Antihyperlipidemic Potential of *Piper nigrum*: A Natural Approach to Lipid Regulation

Abstract

Humans have used herbal medicine to address medical conditions since the inception of civilization. This study seeks to assess the effectiveness of *Piper nigrum* as an anti-hyperlipidemnicdrug and its influence on lipid profiles. We utilized the model to evaluate the effectiveness of the plant antihyperlipidemic activity.SGPT and SGOT levels were statistically significantly reduced ($p < 0.05$) in groups 6 and 5, respectively, at doses of 900 mg/kg and 600 mg/kg. No groups demonstrated statistically significant results in the renal function test. Despite a slight reduction in total cholesterol, HDL, LDL, and overall cholesterol, no group exhibited statistically significant outcomes. However, the elevated dosage of 900 mg/kg showed the most significant reduction in these metrics. The ethanolic extract of this plant demonstrates significant antihyperlipidemic effects, and further research may aid in the advancement of alternative medical uses.

Keywords: *Piper nigrum,* Herbal medicine,antihyperlipidemic, Creatinine. Ethanol, SGOT.

Introduction

Chronic liver disease (CLD) and its related consequences, including cirrhosis and liver cancer, result in considerable mortality, morbidity, and economic burden. The liver, the largest glandular organ, regulates most physiological activities in the human body. The liver is the organ tasked with absorbing an individual's complete blood volume several times each day. It is crucial for human metabolic functions. Excessive alcohol consumption, drug dependency, exposure to some harmful materials, or infection by viruses or parasites may lead to elevated levels of reactive oxygen species (ROS), including hydroxyl radicals (OH), hydrogen peroxide (H_2O_2), and molecular oxygen (O_2) [3]. This may lead to hepatocellular injury. The Centers for Disease Control and Prevention conducted research with 1,492 physicians delivering ambulatory care in private facilities.

The study revealed that hyperlipidemia is the second most prevalent chronic ailment observed by these physicians, surpassed only by hypertension. The study results demonstrate that the primary cause of hyperlipidemia is the excessive consumption of high-fat meals [5]. The liver is crucial for the metabolism of commonly prescribed antihyperlipidemic drugs, such as atorvastatin, pravastatin, fluvastatin, simvastatin, lovastatin, and rosuvastatin. Consequently, the bioavailability of these pharmaceuticals is exceedingly poor [6]. Statins may transiently inhibit the enzyme 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMG-CoAR). This enzyme reduces cholesterol levels. This facilitates the diminution of cholesterol synthesis within the cells. Statins can infiltrate hepatocytes and obstruct HMG-CoAR, which is fundamental to their pharmacological effects [7].

Statin-associated muscle symptoms (SAMS), also known as muscular problems, are the primary side effects that limit the utilization of statins. Two other potentially detrimental effects include the onset of diabetic mellitus (DM) and complications related to the central nervous system [8]. These synthetic drugs not only have considerable adverse effects, but they are also expensive, potentially placing financial strains on patients who must continue their usage during the whole treatment period [9]. Therefore, it is crucial to develop highly effective antihyperlipidemic medicines with minimal side effects. Plants are essential for the discovery and formulation of novel pharmaceuticals [10]. They serve as a significant and abundant source of naturally occurring chemicals for therapeutic applications. Specialists in the domain propose that specific chemical compounds obtained from medicinal flora provide therapeutic properties. Therefore,

researchers consistently pursue novel herbal therapies and other phytotherapeutic agents to manage various ailments effectively [4]. Numerous nations worldwide have traditionally employed traditional medicines derived from botanical sources, nutritional supplements, and alternative treatment methods as remedies. In recent years, the utilization of conventional medicine has significantly increased, with numerous persons around the nation depending on it as their primary healthcare approach. Medicinal plants contain diverse chemical components, enabling them to exert numerous pharmacological and therapeutic effects. These substances encompass several constituents, including tanning agents, glycosides, alkaloids, saponins, polysaccharides, essential oils, terpenoids, resins, and plant lipids [12–14]. Genetically engineered plants enable the exact modulation of chemical concentrations, hence realizing the desired therapeutic effect. Reverse genetics offers several potential uses, one being the augmentation of secondary metabolite biosynthesis, including alkaloid synthesis [15]. Global advancements in scientific research have led to a heightened investigation of the therapeutic qualities of plant species [16]. Individuals are progressively preferring plants because of their inherent safety, potent pharmacological properties, and cost benefits compared to synthetic treatments.

