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# Hiptage benghlensis Leaf Extracts' Hypolipidemic Effect on High-Fat Diet-Induced Hyperlipidaemic Rats

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## ABSTRACT

***The goal of the current research was to assess the hypolipidemic effects of Hiptage benghalensis leaf aqueous extract (HBAE) and ethanolic extract (HBEE) utilizing an animal model of hyperlipidemia caused by a high-fat diet. Male albino wistar rats weighing between 120 and 150 grams were divided into six groups. Rats classified as hyperlipidemic (groups II, III, IV, V, VI, and VII) were fed a high-fat diet in order to induce hyperlipidemia, whereas normal rats (group I) were given a conventional laboratory diet along with 0.3% carboxy methyl cellulose (CMC). Group II, the hyperlipidaemic control group, was given 0.3% CMC (10 mL/kg/day). Group III, the standard group, was given gemfibrozil (50 mg/kg/day, p.o.). Groups IV and V, the HBAE groups, were given an aqueous extract of H. benghalensis (100 and 200 mg/kg/day, p.o.), and groups VI and VII, the HBEE groups, were given an ethanolic extract of H. benghalensis (100 and 200 mg/kg/day, p.o.), all of which were administered in conjunction with a high-fat diet for four weeks in a row. When compared to hyperlipidaemic rats (group II), the HBAE and HBEE treatments resulted in a substantial ($p < 0.05$) reduction in blood lipids (TC, TG, LDL, and VLDL) and rise in cardioprotective HDL. Phytochemical screening identified phytoconstituents that may be responsible for the hypolipidemic effects reported, including alkaloids, flavonoids, saponins, tannins, phenolic compounds, and steroids. According to the results of the current investigation, HBEE (200 mg/kg, p.o.) produced strong hypolipidemic effects.***

## Introduction

A lipid metabolic illness called hyperlipidemia is characterized by elevated levels of triglycerides (TG) and/or total cholesterol (TC). Furthermore, plasma contains lower amounts of high-density lipoproteins (HDL) and higher levels of low-density lipoproteins (LDL).[1] It is well known that hyperlipidemia, particularly high LDL and low HDL, is a significant risk factor for atherosclerosis and cardiovascular illnesses.[2] Moreover, CVD is one of the leading causes of mortality globally[1]. Treatment for hyperlipidemia and atherosclerosis involves lowering plasma levels of cholesterol and triglycerides. It is necessary to discover a means of preventing and managing hyperlipidemia and associated cardiovascular disorders. The majority of synthetic medications, including fibrates, statins, and others, show promise but may also cause serious adverse effects such myositis, diarrhea, altered lipid function, and increased

drug dependency.[3-5] Thus, rather of using synthetic molecules, current research is focusing more on a natural alternative that may lower plasma lipid levels with few or no negative effects.

Beghalensis hiptage (L) In various places, Kurz, syn. Hiptage madablota Geartn. (Family: Malpighiaceae), is also referred to as madhavi, vasantduti, and madhalata.

It is indigenous to the Philippines, Australia, Southeast Asia, and India. From the warmer regions of Maharashtra, Karnataka, Madhya Pradesh, and Chhattisgarh, it is disseminated across India. The traditional medical system uses various plant components, including leaves, bark, and seed kernels, to treat a variety of illnesses, including obesity, chronic rheumatism, asthma, cancer, burning sensations, thirst, and inflammation.[6–8]

Numerous active ingredients, including tannins, phenolic compounds, flavonoids, saponins, and β-sitosterol, are present in the plant.[8, 9] It is possible for these active ingredients to lower plasma lipid levels.[10–12] From this angle, we evaluated the hypolipidemic effects of H. benghalensis on rats who were hyperlipidaemic due to a high-fat diet.

