the refrigerator. The serum was analyzed for blood glucose level, total protein, cholesterol and triglycerides .The plant of hydroalcoholic extracts shown significant ($P<0.05$) reduction in blood glucose level. However, Aegle marmelos extracts (500 mg/kg) was highly effective and results are comparable with that of reference drug, Vildagliptin. Diabetic animals treated with hydroalcoholic extracts of Aegle marmelos shown significant ($P<0.05$) effect on serum protein, cholesterol and triglyceride level. In comparison to different dose of hydroalcoholic leaf extract (500 mg/kg) fraction was found to be more potent in normalizing the blood lipids and protein level in Alloxan induced diabetic rats. It is concluded that Aegle marmelos has significant antidiabetic activity as it lowers the blood glucose levels in diabetic rats and increases the glucose tolerance.

Keywords: Diabetes, Medicinal Plant, Aegle marmelos, Alloxan

INTRODUCTION

Diabetes mellitus is one of the common metabolic disorders with micro-and macrovascular complications that results in significant morbidity and mortality. It is considered as one of the five leading causes of death in the world [1, 2]. In modern medicine no satisfactory effective therapy is still available to cure diabetes mellitus [3]. There is increasing demand by patients to use natural products with antidiabetic activity due to side effects associated with the use of insulin and oral hypoglycemic agents [4–6]. There are numerous traditional medicinal plants reported to have hypoglycemic properties such as Allium sativum (Garlic), Azadirachta indica (Neem), Vinca rosea (Nayantara), Trigonella foenum (Fenugreek), Momordica charantia (Bitter ground), Ocimum santum (Tulsi). Many of these are less effective in lowering glucose levels in severe diabetes.

Aegle marmelos L. Correa (A. marmelos), a medicinal plant of family Rutaceae which is commonly known as Bael, Bengal-quince, golden apple or wood/stone apple tree. It is a medium sized deciduous tree, up to 12-15 m tall with short trunk, thick, soft, flaking bark and spreading, sometimes spiny branches. [5, 6] This plant is native to Northern India, but widely found throughout the Indian Peninsula and in Ceylon, Burma, Bangladesh, Thailand and China. It is also grown in some Egyptian gardens, in Surinam and Trinidad. [7] A. marmelos fruit is globose with smooth, hard and aromatic shell that is gray green in color when raw and yellowish when ripe. Fruit pulp is pale orange, sweet, resinous and highly aromatic. [8, 9]

The aqueous leaf extract of Bael contained alkaloids, flavonoids, phenolic compounds, and saponins. The aqueous extract of Bael leaf consisted of 16.36 mg rutin equivalent total flavonoids and 31.38 gallic acid equivalent total phenolics. The ethanol and aqueous extracts of Bael root have been reported to contain alkaloids, flavonoids, saponins proteins, and tannins. [10]The aqueous and methanol seed extracts of Bael possessed alkaloids, flavonoids, glycosides, phenolics, steroids, tannins, carbohydrates, proteins, amino acids, volatile oils, and fats. [11, 12] Hence on the above fact no study has been carried out on hydroalcoholic extracts of

Aegle marmelos leaves extract in alloxan induced diabetic rats. Thus, the present study is an attempt to test the antidiabetic activity of Aegle marmelos leaves.

MATERIALS AND METHODS

Collection of Plant Materials, Identification and Authentication: *Aegle marmelos* plants were collected from the Gwalior region of Madhya Pradesh and were identified by the :Department of Pharmacy, Shri Ramnath Singh Institute of Pharmaceutical Science & Technology, Gwalior, (Madhya Pradesh).

