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Original Research Article

Effect of Amla (*Emblica officinalis*) on Various Physiological and Biochemical Parameters of Metabolic Syndrome

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Abstract: Amla (*Emblica officinalis*) has effect on physiological and biochemical parameters of metabolic syndrome due to its anti-inflammatory, hypolipidemic, hypoglycaemic, and anti-oxidative effects. We designed a randomized controlled trial to evaluate the role of Amla therapy in glycaemic control, obesity, hypertension and managing dyslipidemia of metabolic syndrome. The method is One Hundred patients of Metabolic Syndrome were randomized to receive conventional treatment with or without Amla. The patients were evaluated for body mass index, waist hip ratio, fasting blood sugar, blood pressure, glycosylated hemoglobin and lipid profile at baseline and 3 months after starting Amla. In results we found that Amla therapy resulted in good glycemic control (both FBS and HbA_1C, $p<0.001$); blood pressure both systolic & diastolic ($p<0.001$) and lipid profile ($p<0.001$) improved significantly in study group after Amla therapy. The parameters regarding obesity control (Body mass index and waist hip ratio) did not show significant improvement. In conclusion The Amla therapy is very efficient as an adjunct with conventional treatment (diet modification and pharmacological intervention) in management of metabolic syndrome.
Keywords: Amla (*Emblica officinalis*); Metabolic Syndrome; body mass index; waist hip ratio; fasting blood sugar; blood pressure; glycosylated hemoglobin; lipid profile.

INTRODUCTION:

The metabolic syndrome (syndrome X, insulin resistance syndrome) consists of a constellation of metabolic abnormalities that confer increased risk of cardiovascular disease (CVD) and diabetes mellitus (DM) [1]. The major features of the metabolic syndrome includes: Central obesity, Hypertriglyceridemia, Low HDL Cholesterol, Hyperglycemia and Hypertension. National Cholesterol Education Program, Adult Treatment Panel III (NCEP: ATP III 2001) criteria[1] for the metabolic syndrome: Three or more of the following

1. Central obesity: Waist Circumference, Male > 102cm, Female > 88cm
2. Hypertriglyceridemia : Triglyceride ≥150mg/dl or specific medication
3. Low HDL Cholesterol : <40mg/dl and <50mg/dl for men and women, respectively or specific medication
4. Hypertension : Blood Pressure ≥130mmHg systolic or ≥85 mmHg diastolic or specific medication
5. Fasting plasma glucose ≥100mg/dl or specific medication or previously diagnosed type II diabetes.

Phyllanthus emblica (Botanical name: *Emblica officinalis*; Common name**:** the Indian gooseberry), or Amla is a deciduous tree of the euphorbiaceae family. It is known for its edible fruit of the same name.

Amla is one of the most often used herbs in Indian ayurveda. Indian gooseberry comprises of the following nutrients: dietary fiber, vitamin C, calcium, Phosphorus, Iron, Carotene, Vitamin B complex, Protein, and Carbohydrates. Indian gooseberry has also been found to be low in saturated fats, cholesterol and sodium, making it good for health.

Only few quality controlled clinical trials are documented despite the widespread use of emblica in traditional health systems. Uses of amla include the following: Anti-inflammatory Effects [2, 3]. Antimicrobial Effects [4], Anti Cancer effects [5],

Hypolipidemic effects [6, 7], anti diabetes effects [8-11], and antioxidative [12].

All these uses of amla as mentioned and availability of very limited clinical evidence to support the use of emblica for any indication, created a great enthusiasm in our mind to go through this study to better serve the humanity by our own country product. The aim of present randomized controlled study is to evaluate the role of Amla therapy in glycaemic control, obesity, hypertension and managing dyslipidemia of metabolic syndrome.

MATERIAL AND METHODS:

This study was conducted in the department of Physiology, S.P. medical College, Bikaner, from August-2012 to october-2013, 100 patients were randomized to receive conventional treatment for metabolic syndrome with or without Amla.

Type of Study: Experimental Study: Randomized Controlled Trial

Selection of Patients: One hundred patients of metabolic syndrome were randomly selected for this study attending the Diabetes Care and Research Center of P.B.M. Hospital, Bikaner.

