

## Comparative Efficacy of four Herbal Antidiabetic Formulations in Albino Rabbits

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### Abstract

A number of herbal formulations are marketed globally, claiming to be useful in diabetes and other associated diseases such as atherosclerosis. In the present study an attempt has been made to study the comparative efficacy of four such marketed herbal oral antidiabetic formulations, for their hypoglycemic and hypolipidemic activities. The study was conducted on healthy albino rabbits of either sex, randomly distributed into control and test groups. The hypoglycemic activity was studied by measuring the reduction in blood glucose levels at different time intervals using GOD/POD method. The hypolipidemic activity was performed by routine techniques.

The formulations tested were compared for their hypoglycemic and hypolipidemic activities for efficacy ranging. The formulations which exhibited significant hypoglycemic activity were then compared with tolbutamide. The results demonstrated a moderate to considerable difference in the hypolipidemic and hypoglycemic activities among the products tested. The present study provides a ready reference to health care practitioners for the appropriate selection of the herbal formulation in clinical practice.

**Key words :** Herbal formulations, hypoglycemic activity, hypolipidemic activity, alternative system.

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### Introduction

Herbal formulations are used by a majority of population throughout the world, since ancient times. In recent years there has been an increase in their clinical use. The side effects and costly treatment associated with the allopathic medicines have forced the health care practitioners to switch over to alternative therapies such as Ayurveda, Homeopathy etc., which are affordable and believed to be free from side effects.

Ayurvedic medicines are composed of either a single drug or combination (polyherbal) having specific diagnostic and therapeutic principles (Kulkarni and Karande, 1998).

Diabetes mellitus is a heterogeneous metabolic disorder characterized by altered carbohydrate, lipid and protein metabolism. But, most of the conventionally used allopathic antidiabetic agents selectively produce only hypoglycemic effect, without correcting any of the associated diseases like atherosclerosis, hyperlipidemia, varieties of infections etc. They have also been reported to produce side effects in the long term use (Khan and Shechter, 1991). To treat the associated diseases in diabetes multi-drug therapy is commonly followed, which may often lead to deleterious and hazardous drug-interactions (Nies and Spielberg, 1996). But the same is not true with the herbal formulations. On the contrary, as per the Herbal compendium the

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combination of plant substances produces enhanced effect and eliminate unwanted side effects (Satyavati *et al.*, 1987; Nadkarni, 1982).

Pharmaceutical research across the world showed that, natural products are the potential sources of novel molecules for drug development (Marles, and Farnsworth, 1995). In this connection a number of herbal formulations are widely marketed, claiming to possess antidiabetic and other properties. But these formulations are not well studied scientifically. Hence, in the present study an attempt has been made to evaluate the potency of four marketed herbal antidiabetic formulations for their hypoglycemic and hypolipidemic activities.

## Materials and Methods

All the four Ayurvedic antidiabetic formulations used in the study were in the form of tablets and the compositions of these formulations as appeared on their labels are as follows:

**“FORMULATION-A” Powders and Bhasmas:** *Curcuma longa* (100mg), *Eugenia jambolana* (50mg), *Swertia chirata* (50 mg), *Shilajit shuddha* (25 mg), *Trivang Bhasma* (25 mg).

**Mass Extracts:** *Cassia auriculata* (100mg), *Embllica officinalis* (100mg), *Enicostemma littorale* (50mg), *Gymnema sylvestre* (50mg), *Pterocarpus marsupium* (50mg), *Tinospora cordifolia* (50 mg) and *Melia azadirachta* (25 mg).

**“FORMULATION – B”** *Salacia oblonga* wall(150 mg), *Tinospora cordifolia* miers (50 mg), *Embllica officinalis* gaertn(50 mg), *Curcuma longa* linn (50 mg) and *Gymnema sylvestre* R.Br.(200 mg).

**“FORMULATION – C”** *Gymnema sylvestre* (100mg), *Eugenia jambolana* seed (120mg), *Embllica officinalis* dried fruit (60mg), *Curcuma longa* dried rhizome (60mg), *Casuarina esculenta* (20mg), *Enicostemma littorale* (20mg) and Asphaltum (30mg).

**“FORMULATION-D”** *Enicostemma littorale*(33.33mg), *Phyllanthus nirum* (33.33mg), *Phyllanthus nirum* (33.33mg), *Eugenia jambolana* (L) (33.33mg), *Eugenia jambolana* (133.33mg), *Melia azadirachta* (33.33mg), *Terminalia arjuna* (33.33 mg), *Aegle marmelos* (133.33 mg), and Asphaltum (66.66 mg).