Physico-chemical analysis of *Aegle marmelos*: The physicochemical evaluation of plant powder is often carried out in accordance with the guidelines of the Indian Pharmacopeia or the WHO. [13, 14]

Preparation of Extract: Leaves were shattered and screened with 40 no. mesh. The shade dried leaves of *Aegle marmelos* were powdered using grinder. The 10 gram of plant material was extracted with 100 ml of 70 % hydro-alcohol (30:70; Water: Ethanol) in a Soxhlet apparatus at 70°C till exhaustion. The obtained extract was concentrated under reduced pressure at 40°C. [15]

Qualitative Phytochemical Investigation Of Extracts: Qualitative phytochemical screening of hydroalcoholic extract of leaves was carried out to identify phytoconstituents. [16]

Fluorescence Analysis: The fluorescence character of the plant powder was studied both in UV light (254nm and 366nm) and daylight and after treatment with different reagents like glacial acetic acid, methanol, sodium hydroxide, sulphuric acid and hydrochloric acid.

Thin Layer Chromatography (TLC): Extracts OF *Aegle marmelos* were subjected to thin layer chromatographic studies, to find out the probable number of compounds present in them. Each solvent extract was subjected to thin layer chromatography (TLC) as per conventional one dimensional ascending method using silica gel. Plate markings were made with silica Gel G. Glass capillaries were used to spot the sample for TLC applied sample volume 1µl by using capillary at distance of 1 cm from the base. In the solvent chamber different solvent system 1 n- Hexane: Ethyl acetate: formic acid (10:5:1), solvent system 2 Benzene: Ethyl acetate (1:0.5) and solvent system 3 Methanol: HCl (9:1) were selected for analysis. [17, 18]

Determination of Phenolic content: The total phenolic content of extracts was determined using to the Folin- Ciocalteu method. Briefly, 0.75 mL of Folin–Ciocalteu reagent (1:9; Folin- Ciocalteu reagent: distilled water) and 10 mL of sample (10 mg/mL) was put into a test tube. The mixture was allowed to stand at room temperature for 5 min. 75 µL of 6% (w/v) Na_2CO_3 was added to the mixture and then mixed gently. The mixture was homogenized and allowed to stand at room temperature for 90 min. Total polyphenol content was determined using a spectrophotometer at 425 nm. The standard calibration (10–100 µg/mL) curve was plotted using gallic acid. [19] The total phenolic content was expressed as Gallic Acid Equivalents (GAE) in milligrams per 100 g plant extract.

$$TPC = \frac{R \times D.F \times V \times 100}{W}$$

Where, R = Result obtained from the standard curve

D.F = Dilution factor

V = Volume of stock solution

100 = For 100 g dried plant

W = Weight of plant used in the experiment

Determination of Flavonoid Content: Total flavonoid content was measured with the aluminium chloride colorimetric assay. 1ml of aliquots and 1ml standard quercetin solution (100, 200, 400, 600, 800, 1000 µg/ml) was positioned into test tubes and 4ml of distilled water and 0.3 ml of 5 % sodium nitrite solution was added into each. After 5 minutes, 0.3 ml of 10 % aluminium chloride was added. At 6th minute, 2 ml of 1 M sodium hydroxide was added. Finally, volume was making up to 10 ml with distilled water and mix well. Orange yellowish colour was developed. The absorbance was measured at 510 nm spectrophotometer using UV-

visible (1800) Shimadzu, Japan Instrument. The blank was performed using distilled water. Quercetin was used as standard. [20] The samples were performed in triplicates. The calibration curve was plotted using standard quercetin.

PHARMACOLOGICAL ACTIVITY

Animal Selection: Albino rats (Wistar strain) male weighing between 225 - 256 gm was used in the study. Animal was housed in polypropylene cages in controlled temperature (25 ± 2°C), relative humidity (60 ± 5°C) and light. They were employed for assessing antidiabetic activity study. The animals were allowed free access to commercial rat pallet diet (Lipton India ltd., Mumbai, India). The bedding material of the cages was changed every day. All the experimental procedures were carried out accordance with committee for the purpose of control and supervision of experiments on animal (CPCSEA) guidelines. [21, 22] The experimental procedures were approved by the institutional animal ethical committee.