Exclusion Criteria: Patients suffering from any other diseases in addition to metabolic syndrome and non-cooperative patients were excluded from the study.

Method: The selected patients were divided randomly into two groups each were comprising of 50 patients.

Group I: These patients were given conventional treatment only (diet modification and pharmacological intervention) and served as the control group.

Group II: These patients besides conventional treatment were given Amla juice and served as the study group.

Amla Juice:

- **Manufacturer** : Patanjali Ayurveda Limited, Unit III
- **Preparation** : 1 Liter bottle, with sealed air tight lid
- **Composition** : Each 5ml contains**:** Amla swaras (*Emblica officinalis*) Indian gooseberry Juice 5ml
- **Preservative:** Sodium benzoate 0.20% weight/volume.

Procedure: Patients included in the study group were asked to take 25ml of Amla Juice (*Emblica officinalis*) mixed with equal amount of water, two times a day (morning & evening) empty stomach for three months regularly.

Before starting Amla Juice baseline parameters were taken for every patient i.e. body mass index, waist hip ratio, fasting blood sugar, blood pressure, glycosylated hemoglobin and lipid profile. Patients were evaluated weekly for Body Mass Index, Waist Hip Ratio, Fasting Blood Sugar and Blood Pressure. After three months besides above tests glycosylated hemoglobin and lipid profile were also estimated. Those under control group were also be evaluated weekly and after three months for these above mentioned parameters.

Body Mass Index(BMI): BMI = Weight (kg)/Height$(m)^2$

Waist Hip Ratio (WHR): It is the ratio of body circumference measured mid way between the iliac crest and lowest rib to that at the level of the greater trochanters.

Fasting Blood Sugar (FBS): FBS measured by glucose oxidase method, using enzymatic kits (GOD-POD method).

Glycosylated Hemoglobin: Measured by ion-exchange resin method/ Boronate affinity assay using HbA_1C Kit.

Serum Lipid Profile

Estimation of serum triglyceride: was done colorimetrically using enzymatic kits (GPO-POD method).

Estimation of total Cholesterol: was done colorimetrically using enzymatic kit (CHOD-POD method).

Estimation of HDL-Cholesterol: was done colorimetrically using enzymatic kit (Precipitating reagent).

Estimation of VLDL Cholesterol and LDL cholesterol: was calculated by using Friedwald (1972) formula

VLDL (mg/dl) = Triglyceride/5

LDL (mg/dl) = Total Cholesterol – (HDL + VLDL)

Measurement of Blood Pressure by Sphygmomanometry : In sitting position, Mean of two readings were recorded.

For statistical comparison of data, appropriate statistical model were applied using SPSS trial version 10 software for statistics.

Patients Characteristics at baseline are depicted in Table 1&2.

Table: 1 Comparison between two groups according to their age and sex

Age Group (years)	Control Group				Study Group			
	Female		Male		Female		Male	
	No.	%	No.	%	No.	%	No.	%
<40	6	20.0	0	-	1	3.4	7	33.3
41-50	12	40.0	9	45.0	11	37.9	9	42.9
51-60	8	26.7	7	35.0	9	31.0	2	9.5
>60	4	13.3	4	20.0	8	27.6	3	14.3
Total	30	60.0	20	40.0	29	58.0	21	42.0

Table:2 Mean age of subjects under study

	Female		Male		Total	
	Control Group	Study Group	Control Group	Study Group	Control Group	Study Group
Mean	49.30	55.00	53.35	46.48	50.92	51.42
SD	8.80	9.85	8.85	10.13	8.95	10.74
SE	1.61	1.83	1.98	2.21	1.27	1.52
t	2.346		2.310		0.253	
p	0.022		0.026		0.801	

RESULT:

(A) **Effects over Lipid Profile**

Triglyceride (TAG): The mean pre-intervention value in control and study group were 197.47±70.51 and 205.47±72.08, respectively (p=0.576), (Table no. 3). Mean post-intervention value in control and study group were 195.04±70.13 and 188.97±67.90 respectively (p=0.661), (Table no. 4). Comparison between differences of means (post intervention value - Pre intervention value) in control and study group were 2.428±4.572 and 16.503±8.964 (p<0.001), (Table no. 5).

