

An Assessment of Hepato-protective activity of *Psidium guajava* fruit extract against Hepatic injured Rodent Model

Abstract:

Herbal remedies are the art or practice of using herbs and herbal medicines to maintain health and prevent, treat, or cure sickness. The lipid profiles of *Psidium guajava* extract were studied in rats. In the case of Serum glutamic pyruvic transaminase (SGPT) and serum glutamic-oxaloacetic transaminase (SGOT), only the high dose produced statistically significant ($p < 0.05$) outcomes as compared to the negative control group. At low, medium, and high dosages, creatinine levels decreased statistically significant ($p < 0.05$). However, none of the dosages in case of urea produced statistically significant ($p < 0.05$) effects. Only at high dosages did total cholesterol levels reduce statistically significantly ($p < 0.05$) when compared to the negative control group. Only at high doses did High Density Lipoprotein (HDL) levels improve statistically significantly ($p < 0.05$). High and medium dosages of Low Density Lipoprotein (LDL) significantly ($p < 0.05$) reduce the quantity in the blood. Triglyceride levels were reduced only at high dosages as compared to the negative control group.

These discoveries may benefit those suffering from liver disorder.

Keywords: *Psidium guajava*, SGPT, Herbal medicine, phytopharmacology. Cholesterol.

Introduction:

“The liver is the body's biggest and most complicated internal organ, accounting about 2-3% of an adult human's total body weight. Chronic Liver Diseases (CLD) affect an estimated 1.5 billion individuals globally; in the United States, the rate has grown by 31% among those aged 45-64 years” [1]. “The liver is especially vulnerable to cellular damage caused by an increase in ROS activity OH, H₂O₂, O₂ caused by excessive alcohol intake, drug abuse, exposure to certain toxic substances, or viral or parasite infection” [2]. “L-glutathione (L-cysteine, glycine, and L-glutamate) is a low molecular weight, water-soluble tripeptide that acts as a free-radical scavenger and is frequently combined with ascorbic acid as an oral dietary supplement. They have valuable detoxifying and anti-oxidant properties and are known to strengthen the immune system” [3-6]. “However, they can cause digestive problems, stomach cramps, bloating, diarrhea, breathing difficulty owing to bronchoconstriction, and allergic reactions such as dermatitis. Plants have an important role in the discovery and synthesis of novel drugs because they provide a rich, diverse, and prolific supply of naturally occurring therapeutic chemicals. These might either operate as a safer, more effective alternative to the present medicine molecule or be researched further. Unique chemical compounds produced by medicinal plants, according to medicinal plant scientists, may have therapeutic effects. As a result, scientists are always looking for alternative or plant-based herbal medications to treat a wide range of ailments. These medicinal plants can provide a wide range of pharmacological and therapeutic effects due to the presence of numerous chemical constituents such as phenols, alkaloids, terpenoids, saponins, glycosides, tannins, flavonoids, resins, polysaccharides, plant lipids, essential oils, and so on” [7-9]. “The concentration of the plant's chemical components, whether increasing or decreasing, may provide the desired therapeutic effect, which may be achieved by plant genetic manipulation. For example, using reverse genetics, we can boost the biosynthesis of secondary metabolites such as alkaloid” [10-11]. Hepatoprotective action is shown in *Acacia mellifera*, *Adansonia digitata* L, and *Cannabis sativa* L [12-14].

“*Psidium guajava* L is a fruit-bearing tree in the Myrtaceae family that is generally known as guava. Guava is a tiny tree or shrub native to the Caribbean, Central America, and South America” [15]. The plant contains Alkaloids, Flavonoids, Phenol, Saponins, Tannins,

Triterpenes, and other compounds [16-17]. Natural compounds originating from plants, such as flavonoids,

terpenoids, and sterols, have attracted a lot of interest in recent years because of their various pharmacological characteristics, such as antioxidant and hepatoprotective activity [18]. Silymarin, a flavonolignan derived from the plant "milk thistle" (*Silybum marianum*), is virtually solely utilized for hepatoprotection [19].

The goal of this study is to look at the potential hepatoprotective action of in a *P. guajava* CCl₄-induced experimental rat model as well as their potential adverse effects on the liver in the hunt for a better, safer, more inexpensive, and more effective drug.