In-Vivo Antidiabetic activity study: Screening of antidiabetic activity of the extracts of *Aegle marmelos* was done in alloxan induced male albino rats. In this study the prolonged effect of the extracts of leaves in blood glucose (BG) and biochemical parameters such as serum total cholesterol (TC), Triglycerides (TG), HDL and LDL were studied in alloxan induced diabetic rats. [23]

Experimental Design: Six groups of rats, six in each received the following treatment schedule.

- Group 1: Normal control (0.9% NaCl) (NC)
- Group 2: Diabetic control (Alloxan 150 mg/kg) (DC)
- Group 3: Diabetic control (Alloxan 150 mg/kg) + Vildagliptin (0.3mg/kg)
- Group 4: Diabetic rat + leaf extract of Aegle marmelos (125mg/kg low dose) (AMEE 125)
- Group 5: Diabetic rat + leaf extract of Aegle marmelos (250mg/kg medium dose) (AMEE 250)
- Group 6: Diabetic rat + leaf extract of Aegle marmelos (500mg/kg high dose) (AMEE 500)

Leaves extract and standard drug vildagliptin (0.3 mg/kg) and saline were administered with the help of feeding cannula.

Statistical Calculation: For the One-way Anova calculations for all the sets of data obtained, SPSS version 21.0 was used. The IC_{50} values were calculated using Graph Pad Prism version 6.0 Software followed by paired t test. [24, 25]

RESULTS AND DISCUSSION

Physico–Chemical Properties Of Leaves: The physical nature of leaves of *Aegle marmelos* is shown in Table 1. The results indicate that the leaves showed total ash content of 11%, acid insoluble ash content of 20% and water soluble content of 12%. The ash values are useful in the determination of quality and purity of the plant sample.

Hydro-Alcoholic Extractive Values: Soxhlet method was used for the extraction of leaves of *Aegle marmelos*. The hydroalcoholic extractive values of *Aegle marmelos* leaves are given in Figure 1.

Qualitative Phytochemical Screening Of Extracts Of Aegle Marmelos: The phytochemical constituents of leaves and fruits extracts of *Aegle marmelos* were screened by Soxhlet process. The results are given in Figure 2. Alkaloids, flavonoids, steroids, tannins and phenolics, glycosides and carbohydrates are present in all the extracts. Proteins were absent in all the extracts of leaves and fruits. The interesting fact is that the saponins are present in leaves extract. Hence the results revealed that hydro-alcoholic leaves extract has the ability to extract more polar compounds.

International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 30, Issue 12, December 2024 **ijppr.humanjournals.com** ISSN: 2349-7203

Figure 1: Hydroalcoholic extraction of drug

Figure 2: Qualitative Phytochemical Screening Of Extract

Fluorescence Analysis: The leaves powder of *Aegle marmelos* exhibit colours when treated with different reagents which constitutes major photo compounds. After detecting the phytochemicals, the fluorescence analysis of *Aegle marmelos* in chemical test by daylight and UV light the extract appeared dark green, brown and greenish brown colour. The plant is reliable and possess medicinal value and the colour was undertaken as a pharmacognostic standardization.

Table 1: Fluorescence analysis of powdered leaves

S. No	Powdered Drug	Visible Light/Day Light	UV 254nm
1	Untreated leaves powder	Dark green	Dark green
2	Leaves powder treated with methanol	Dark green	Dark green
3	Leaves powder treated with 1% glacial acetic acid	Deep greenish brown	Greenish brown
4	Leaves powder treated with 10% NaOH	Dark green	Dark green
5	Leaves powder treated with 1M H_2SO_4	Green	Green
6	Leaves powder treated with 1M HCl	Green	Green

Thin Layer Chromatography (TLC): Large number of solvent systems such as n-Hexane: Ethyl acetate: formic acid (10:5:1), Benzene: Ethyl acetate (1:0.5) and Methanol: HCl (9:1) were tried to achieve a good resolution (Table 2). Finally, the solvent system of Methanol: HCl (9:1) gave the best result. Many of other solvent system were investigated before developing the solvent systems but none of them gave the satisfactory results. TLC of Aegle marmelos leaves extract having Rf values by Soxhlet process of 0.83. These spots and Rf values are similar to the flavonoids (quercetin/rutin) and confirms the presence of flavonoids in leaves and fruits extracts of Aegle marmelos.