## Materials and methods

## Plant Material

*Fresh leaves of H. benghalensis were gathered in September at the Agriculture College in Bi laspur, Chhattisgarh. The plant's authenticity was confirmed by the National Institute of Science Communication and Information Resources, New Delhi, India (Ref.-NISCAIR/RMHD/Consult/2011-12/1812/112).*

### *Chemicals and Drugs*

*In this investigation, plasma TC, TG, HDL, and glucose kits (Span Diagnostics Ltd. and Agappe Diagnostic Ltd.) were used together with cholesterol (Central Drug House P. Ltd., New Delhi) and gemfibrozil (Lopid, Pfizer). Every chemical utilized was of the analytical kind.*

### *Removal*

H. benghalensis leaves were dried at room temperature while shaded. Using a hand grinder, the dried plant material that had been shaded was roughly pulverized. 90% ethanol and water were used to extract H. benghalensis leaves that had been coarsely pulverized. A cold aqueous percolation approach was used to create aqueous extracts (HBAE), whereas a hot continuous extraction procedure by isolation was used to prepare ethanolic extract (HBEE).[13] For further phytochemical and pharmacological analyses, the extracts were lyophilized at -2°C after being concentrated in a water bath at 40°C.

### Screening with phytochemicals

To find out whether there were any phytoconstituents present, the HBAE and HBEE underwent qualitative testing. We conducted qualitative testing using the techniques provided by Iqbal et al. (2015).[14]

Animals For this investigation, albino wistar rats weighing between 120 and 150 grams were used. The animals were obtained from the Guru Ghasidas Vishwavidyalaya, Bilaspur animal house (Reg. NO. 994/a/GO/06/CPCSEA) and kept in standard environmental conditions (23 ± 2°C, with 55 ± 5% humidity and a 12-hour light/dark cycle) in accordance with the guidelines of the Committee for the purpose of Control and Supervision of Experiments on Animals (CPCSEA). They were given water on demand along with a conventional laboratory diet from Pranav Agro Industries (P) Ltd., Baroda, Gujarat, India. The SLT Institute of Pharmaceutical Sciences, Bilaspur, (C.G.) Institutional Animal Ethical Committee (IAEC) authorized the whole experimental protocol (Ref No.: IAEC/Pharmacy/2012/45), and the studies were carried out in accordance with the ethical standards and principles supplied by CPCSEA.

### Design Experiments

Two diet groups—normal rats and hyperlipidaemic rats—were created from male wistar rats weighing 120–150 grams. Throughout the trials, normal rats were given a standard laboratory diet (SLD), whereas hyperlipidaemic rats were administered a high-fat diet (HFD) in order to induce hyperlipidemia (Table 1). Rats with hyperlipidemia were

separated into groups of six individuals each. For four weeks, the experimental groups received the prescribed medication regimens shown in Table 2.

Weakly, body weight growth was investigated. After an overnight fast, animals' blood was drawn via a retro-orbital puncture. Blood was taken in tubes containing EDTA, centrifuged for 15 minutes at 3000 rpm at 8 oC, and the plasma was separated. It was then kept at 8 oC until biochemical analysis.

**Biochemical Evaluation**

Diagnostic kits were used to evaluate biochemical parameters, such as glucose, HDL, TC, and TG in plasma, utilizing the spectrophotometric approach. An enzymatic technique based on CHOD/PAP was used to quantify TC.[15] The GPO/PAP technique was used to calculate TG.[16] The enzymatic approach, which is based on the specific precipitation of VLDL and LDL in the presence of magnesium ions, was used to assess the HDL content in plasma.[17] The technique of GOD/POD was used to estimate plasma glucose.[18]

Friedwald's (1972) method[19] was used to compute LDL, and the following formula was used to calculate VLDL:

$$\text{LDL (mg/dL)} = \text{TC} - \text{HDL} - \text{TG}/5$$
$$\text{VLDL} = \text{TG}/5$$

**Statistical Analysis**
The findings were presented as mean ± standard error of the mean of six observations (SEM). Variance analysis was used to evaluate the group differences (ANOVA).
At $p < 0.05$, differences were deemed statistically significant.

## Results

**Effects of HBAE and HBEE on Body Weight Gain**
Fig. 1 shows the findings of the investigation into how oral HBAE and HBEE administration affected body weight increase.

