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Influence of Combination of Crude Extract of *Aegle marmelos* Leaves and *Tamarindus indica* Seeds on Sugar and Lipid level in Normal and Streptozocin Induced Diabetic Rats

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ABSTRACT

To evaluate the effects of the combination of crude extract from the leaves of *Aegle marmelos* and seeds of *Tamarindus indica* on blood glucose and serum lipid level in normal and diabetic rats. Diabetes was induced by intraperitoneal (*ip*) injection of Streptozocin dissolved in 0.1 M cold sodium citrate buffer, pH 4.5, at a dose of 35 mg/kg and maintained on ice prior to use. A mixture of crude extract by oral gavage at the dose of 350mg/kg, 700mg/kg and 1400mg/kg per day for 45 days. A significant diminution of fasting blood sugar level from 7 days onwards as compared to diabetic control and glibenclamide treated rats but there was no significant difference among normal rats. Continuous supplementation of this extract for 45 days resulted significant decrease of serum triglycerides, LDL, VLDL and elevation of HDL cholesterol level in treatment group with respect to control group. Results clearly suggest that, this crude test drug combination has enormous antidiabetic and antihyperlipidemic value. Moreover, it is very important to elucidate the phytochemical compounds responsible for these activities and the specific mechanism for its antidiabetic and antihyperlipidemic effect.

Keywords: *Aegle marmelos*, *Tamarindus indica*, glibenclamide, antidiabetogenic, antihyperlipidemic

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INTRODUCTION

Diabetes mellitus is a heterogeneous metabolic disorder characterized by derangements in carbohydrate, protein and fat metabolism, caused by complete or relative insufficiency of insulin secretion and insulin action [16]. Elevated levels of plasma low-density lipoprotein cholesterol (LDL) and triglycerides, accompanied by reduced high-density lipoprotein (HDL) levels, is often associated with an increased risk of coronary heart disease [20]. The pharmaceutical drugs are either too expensive or have undesirable side effects. The global prevalence of diabetes is predicted to rise to 300 million by 2025 [17, 18]. Diabetes patients in India are expected to rise to 57 million by 2025 [18].

The medicinal plants might provide a useful source of new oral hypoglycemic compounds for development of pharmaceutical entities or as a dietary adjunct to existing therapies. Few of the plants used for the treatment of diabetes have received scientific or medical scrutiny and even the WHO expert committee on diabetes recommends that this area warrant further attention.

Aegle marmelos (*Family-Rutaceae*) commonly called as 'Bael' in Hindi is indigenous to India. It is a medium sized, armed deciduous tree found wild, especially in dry forests and is also cultivated throughout Indian subcontinent for its fruit. The fruit are globose with smooth, hard and aromatic rind. The ripe fruit is used for digestive and stomachic complications. Leaves, fruits, stem and roots of *Aegle marmelos* have been used in ethno medicine for several medicinal properties: astringent, antidiarrheal, antidysenteric, demulcent, antipyretic, antiscourbutic, haemostatic, aphrodisiac and as an antidote to snake venom [3]. Fresh aqueous and alcoholic leaf extracts of *Aegle marmelos* were reported to have a cardio tonic effects in mammals [3]. *Aegle marmelos* leaf extract has been reported to regenerate damaged pancreatic beta cells in diabetic rats and increased the activities of peroxidase in the liver tissues of Isoproterenol treated rats [1]. *Aegle marmelos* leaf extract was found to be a potential antioxidant drug, which reduces the blood sugar level in alloxan induced diabetic rats. It was found to be as effective as insulin in the restoration of blood glucose and body weight to normal levels on hyperglycemic state [3, 4].

Tamarindus indica is tree-type of plant belonging to the *Caesalpiniacae* family and it is extremely found all over India. The tree carries brittle, ligneous pods about the size of a human digit, containing up to 10 shiny seeds surrounded by a sticky, sour pulp that is used in food and drinks. There fruits are also found mainly summer season and seed coat is brownish black in color though the kernel is white in color. Its fruit is regarded as a digestive, carminative, laxative, expectorant and blood tonic [6, 2]. Other parts of the plant present antioxidant, antihepatotoxic, antiinflammatory, antimutagenic and antidiabetic activities [10].