Table 2: TLC of extract

Solvent System	Distance travel by solvent (A) (cm)	Distance travel by solute (B) (cm)	Retention Factor (Rf)= B/A	Conclusion
n-Haxane: Ethyl acetate: formic acid (10:5:1)	-	-	-	Poor
Benzene: Ethyl acetate (1:0.5)	-	-	-	Poor
Methanol: HCl (9:1)	13	10.9	0.83	Very Good

Total Phenolic content: Total Phenolic content of leaves extract of *Aegle marmelos* is 2.13±0.003 mg GAE/gm by maceration process. However, in Soxhlet process the total phenolic content was 2.13±0.003 mg GAE/gm of dried plant part respectively. Total phenolic content are expressed as mg gallic acid equivalent (GAE). Total Phenolic contents have been implicated as natural antioxidants in leaves. They contribute to quality and nutritional value and also provide health beneficial effects.

Table 3: Total Phenolic content

S. No.	Extraction Process	Extract	Total phenolic content mg GAE/gm
1	Soxhlet	Leaves Extract	2.13±0.003

Data are presented as mean ± SE of each triplet test.

Total Flavonoid content: Flavonoid content of all extracts were measured and expressed as mg quercetin equivalents (QE). Total flavonoid content of leaves extract of *Aegle marmelos* was 1.03 ± 0.0006. The highest flavonoid content was found in fruits extract prepared by Soxhlet method.

Table 4: Total Flavonoid content

S. No.	Extraction Process	Extract	Total phenolic content mg GAE/gm
1	Soxhlet	Leaves Extract	1.03 ± 0.0006

Data are presented as mean ± SE of each triplet test.

Pharmacological Activity

Acute Toxicity Test: The acute toxicity study showed that the administration of graded doses of hydroalocholic extracts of *Aegle marmelos* did not generate any observable signs of toxicity up to the dose of 2000 mg/kg. This was confirmed by the absence of significant changes in behaviours such as alertness, motor activity, weight loss, sluggishness, paralysis, breathing, restlessness, diarrhoea, convulsions, and coma. In addition, no death was observed for two weeks and they were physically active. The result proves that the plant extracts had no observable adverse effect at the doses tested; implying that the medium lethal dose (LD_{50}) is greater than 2000 mg/kg body weight in rats. Since its actual median lethal dose (LD_{50}) is greater than 2000 mg/Kg, extract of Aegle marmelos is non-toxic.

In- Vivo Antidiabetic Activity

Body Weight: The data of body weight obtained in the present study of all the groups of male albino rats are shown in table no 5. There was no significant change in the body weight of normal control animals during the experimental period of 28 days. Diabetic control (DC) rats showed a loss of 7.7% body weight on 28th day. They showed a significant reduction ($p< 0.001$) in body weight when compared with normal control with their initial weight and final weight. Alloxan mediated body weight reduction was significantly reversed by hydroalcoholic leaves and fruits extract in dose dependent fashion with (125, 250 and 500 mg/Kg) when compared with diabetic control ($p< 0.001$). The body weight of these animals does not show any significant increase in their respective weights of initial and final day of the experiment.

Table 5: Effect of *Aegle marmelos* extracts on body weight in control and experimental rats.