The study was conducted on healthy albino rabbits of either sex, weighing between 1.5 to 2.0 kg. They were caged individually in similar environmental conditions and were randomly categorized into five groups, each group comprised of six animals. The animals were fasted for 18 hours prior to experiment. During this period the animals were allowed to take adequate water. The fasting was continued till the end of experiment. After 18 hours of fasting “zero” hour blood samples were collected from all the animals of each group and then the drugs were administered orally in the form of suspensions, prepared using 1%w/v gum acacia in distilled water.

GROUP – I : Formulation – A (141.75 mg / 1.5 kg)

GROUP – II : Formulation – B ( 105 mg / 1.5 kg )

GROUP – III: Formulation – C (86.1 mg / 1.5 kg )

GROUP – IV : Formulation – D (105 mg / 1.5 kg )

GROUP – V : Tolbutamide(40 mg/kg), which served as control

**Serum analysis:** The blood samples were collected from the marginal ear vein at 0, 2, 4, 6, 8, 12, 24, 30, 36 and 48 hours and blood glucose levels were analysed by using GOD/ POD method (Trinder’s method, 1964).

The estimation of different serum lipid levels was carried out using following methods:

- GPO Trinder method for triglycerides (Tiffany *et al.*, 1974),
- Enzymatic CHOD/POD for cholesterol (Allian *et al.*, 1974) and

- Auto enzyme HDL-cholesterol kit for HDL, LDL and VLDL cholesterol was used (Burstein *et al.*, 1970).

The hypoglycemic activity of all the four formulations at any required time interval “t” was calculated as the percentage of blood glucose reduction at that time with respect to initial blood glucose level.

**Statistical Analysis:** The values are reported as mean±SEM. Statistical significance was analysed by using one-way analysis of variance (ANOVA). Post-hoc comparisons were done by using Tukey-Kramer multiple comparisons. *P* values lower than 0.05 were considered statistically significant.

Table 1. The hypoglycemic effect of four herbal formulations compared with tolbutamide in healthy albino rabbits.

Time in hours	Percent blood glucose reduction with different formulations compared with tolbutamide( mean ± S E M )				
	Formulation A	Formulation B	Formulation C	Formulation D	Tolbutamide (40mg/kg p.o)
0	0	0	0	0	0
2	6.28±1.66	15.17±8.31	6.99±4.39	2.04±2.04	17.81±3.33
4	11.43±2.38	18.13±9.52	16.27±2.87	3.23±3.23	27.68±3.73*
6	16.60±2.60	22.32±5.02	17.13±1.98	13.21±5.11	33.5±5.04*
8	22.45±1.74	27.70±7.77	17.42±4.37	16.63±3.80	36.85±4.21*
12	33.82±0.27	31.40±6.94	22.27±3.41	30.53±0.61	35.19±4.97
24	37.27±1.23	33.77±3.84	31.15±2.12	25.43±8.67	19.26±2.94
30	29.88±2.27***	21.56±2.66	20.55±3.05	13.57±2.14	15.89±1.24
36	14.80±1.98*	21.55±2.57***	11.99±3.39	3.61±2.08	09.20±1.06
48	2.14±2.15	4.49±4.50	3.25±0.39	1.20±0.43	01.04±1.76

Values are mean ± S E M, determined at different time intervals after treatment, n=6 in each group.

\**P*< 0.05 and \*\*\**P*< 0.001

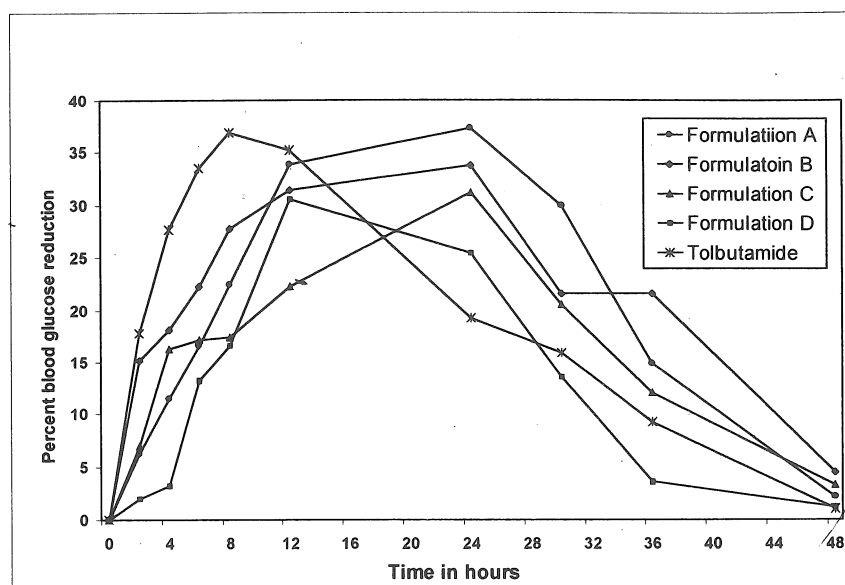


Fig 1. The hypoglycemic effect of four herbal formulations in healthy albino rabbits compared with tolbutamide.

