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EVALUATION OF METHANOLIC EXTRACT OF *SCOPARIA DULCIS* FOR HEPATOPROTECTIVE ACTIVITY IN RATS.

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Abstract

The present study was undertaken to evaluate the hepatoprotective potential of the methanolic extract of Scoparia dulcis (MESD) against paracetamol-induced hepatotoxicity in experimental animals. A review of existing literature indicated limited scientific evidence supporting the hepatoprotective use of this plant, prompting a systematic investigation. Preliminary phytochemical screening of MESD revealed the presence of glycosides, flavonoids, tannins, carbohydrates, and proteins, suggesting bioactive constituents with therapeutic relevance.

Hepatoprotective activity was assessed using biochemical markers such as SGOT, SGPT, ALP, LDH, ACP, total bilirubin, and total protein, along with antioxidant parameters (SOD, CAT, GSH, LPO) in albino mice and Wistar rats. Both low and high doses of MESD were compared with the standard hepatoprotective drug, silymarin. Paracetamol administration produced significant hepatic damage, as evidenced by elevated liver enzymes, oxidative stress markers, and histopathological alterations including centrilobular necrosis, congestion, and inflammatory infiltration. Treatment with MESD significantly restored biochemical parameters toward normal levels and markedly reduced histopathological lesions, indicating strong hepatoprotective and antioxidant activity.

The hepatoprotective effect of MESD was comparable to that of silymarin, confirming its therapeutic potential. These findings suggest that Scoparia dulcis possesses effective protective activity against chemically induced liver damage, possibly through the enhancement of endogenous antioxidant defense mechanisms. Further studies are warranted to isolate and characterize the specific active constituents responsible for this activity.

Keywords: *Scoparia dulcis, hepatoprotective, MESD, paracetamol-induced*

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INTRODUCTION:

Plants have framed the reason for treatment of sicknesses in customary medication for millennia and keep on assuming a significant part in the necessary medical care of approximately 80% of the world's population[1]. Each plant has conceivably 10,000 unique constituents[2]. By definition, customary utilization of home grown medications suggests significant chronicled use, and this is unquestionably valid for some items that are accessible as conventional natural medicines. In many non-industrial nations, a huge extent of the populace depends on customary specialists and their armamentarium of restorative plants to meet medical services needs. In this cutting edge setting, fixings are once in a while advertised for utilizes which never were considered in the conventional recuperating frameworks from which they came out. The utility of Ephedra in loss of weight or enhanced sportive ability is an example.

The disclosure and improvement of adequate remedial specialists from characteristic sources gave persuading proof that plants could be a rich source of new medicines. In the western medication utilize numerous medications extricated from characteristic items: cocaine, atropine, ephedrine, hyoscine, digitoxin, morphine, codeine, quinine, pilocarpine, taxol, reserpine, menthol, warfarin, and so on whereas the characteristic item separated as well as the dynamic product would not generally reasonable to advancement as a successful medication, it's possible give an appropriate guide to transformation into a medically valuable specialist[2] [2].

Ayurveda is a clinical framework basically rehearsed approximately 5000 years in India. It combines diet and home-grown remedies while concentrating on the body, psyche, and soul in the prevention and treatment of illness[3]. The point of Ayurveda is to boost the standard of living, in saving and advancing the wellness of people. Ayurveda consistently gives an essential significance to the upkeep of sound wellbeing and the avoidance of sickness by the straightforward gadget of raising the individual obstruction of the body and giving dynamic insusceptibility[4].

The plants and their auxiliary metabolites have a history of use in current western medicaments, as well as in unique systems of ancient medicine. Various resources, including the European Scientific Cooperative on Phytotherapy [ESCP], provide monographs on particular spices 'Common Medicines Comprehensive Database,' The 'World Health Organization[5] and 'The total German Commission E monograph.' For example, the WHO monographs depict the spice itself using various standards such as identical terms and native names, and the spice section usually used topographical distribution, identification test and represent the spice (together with the perceptible and tiny evaluation and virtue examination), complex standards, measurements frames and dosing, restorative uses, pharmacology, contraindications and unfavorable responses. Data about other accessible information bases has been distributed[6].