No.	Groups	Body weight Mean ± S.D.		Percentage change (%)
		Initial day	28th day	
1	(0.9% NaCl)	240.45 ± 3.65	241.78 ± 4.76	0.25 ↑
2	Diabetic control (DC) (Alloxan) 150 mg/Kg	236.34 ± 5.11	218.67 ± .432abc***	7.12 ↓
3	Diabetic rats fed Vildagliptin (RD) 0.3 mg/Kg	237.45 ± 3.76	234.56 ± 3.64c***	1.39 ↓
4	Diabetic rats fed leaves extract of *A. marmelos* (AMEE-125 mg/Kg)	235.45 ± 7.72	238.54 ± 7.61c***	1.61 ↑
5	Diabetic rats fed leaves extract of *A. marmelos* (AMEE-250 mg/Kg)	235.45 ± 2.67	239.34 ± 4.29c ***	1.70 ↑
6	Diabetic rats fed leaves extract of *A. marmelos* (AMEE-500 mg/Kg)	237.03 ± 4.75	244.54 ± 5.34c ***	3.37 ↑

[a] when compared with normal control (NC); [b] when compared with normal control (EC); [c] when compared with diabetic control (DC). * P < 0.05 ** P < 0.01 *** P < 0.001

Oral Glucose Tolerance Test: Zero hour (fasting) blood glucose level was determined from overnight fasted animals. After 30 minutes of drug treatment animals were fed with glucose (2gm/Kg) and blood glucose level was determined after 30, 60, 90 and 120minutes of the glucose load. Blood glucose concentration was estimated by the glucose oxidase enzymatic method by using commercial one touch electronic glucometer and test stripes. The recorded blood glucose levels and percentage glycemic change for every 30, 60, 90 and 120 minutes of each group are shown in table 6. After 30 minutes of oral administration of glucose there was a significant rise in blood glucose levels of all groups of animals and gradually the values decreased pre- prandial level. The hydroalcoholic extract of leaves at the dose of 125, 250 and 500 mg/Kg produced blood glucose levels significantly lower than those of the diabetic control group at 30, 60, 90, and 120 minutes after glucose administration.

Table 6: Effect of *A. marmelos* extracts on oral glucose tolerance test (OGTT) in control and experimental rats

Groups	Blood glucose concentration (mg/dl) (mean ± S.D.) n = 6				
	In fasting	30 min	60 min	90 min	120 min
Normal control (0.9% NaCl)	67.56±2.54	83.12±1.47	80.23±1.21	78.12±1.24	77.54±1.76
Diabetic control (DC) (Alloxan-150 mg/kg)	246.67± 6.56a	315.32± 6.76a	306.645± 5.76a	292.47± 3.54a	290.56± 3.27a
Diabetic rats fed Vildagliptin (0.3 mg/kg)	246.72± 4.56ab	296.45± 2.68ab	271.78± 3.68ab	268.56± 4.67ab	253.67± 2.57ab
AME-125 mg/Kg	245.27± 3.11a	245.95± 2.63abc	242.54± 2.32abc	240.65± 1.54abc	239.19± 1.44abc
AMEE-250 mg/Kg	235.37± 2.12abc	245.65± 2.67abc	243.76± 1.36abc	242.11± 2.29abc	240.59± 3.97abc
AMEE-500 mg/Kg	223.34± 2.46abc	245.57± 1.67abc	244.46± 1.22abc	243.47± 2.32abc	242.67± 2.66abc

a P < 0.001 compared with normal control.

b P <0.001 compared with diabetic control

c P<0.001 compared with reference drug group

Blood Glucose Determination: The leaves extract of *Aegle marmelos* (at 125, 250, and 500 mg/Kg) exhibited a dose dependent significant anti hyperglycemic activity on 28th day post treatment. The leaves extract dose of 125 mg/Kg caused 15.78% reduction in blood glucose level (p<0.001). Among leaves extract treatment maximum reduction in blood glucose level (46.93%) was observed when the extract was given in the dose of 500 mg/Kg. The Antihyperglycemic effect of leaves extract was found less effective than the standard drug vildagliptin fed Group 4. Vildagliptin produced a significant reduction in blood glucose compared to diabetic control (p< 0.001).