The average body weight of the hyperlipidaemic control group increased significantly ($p < 0.05$) in a time-dependent manner starting in the second week, as compared to the normal control group. On the other hand, after four weeks of oral HBAE and HBEE treatment at 200 mg/kg each

Table 1: The makeup of diets under experimentation

| *SLD Ingredients* | *Quantity in %* | *HFD Ingredients* | *Quantity in %* |
|---|---|---|---|
| Moisture | 8.52 | SLD | 63 |
| Crude Protein | 21.92 | Butter | 15 |
| Curd Fat | 4.36 | Ground Nut Oil | 10 |
| Crude Fibre | 4.30 | Cassin | 5 |
| Calcium | 1.26 | Sugar | 5 |
| Phosphorus | 0.79 | Cholesterol | 1 |
| Total Ash | 6.46 | Bile Salt | 0.5 |
| Carbohydrates | 54.0 | Salt Mixture[¥] | 0.5 |

[¥]Salt mixture- NaCl (1 g), KCl (1 g), and $CaCl_2$ (3 g), HFD- High-fat diet, and SLD- Standard Laboratory Diet. Content of SLD was provided by the manufacturer, Pranav Agro Industries (P) Ltd., Baroda, Gujarat, India

**Table 2:** Experimental groups and their treatments

| *Group no.* | *Groups* | *Treatment (four weeks)* |
|---|---|---|
| I | Normal Control | SLD + 0.3% CMC (1 ml) |
| II | Hyperlipidaemic Control | HFD + 0.3% CMC (1 ml) |
| III | Standard | HFD + Gemfibrozil (50 mg/kg, p.o.) |
| IV | HBAE-1 | HFD + HBAE (100 mg/kg, p.o.) |
| V | HBAE-2 | HFD + HBAE (200 mg/kg, p.o.) |
| VI | HBEE-1 | HFD + HBEE (100 mg/kg, p.o.) |
| VII | HBEE-2 | HFD + HBEE (200 mg/kg, p.o.) |

CMC- carboxy methyl cellulose, HBAE- *Hi. benghalensis* aqueous extract, HBEE- *H. benghalensis* ethanolic extract, HFD- high-fat diet, and SLD- standard laboratory diet.

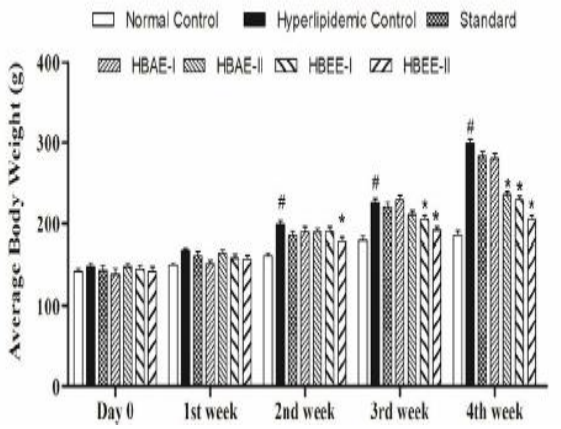

**Fig. 1:** effects on average body weight of HBAE and HBEE. The values are given as mean ± S.E.M., for n = 6. #P < 0.05 indicates a significant difference from the usual control group. The study found that, at 100 and 200 mg/kg dosage levels, there was a substantial ($p < 0.05$) decrease in average body weight when compared to the hyperlipidaemic control group (two-way ANOVA followed by Bonferroni posthoc test). Furthermore, there were no significant differences in the average body weight between the hyperlipidaemic control group and the HBA E-I and gemfibrozil groups. According to the results, HBEE was superior than HBAE and gemfibrozil in terms of weight loss.

## Discussion

In a high-fat diet-induced hyperlipidaemic animal model, the purpose of the current research was to examine the hypolipidemic effects of HBAE and HBEE as well as their impact on plasma glucose and body weight increase. Increased dietary intake of fat, carbs, and extra energy is one of the main causes of obesity.[20] Hyperlipidemia may result from obesity, which raises the blood's content of lipids.[21] The average body weight and plasma TC, TG, and LDL levels of the male wistar albino rats in the hyperlipidaemic control group—which were fed a high-fat diet—rose significantly in comparison to the normal group. Hyperlipidemia is the term used to describe elevated TC, TG, or both values.

