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Hepatoprotective Activity of Methanolic Extract of Hibiscus Plantifolius in Paracetamol Induced Hepatotoxic Rats

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Abstract

Objective: Objective of the present study was to carry out hepato protective activity of methanolic extract of *Hibiscus Plantifolius* belonging to family Malvaceae. **Methods:** The shade dried stem part of *H.Plantifolius* (1 kg) was powdered and extracted with methanol using soxhletion. The extract was concentrated using rotary evaporator under reduced pressure at 40°C, till free from the solvents and thereby providing crude methanol extract which was subsequently employed for further studies. Hepato protective activity was studied by using paracetamol used hepato toxicity by using 7 experimental groups like normal control, 10% DMSO, standard, test groups at a dose of 50, 150, 300 mg/kg. And also, blood was collected, and the serum was separated by centrifuging at 300 rpm for 10 min. The collected serum was used for the assay of marker enzymes. The serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) and alkaline phosphatase (ALP) and Total bilirubin and also activity were compared with standard drug. **Results:** Blood samples from rats are treated with methanolic extract of *H.Plantifolius* (50, 150, 300 mg/kg) had significant reductions in serum markers in paracetamol administered animals, indicating the effect of the extract in restoring the normal functional ability of hepatocytes. Silymarin was used as a reference drug. **Conclusion:** The results of the experimental study confirmed that methanolic extract of *Hibiscus Plantifolius* exhibits protective effects against paracetamol induced hepatotoxicity.

Keywords
Hibiscus Plantifolius, Paracetamol, Silymarin

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INTRODUCTION:

Herbs play a major role in the management of various liver disorders along with other system associated diseases. Liver is a key organ regulating homeostasis within the body by various functions. Liver injury caused by toxic chemicals and certain drugs has been recognized as a toxicological problem. Hepatotoxicity is one of very common aliment resulting into serious debilities ranging from severe metabolic disorders to even mortality. Plant derived natural products such as flavonoids, terpenoids and steroids have received considerable

attention in recent years due to their diverse pharmacological properties including antioxidant and hepato- protective activity [1-3]. Among these plants, Hibiscus plantifolius (Maple-Leaved Mallow) is a species of flowering tree in the mallow family, Malvaceae that is native to the India and Sri Lanka. In Sri Lankan texts, the plant is widely known by its synonym H. eriocarpus. The tree is about 8m tall. Leaves are cordate at base; hairy; trilobed. Flowers show axillary panicles where flowers show typical Hibiscus flower colors, pink with dark center. Fruit is a capsule. Common Names for this plant in kannada: Bili daasavaala, Daasaala, Daasaani and in telugu: Telugu - Kondabenda, Kondagogu, Kondajana punara. Paracetamol (acetaminophen) is a widely used antipyretic and analgesic which produces acute liver damage if overdoses are consumed. Paracetamol is mainly metabolized in liver to excretable glucuronide and sulphate conjugates [4,5]. However, the hepatotoxicity of paracetamol has been attributed to the formation of toxic metabolites when a part of paracetamol is activated by hepatic cytochrome P-4506 to a highly reactive metabolite N-acetyl benzoquinone imine (NAPQI)[7]. NAPQI is initially detoxified by conjugation with reduced glutathione (GSH) to form mercapturicacid8. However, when the rate of NAPQI formation exceeds the rate of detoxification by GSH, it oxidizes tissue macromolecules such as lipid or SH group of protein and alters the homeostasis of calcium after depleting GSH. Silymarin is marketed as one of the standard hepatoprotective herbal formulation.

MATERIALS AND METHODS:

Procurement and authentication of plant:

Hibiscus Plantifolius was identified and authenticated by P.Satynarayana Raju, Plant Taxnomist, Department of Botany and Microbiology, Acharya Nagarjuna University

Plant Material:

1 kg of the stem of Hibiscus plantifolius were collected from the Thirumala forest in Andhra Pradesh State, India, in the months of June and July 2017. The stem of Hibiscus plantifolius was washed and allowed to dry for 15 days. The dried stem was then ground to fine powder by using the laboratory Hammer mill. Powdered samples were stored desiccators until required for extraction.