Our hypothesis is to see the activity of the mixture of leaves of *Aegle marmelos* and seeds of *Tamarindus indica* without doing any kind of distillation because we are agree with the concept of synergism and minimal adverse effects due to additive and counter balancing nature of the constituents present in crude powder form. There is no substantial scientific study done

with combination of fine crude powder of *Aegle marmelos and Tamarindus indica* to prove its antidiabetic and antihypelipidemic activity, hence the present study has been undertaken to investigate if fine crude powder of *Aegle marmelos* leaves and *Tarmarindus indica* seeds in combination has synergistic influence on sugar and lipid level in normal and streptozocin induced diabetic rats.

MATERIALS AND METHODS

Animals

Adult male and female Wistar albino rats weighing 150–300 g were housed in separate polypropylene cages, maintained under standard conditions with temperature (22–24^0 C), 12- h light/12-h dark cycle and relative air humidity 40–60%. Rats had continuous access to normocaloric standard rat pellet diet (Hindustan Lever Ltd., Mumbai, India) and to tap water. The animals were acclimatized to the laboratory conditions for one week before the start of the experiment. The experimental protocol was approved by the Institutional Animal Ethical Committee and experiments were conducted according to the ethical norms approved by Ministry of Social Justices and Empowerment, Government of India and Committee for the purpose of control and supervision on experiments on animals (CPCSEA) guidelines on the use and care of experimental animals.

Preparation of Plant Material

Leaves of *Aegles marmelos* and seeds of *Tamarindus indica* were collected from Udupi district of Karnataka. Separately fresh leaves of *Aegles marmelos* and seeds of *Tamarindus indica* were dried in an incubator at 45°C for 48 hours, powdered using electric grinder, and stored in a decicator. 250 g of fine crude powder of *Aegles marmelos* was mixed with 250 g of fine crude powder of *Tamarindus indica* and the mixture was lyophilized to use as herbal drug.

Drugs and Reagents

Streptozocin was procured from Sigma Aldrich, Mumbai (India). One touch glucometer (Accu-Chek Active) with glucose oxidase-peroxidase reactive strips was purchased from Roche Diagnostics, Germany. Glibenclamide (Daonil) was obtained from hospital pharmacy of Kasturba Hospital, Manipal. The reagent kits for lipid profile estimation were purchased from ASPEN Laboratories, New Delhi (India). The other chemical reagents used in the study were obtained from Merck Chemicals, Bangalore, India.

Induction of Diabetes

After fasting, diabetes was induced by intraperitoneal (*ip*) injection of Streptozocin dissolved in 0.1 M cold sodium citrate buffer, pH 4.5, at a dose of 35 mg/kg and maintained on ice prior to use. The animals were allowed to drink 5% glucose solution overnight to overcome the drug induced hypoglycemia. After a week time for the development of diabetes, the rats

with moderate diabetes having glycosuria and hyperglycemia (fasting blood glucose range of above 250 mg/dl) were considered as diabetic rats and used for the experiment.

Selection of the dose of the test drug

Three different doses (350mg/kg, 700mg/kg and 1400mg/kg) of the mixture of the crude test drug were selected after the acute toxicity study according to the Acute Toxicity Class (ATC) method (OECD guideline 423).

Estimation of biochemical parameters

Blood glucose was estimated by using one touch glucometer. Triglyceride, total cholesterol and high density lipoprotein cholesterol levels in serum were measured by prescribed methods given along with the respective reagent kit using semi autoanalyzer. Urine sugar was detected by O-toluidine method. Low density and very low density lipoprotein cholesterol were calculated from the above measurement by using Friedwald formula.

Change in body weight

The change in body weight of individual animals was noted down before the start and at the end of experiment.

Experimental Procedure

A total of 54 adult male Wistar albino rats were divided into nine groups (n=6) based on the treatment protocol. Treatment was done for 45 days as follows:

Group I: Normal control rats were given 1ml/kg of 2% gum acacia.
Group II: Streptozocin (35mg/kg, i.p.) induced diabetic rats were given 1ml/kg of 2% gum acacia orally for 45 days
Group III: Streptozocin (35mg/kg, i.p.) induced diabetic rats were given glibenclamide (0.5mg/kg) orally for 45 days
Group IV: Non-diabetic control rats were given 350mg/kg of test drug orally for 45 days
Group V: Non-diabetic control rats were given 700mg/kg of test drug orally for 45 days
Group VI: Non-diabetic control rats were given 1400mg/kg of test drug orally for 45 days
Group VII: Streptozocin (35mg/kg, i.p.) induced diabetic rats were given 350mg/kg of test drug orally for 45 days
Group VIII: Streptozocin (35mg/kg, i.p.) induced diabetic rats were given 700mg/kg of test drug orally for 45 days
Group IX: Streptozocin (35mg/kg, i.p.) induced diabetic rats were given 1400mg/kg of test drug orally for 45 days