It implies that a high-fat diet was enough to cause hyperlipidemia in only four weeks. elevated lipid levels,

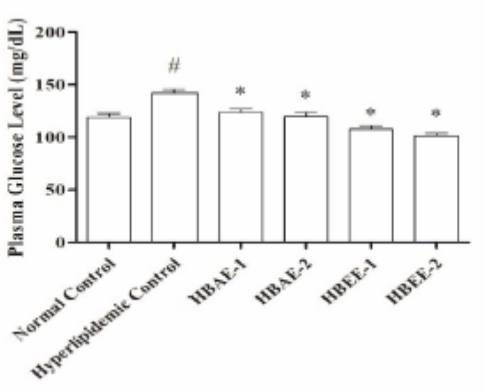


**Fig. 2:** The impact of HBEE and HBAE on the level of plasma glucose. The values are given as mean ± S.E.M., for n = 6. #P < 0.05 indicates a significant difference from the usual control group. *P < 0.05 indicates a significant difference from the hyperlipidaemic control group (one-way ANOVA with Turkey posthoc testing in between).
Table 3 shows the level of plasma lipids after oral HBAE and HBEE treatment.

| | *TC (mg/dL)* | *TG (mg/dL)* | *LDL (mg/dL)* | *VLDL (mg/dL)* | *HDL (mg/dL)* |
|---|---|---|---|---|---|
| Normal Control | 78.94 ± 2.85 | 83.31 ± 2.16 | 24.36 ± 1.80 | 17.46 ± 0.43 | 37.11 ± 0.89 |
| Hyperlipidaemic Control | 129.11 ± 2.46$^{\#}$ | 172.35 ± 3.33$^{\#}$ | 62.46 ± 3.37$^{\#}$ | 34.47 ± 0.67$^{\#}$ | 32.17 ± 0.92$^{\#}$ |
| Standard | 99.82 ± 3.0* | 105.15 ± 2.71* | 36.57 ± 4.30* | 21.03 ± 0.54* | 42.22 ± 1.16* |
| HBAE-1 | 113.57 ± 3.75* | 124.52 ± 1.74* | 47.42 ± 3.78* | 24.90 ± 0.35* | 41.24 ± 0.42* |
| HBAE-2 | 103.08 ± 2.40* | 113.51 ± 1.74* | 37.84 ± 1.88* | 22.70 ± 0.35* | 42.54 ± 0.58* |
| HBEE-1 | 99.32 ± 2.71* | 99.68 ± 2.10* | 36.26 ± 2.82* | 19.94 ± 0.42* | 43.12 ± 0.85* |
| HBEE-2 | 90.22 ± 2.33* | 91.23 ± 1.40* | 25.28 ± 2.24* | 18.25 ± 0.28* | 46.69 ± 0.73* |

Values are expressed as mean ± S.E.M., (n= 6). $^{\#}P < 0.05$ significant values as compared to the normal control group. $^{*}P < 0.05$ significant values as compared to hyperlipidaemic control (one-way ANOVA followed by Turkey posthoc test)

The presence of cholesterol, bile acid, sugar, and high fat in high-fat meals may lead to hyperglycemia and obesity. By interfering with cholesterol absorption, metabolism, breakdown, serum clearance, and excretion, cholesterol and bile acid cause hypercholesterolemia.[22, 23] Due to its greater fat content, sucrose causes insulin resistance, hypertriglyceridemia, and obesity [24, 25].[26]

The current study's results demonstrate that the HBAE and HBEE therapies dramatically decreased average body weight, plasma lipids such as TC, TG, LDL, and VLDL, and significantly enhanced the amount of cardioprotective HDL when compared to the hyperlipidemic control group. Based on the data, it can be concluded that HBEE, at a dose of 200 mg/kg, showed significant hypolipidemic effects that were superior to those of HBAE.