HDL: The mean pre-intervention value in control and study group were 39.39±3.66 and 38.26±4.27 respectively (p=0.158), (Table no. 3). Mean post-intervention value in control group and study group were 38.56±3.69 and 39.22±4.05 respectively (p=0.394), (Table no. 4). Comparison between differences of means in control and study group were 0.832±1.183 and 0.964±2.799 (p=<0.001), (Table no. 5).

TOTAL CHOLESTEROL: The mean pre-intervention value in control and study group were 203.77±42.19 and 218.58±39.57 respectively (p=0.073), (Table no. 3). Mean post-intervention value in control group and study group were 201.52±41.59 and 200.30±36.72, respectively (p=0.877), (Table no. 4). Comparison between differences of means in control and study group were 2.248±3.092 and 18.280±8.985 (p=<0.001), (Table no. 5).

LDL: The mean pre-intervention value in control and study group were 124.88±40.01 and 129.74±34.81 respectively (p=0.519), (Table no. 3). Mean post-intervention value in control group and study group were 123.95±39.40 and 124.50±33.21 respectively (p=0.940), (Table no. 4). Comparison between differences of means in control and study group were 0.930±3.181 and 5.234±29.643 (p=<0.001), (Table no. 5).

VLDL: The mean pre-intervention value in control and study group were 39.49±14.10 and 41.09±14.42 respectively (p=0.576), (Table no. 3). Mean post-intervention value in control group and study group were 39.01±14.03 and 37.79±13.58 respectively (p=0.661), (Table no. 4). Comparison between differences of means in control and study group were 0.486±0.914 and 3.301±1.793 (p=<0.001), (Table no. 5).

(B)**Effect over Obesity control**

Body Mass Index (BMI): The mean pre-intervention value in control and study group were 29.71±5.22 and 29.77±4.20 respectively (p=0.942), (Table no. 3). Mean post-intervention value in control group and study group were 29.69±5.23 and 29.77±4.20, respectively (p=0.930), (Table no. 4).Comparison between differences of means in control and study group were 0.014±0.071 and 0.00±0.00 (Table no. 5).

WAIST-HIP RATIO (WHR): The mean pre-intervention value in control and study group were 0.96±0.08 and 0.95±0.06, respectively (p=0.374), (Table no. 3). Mean post-intervention value in control group and study group were 0.97±0.07 and 0.95±0.05 respectively (p=0.224), (Table no. 4). Comparison between differences of means in control and study

group were 0.003±0.024 and 0.004±0.013 (p>0.05), (Table no. 5).

(C)**Effect over Blood Pressure**

Systolic Blood-Pressure: The mean pre-intervention value in control and study group were 151.36±10.94 and 142.16± 11.53, respectively (p<0.001), (Table no. 3). Mean post-intervention value in control group and study group were 149.12±10.73 and 133.54±9.41, respectively (p<0.001), (Table no. 4). Comparison between differences of means in control and study group were 2.240±.255 and 8.62±5.22 (p<0.001), (Table no. 5).

Diastolic Blood-Pressure: The mean pre-intervention value in control and study group were 94.16±7.62 and 89.00±3.06 respectively (p<0.001), (Table no. 3). Mean post-intervention value in control group and study group were 92.40±7.08 and 83.04±3.62 respectively (p<0.001), (Table no. 4). Comparison between differences of means in control and study group were 1.760±1.492 and 5.96±3.44 (p<0.001), (Table no. 5).

(D)**Effects over Glycaemic Control**

Fasting Blood sugar: The mean pre-intervention value in control and study group were 161.49±66.49 and 201.02±68.74 respectively (p=0.004), (Table no. 3). Mean post-intervention value in control group and study group were 158.44±65.95 and 172.86±55.58 respectively (p=0.240), (Table no. 4). Comparison between differences of means in control and study group were 3.052±3.047 and 28.16±20.62 (p=<0.001), (Table no. 5).