South Africa[7] an enormous number of South Africans counsel customary healers, by and large notwithstanding clinical experts. There are around 2,00,000 (0.2 million) conventional healers in the nation. The pharmacological treatment of infection started quite a while in the past with the utilization of spices. Ayurveda system is an antiquated medical care framework which originated and explored in India goes back to around 5000 years prior. According to the antiquated written works on ayurveda, it was worked on during Vedic time of Indian has around 700 plants were portrayed in Charaka Samhita and Sushruta Samhita during the millennium BC[8].

Home grown medications has for some time been utilized restoratively for countless human problems are as yet being utilized for a significant number of the well-being needs of an enormous populace of the world. The WHO has recognized the current use of conventional and home grown medication, which has been in presence for in excess of a hundred years, much before the advancement of present day medication. India has around 45,000 plant species and in excess of 35,000 plant species have been professed to have restorative properties and are being utilized in different human societies around the globe for therapeutic purposes[9]. As per WHO, it was discovered that there were 35,000 to 70,000 types of plants which are utilized as medicaments. As a matter of fact the restorative plants are the plants which have property to fix illness[10].

There are around 45,000 restorative plant species in India, with amassed spots in the district of Eastern Himalayas, Western Ghats and Andaman and Nicobar Islands. The authoritatively archived plants with restorative potential are 3000 however customary specialists utilize more than 6000. India is the biggest maker of therapeutic spices and is known as the professional flowerbed of the world. There are as of now around 2,50,000 (0.25 million) enrolled clinical experts of the Ayurvedic framework, when contrasted with around 7,00,000 (0.7 million) of the advanced medication framework. In country India, 70% of the populace relies upon the customary sort of medication. India is a nation known for old contents, the number framework, innovation of zero and Vedas meds in India are utilized by around 60% of the total populace[11].

Chinese, Indian, Arabian and other customary frameworks of prescriptions utilize around five thousands plants and many of herbs. India is pleased to be wealthy in natural variety and placed in tenth position among countries with an abundance of plants of Asia and 6th in the places of various agro diversity are known. Almost three fourth portions of the medications and fregrancial materials utilized on the planet are accessible in regular realm in the nation. Plants are one of the significant hotspots for drugs utilized in the counteraction and fix of infections and furthermore for restoration. Home grown medication is a significant part in conventional medication of every native individual and a typical component in Ayurveda, Siddha, Amchi, Unani, Homeopathic, Naturopathic and Native American Indian medicine[12]. Quantities of biologically active mixes of plants, for example, flavanoids, Triterpenes, tannins, sterols, alkaloids, and so on, have been noted to have important functions in the biology, physiology, and control of sicknesses[13].

At present, there are fifty thousand plant species utilized in the readiness of drugs because of mix of optional mixes, for example, fundamental oils, sweet-smelling, tar, gum and sap in different body part, for example, fruits, flowers, leaves, stems, roots, blossoms, products of seeds[14]. Epidemiologic investigations from network emergency clinics and tertiary consideration reference focuses gauge that intense liver disappointment influences around 1600 to 2000 individuals for each year in the United States[15].

MATERIALS AND METHODS:

Collection and identification of the tested plant material

The dried powdered plant material of Scoparia dulcis were collected from Ranga Reddy District, Telangana. The plant was identified and authenticated by Dr. K. Madhava Chetty, Assistant Professor, Department of Botany, S.V. University, and Tirupati. A specimen voucher was deposited at the Department of Pharmacology in our institution.

Extraction of plant material

The plant material, which was powdered and stored, was used for extraction. A weighed quantity of each of the plant powdered material was extracted by cold maceration with 50% methanol for 72 hrs with intermediate heating at 40°C once a day. After that the residues was extracted with water for aqueous extract. The extract was filtered using Whatmann filter paper and then the filterate was concentrated under reduced pressure and controlled temperature (40-50°C). The marc was dried and weighted. This marc was again extracted with water by cold maceration for 72 hrs to yield aqueous extracts.[14]

Determination of solvent extractive values:

Five grams of powdered drug was macerated with 100 ml of water closed flask for 24hr and was occasionally shaked with 6hr time period and was allowed to stand for 18hr. After filtration the 23ml of the filterate evaporated to dryness in a tared flat bottomed shallow dish. Dry at 103ºC and weighed. Percentage of water soluble extractive value was calculated concerning the air dried drug.

Determination of alcohol soluble extractive value:

Five grams of powdered drug was macerated with 100ml of ethanol closed flask for 24hr and was occasionally shaked with 6hr time period and was allowed to stand for 18hr. After filtration the 23 ml of the filtrate evaporated to dryness in a tared flat bottomed shallow dish. Dry at 103ºC and weighed. Percentage of ethanol-soluble extractive value was calculated with reference to the air-dried drug.