Preparation of Hibiscus Plantifolius Extract:

The powdered materials of Hibiscus plantifolius was extracte with methanol using soxhlet apparatus for 18 hours. The extract was concentrated using rotary evaporator till free from the solvents and obtained yield was respectively 25 g/kg respectively.

Chemicals:

Paracetamol was purchased from, CIPLA LTD., Vill. J uddikalan, Baddi, H.P. Silymarin was supplied by Pan acea Biotech Ltd, New Delhi. All other chemicals and other biochemicals used in the experiments were of analytical grade from different firms. The organic s olvents were distilled before use.

Animals:

Wistar Albino rats of either sex weighing between 100-200 g were used for this purpose. The animals were housed in polypropylenecages and maintained at 24±2oC under 12h light dark cycle and were fed adlibitum with standard pellet diet and had free access to water maintenance and use of animals as per the experiment was approved by the institutional Animal Ethics Committee(014/IAEC/NCPA/PHD/2018-19).

Paracetamol Induced Hepatotoxicity:

The hepatoprotective activity of MEHP was determined using the paracetamol-induced hepatotoxicity test in rats. The animals were randomly divided into 7 experimental groups and administered with test solutions as follows.

Group I Normal control
Group II 10% DMSO.
Group III Received Paracetamol (2 gm/kg bd. wt.)
Group IV Received Silymarin (10 mg/kg bd. wt.)
Group V Received 50mg/kg MEHP
Group VI Received 150mg/kg MEHP
Group VII Received 300mg/kg MEHP

The animals were fasted for 48 hours prior to the experiment under standard laboratory conditions but allowed free access to distilled water *ad libitum.* After 48 hours, each group received the respective dose of test solution orally once daily for 7 consecutive days. The oral administration of paracetamol was performed 3 hours after the last extract administration on the 7th day.

At the end of the experimental period, animals were under mild ketamine anesthesia, blood was collected, and the serum was separated by centrifuging at 300 rpm for 10 min. The collected serum was used for the assay of marker enzymes. The serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) and Alkaline phosphatase (ALP) and Total bilirubin.

Statistical Analysis:

Data obtained from this work were analyzed statistically using Student's t-test and ANOVA (One-way) followed by a post-test (Tukey-Kramer multiple comparison test). Differences between means were considered significant at 0.1% and 5% level of significance i.e $p \leq 0.001$ and 0.05.

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RESULTS:

Effect of MEHP on serum SGOT, SGPT, Total bilirubin and ALP in Paracetamol (2gm/kg bd.wt) treated rats

Group	Treatment	SGOT(U/L)	SGPT(U/L)	ALP(U/L)	Total Bilirubin (mg/dl)
I	Normal control	59±1.76	56.67±1.87	198.33±2.83	0.82±0.11
II	10% DMSO	61.5±1.2	61.17±1.04	200.67±5.63	1.07±0.10
III	Paracetamol (2 gm/kg bd. wt.)	124.33±2.59^{a***}	128±3.65^{a***}	369.5±10.1^{a***}	3.07±0.16^{a***}
IV	Silymarin (10 mg) /kg bd.wt.)	68.5±0.39^{b***}	68.67±0.61^{b***}	239.33±2.74^{b***}	1.23±0.12^{b***}
V	MEHP 50 mg/kg bd.wt	97.17±4.04	89±2.37	317.17±7.41	2.57±0.10
VI	MEHP 150 mg/kg bd.wt.	83.5±2	81±1.41	288.67±3.62	2.12±0.13
VII	MEHP 300 mg/kg bd.wt.	76.33±0.99^{c**}	75.83±1.26^{c**}	262.33±3.97 ^{c**}	1.5±0.12 ^{c**}

Data were expressed as Mean±SEM. Significant at ^{a***}P< 0.001 compare with normal control. b ***P< 0.001 compare with paracetamol treated rats. Significant at ^{c**}p< 0.01 compared paracetamol treated rats