Glycosylated Haemoglobin (HbA_1C): The mean pre-intervention value in control and study group were 7.59±0.55 and 7.98±0.96 respectively (p=0.016), (Table no. 3). Mean post-intervention value in control group and study group were 7.38±0.55 and 7.24±0.89 respectively (p=0.320), (Table no. 4). Comparison between differences of means in control and study group were 0.210±0.133 and 0.742±0.306 (p<0.001), (Table no. 5).

Table: 3 Comparison of different parameters between the groups at pre-intervention

Parameters		Control Group		Study Group		p
		Mean	SD	Mean	SD	
BMI		29.71	5.22	29.77	4.20	0.942
WHR		0.96	0.08	0.95	0.06	0.374
Blood Pressure	Systolic	151.36	10.94	142.16	11.53	<0.001
	Diastolic	94.16	7.62	89.00	3.06	<0.001
Glycemic Control	FBS	161.49	66.49	201.02	68.74	0.004
	HbA_1C	7.59	0.55	7.98	0.96	0.016
Lipid Profile	TC	203.77	42.19	218.58	39.57	0.073
	TG	197.47	70.51	205.47	72.08	0.576
	HDL	39.39	3.66	38.26	4.27	0.158
	LDL	124.88	40.01	129.74	34.81	0.519
	VLDL	39.49	14.10	41.09	14.42	0.576

Table: 4 Comparison of different parameters between the groups at post-intervention

Parameters		Control Group		Study Group		p
		Mean	SD	Mean	SD	
BMI		29.69	5.23	29.77	4.20	0.930
WHR		0.97	0.07	0.95	0.05	0.224
Blood Pressure	Systolic	149.12	10.73	133.54	9.41	<0.001
	Diastolic	92.40	7.08	83.04	3.62	<0.001
Glycemic Control	FBS	158.44	65.95	172.86	55.58	0.240
	HbA_1C	7.38	0.55	7.24	0.89	0.320
Lipid Profile	TC	201.52	41.59	200.30	36.72	0.877
	TG	195.04	70.13	188.97	67.90	0.661
	HDL	38.56	3.69	39.22	4.05	0.394
	LDL	123.95	39.40	124.50	33.21	0.940
	VLDL	39.01	14.03	37.79	13.58	0.661

Table: 5 Comparison between differences of means of anthropometric and biochemical parameters in both groups at 0 to 3 months

Parameters		Control Group		Study Group		p
		Mean	SD	Mean	SD	
BMI		0.014	0.071	0.00	0.00	-
WHR		0.003	0.024	0.004	0.013	>0.05
Blood Pressure	Systolic	2.240	1.255	8.62	5.22	<0.001
	Diastolic	1.760	1.492	5.96	3.44	<0.001
Glycemic Control	FBS	3.052	3.047	28.16	20.62	<0.001
	HbA_1C	0.210	0.133	0.742	0.306	<0.001
Lipid Profile	TC	2.248	3.092	18.280	8.985	<0.001
	TG	2.428	4.572	16.503	8.964	<0.001
	HDL	0.832	1.183	0.964	2.799	<0.001
	LDL	0.930	3.181	5.234	29.643	<0.001
	VLDL	0.486	0.914	3.301	1.793	<0.001