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Fasting blood samples were drawn on from all the experimental rats before administration of gum acacia or streptozocin or test drug. Day of drug administration was counted as 0th day. Fasting blood samples of group I, II after administration of gum acacia and of rest other groups after single administration of standard drug and test drug on 1st day and on 7th, 15th, 30th and 45th day before administration of next dose of gum acacia for group I, II and standard drug glibenclamide for group III and test drug for group IV, V, VI, VII, VIII and IX. All the fasting blood samples were drawn on from tail vein of rats for the estimation of blood glucose by glucose oxidase-peroxidase reactive strips.

Statistical analysis

Data were analyzed by one way analysis of covariance (ANOVA) followed by post hoc Tukey test and analysis of covariance (ANCOVA) using SPSS software package version 16.0 (Statistical Program for Social Science). P value less than 0.05 was considered as statistically significant.

RESULTS

Fasting blood glucose level - (Table-1)

Table-1: Effect Crude Extract of *Aegle marmelos* Leaves and *Tamarindus indica* Seeds on on fasting blood glucose level in rats

Groups	Fasting blood glucose level (mg/dl) Mean±SEM				
	Day 1	Day 7	Day 15	Day 30	Day 45
Normal rat- 2% gum acacia (1ml/kg)	67.33	70.66	60.00	69.33	84.00
	± 1.70	± 9.10	± 2.48	± 2.66	± 1.54
Diabetic rat- 2% gum acacia (1ml/kg)	248.83[a]	218.83[a]	313.83[a]	303.50[a]	389.00[a]
	± 17.11	± 9.56	± 6.90	± 4.03	± 19.60
Diabetic rat- Glibenclamide (0.5mg/kg)	254.00[a]	178.50	147.66[b]	194.50[b]	225.50[b]
	± 22.04	± 40.06	± 38.36	± 41.62	± 40.21
Normal rat 350mg/kg	43.33	65.66	58.16	79.50	77.16
	± 1.64	± 2.15	± 4.23	± 5.34	± 2.84
Normal rat 700mg/kg	36.83	64.16	77.50	89.66	83.83
	± 1.97	± 4.06	± 5.68	± 3.62	± 3.17
Normal rat 1400mg/kg	37.50	76.66	81.50	70.83	83.83
	± 4.03	± 4.67	± 4.13	± 3.71	± 1.16
Diabetic rat 350mg/kg	240.33[a]	103.83[b]	151.00[b,h]	110.50[b]	124.50[b,c]
	± 11.32	± 22.57	± 15.75	± 6.82	± 10.37
Diabetic rat 700mg/kg	313.00[a]	95.3333[b,c]	245.00[c,i]	157.16[b]	167.50[b]
	± 30.72	± 14.73	± 26.70	± 32.39	± 29.77
Diabetic rat 1400mg/kg	351.00[a]	105.83[b]	147.66[b]	132.33[b]	178.66[b]
	± 37.97	± 11.95	± 33.34	± 28.01	± 26.76

P ≤ 0.05 Significant as compared to **a** Normal control, **b** diabetic control, **c** diabetic+Glibenclamide, **h** diabetic rat-700mg/kg, **i** diabetic rat-1400mg/kg

There was no any significant difference in blood glucose level of normal rats treated with all the three doses of test drug and normal control rats ($p>0.05$). Throughout the experiment, there was significant decrease in blood glucose level in the diabetic rats treated with 350mg/kg, 700mg/kg and 1400mg/kg of test drug as compared to diabetic control rats and the anti-hyperglycaemic effect of test drug was more pronounced in 350mg/kg treatment group of diabetic rats ($p<0.0001$). Whereas, the significant decrease of blood glucose level in glibenclamide treated diabetic rats as compared to diabetic control rats appeared from 15th day onwards. On 45th day, there was more significant decrease in blood glucose level in diabetic rats treated with 350mg/kg of test drug as compared to diabetic rats treated with glibenclamide ($p=0.026$).