Pharmacological Study

Animals

A total of 30 Albino Mice with an approximate age of 60 days were purchased from, Jeeva life sciences, Hyderabad. On their arrival a sample of animals was chosen at random and weighed to ensure compliance with the age requested. The mean weights of mice were 25 - 30 g respectively. The animals were housed in metabolic cages (55 x 32.7 x 19 cm), with sawdust litter, in such a way that each cage contained a maximum of 5 animals of the same sex. All animals underwent a period of 7 days of observation and acclimatization between the date of arrival and the start of treatment. During the course of this period, the animals were inspected by a veterinary surgeon to ensure that they fulfilled the health requirements necessary for initiation of the Study. They were distributed among the experimental groups using a random distribution method. This procedure allows approximate equalization of initial bodyweights whilst allowing random allocation to experimental groups.

Acute Oral Toxicity Study[15]

Healthy Wistar rats (180-220 g) of both sex were used in acute toxicity studies as per OECD guidelines-425. The animals were fasted overnight and divided into 3 groups with 5 rat in each group. Extracts were administered at dose of 100, 500 and 2000 mg/kg, p.o. body weight. The mice were observed continuously for behavioural and autonomic profiles for 2 hrs and for any signs of toxicity or mortality up to 48 hrs (OECD-425, 2001).

The test substance was administered orally. The mice belonging to the control group were treated with the vehicle (distilled water) at the same administration volume as the rest of the treatment

groups. The administration volume for oral administration was 10 ml/kg. The quantity of test substance administered to each animal was calculated from its body weight on the day of the treatment.

Induction of Hepatotoxicity

Pre-treatment Group

All pretreated groups of albino mice except control groups receives a daily dose of Paracetamol (3g/ Kg of body weight), Silymarin (100mg/kg) and methanolic Extract of *Scoparia dulcis* leaves (EECS) (250 and 500mg/kg) for 14 day.

Experimental Design

Group 1: Receives (Distilled water) as control for 14 days.

Group 2: Receives a daily dose of Paracetamol (3g/ Kg of body weight, p.o) for 14 days (p.o)

Group 3: Receives a daily dose of Paracetamol (3g/ Kg of body weight) and after one hour a daily dosage of Standard Silymarin (100mg/kg) of body weight for 14 days (p.o)

Group4: Receives a daily dose of Paracetamol (3g/ Kg of body weight) and one hour a daily dosage of MECP 250mg / Kg of body weight for 14 days (p.o)

Group 5: Receives a daily dose of Paracetamol (3g/ Kg of body weight) and one hour a daily dosage of MECP 500mg / Kg of body weight for 14 days (p.o)

Sample collection

At the end of the 14th day treatment, samples of blood were withdrawn from the orbital sinus of mice from each group, under light ether anesthesia after fasting for 16 hours. The collected blood samples also centrifuged 10000 rpm in 10 minutes to separate the serum. The separated serum used to evaluate biochemical parameters like SGOT, SGPT, ALP and BILIRUBIN. After separation of serum for biochemical estimation, the mice were sacrificed, liver of mice were isolated and washed with normal saline and stored for 12 h for in vivo antioxidant studies.

Measurement of Body weight

The body weight of the animals was monitored daily by weighing on an electrical balance with accuracy to ± 0.1 g. All measurements were made every day between 8.30 and 9.15 h, immediately before administration of the distilled water in the case of control and the drugs paracetamol.

Determination of Biochemical Parameters

Determination of aspartate aminotransferase (AST)/ SGOT

Procedure

Rietman and Frankle method was adopted for the estimation of SGOT[16]. The reaction systems used for this study included blank, standard, test (for each serum sample) and control (for each serum sample). 0.25 ml of buffered aspartate was added into all the test tubes. Then 0.05 ml of serum was added to the test group tubes and 0.05 ml of working pyruvate standard into the standard tubes. After proper mixing, all the tubes were kept for incubation at 37°C for 60 min, after which 0.25 ml each of 2, 4-DNPH reagent was added into all the tubes. Then, 0.05 ml of distilled water and 0.05 ml of each serum sample was added to the blank and the serum control tubes respectively. The mixture was allowed to stand at room temperature for 20 min. After incubation, 2.5 ml of solution I was added to all test tubes. Mixed properly and optical density was measured in a spectrophotometer at 505 nm within 15 min.