Materials and Methods:

Plant Collection and Extract Preparation

Fruits of *P. guajava* were collected from local market of Dhaka. The material was authenticated by the University of Dhaka's Department of Pharmacy. The moist fruit of *P. guajava* was air-dried and severely crushed. The powdered fruit was then extracted for 15 days in 50% ethanol. The extract was filtered at three-day intervals. The extracted material was dried in a rotary evaporator at a low temperature and pressure. Finally, the crude residue was subjected to the required pharmacological testing.

Drugs and Chemicals

Carbon tetrachloride (CCl₄), a well-known hepatotoxicity causing chemical, was purchased from the Sigma firm in the United States. The typical anti-oxidant medication silymarin was purchased as Livasil 140 mg from Incepta Pharmaceuticals Ltd.

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). They were given a conventional food and

were permitted to drink clean water. All of the animals were maintained in this habitat for at least one week prior to the research for adaption. All experimental methods followed the recommendations of the Institutional Animals Ethics Committee (IEAC).

Animal Model Sample Size Detection

A total of 100 rats were allocated at random into 10 groups of ten rats each. The rats were assigned to each group at random in all of the studies. We used ten rats in each group to increase the investigation's validity. During the mating season, we, on the other hand, maintained a close eye on the rat every day. We included both positive and negative control groups in our study.

Dose Selection and Route of Administration for Respective Study

Carbon tetrachloride (CCL₄) is a common chemical agent used in laboratories to study a range of liver diseases, both acute and chronic. Trichloromethyl free radical (CCL₃), a CYP2E1 isozyme-produced CCL₄ metabolite, reacts with cellular lipids and proteins to form trichloromethyl peroxy radical, which attacks lipids on the endoplasmic reticulum membrane faster than the trichloromethyl free radical, causing lipid peroxidation and lobular necrosis. A single oral treatment of CCL₄ 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. *P. guajava* extracts were administered to animals with hepatic injury as a post-treatment. The extract was administered orally in various quantities.

Evaluation of Hepato-Protective Activity

For this experiment, 100 rats were randomly picked and equally divided into fourteen groups (Table 1).

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 + Silymarin	Silymarin	80	A + S ₈₀
4	CCl ₄ + Silymarin	Silymarin	120	A + S ₁₂₀
5	CCl ₄ + Silymarin	Silymarin	150	A + S ₁₅₀
6	CCl ₄ + <i>Psidium guajava</i>	<i>Psidium guajava</i>	400	A + PG ₄₀₀
7	CCl ₄ + <i>Psidium guajava</i>	<i>Psidium guajava</i>	700	A + PG ₇₀₀
8	CCl ₄ + <i>Psidium guajava</i>	<i>Psidium guajava</i>	1000	A + PG ₁₀₀₀
9	Silymarin	Silymarin	80	S ₈₀
10	<i>Psidium guajava</i>	<i>Psidium guajava</i>	400	PG ₄₀₀

Statistical analysis:

All of our findings (raw data) in terms of numerical parameters were recorded and analyzed on a broadsheet using the MS Excel application. The gathered data were subjected to descriptive statistics, with the findings reported as mean SD. To evaluate statistical significance, we used the SPSS 16 software's "One-way Anova test" to interpret inter-group heterogeneity in terms of several biological factors. The occurrences are considered statistically significant since the 'p' value was less than 0.05 ($p < 0.05$).

Results:

In the case of SGPT and SGOT, only the high dosage 1000mg/kg produced statistically significant ($p < 0.05$) outcomes when compared to the negative control group. In low, medium, and high dosages, creatinine levels decreased statistically significant ($p < 0.05$). However, none of the dosages in case of urea had statistically significant ($p < 0.05$) outcomes. Only at high dosages did total cholesterol levels drop statistically significantly ($p < 0.05$) as compared to the negative control group. Only at high doses did HDL levels increase statistically significantly ($p < 0.05$). In

the case of LDL, high and medium dosages significantly ($p < 0.05$) reduce the quantity in the blood. When compared to the negative control group, triglyceride levels dropped only at high dosages.