Serum triglyceride level - (Table-2)

Table-2: Effect Crude Extract of *Aegle marmelos* Leaves and *Tamarindus indica* Seeds on serum triglyceride level in rats

Groups	Serum triglyceride (in mg/dl)Mean±SEM	
	Baseline	Day 45
Normal rat- 2% gum acacia (1ml/kg)	78.93	50.63
	± 7.41	± 0.89
Diabetic rat- 2% gum acacia (1ml/kg)	68.56	92.03[a]
	± 1.14	± 2.66
Diabetic rat- Glibenclamide (0.5mg/kg)	57.59	38.25[b]
	± 7.37	± 3.68
Normal rat 350mg/kg	60.14	31.35[a]
	± 9.31	± 4.54
Normal rat 700mg/kg	51.74	27.87[a]
	± 4.71	± 3.91
Normal rat 1400mg/kg	64.62	41.28[e]
	± 10.55	± 4.15
Diabetic rat 350mg/kg	66.41	50.92[b,c]
	± 6.62	± 5.23
Diabetic rat 700mg/kg	57.11	36.78[b,g]
	± 5.35	± 2.35
Diabetic rat 1400mg/kg	57.35	48.61[b,h]
	± 8.13	± 4.90

P ≤ 0.05 Significant as compared to **a** Normal control, **b** diabetic control, **c** diabetic+Glibenclamide, diabetic rat-350mg/kg, diabetic rat- **e** Normal rat+700mg/kg, **h** Diabetic rat+700mg/kg**, i** diabetic rat-1400mg/kg

There was significant decrease in serum triglyceride level in normal ($p<0.05$) and diabetic rats ($p<0.0001$) treated with all the three doses of test drug as compared to normal and diabetic control group respectively ($p<0.05$) and more decrease was seen at 700mg/kg of test drug in both normal and diabetic rats. There was no significant difference in triglyceride level in glibenclamide treated diabetic rats as compared to diabetic rats treated with 750mg/kg and 1400mg/kg of test drug.

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Serum total cholesterol level - (Table-3)

Table-3: Effect Crude Extract of *Aegle marmelos* Leaves and *Tamarindus indica* Seeds on serum total cholesterol level in rats

Groups	Serum total cholesterol(in mg/dl)Mean±SEM	
	Baseline	Day 45
Normal rat- 2% gum acacia (1ml/kg)	64.75	77.64
	± 3.38	± 4.08
Diabetic rat- 2% gum acacia (1ml/kg)	64.10	89.26
	± 1.71	± 2.12
Diabetic rat- Glibenclamide (0.5mg/kg)	52.54	76.75
	± 3.88	± 10.34
Normal rat 350mg/kg	76.20	67.32[a,c]
	± 3.69	± 5.02
Normal rat 700mg/kg	58.61	60.11[c]
	± 2.80	± 3.99
Normal rat 1400mg/kg	74.79	83.10[d]
	± 4.40	± 1.62
Diabetic rat 350mg/kg	60.00	82.78
	± 8.75	± 4.65
Diabetic rat 700mg/kg	70.62	80.73
	± 8.88	± 8.82
Diabetic rat 1400mg/kg	59.05	88.73
	± 5.20	± 5.64

P ≤ 0.05 Significant as compared to **a** Normal control, **c** diabetic+Glibenclamide, **d** Normal rat+350mg/kg

There was significant decrease in serum total cholesterol level in normal rats treated with 350mg/kg of test drug as compared to normal control rats (p≤0.05). There was no significant difference seen in rest of the normal treated rats and diabetic treated rats in comparison with normal control and diabetic control group (p>0.05).

Serum high density lipoprotein cholesterol level - (Table-4)

Table-4: Effect Crude Extract of *Aegle marmelos* Leaves and *Tamarindus indica* Seeds on serum high density lipoprotein-C level in rats

Groups	Serum HDL-C level (in mg/dl)Mean	
	Baseline	Day 45±SEM
Normal rat- 2% gum acacia (1ml/kg)	29.91± 2.93	39.42± 1.99
Diabetic rat- 2% gum acacia (1ml/kg)	23.25± 0.96	11.04± 0.90[a]
Diabetic rat- Glibenclamide (0.5mg/kg)	29.20± 3.49	20.17± 3.12[a]
Normal rat 350mg/kg	29.76± 5.58	27.43± 3.68[a]
Normal rat 700mg/kg	22.83± 3.71	20.78± 3.61[a]
Normal rat 1400mg/kg	32.70± 3.15	36.95± 4.98[e]
Diabetic rat 350mg/kg	30.22± 4.27	39.75 ± 6.96[b c]
Diabetic rat 700mg/kg	35.45± 4.50	23.03 ± 1.30[b]
Diabetic rat 1400mg/kg	31.56± 3.43	33.60 ± 4.93[b c]