Table 7: Effect of *A. marmelos* extracts on fasting blood glucose in control and experimental rats

Group No.	Groups	Fasting blood glucose level Mean ± S.D.		Percentage change (%)
		Initial day	28th day	
1.	NC	79.45 ± 2.64	79.99 ± 3.45	0.02 ↓
2	DC	292.34 ± 2.52	286.55 ± 5.11	1.72 ↓
3	RD	277.13 ± 3.46	132.34 ± 3.43ab***	54.26 ↓
4	AMEE-125	287.85 ± 1.37	245.12 ± 4.65ab***	15.78 ↓
5	AMEE-250	285.54 ± 3.04	203.65 ± 3.54ab***	29.27 ↓
6	AMEE-500	280.34 ± 3.02	156.16 ± 7.60ab***	46.93 ↓

All values analysed for One Way ANOVA and paired t test

a when compared with diabetic control P < 0.001

b when compared with initial and 28th day value P < 0.001

International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 30, Issue 12, December 2024 ijppr.humanjournals.com ISSN: 2349-7203

Analysis of Lipid profile: Effect of leaves extract of *Aegle marmelos* a in normal control and experimental animals on lipid profile are shown in table 8. Alloxan induced diabetic rats showed significant hypercholesterolemia and hypertriglyceridemia as compared to normal control animals. Treatment with different doses of leaves extract significantly changed the lipid profile of experiment animals compared to the untreated diabetic rats.

Table 8: Effect of *Aegle marmelos* extracts on lipid profile

Groups	Lipid Profile mg/dl			
	Total cholesterol	% change	Triglyceride	% change
NC	85.92 ±4.01	-	70.14 ±2.27	-
DC	172.65±7.58ab***	104.77	167.11±10.54 ab***	58.40
RD	155.67±7.33abc***	33.46	103.21±4.12abc***	40.85
AMEE125	152.54±8.56abcd***	12.06	135.46±2.34abcd***	19.48
AMEE250	121.23±3.56abcd***	29.27	120.43±4.23abcd***	28.58
AMEE500	112.57 ±4.11abcd***	36.45	103.43±2.32abcd***	36.64

a -P<0.001 when compared with normal control, b-P<0.001 when compared with experimental control, c-P<0.001 when compared with diabetic control, d-P<0.001 when compared with reference drug group. Analysis by One Way ANOVA. *** p < 0.001

Table 9: Effect of *Aegle marmelos* extracts on lipid profile

Groups	Lipid Profile mg/dl			
	HDL	% change	LDL	% change
NC	45.63 ±3.27	-	88.11±2.77	-
DC	17.65±3.61 ab***	62.15	189.65±2.54 ab***	109.65
RD	26.43±2.54abc***	51.99	90.86±1.50abc***	53.17
AMEE125	24.45±2.68abc***	43.83	112.21±3.11abcd***	39.43
AMEE250	30.54±2.21abcd***	69.60	101.1±4.18abcd***	48.43
AMEE500	35.23±3.11abcd***	104.11	87.11±3.98abcd***	54.60

a -P<0.001 when compared with normal control, b-P<0.001 when compared with experimental control, c-P<0.001 when compared with diabetic control, d-P<0.001 when compared with reference drug group. Analysis by One Way ANOVA. *** p < 0.001

Analysis of in vivo antioxidant activity:

i) Superoxide dismutase (SOD): The results showed that the SOD that the SOD level of animals treated with alloxan (DC) declined significantly than normal control groups. Administration of leaves and fruits extract of *Aegle marmelos* at a dose of 125, 250 and 500 mg/Kg for 28 days markedly increased the level of SOD. Standard vildagliptin treated group also significantly increased (50.39%) the level of SOD in diabetic rats.

ii) Lipid peroxidation (MDA Analysis): The results of MDA level of various groups are mentioned in table 10. In the liver of alloxan treated diabetic rats, lipid peroxidation levels as evidenced by MDA determination increased significantly as compared to normal control group (p< 0.001). In diabetic rats treated with reference drug vildagliptin a significant decreases in MDA were observed. In diabetic rat's extract of *Aegle marmelos* leaves (125, 250, 500 mg/Kg) treatment significantly inhibited the increase in MDA.