Table 2. Effect of four herbal antidiabetic formulations on serum lipid levels (mg/dl) in healthy albino rabbits.

Formulations	Total cholesterol	Triglycerides	LDL Cholesterol	VLDL Cholesterol	HDL Cholesterol
<b>Control</b>					
0 hour	84 ± 1.15	64 ± 1.53	42.2 ± 0.6	12.8 ± 0.30	20 ± 0.58
24 hours	83.33 ± 2.40	65.66 ± 1.20	41.86 ± 4.17	13.13 ± 0.24	28.33 ± 1.76
<b>Formulation-A</b>					
0 hour	81.34 ± 4.05	63.67 ± 2.03	43.6 ± 4.01	12.73 ± 0.40	25 ± 1.73
24 hours	77.67 ± 6.44*	58 ± 3.46	37.07 ± 6.53	11.6 ± 0.69	29 ± 0.58
<b>Formulation-B</b>					
0 hour	80 ± 1.54	65 ± 2.08	38 ± 1.91	13 ± 0.42	29 ± 0.58
24 hours	52.34 ± 6.89***	46.34 ± 1.20	7.6 ± 4.86**	10.26 ± 0.24*	36 ± 3.46
<b>Formulation-C</b>					
0 hour	80 ± 17.70	67.67 ± 9.53	34.4 ± 17.95	13.4 ± 1.90	32.34 ± 1.76
24 hours	101.67 ± 10.17	38 ± 99.30	59.4 ± 13.39	7.6 ± 1.86	34.67 ± 1.76
<b>Formulation-D</b>					
0 hour	80 ± 1.54	64 ± 1.15	39.53 ± 1.05	12.8 ± 0.23	27.67 ± 0.88
24 hours	50.34 ± 3.38***	52.34 ± 5.24	10.53 ± 5.20**	10.47 ± 1.05	29.34 ± 0.88

Values are Mean ± SEM

Significant at 0.05\*, 0.01\*\*, and 0.001\*\*\* n=6, in each group.