Elevated TC and LDL values are recognized as key risk factors for coronary heart disease.[27] Reduced HDL, however, is a risk factor for atherosclerosis on its own. Furthermore, a 1% increase in HDL was associated with a 3% reduction in the chance of developing clinical atherosclerosis and coronary heart disease, according to a research on HDL intervention.[28] It can be concluded that the leaves of H. benghalensis have a potent cardioprotective action, and that this effect may be caused by an increase in the activity of lecithin cholesterol acyltransferase (LCAT), which helps to regulate blood lipids, given the enhancement of the cardio protective lipid HDL following the administration of HBAE and HBEE.[29] For free cholesterol to be converted to HDL and subsequently transported back to VLDL or IDL, which the liver cells then absorb, LCAT is necessary.[30, 31] The experiment's other significant discovery is the lower blood TG level, which may be linked to an increase in endothelium-bound lipoprotein lipase, which hydrolyzes triglycerides into fatty acids. TG is also independently linked to cardiovascular health.[32]

Table 4: The plasma lipid fraction ratio

| | *TC/HDL* | *LDL/HDL* |
|---|---|---|
| Normal control | 2.12 ± 0.04 | 0.65 ± 0.04 |
| Hyperlipidemic control | 4.04 ± 0.18$^{\#}$ | 1.96 ± 0.15$^{\#}$ |
| Standard | 2.38 ± 0.12* | 0.88 ± 0.12* |
| HBAE-1 | 2.75 ± 0.08* | 1.15 ± 0.09* |
| HBAE-2 | 2.42 ± 0.04* | 0.89 ± 0.04* |
| HBEE-1 | 2.30 ± 0.06* | 0.84 ± 0.07* |
| HBEE-2 | 1.93 ± 0.05* | 0.54 ± 0.05* |

Values are expressed as mean ± S.E.M., (n= 6). $^{\#}P < 0.05$ significant values as compared to the normal control group. $^{*}P < 0.05$ significant values as compared to hyperlipidaemic control (one-way ANOVA followed by Turkey posthoc test)

The results of the photochemical screening showed that HBEE included carbohydrates, alkaloids, flavonoids, saponins, tannins, phenolic compounds, and steroids, while HBAE solely contained the aforementioned phytoconstituents.
These phytoconstituents may be the cause of HBAE and HBEE's hypolipidemia. By competing with cholesterol-binding sites or obstructing the manufacture of cholesterol, saponins have been shown to lower blood cholesterol.[35, 38] Additionally, in the colon, saponins combine with cholesterol to produce insoluble complexes that hinder absorption.[39] By inhibiting dyslipidemia, hepatosteatosis, and oxidative stress, polyphenols and tannins have been shown to have anti-obesity, hypolipidemic, and hypoglycemic actions in obese and diabetic rats[26, 40]. As a result, they may be in charge of reducing TC and LDL and raising HDL in hyperlipidemic rats.
It has been shown that flavonoids reduce LDL levels and boost the body's resilience to LDL oxidation, which may prevent atherosclerosis.[11, 41] By promoting the breakdown of cholesterol and lipoprotein lipase and plasma LCAT, flavonoids help prevent lipogenesis.[10] It has previously been established that H. benghalensis contains β-sitosterol.[42] A plant sterol called β-sitosterol has been suggested to have cholesterol-lowering properties.[30, 43] According to published research, β-sitosterol lowered the absorption of cholesterol by 42% when consumed with 500 mg of cholesterol.[44] Thus, it is possible that β-sitosterol is one of the bioactive phytoconstituents in H. benghalensis leaves that lowers plasma cholesterol via lowering the absorption of cholesterol.

## Conclusion

The effects of a high-fat diet on a genesis of hyperlipidemia and hyperglycemia are summarized in the current research. The combined findings imply that H. benghalensis reduces blood glucose levels and body weight increase while also having strong hypolipidemic effects. It could enhance lipid metabolism and counteract the consequences of hyperlipidemia. Phytochemical study identified a number of different phytoactive components. Therefore, isolation is required in order to identify their method of action and conduct further pharmacological assessments.

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