Original Research Article

An Assessment of Anti-hyperlipidemic Activity of Ethanolic Extract of *Gymnema Sylvestre* on Rat Model

Abstract:
According to World Health organization (WHO), cardiovascular diseases (CVDs) are now the leading cause of global death. Almost 17.9 million people die every year due to cardiovascular diseases. Hyperlipidemia is one of the major causes of CVDs. Increased cholesterol level increases the risk of stroke and other heart diseases. To reduce the occurrence of CVDs, hyperlipidemia must be controlled. There are already several drugs such as instance Atorvastatin (Lipitor), Simvastatin (Zocor), Fluvastatin, Lovastatin etc. available in the market. But the drugs have some side effects also. To decrease the side effect and ensure natural treatment several medicinal plants are being searched for having antihyperlipidemic activity. *Gymnema Sylvestre* is one of them. If the drug gives antihyperlipidemic activity then it will open a new door way for natural medicine in the treatment of CVDs. To inspect that, leaves of the plant were collected, purified, dried and then soaked in ethanol. This infusion was then preserved. 80 adult Wister rats were divided into 9 groups. Hyperlipidemia was introduced group 2 to 6 by giving high fat diet. Then Negative control group has no disease nor treated with any drug. One of the disease groups was treated with marketed drug. Three groups were treated with the *Gymnema Sylvestre* infusion in low, medium and high doses. Three groups without disease were done the same to inspect the drug activity on normal physiological function. High dose of *Gymnema Sylvestre* decreases the total cholesterol level significantly. Medium and high dose causes same in case of triglyceride level. In liver function test, medium and high dose of the drug causes significant decrease in SCPT and SGOT level. In case of kidney function test, all doses decrease creatinine level and only high dose decrease urea level. So, we can the drug has antihyperlipidemic activity and has no remarkable side effects. Thus, it can be used as antihyperlipidemic agent.

Keywords: cardiovascular disease,), fluvastatin, hyperlipidemia, *Gymnema Sylvestre*, natural medicine

Introduction:
modern times cardiovascular diseases represent 32% of all global deaths. In the year 2019, an estimated 17.9 million people died from CVDs. (1) The way CVDs became an existential crisis for humans is where hyperlipidemia steps in. Hyperlipidemia presents significant challenges to human existence due to its potential impact on health. Hyperlipidemia (high cholesterol) is an

overabundance of lipids or fats in the blood. This can raise the risk of heart attack and stroke because blood can't flow through arteries smoothly. (2) Hyperlipidemia is a significant risk factor for cardiovascular diseases like heart attacks, hypertension, strokes, coronary artery disease, type-2 diabetes, etc. Globally, raised total cholesterol affects approximately 39% of adults. (2) Ninety-three million American adults (age 20 and older) have a total cholesterol count above the recommended limit of 200 mg/dL. (2) For this reason, it is incumbent upon us to deem anti-hyperlipidemic agents. Antihyperlipidemic agents promote the deduction of lipid levels in the blood. Some antihyperlipidemic agents aim to lessen the levels of low-density lipoprotein (LDL) cholesterol, some decrease triglyceride levels, and some aid in raising the high-density lipoprotein (HDL) cholesterol. (3)

There are already some available drugs on the market. For instance Atorvastatin (Lipitor) Simvastatin (Zocor), Fluvastatin, Lovastatin, (4) There are side effects of these drugs
Common side effects unique to atorvastatin include constipation, fatigue, gas, heartburn, common cold, urinary tract infection, and joint pain. Simvastatin, on the other hand, can cause nausea, vomiting, gas, and allergic reactions. The most serious possible side effect of both Lipitor and Zocor is liver damage. (5) These drugs come with a financial burden alongside the side effects.

In modern-day, scientists introspect medicinal plant compounds to formulate new drugs. Medicinal plants provide natural antidotes for a vast span of health problems, usually with infrequent side effects corresponding to synthetic drugs. It's possible to get numerous treatments from a plant. For instance, Anti-inflammatory, Cardiovascular Health, Anti-diabetic, Antidiuretic, Anticancer, and Hepatoprotective activity. Medicinal plants Trigonella foenum graecum L Cynara cardunculus(Artichoke), Medicago sativa (Alfalfa), Allium sativum L(garlic) Silybum marianum L, Thistle Maryam, Seville, and some additional herbs are among the greatly essential plants that are used for hyperlipidemia. (6) In traditional medicine, Trigonella foenum graecum L is prescribed to treat diseases like diabetes, high cholesterol, bronchitis, constipation, dyspepsia, and renal problems. Italian scientists used to prescribe the cynarin compound (an effective substance of artichoke) to stimulate the liver and gallbladder and to treat elevated cholesterol(6) and the list goes on.