Table 10: Effect of AM extracts on antioxidant levels in control and experimental rats on 28th day

Groups No.	Groups	in vivo antioxidants µg Mm/tissue	
		SOD	MDA
1	NC	70.55 ± 5.95	19.08±2.19
2	DC	21.40 ± 2.57ab***	43.09±4.31ab***
3	RD	32.45 ± 3.69abc***	29.54±1.61 abc***
4	AMEE-125	31.74 ± 2.18 abc***	38.41±2.63 abcd***
5	AMEE-250	41.12 ± 2.85 abcd***	33.15±2.54 abcd***
6	AMEE-500	50.39±3.18abcd***	30.99±2.47 abcd***

CONCLUSION

In conclusion, these observations clearly demonstrated that the Aegle marmelos leaves and exerts remarkable hypoglycemic and Antihyperglycemic activity due to its possible multiple effects involving both pancreatic and extra pancreatic mechanism. It has also determines that the extract possessed a capability to inhibit the enzymes like SOD in diabetes, so the observed antioxidant potential of *Aegle marmelos* extract may partially responsible for its antidiabetogenic properties. Antihyperglycemic activities of most effective plants were in part explained by the ability of phytoconstituents to increase glucose transport and metabolism in muscle and / or to stimulate insulin secretion. invitro inhibitory activities can be related to invivo activity. The data obtained from invitro inhibitory activity of Aegle marmelos were very promising and therefore it is used for preclinical animal study. Hence, the results of this study can be justified by the facts that the leaf extract of Aegle marmelos enhances the faster lay down of collagen fibres and improves the antioxidant status in the diabetic animals and decrease diabetes level and can used as antidiabetic drug.