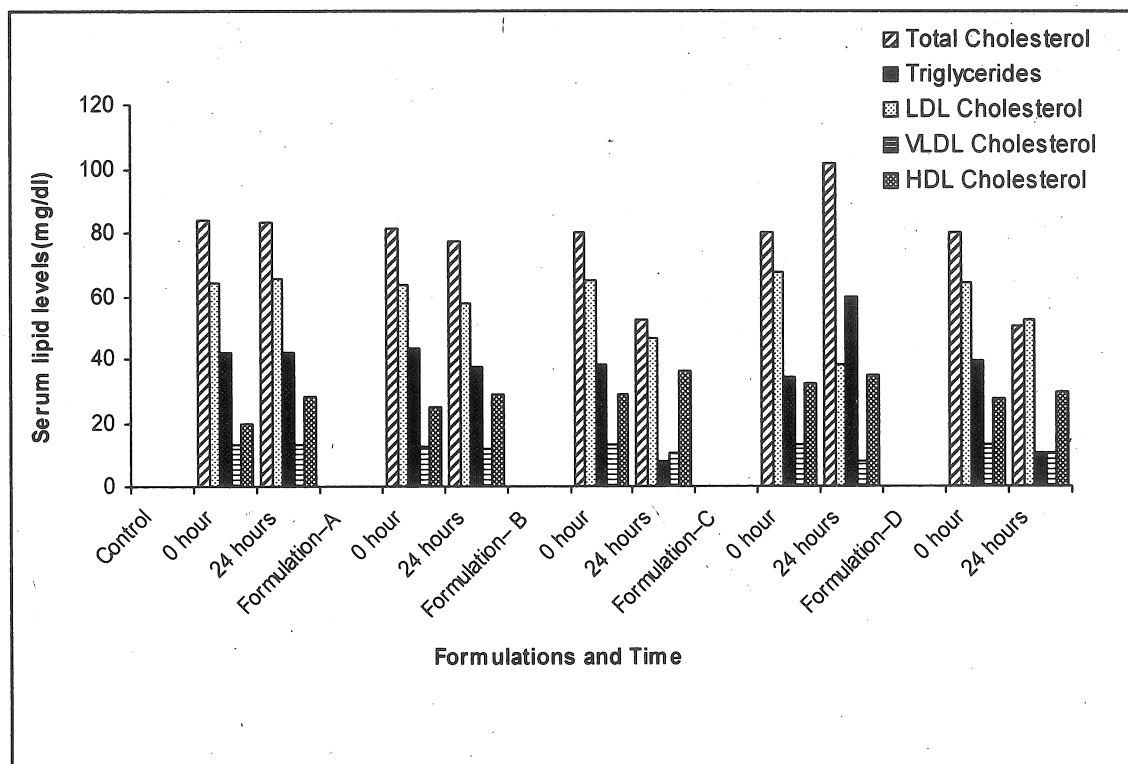


Fig 2. Serum lipid levels (mg/dl) with four herbal antidiabetic formulations in healthy albino rabbits.

## Results and Discussion

The results of the study are summarized in the Tables 1, 2 and graphically depicted in Figures 1 and 2, respectively.

The present study includes the comparison of efficacy of four herbal formulations for their hypoglycemic and hypolipidemic activities. For the assessment of hypoglycemia the parameters considered were onset of action, peak effect and duration of action. However, the duration of action was considered as the most important parameter for evaluation of efficacy. Similarly, the emphasis was also laid down on the ability of different formulations to keep control over the serum lipid profile.

*Hypoglycemic activity:* A minimum of 30% reduction in blood glucose levels was considered as positive hypoglycemic effect for all the four formulations.

From the Tables-1, 2 and Figures-1, 2 the following can be deduced.

### FORMULATION - A:

*Hypoglycemic activity:* The onset of action was less than 12 hours and the peak effect was observed at 24<sup>th</sup> hour with the reduction of blood glucose levels by  $37.27 \pm 1.23\%$ . The duration of action was more than 18 hours.

*Serum lipid levels :* No significant effect.

#### FORMULATION – B :

*Hypoglycemic activity:* The onset of action was between 8–12 hours, peak effect was observed at 24<sup>th</sup> hour with reduction in blood glucose levels by  $33.77 \pm 3.84\%$ . The duration of action was for about 16–22 hours.

*Serum lipid levels :* Highly significant effect.

#### FORMULATION – C :

*Hypoglycemic activity:* The onset of action was around 24<sup>th</sup> hour, the formulation failed to achieve the peak effect and the duration of action was also less than 6 hours.

*Serum lipid levels:* Significant effect on triglycerides and VLDL-cholesterol levels.

#### FORMULATION – D :

*Hypoglycemic activity:* The onset of action was at 12<sup>th</sup> hour, this drug also failed to reach the peak effect and the duration of action was lower than 12 hours.

*Serum lipid levels:* Highly significant effect on serum cholesterol and LDL-cholesterol levels.

Based on the above results and statistical analysis the four marketed popular herbal formulations can be ranged for their hypoglycemic and antihyperlipidemic activities in the following orders respectively:

*Hypoglycemic effect:* Formulation A > Formulation B > Formulation C > Formulation D

*Antihyperlipidemic effect:* Formulation B > Formulation D > Formulation C > Formulation A

It is very clear from the above results that, though the formulation A exhibited significant hypoglycemic effect ( $P < 0.001$ ), it failed to produce hypolipidemic effect significantly ( $P < 0.05$ ). Whereas the formulation B, despite showing significant hypoglycemic effect ( $P < 0.01$ ) also exhibited significant hypolipidemic activity on total cholesterol ( $P < 0.001$ ), LDL-cholesterol ( $P < 0.01$ ) and VLDL-cholesterol ( $P < 0.05$ ). The other two formulations C and D showed a very weak hypoglycemic activity compared to A and B. Moreover, the peak hypoglycemic activity exhibited by the formulations A and B are closely comparable with that of tolbutamide. But the duration of action of both formulations A and B are longer than the tolbutamide. Hence, it can be readily concluded from the above discussion that, the formulation B is superior out of four formulations with respect to hypoglycemic and hypolipidemic activities ( $B > A > D > C$ ). However it is very difficult to point out the specific ingredient in the formulation responsible for these favorable responses. Since, the concept of efficacy in phytotherapy is based on the mixture of substances contained in the medicinal plants. Further studies are in progress so as to confirm these results in pathophysiological conditions such as diabetes mellitus in animal models.

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