Piper nigrum Linn (Piperaceae), generally referred to as black pepper, has been traditionally employed for cholera, dyspepsia, stomach disorders, and diarrhoea [17]. The chemical contents of PnL comprise polyphenols, alkaloids, terpenoids, tannins, and oils, with the principal chemicals being piperine, piperidine, pellitorine oil, cephradine, piperolactum, piperazine, sylvanite [18]. Research on the biological activity of *Piper nigrum*has been sparse thus far: *Piper nigrum* has demonstrated antidiabetic capabilities [19], along with hepatoprotective and antioxidant benefits in rats [20].

This study aims to determine if an ethanolic extract of *Piper nigrum*can benefit individuals with diabetes and to examine its impact on lipid profiles. This study provides significant insights into the possible antidiabetic and lipid-modulating actions of *Piper nigrum*extract in an alloxan-induced diabetes model. It underscores the importance of herbal medicines in the pursuit of alternative, natural therapies for hyperlipidemia, a worldwide health issue. The study presents first data on the biochemical impacts of several dosages of *Piper nigrum*on liver and kidney function, facilitating subsequent research into its medicinal effectiveness and safety.

Materials and methods

Plant Collection and Extract Preparation

*Piper nigrum*L. were collected from Dhaka University area. The specimen was verified by the Bangladesh National Herbarium, which also gave it the accession number 568765 for future use. *P. nigrum* was first cleaned properly with distilled water and air-dried. Next, it was severely grinded with mechanical grinder. The powder was soaked in 90% ethanol with 1:2 ratio and kept for 15 days. By this time the solution was vigorously shaken occasionally. Then, the extract was filtered with Whitman filter paper with gravitational filtration and the filtrate is collected. The filtrate was dried in a rotary evaporator at a 60□ temperature.

Drugs and Chemicals

Carbon tetrachloride (CCl_4), a well-known hepatotoxicity-causing chemical, was purchased from the Sigma Aldrich. The API of typical anti-oxidant medication silymarin was received as a free gift from Incepta Pharmaceuticals Limited.

Experimental Animal Procurement, Nursing, and Grouping

A total of 100 male rats weighing between 120 and 150 grams were obtained from Jahangirnagar University in Savar, Dhaka. Each of them was housed in a climate-controlled environment (temperature 25±3°C, relative humidity 55±5%, and a 12-h light/dark cycle) at the University of Dhaka's Institute of Nutrition& Food Science (INFS). Group 1 is negative control group and group 2 is positive control group whereas group 3-group10 is treatment group. They were given a standard diet and were provided with clean water. All of the animals were acclimatized in this habitat for at least one week prior to the research for adaption. All experiments have been examined and approved by the ethical committee under permission number. 278/LUB.Pharm. All experimental methods followed the recommendations of the Institutional Animals Ethics Committee (IEAC).

Animal Model Sample Size Detection

There were 100 rats in all, and they were randomly divided into ten groups of ten. The rats were randomly allocated to one of the groups. The rats were watched closely each day to ensure better health status.

Dose Selection and Route of Administration for Respective Study

Carbon tetrachloride (CCL_4) is a common chemical agent used in laboratories to study arrange of liver diseases, both acute and chronic. Trichloromethyl free radical (CCL_3), a CYP2E1isozyme-

produced CCL_4 metabolite, reacts with cellular lipids and proteins to form trichloromethylperoxy radical, which attacks lipids on the endoplasmic reticulum membrane faster than thetrichloromethyl free radical, causing lipid peroxidation and lobular necrosis. A single oral treatment of CCl_4 mixed with olive oil as a vehicle in a 1:1 ratio (3 ml/kg of rat body weight) produced hepatic damage in all animal groups except the usual control group. *Piper nigrum*extracts were administered to animals with hepatic injury as a post-treatment. The extract was administered orally at doses of 300,600 and 1200mg/kg with Tween-80 solution.

Evaluation of Hepato–ProtectiveActivity

For this experiment, 100 rats were randomly picked and equally divided into fourteen groups.

Table 1: Application of treatment efficacy

Group Number	**Group Specification**	**Treatment species**	**Dose treatment species (mg/kg)**	**Abbreviation of Groups**
1	Negative Control	Physiological saline	10 ml/kg	N
2	CCl_4 Control	N/A	N/A	A
3	CCl_4 + S_{10}	Silymarin	10	S_{10}
4	CCl_4 + PN_{300}	*Piper nigrum*	300	SN_{300}
5	CCl_4 + PN_{600}	*Piper nigrum*	600	SN_{600}
6	CCl_4+ PN_{900}	*Piper nigrum*	900	SN_{1200}
7	S_{10}	*Piper nigrum*	10	S_{10}
8	PN_{300}	*Piper nigrum*	300	PN_{300}
9	PN_{600}	*Piper nigrum*	600	PN_{600}
10	PN_{900}	*Piper nigrum*	900	PN_{900}

Biological Sample Collection:

Blood was drawn from the animals via cardiac puncture and transferred to a centrifuge tube by euthanizing the rats with chloroform. The samples were centrifuged at 5,000 rpm for 5 minutes to create the supernatant fluid. Biochemical testing subsequently required the transfer of this fluid to an additional micro-centrifuge tube.