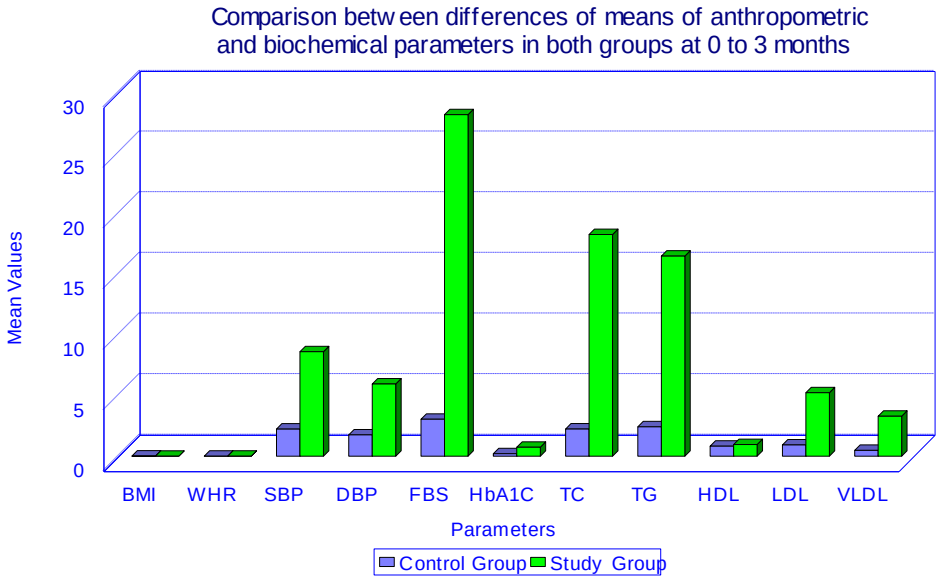

Fig-1: Comparison between differences of means of anthropometric and biochemical parameters in both groups at 0 to 3 months

DISCUSSION:

Greater understanding about the pathogenesis of metabolic syndrome and potential causes suggests that plant polyphenols might be useful as a treatment. Dietary excess energy can be stored in adipocytes, leading to the release of proinflammatory cytokines and adipose-related hormones that cause vascular injury. Plant polyphenols, organic compounds found in numerous plant species and their fruits, are being actively studied as potential treatments for components of the metabolic syndrome. Individual polyphenols that have been examined include resveratrol [13], quercetin, and epigallocathechin-3-gallate [15]. Resveratrol lowers weight, blood pressure, glucose, and insulin resistance in rodents and a human trial is currently underway. Quercetin decreases lipid and glucose levels in obese rats, and in a human investigation of subjects with the metabolic syndrome has lowered blood pressure without significant alteration of lipids [14]. Epigallocathechin-3-gallate–induced weight loss, has attenuated glucose levels and insulin resistance in rodents and improved hemoglobin A_1C and lipid profile in human studies [15].

THE PROTECTIVE ROLE OF AMLA AGAINST METABOLIC SYNDROME

In the year 2010, Kim *et al.;* [7] investigated the effects of amla (*Emblica officinalis* Gaertn.) on fructose-induced metabolic syndrome using a rat model. The elevated levels of hepatic TAG and total cholesterol in rats given the high-fructose diet were significantly reduced by 33.8 and 24.6%, respectively ($P<0.001$), on the administration of the ethyl acetate extract of amla at the dose of 20 mg/kg with the

regulation of sterol regulatory element-binding protein (SREBP)-1 expression. There are very limited data available on human studies making our study important. In our study, we obtained highly significant differences of means for both Triglycerides and Total cholesterol levels ($p<0.001$).

EFFECT OF *EMBLICA OFFICINALIS* IN FAT MASS AND OBESITY

In the year 2010, Sato *et al.; et al.;* [16] did a study to investigate the anti-obesity effects of *Emblica officinalis* (EO) in mice fed 58% kcal high-fat-diet (HFD) for 16 weeks. Male C57BL/6J mice were randomized into four groups: 1) control, 2) EO (10% w/w), 3) HFD and 4) HFD + EO. EO had no significant effect on daily food intake but significantly inhibited body weight gain as well as adipose tissue weights in mice fed HFD. Mechanistic studies indicated that EO normalized adipose mRNA expression of nuclear transcription factor, Peroxisome proliferator-activated receptor gamma (PPAR). Bioactive-guided fractionation of EO demonstrated that aqueous extract was more effective in inhibiting lipid accumulation in 3T3-L1 mouse adipocytes treated during differentiation. However, in our study, no significant improvement was observed in BMI and Waist Hip ratio ($p>0.05$). This may stem from the fact that changes in BMI and WHR is a slow process and takes a longer time to manifest. Since our study time was shorter, these beneficial effects could not manifest.