Gymnema Sylvestre plant is located in Asia, Africa, and Australia. Also known as It is known to have blood glucose-lowering potential and, thus, is widely used in traditional and Ayurvedic systems of medicine. It's also known to have anti-oxidant, antibiotic, anti-inflammatory, antiviral, gastro and hepatoprotective, anticancer, and lipid-lowering activities. (7)

Gymnema Sylvestre leaf extract was observed to possess very potent hypolipidaemic activity.
Stems of Gymnema Sylvestre contain stigmasterol. These compounds have multiple therapeutic potentials including antidiabetic, hypoglycemic, antioxidant, and anticancer activities. Triterpenoid saponins also exhibited anti-tumor, anti-fungal, hepatoprotective, and antidiabetic potential in several studies. (8)

Ethanol extract of this plant is reported to reduce glucose level by 46% whereas the water extract reduced glucose level by 26% and methanol extract by 12%.
One of the constituents of Gymnema Sylvestre is gymnemic acid which is a mixture of saponins (Yoshikawa et al., 1993). It blocks the receptor site for sugar in the intestines, preventing the absorption of sugar which reduces blood sugar levels. (7) The extract of G. sylvestre is reported to be liver tonic, emetic, diuretic, thermogenic, stomachic, stimulant, anthelmintics, laxative, cardiotonic, expectorant, antipyretic, and uterine tonic. The plant also exhibits medicinal importance in the treatment of jaundice, constipation, cardiomyopathy, asthma, bronchitis, amenorrhoea, conjunctivitis, renal and vesical calculi, dyspepsia, leucoderma, and Parkinsonism. (10)
The prevalence of coronary artery disease is the cause of a higher incidence of mortality than other causes combined (11) The prominent aspect contributing to coronary artery diseases is hyperlipidemia. Reduction in serum cholesterol levels may significantly reduce the chances of coronary heart disease (11). Gymnemasylvestre improves Cholesterol and Triglyceride Levels, reducing the risk of Heart Disease. Gymnema Sylvestre may help lower “bad” LDL cholesterol levels and triglycerides. While Gymnema gets its fame from lowering blood sugar levels and reducing sugar cravings, research shows that it may also influence fat absorption and lipid levels. (14). Gymnema has a trophorestorative action of the beta cells of the pancreas. The leaf is the plant part used medicinally. The key constituents of Gymnema include saponins and gymnemic acids (12). Gymnema leaves exert their action through stimulation of insulin secretion from the

pancreas (9). Hydroalcoholic extract of Gymnema leaves showed a significant reduction in the levels of all lipids with an increase in HDL-C as compared to high cholesterol diet control (13).

Hence, this plant is an immaculate nominee for anti-hyperlipidemic activity.

Materials and Methods:

Collection and extraction of the plant:

The leaves of Gymnema Sylvestre were gathered from the medicinal plant garden of the Faculty of Pharmacy at the University of Dhaka. The leaves underwent a meticulous process of purification, commencing with a thorough cleansing, followed by a delicate oven-drying procedure. Subsequently, the desiccated leaves were meticulously made into a fine powder, which was then soaked in an ethanol solution. This infusion underwent vigilant scrutiny and continuous assessment. After 14 days the solution was filtered. The resulting solution was subjected to an intricate process of concentration through the employment of a rotary evaporator.

Materials:

1. Drug and Chemical:
2. Ethanol
3. CCl4
4. Standard drug- Atorvastatin
5. Stress chemical-high fat components- Ghee, butter, oil, mutton fat, dalda, etc
6. Kits to check creatinine level
7. Humalyzer 3000
8. LDL, HDL, SGPT, Cholesterol

Atorvastatin is a standard drug that is to treat hyperlipidemia. We got this medical sample as a gift from Insepta Pharmaceutical Limited.

Method:

After extracting the antihyperlipidemic drug from Gymnema Sylvestre leaves the next step was housing the rats dividing them into 9 groups and feeding them a high-fat diet. While giving some

rats drug store medicine and some plant-based medicine some rats were not provided such a high-fat diet. Then we had a rigorous observation checking the condition of rats upon various measurements. After feeding the rats high-cholesterol drugs and giving them medications we tested their blood using various kits. For example, to measure creatinine level we mixed the blood serum of the rat with certain chemicals and used a creatinine kit for it. The same goes for SGPT, HDL, LDL, total Cholesterol, and triglycerides