P ≤ 0.05 Significant as compared to **a** Normal control, **b** diabetic control, **c** diabetic-Glibenclamide, **e** Normal rat+700mg/kg

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There was significant increase in serum high density lipoprotein cholesterol level in normal rats treated with 1400mg/kg of test drug as compared to test drug treated normal rats at the dose of 700mg/kg (p=0.004). There was significant increase in HDL cholesterol level in diabetic rats treated with test drug at all the three doses 350mg/kg, 700mg/kg and 1400mg/kg as compared to diabetic control rats (p<0.0001). Significant increase in HDL cholesterol was also observed in diabetic rats treated with test drug at the dose of 350mg/kg (p=0.001) and 1400mg/kg (p=0.018) with respect to diabetic rats treated with glibenclamide. The remarkable increase in HDL cholesterol level was seen in diabetic rats treated with test drug at the dose of 350mg/kg.

Serum low density lipoprotein cholesterol level - (Table-5)

Table-5: Effect Crude Extract of *Aegle marmelos* Leaves and *Tamarindus indica* Seeds on serum low density lipoprotein-C level in rats

Groups	Serum LDL-C level (in mg/dl)Mean±SEM	
	Baseline	Day 45
Normal rat- 2% gum acacia (1ml/kg)	19.06± 4.84	28.09± 5.68
Diabetic rat- 2% gum acacia (1ml/kg)	27.14± 1.69	59.81± 2.14 [a]
Diabetic rat- Glibenclamide (0.5mg/kg)	11.82± 4.94	48.93± 10.02
Normal rat 350mg/kg	34.41± 5.59	33.61± 5.76
Normal rat 700mg/kg	25.43± 5.05	33.75± 5.07
Normal rat 1400mg/kg	29.17± 5.19	42.30± 4.50
Diabetic rat 350mg/kg	18.89±3.96	32.85± 10.24 [b]
Diabetic rat 700mg/kg	23.75± 5.08	50.34± 7.58
Diabetic rat 1400mg/kg	16.03± 2.50	45.40± 6.01

P ≤ 0.05 Significant as compared to **a** Normal control, **b** diabetic control,

There was significant decrease in serum low density lipoprotein cholesterol level in diabetic rats treated with 350mg/kg of test drug as compared to diabetic control rats (p=0.012). There was no significant difference seen in rest of the treatment group of normal and diabetic rats as compared to normal control and diabetic control group (p>0.05).

Serum very low density lipoprotein cholesterol level - (Table-6)

Table-6: Effect Crude Extract of *Aegle marmelos* Leaves and *Tamarindus indica* Seeds on serum very low density lipoprotein-C level in rats

Groups	Serum VLDL-C level (in mg/dl)	
	Baseline	Day 45
Normal rat- 2% gum acacia (1ml/kg)	15.78± 1.48	10.12± 0.17
Diabetic rat- 2% gum acacia (1ml/kg)	13.71± 0.22	18.40± 0.53 [a]

Diabetic rat- Glibenclamide (0.5mg/kg)	11.51± 1.47	7.64± 0.73 [b]
Normal rat 350mg/kg	12.02± 1.86	6.26± 0.90 [a]
Normal rat 700mg/kg	10.34± 0.94	5.57± 0.78 [a]
Normal rat 1400mg/kg	12.92± 2.11	8.25± 0.83 [e]
Diabetic rat 350mg/kg	13.28± 1.32	10.17 ± 1.04 [b c]
Diabetic rat 700mg/kg	11.41± 1.07	7.35 ± 0.47 [b g]
Diabetic rat 1400mg/kg	11.46± 1.62	9.72 ± 0.98 [b h]

P ≤ 0.05 Significant as compared to **a** Normal control, **b** diabetic control, **c** diabetic+Glibenclamide, e Normal rat 700mg/kg, **g** diabetic rat-350mg/kg, **h** diabetic rat-700mg/kg

There was significant decrease in serum very low density lipoprotein cholesterol level in normal rats ($p<0.05$) and diabetic rats ($p<0.0001$) treated with test drug as compared to normal and diabetic control group respectively. There was drastic decrease in VLDL cholesterol level in diabetic rats treated with 350mg/kg of test drug as compared to its higher doses.