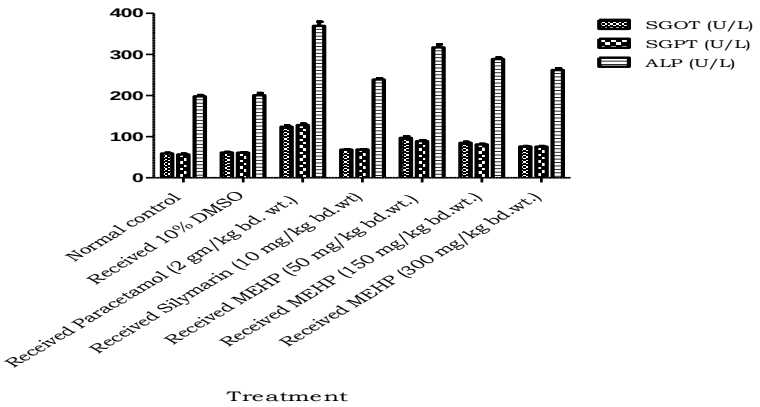

Fig.1: Effect of MEHP on serum SGOT, SGPT and ALP in Paracetamol (2 gm/kg bd.wt) treated rats

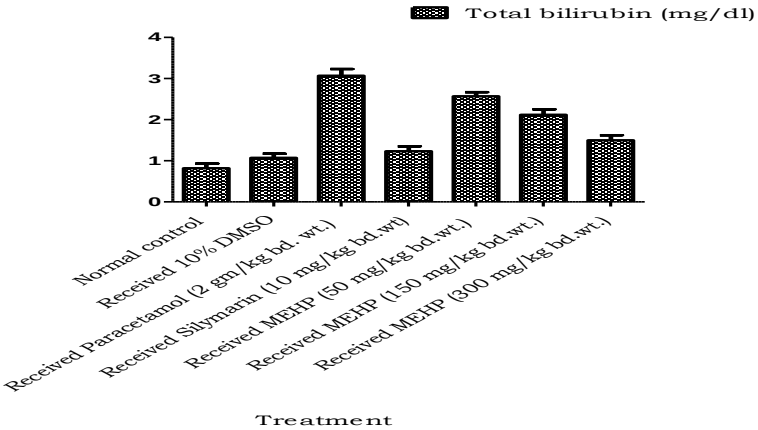

Fig.2: Effect of MEHP on serum total bilirubin in Paracetamol (2 gm/kg bd.wt) treated rats

DISCUSSION:

In the present study, the methanolic extract of *Hibiscus plantifolius (MEHP)* was evaluated for hepato protective activity against paracetamol – induced hepatotoxic rats. The serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) and alkaline phosphatase (ALP) and total bilirubin assessed to study the hepatoprotective activity of the plant and were compared with standard drug.

Hepatocytes are the main components of liver which regulates various metabolic activities and their distortion leads to disorder in body metabolism. At high doses, paracetamol produces acute toxic effects which lead to liver damage. The drug is bioactivated to a toxic electrophile, *N*-acetyl *p*-benzoquinone imine (NAPQI), which covalently binds to tissue macromolecules, probably oxidizes lipids, or the critical sulfhydryl groups (protein thiols) and alters the homeostasis of calcium Massive production of reactive species may lead to depletion of protective physiological moieties (glutathione and α-tocopherol, etc.), causing damage to the macromolecules in vital bio membranes and liver injury.

Silymarin forms a complex that hinders the entrance of toxins into the interior of liver cells and metabolically stimulates hepatic cells and activates the RNA biosynthesis of ribosomes to stimulate protein formation. It is most frequently used natural compound all over the world due to its anti-toxic, anti-oxidant, anti-inflammatory, anti-fibrotic activities.

CONCLUSION:

Nature has been a source of medicinal medicine. Higher plants, as sources of medicinal compounds, have continued to play a dominant role in the maintenance of human health since the ancient times. Hepatoprotective activity was exhibited due to presence of flavonoids and tannins, phenolic compounds which was present methanolic extract of Hibiscus plantifolius. Present study shows that poly-phenols content in the methanolic stem extracts of Hibiscus plantifolius is high and these extracts exhibit strong activity compared to that of the standard compounds. It is an easily available plant for natural remedies.

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CONFLICT OF INTERESTS:

Declared None.

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