Group 1: Negative control- They were fed normal food. No high-fat food was provided
Group 2- Disease control- Disease was created by feeding a high-fat diet but no drugs were fed.
Group 3- We gave the rats a marketed drug (Atorvastatin) upon developing hyperlipidemia.
Group 4- Disease + plant-based drug in low concentration
Group 5- Disease + plant-based drug in medium concentration
Group 6- Disease + plant-based drug in high concentration
Group7- plant-based plant-based drug in low concentration was given to rats with no disease
Group 8- Plant-based drug in medium concentration was given to rats with no disease
Group 9- Plant plant-based drug in high concentration was given to rats with no disease
Then the result was meticulously observed

Result

Animal housing:

A total of 80 adult male Wistar rats, weighing between 100 and 170 grams, were acquired. These rats were housed in cages in the Institute of Nutrition and Food Science at the University of Dhaka, where they were subjected to a 12-hour light/dark cycle and maintained at a constant temperature of 25°C.+/-3°C. Humidity 55+/-5% They were provided with a standard pellet diet and before clean water. Before commencing the study, the rats were allowed to acclimatize to their environment. Subsequently, the 80 rats were divided into 16 groups, with each group consisting of 5 rats. All experiments involving these rats were conducted in compliance with the ethical guidelines of the institutional animal ethics committee.

Table 1.Variation of Total Cholesterol, HDL, LDL and Triglyceride among different groups

Group	Total Cholesterol (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	Triglyceride (mg/dl)
1	87.32±3.82	78.70±2.41	30.42±1.63	53.44±3.19

2	209.36±14.11	41.43 ±1.29	70.14±2.41	108.49±11.62
3	109.48±13.26	61.29±4.73	48.42±3.15	71.55±8.90
4	206.54 ± 12.21	43.41 ±4.19	68.48±2.49	104.26 ±7.30
5	202.31±14.21	41.26±5.30	64.65±6.73 *	98.65±7.90 *
6	196.51±9.13 *	40.70±4.16	59.37±5.19 *	91.85±8.84 *
7	83.22±4.16	75.50 ± 3.91	32.91±2.19	52.46±1.43
8	85.43±3.21	79.81±2.90	34.59±1.60	55.51±2.30
9	87.80±4.22	77.40±3.14	31.63±2.20	52.46±1.2

Table 2.Variation of SCPT, SGOT, Urea and Creatinine among different groups

Group	SCPT (U/L)	SGOT(U/L)	Urea (mg/dL)	Creatinine(mg/dL)
1	37.37±2.46	40.71±3.6	35.91±1.29	0.52±0.03
2	91.73±8.24	102.91±9.39	93.46±8.61	2.49±0.09
3	64.25±6.29	70.35 ±7.41	62.52±7.30	1.30±0.06
4	88.36±7.59	98.34±8.23	92.45±7.39	2.00±0.05 *
5	83.36±8.39 *	91.63±7.53 *	89.57±4.21	1.73±0.08 *
6	76.24±5.48 *	82.14±8.39 *	88.99 ±6.32 *	1.41±0.03 *
7	35.41±1.83	41.63±2.30	37.41±2.19	0.67±0.04
8	35.22±1.39	37.15±3.39	34.33±2.41	0.69±0.08
9	38.41±1.11	39±1.93	36.16±2.30	0.82±0.07

Discussion

Cardiovascular disease has become one of the major concerns of the time. Hyperlipidemia is a important factor in the development of any cardiovascular disease. The study is done to evaluate the antihyperlipidemic activity of *Gymnema Sylvestre* (leaves).

To assess the lipid profile, serum total cholesterol, LDL, HDL and triglyceride level is demonstrated in table 1. Though we do not see significant changes in HDL level in case of group 4,5,6 when compared with positive control group, we can see significant change in total serum cholesterol level when given in high doses. In case of LDL and triglyceride level, significant decrease has been observed ($p<0.05$) in medium and high doses.

For liver function test, SCPT and SGOT levels were recorded. At lower dose (group 4) no significant change has been observed. Medium dose (group 5) decreases SCPT and SGOT levels significantly ($p<0.05$). But drastic lowering has been observed in case of high dose when compared with the positive control group.

In case of kidney functioning test, creatinine level was decreased significantly ($p<0.05$) in group 4,5 and 6 for administering low, medium and high dose respectively. But urea level only decreased significantly in case of high dose when compared to high dose.

In case of group 7,8 and 9, treated only with low, medium and high dose respectively, has showed no significant changes when compared with the negative control group. This concludes that the drug has no impact on the normal physiological function.

Conclusion:

According to our findings it can be concluded that our plant *Gymnema Sylvestre*possesses therapeutic potential to subside hyperlipidemic state but concentration of therapeutic compound responsible for imparting anti-hyperkipidemic activity; exist in tiny concentration as it could not induce significant activity ($p<0.05$)at low dose. So, more vigorous study is required to isolate the therapeutic compound to assess the activity more precisely.

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