Table 2: Lipid profile of rat after administration of drug and *P. guajava* extract

GROUP	SGPT	SGOT	Total cholesterol	HDL	LDL	Triglyceride	Urea	Creatinin
N	33.4±0.9 7	44.69±0. 87	95.34±5.60	66.32±4.5 3	36.92±4.37	47.42±3. 50	27.39±2. 31	0.6
D	92.35±5. 46	95.90±6. 32	149.34±4.10	42.93±4.2 3	84.53±5.99	99.34±8. 31	89.35±8. 46	1.9
D+Drug	57.35±3. 94	53.50±4. 97	121.34±4.60	55.53±3.9 7	65.19±6.39	70.53±7. 18	67.32±4. 93	1.2
D+P _{low}	89.24±6. 37	94.91±7. 37	146.42±5.30	44.24±3.9 7	82.45±5.30	96.19±7. 50	89.16±7. 42	1.5*
D+P _{med}	87.58±4. 28	90.16±6. 35	144.35±4.73	45.43±5.3 7	77.53±4.62*	94.54±3. 16	87.32±6. 57	1.1*
D+P _{high}	81.36±5. 59*	85.47±8. 23*	139.32±4.67 *	51.16±4.8 2*	73.45±3.90*	91.10±6. 32*	84.99±6. 36	0.80*
Drug	30.20±0. 84	39.63±0. 94	92.57±4.93	65.31±5.1 9	36.24±3.16	46.10±3. 10	31.32±1. 46	0.6
Low	33.96±0. 81	44.16±0. 97	90.46±3.10	64.24±3.9 7	30.10±4.10	48.40±4. 15	30.15±0. 93	0.7
Medium	32.46±0. 69	47.30±0. 86	94.91±5.30	68.46±4.5 7	32.97±2.41	44.82±3. 59	28.41±1. 32	0.4
High	35.81±0.	42.94±0.	93.10±4.30	65.42±4.1	35.47±4.4	45.45±5.	29.61±2.	0.6

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Values are expressed as mean \pm SEM or percentage ($n = 5$). The data were analyzed by one-way ANOVA followed by Dunnett's test. Asterisks indicated statistically significant values from control. * $p < .05$, ** $p < .01$ and *** $p < .001$ compared with control.

Discussion:

It is customary to assess plant hepatoprotective properties using a variety of approaches to quantify specific biochemical markers. There is no simple universal paradigm for measuring hepatoprotective activity precisely and qualitatively. Toxic damage occurs more frequently in the liver than in any other organ. When a medicine is extensively used, drug-induced liver injury becomes a severe health concern in modern society; thus, study on the mechanism of drug-induced liver injury is highly beneficial in drug-induced liver injury therapy and prevention. In the lack of dependable hepatoprotective medications in contemporary medicine, a wide range of herbal treatments for the treatment of liver problems has grown in popularity [20]. A variety of herbals, notably Silymarin, have shown potential efficacy in the treatment of liver cirrhosis. In the case of SGPT and SGOT, only the high dosage produced statistically significant ($p < 0.05$) outcomes when compared to the negative control group. Creatinin levels decreased statistically substantially ($p < 0.05$) in low, medium, and high dosages. However, no dosage of urea produced statistically significant results. Only at high dosages were total cholesterol levels statistically significant lower as compared to the negative control group. Only at high dosages did HDL levels increase statistically significantly. In the case of LDL, high and medium dosages reduce the quantity in the blood by a statistically significant amount. When compared to the negative control group, triglycerides fell only at high dosages. Many studies using plant extracts, including *Andrographis paniculata*, *Diplazium esculentum*, and *Tamarindus indica*, yielded similar findings [21-23]. *P. guajava* contains a high concentration of kaempferol, an aglycone flavonoid [24]. This chemical can be found in many plant sections. Kaempferol is a powerful antioxidant that can scavenge reactive oxygen and nitrogen species such as superoxide anion, hydroxyl radical, and peroxy nitrite, as well as inhibit the formation of hydroxyl radical [25]. The rise in total antioxidant status was most likely owing to increased antioxidant consumption from

guava, which is abundant in antioxidant vitamins such as ascorbic acid, carotene, lutein, zeaxanthin, and lycopene [26].

Following the isolation of the individual beneficial molecules, more research might be conducted. By using modern procedures such as NMR and mass spectrometry, a novel therapeutic drug can be created in the Anti-hyperlipidemic management system.

Conclusion

The ethanolic extract of *P. guajava* was found to have hepatoprotective effects in this investigation. This extract alleviates the negative effects of a high fat diet on lipid buildup and liver diseases. This requires more research to determine which component from the whole extract truly provides the anti-hyperlipidemic action by a screening approach.

Ethical Approval:

All experimental methods followed the recommendations of the Institutional Animals Ethics Committee (IEAC).

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