REFERENCES

1. Vats V, Yadav SP, Grover JK. Ethanolic extract of Ocimum sanctum leaves partially attenuates streptozotocin-induced alterations in glycogen content and carbohydrate metabolism in rats. Journal of Ethnopharmacology. 2004;90(1):155–160. doi: 10.1016/j.jep.2003.09.034. [DOI] [PubMed] [Google Scholar]
2. Kumar GPS, Arulselvan P, Kumar DS, Subramanian SP. Anti-diabetic activity of fruits of Terminalia chebula on streptozotocin induced diabetic rats. Journal of Health Science. 2006;52(3):283–291. [Google Scholar]
3. Sumana G, Suryawashi SA. Effect of vinca rosea extracts in treatenent of alloxan diabetes in male albino rats. Indian Journal of Experimental Biology. 2001;39:748–758. [PubMed] [Google Scholar]
4. Holman RR, Turner RC. Oral agents and insulin in the treatment of NIDDM. In: Pickup J, Williams G, editors. Text Book of Diabetes. Oxford, UK: Blackwell; 1991. pp. 467–469. [Google Scholar]
5. Kameswara Rao B, Kesavulu MM, Apparao Ch. Antihyperglycemic activity of Momordica cymbalaria in alloxan diabetic rats. Journal of Ethnopharmacology. 2001;78(1):67–71. doi: 10.1016/s0378-8741(01)00324-5. [DOI] [PubMed] [Google Scholar]
6. Kameswrarao B, Giri R, Kesavalu MM, Apparao Ch. Herbal medine. In: Bajaj JS, editor. The Management by Indigenous Resources. New Delhi, India: Diabetes Mellitus in Developing Countries. Interprint; 1997. pp. 375–377. [Google Scholar]
7. Jaleel CA, Gopi R, Lakshmanan GMA, Panneerselvam R. Triadimefon induced changes in the antioxidant metabolism and ajmalicine production in Catharanthus roseus (L.) G. Don . Plant Science. 2006;171(2):271–276. [Google Scholar]
8. Jordan MA, Thrower D, Wilson L. Mechanism of inhibition of cell proliferation by Vinca alkaloids. Cancer Research. 1991;51(8):2212–2222. [PubMed] [Google Scholar]
9. Kulkarni RN, Baskaran K, Chandrashekara RS, Kumar S. Inheritance of morphological traits of periwinkle mutants with modified contents and yields of leaf and root alkaloids. Plant Breeding. 1999;118(1):71–74. [Google Scholar]
10. Sharma PC, Bhatia V, Bansal N and Sharma A (2007): A review on Bael tree. Natural Products Radiance., 6(2):171-178.
11. Gaur SD (1969): Aegle marmelos, in Dhanvantri, Ed by Trivedi KP. Dhanvantri Karyalaya, Aligarh, p 204.
12. Baliga MS, Bhat HP, Joseph N and Faza F (2011): Phytochemistry and medicinal uses of the bael fruit (Aegle marmelos Correa): A concise review. Food Research International, 44(7): 1768-1775.
13. Kamalakkannan N and Prince PS (2003): Hypoglycaemic effect of water extracts of Aegle marmelos fruits in streptozotocin diabetic rats. J. Ethnopharmacol., 87(2-3):207-210.
14. Jagetia GC, Venkatesh P and Baliga MS (2004): Fruit extract of Aegle marmelos protects mice against radiation-induced lethality. Integr. Cancer Ther., 3(4):323-332.
15. Rao CHV, Amresh KR, Irfan A, Rawat AKS and Pushpangadan P (2003): Protective effect of Aegle marmelos fruit in gastrointestinal dysfunction in rats. J.Pharm. Biol., 4:558-563.
16. Raja SB, Murali MR, Malathi GK, Anbarasu K and Devaraj SN (2009): Effect of aqueous extract of Aegle marmelos fruit on adherence and β-lactam resistance of Enteropathogenic Escherichia coli bydown regulating outer membrane protein C. Am. J. Infect. Dis., 5(2):154-162.
17. S.S. Gupta Prospects and perspectives of natural plant products in medicine, Indian Journal of Pharmacology,1994 ,26,1-12
18. A . Purohit , V.P. Dixit , Hypoglycemic effect of membrane and flower on streptozotocin-induced diabetes in mice. Ancient science of life.,1991;11:28-30
19. M.N. Ghosh, Fundamentals of Experimental Pharmacology.5th edn.1984, P.153-158 .
20. C .Stephen, D .McCarthy, H.H .De cory, M .Nasler and J .Garilleson, Phase I: The First Opportunity for Extrapolation from Animal Data to Human Exposure. Proc.of 5th Int.Symp. On Drug Discovery. Mumbai.Jan 2003.
21. Giordano BP, Thrash W, Hollenbaugh L, et al. Performance of seven blood glucose testing systems at high altitude. The Diabetes Educator. 1989;15(5):444–448. doi: 10.1177/014572178901500515. [DOI] [PubMed] [Google Scholar]
22. Roeschlau P, Bernt E, Gruber W. Enzymatic determination of total cholesterol in serum. Zeitschrift für klinische Chemie und Klinische Biochemie. 1974;12(5):p. 226. [PubMed] [Google Scholar]

23. Mueller PH, Schmuelling RM, Liebich HM. A fully enzymatic triglyceride determination. Journal of Clinical Chemistry and Clinical Biochemistry. 1977;15(9):457–464. [PubMed] [Google Scholar]
24. Allain CC, Poon LS, Chan CSG. Enzymatic determination of total serum cholesterol. Clinical Chemistry. 1974;20(4):470–475. [PubMed] [Google Scholar]
25. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clinical Chemistry. 1972;18(6):499–502. [PubMed] [Google Scholar]

How to cite this article:
Mohan Kashyap et al. Ijppr.Human, 2024; Vol. 30 (12): 480-488.
Conflict of Interest Statement: All authors have nothing else to disclose.