Body weight - (Table-7)

Table-7: Effect Effect Crude Extract of *Aegle marmelos* Leaves and *Tamarindus indica* Seeds on body weight rats

Groups	Body weight (in gram)Mean±SEM	
	Baseline	**Day 45**
Normal rat- 2% gum acacia (1ml/kg)	185.33± 20.27	180± 19.20
Diabetic rat- 2% gum acacia (1ml/kg)	170.66± 5.71	148.33± 5.73
Diabetic rat- Glibenclamide (0.5mg/kg)	172.66± 5.80	183.83± 15.10 [b]
Normal rat 350mg/kg	227.33± 18.09	260.16± 12.68 [a]
Normal rat 700mg/kg	245.16± 8.40	243.50± 8.09 [a]
Normal rat 1400mg/kg	196.00± 11.19	196.83± 14.16
Diabetic rat 350mg/kg	116.16± 6.83	133.66± 6.76
Diabetic rat 700mg/kg	118.00± 5.57	138.50± 8.53
Diabetic rat 1400mg/kg	122.16± 9.16	130.33± 7.13 [c]

P ≤ 0.05 Significant as compared to **a** Normal control, **b** diabetic control, **c** diabetic+Glibenclamide

There was no significant difference in body weight of normal rats and diabetic rats treated with test drug as compared to normal and diabetic control group respectively ($p>0.05$). But, there was significant increase in body weight of normal rats treated with test drug at the dose of 350mg/kg in comparison with normal control rats.

DISCUSSION

The results of present study reveals antidiabetic effect of combination of crude extract of leaves of *Aegle marmelos* and seeds of *Tamarindus indica* on normal and streptozotocin-induced diabetic rats in duration dependent fashion. Streptozotocin injection results diabetes mellitus, which may be due to destruction of β cells of Islets of Langerhans [8]. After 7 days

supplementation of mixture of the crude extract resulted significant diminution of fasting blood glucose level in respect to diabetic control rats, but no significant alteration of fasting blood glucose level to the normal rats, which further strengthen the antihyperglycaemic action of this extract. At present juncture, it is not possible either to pin point the exact mechanism of the antidiabetic effect of combination of crude extract of leaves of *Aegle marmelos* and seeds of *Tamarindus indica* or to identify the active principle(s) responsible for such effect. The one possible way of antidiabetic action of this supplementation is by improvement of glycogenesis process in muscle and liver [2, 3]. Streptozotocin-induced type-I diabetes is also developed due to reduction of G-6-PDH activity in liver that obstruct glucose utilisation through pentose phosphate pathway as this enzyme activity is insulin dependent [4, 6]. The mixture of crude extract of leaves of *Aegle marmelos* and seeds of *Tamarindus indica* might have significantly improved this enzyme activity in hepatic tissue which enlighten its another possible way of antidiabetic activity. Symptoms like loss of body weight, weakness, polyuria and polyphagia that accompany type-I diabetes mellitus were significantly absent in this crude test drug supplemented group. Moreover, improvement of body weight of the supplemented animal's further support the antidiabetic effect of this extract as diabetic condition is associated with loss of body weight.

The levels of serum lipids are usually elevated in diabetes mellitus and such an elevation represents the risk factor for coronary heart diseases [7]. The marked hyperlipemia that characterizes the diabetic states may be regarded as consequence of the uninhibited actions of lipolytic hormones on the fat depots [7]. Moreover, supplementation of combination of crude extract of leaves of *Aegle marmelos* and seeds of *Tamarindus indica* for 45 days produced significant beneficial effects in the lipid profile in normal and diabetic rats by reducing triglycerides, total cholesterol and increasing HDL levels significantly (Table-2, 3, 4). This effect may be due to low enzymatic activity during cholesterol biosynthesis or low level of lipolysis which are under the control of insulin. From such informations it may be stated primarily that mixture of this crude extract may contain some biomolecule(s) that may sensitize the insulin receptor to insulin or stimulate the β stem cell of Islets of Langerhans in pancreas in streptozotocin-induced diabetic rat that may restore plasma level of insulin or it may results the improvement of carbohydrate metabolic enzymes towards the reestablishment of normal blood glucose level. The increase in insulin secretion and the consequent decrease in blood glucose level may lead to inhibition of lipid peroxidation and control of lipolytic hormones [7, 8, 9, 10].

From this study, we can conclusively state that combination of crude extract of leaves of *Aegle marmelos* and seeds of *Tamarindus indica* fhas beneficial effects on blood glucose level as well as improving hyperlipidemia due to diabetes. Further pharmacological and biochemical investigations are underway to elucidate the exact mechanism for its antidiabetic and antihyperlipidemic effect.

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