MECHANISM OF HYPOLIPIDEMIC EFFECT OF *EMBLICA OFFICINALIS*

Emblica officinalis contains flavonoids which reduce the levels of lipid in serum. A number of animal experiment report improved lipid profiles [6]. Flavonoid extracts from the fruits of emblica inhibited synthesis of cholesterol via decreasing hepatic 3-hydroxy-3-methyl glutaryl-coenzyme A (HMG-CoA) reductase and also enhanced degradation of cholesterol.

The PPAR alpha is known to regulate the transcription of genes involved in lipid and cholesterol metabolism. The PPAR alpha protein level in liver was reduced in aged control rats. However, the oral administration of amla significantly increased the hepatic PPAR alpha protein level. In addition, oral administration of amla significantly inhibited the serum and hepatic mitochondrial thiobarbituric acid-reactive substance levels in aged rats. In our study we observed that lipid profile improved significantly in study group. Differences of means for HDL, LDL & VLDL were highly significant ($p<0.001$).

ANTI-HYPERTENSIVE ACTIVITY OF *EMBLICA OFFICINALIS*

Emblica officinalis (EO) has antioxidant properties that could improve redox-sensitive vascular, cardiac and renal changes associated with deoxycorticosterone acetate/1% NaCl high salt (DOCA/HS)-induced hypertension. In the year 2011, Bhatia *et al.;* [17] determined whether hydro alcoholic lyophilized extract of EO may influence DOCA/HS-induced hypertension by modulating activity of endothelial nitric oxide synthase (eNOS) and endogenous antioxidants. Hypertension was induced in rats by DOCA-salt (20 mg/kg, S.C.) twice weekly for 5 weeks and replacing drinking water with 1% NaCl solution. These rats received co-treatment of different doses of EO (75, 150 and 300 mg/kg/day) for 5 weeks. EO significantly decreased arterial blood pressure and heart rate along with cardiac and renal hypertrophy in a dose-dependent fashion as compared to DOCA control rats.

In our study we found that systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) improved significantly in study group after Amla therapy. The differences of means were statistically highly significant ($p<0.001$) for SBP &DBP.

MECHANISM OF HYPOGLYCEMIC ACTIVITY OF *EMBLICA OFFICINALIS*

Emblica officinalis fruits have been found to inhibit enzymes of carbohydrate absorption, including α-glucosidase (IC_{50} of 1.0µg/mL) and α-amylase (IC_{50} of 94.3µg/mL) [12].

Glycation (a reduction between sugars and amino acids) has been noted to be reduced with the fruits, albeit with an IC_{50} of 182.9µg/mL[12]. *Emblica officinalis* may reduce glycation at the concentrations that it also reduces LDL oxidation (i.e. high enough that it might not be biologically relevant) which is thought to simply be due to antioxidative effects.

In our study we found that Amla therapy had good glycemic control, both FBS and HbA_1C improved significantly in study group after Amla therapy. Differences of means for FBS & HbA1c in control and study groups were highly significant ($p<0.001$).

Insulin Sensitivity

Emblica officinalis has shown insulin sensitizing properties in adipocytes by increasing glucose uptake in the 50-200µg/mL range (dose-dependent) [18]. *Emblica officinalis* normalizes adipose mRNA expression of nuclear transcription factor peroxisome proliferator activated receptor gamma (PPAR). Activation of PPAR promotes secretion of anti-hyperglycemic adipokines like adiponectin, and shifts the deposition of NEFAs (non esterified fatty acids) towards adipose tissue and away from liver and skeletal muscle – insulin sensitizing activity [19].

Aldose reductase (AR) has its involvement in the development of secondary complications of diabetes including cataract. EO is proved as an important inhibitor of AR. Exploring the therapeutic value of natural ingredients that people can incorporate into everyday life may be an effective approach in the management of diabetic complications [20].

CONCLUSION:

In our study we found that Amla therapy confers good glycemic control, manifesting as improved FBS and HbA_1C. We also found significant improvement in systolic Blood Pressure, Diastolic Blood Pressure and lipid profile. Amla therapy can be used as an adjunct with conventional treatment (diet modification and pharmacological intervention) in management of metabolic syndrome.

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