Estimation of Biochemical Parameters

Lipid profile (total cholesterol, triglyceride, HDL, LDL), kidney (urea and creatinin), and liver function tests(SGPT and SGOT) were performed in Humaluzer 3000 using respective parameter Kit.

Statistical analysis:

All of our findings (raw data) about numerical parameters were documented and evaluated on a spreadsheet utilizing the MS Excel tool. The collected data underwent descriptive statistical analysis, with results presented as mean and standard deviation. We employed the "One-way ANOVA test" in SPSS 16 program to assess inter-group heterogeneity about several biological parameters for evaluating statistical significance. The events are deemed statistically significant as the 'p' value was below 0.05 ($p<0.05$).

Results and Discussion

Herbal medicine refers to the use of medicinal herbs to prevent and treat sickness. This might range from traditional and popular cures found across cultures to the use of standardized and titrated plant extracts. In this study, we examined the lipid profiles of the plant Piper nigrum in mice. SGPT and SGOT levels fell significantly ($p < 0.05$) in groups 6 and 5, respectively, at doses of 900mg/kg and 600mg/kg. Other research into comparable experiments yielded the same findings [21]. In the renal function test, no groups had statistically significant results. The 900mg/kg dosage resulted in the most significant drop in urea and creatinine levels, with values of 100.57±6.73 and 1.46±0.73, respectively. Further investigation into such an experiment provides the same results [22]. Despite a slight decrease in total cholesterol, HDL, LDL, and total cholesterol, no group achieved statistically significant results. However, the highest dosage of

900mg/kg resulted in the most significant drop in these parameters. Further investigation into such an experiment provides the same results [23].

Table 2: Different biochemical parameters of*Piper nigrum*

Groups	SGPT	SGOT	Urea	Creatinine	Total Cholesterol	HDL	LDL	Triglyceride
N	44.29±3.71	39.83±5.32	40.52±3.18	0.74±0.06	116.29±6.90	94.57±6.28	23.91±3.10	52.57±4.10
CCl_4	112.63±9.23	93.65±9.30	107.91±6.39	3.2±0.83	214.50±15.39	45.29±7.70	146.74±10.76	118.79±8.87
CCl_4+S_{10}	65.30±6.25	60.21±6.80	53.93±5.21	1.5±0.77	145.70±10.50	76.91±7.28	65.56±7.29	78.75±6.10
CCl_4+PN_{300}	109.34±12.47	90.23±7.81	105.39±8.18	2.64±0.67	211.42±14.62	50.28±4.90	146.70±8.08	114.10±7.50
CCl_4+PN_{600}	105.23±8.46	87.25±7.53*	103.49±7.77	1.81±0.83	205.91±12.73	54.67±6.29	141.29±7.52	112.29±4.97
CCl_4+PN_{900}	100.30±7.53*	84.73±6.75	100.57±6.73	1.46±0.73	201.82±11.97	58.28±4.71	138.70±6.29	107.50±6.70
S_{10}	42.47±6.21	42.32±6.40	41.37±4.21	0.65±0.07	110±0.05	45±0.87	100±0.12	82±0.12
PN_{300}	44.34±7.21	44.51±5.24	42.30±3.08	0.77±0.08	114.93±7.53	94.67±2.87	26.10±4.28	51.08±5.20
PN_{600}	40.23±6.73	40.72±5.21	43.18±4.18	0.78±0.06	116.57±5.28	92.61±3.46	24.50±3.10	54.28±4.29
PN_{900}	41.43±5.73	41.32±4.24	41.28± 4.73	0.83±0.05	119.29.6.27	90.80±6.70	24.67±4.50	53.90±4.68

Note: The results were expressed in Mean±SEM (standard mean error) *p< 0.05, **p< 0.01, and ***p< 0.001 were considered as statistically significant. The statistical analysis was followed by a one-way analysis of variance (Dunnett's test) compared to the control.

Conclusion

The findings of this research indicate that an ethanol extract of *Piper nigrum*may have preventive benefits against hypercholesterolemia, liver damage, and reduced kidney function. However, despite its anti-hyperlipidemic capabilities, the extract had no meaningful effect on the desired

results. Additional research is required to isolate and identify the active molecules responsible for these effects. Once discovered, extensive research may be done to understand their methods of action better.

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