The enzyme activity was calculated as:-

AST (GOT) activity in IU/L) = [(Absorbance of test - Absorbance of control)/ (Absorbance of standard - Absorbance of blank)] x concentration of the standard.

Determination of alanine aminotransferase (ALT) or Serum Glutathione peroxidase (SGPT)

Procedure

Rietman and Frankle method (1957)[17] was adopted for the estimation of SGPT.

The reaction systems used for this study included blank, standard, test (for each serum sample) and control (for each serum sample). 0.25 ml of buffered alanine was added into all the test tubes. This was followed by the addition of 0.05 ml of serum into the test group tubes and 0.05 ml of working pyruvate standard into the standard tubes. After proper mixing, all the tubes were kept for incubation at 37oC for 60 minutes, after which 0.25 ml each of 2,4- DNPH reagent was added into all the tubes. Then, 0.05 ml of distilled water and 0.05 ml of each serum sample was added to the blank and the serum control tubes respectively. The mixture was allowed to stand at room temperature for 20 min. After incubation, 2.5 ml of solution I was added to all test tubes. Mixed properly and optical density was read against purified water in a spectrophotometer at 505 nm within 15 min.

The enzyme activity was calculated as:- ALT (GPT) activity in IU/L) = [(Absorbance of test - Absorbance of control)/ (Absorbance of standard - Absorbance of blank)] x concentration of the standard.

Determination of alkaline phosphatase (ALP)/serum alkaline phosphatase (SALP)

Procedure:

ALP was determined using the method of Kind and King[18].

The working solution was prepared by reconstituting one vial of buffered substrate with 2.2 ml of water. 0.5 ml of working buffered substrate and 1.5 ml of purified water was dispensed to blank, standard, control and test. Mixed well and incubated at 370C for 3 min. 0.05 ml each of serum and phenol standard were added to test and standard test tubes respectively. Mixed well and incubated for 15 min at 370C. Thereafter, 1 ml of chromogen reagent was added to all the test tubes. Then, added 0.05 ml of

serum to control. Mixed well after addition of each reagent and the O.D of blank, standard, control and test were read against purified water at 510 nm. Serum alkaline phosphatase activity in KA units was calculated as follows

[(O.D. Test-O.D. Control) / (O.D. Standard- O.D. Blank)] x 10 Alkaline phosphate was expressed as U/l.

Alkaline phosphate was expressed as U/l.

Determination of bilirubin;

The bilirubin level in serum was determined by Dangerfield and Finlayson, (1953)[19].

Sulfanilic acid reacts with sodium nitrite to produce deoxidized sulfanilic acid. Total bilirubin couples with deoxidized sulfanilic acid in the presence of methylsulfoxide to produce azobilirubin which may be measured at 532-536 nm. In the absence of methyl sulfoxide, only direct (conjugated) bilirubin forms azobilirubin complex.

Procedure

Estimation of total bilirubin:

To 1.0 ml total bilirubin reagent, 0.02 ml of activator and 0.1 ml of serum were added, mixed well and incubated for exactly 5 minutes at room temperature. Sample blank was prepared by mixing 1.0 ml total bilirubin reagent with 0.1 ml of distilled water, mixed well and incubated for exactly 5 minutes at room temperature. The absorbance of each sample blank and test were measured at 532- 546 nm against distilled water blank. Total bilirubin and direct bilirubin level in serum was expressed as mg/dl.

The Bilirubin content was calculated using the following equation:

Total bilirubin (mg/dt) = Abs of the sample blank x 15.

Direct Bilirubin(mg/dt) = Abs of sample blank x 10.

Determination of Total proteins:

Principle

Lowry method was adopted for the estimation of total protein[20].

To 0.1 ml of the liver homogenate, 0.9 ml of water, 4.5 ml of alkaline copper sulphate reagent were added and allowed to stand in the room temperature for 10 min. To this 0.5 ml of Folin's reagent was added. After 20 min, the blue colour developed was measured at 640 nm.

The level of protein present was expressed as mg/g tissue or mg/dl

Lactate Dehydrogenase Assay

The method described here is derived from the formulation recommended by the IFCC and was optimized for the performance and stability[21].

Determination of Antioxidant Enzymes and Lipid Peroxidation

Determination of superoxide dismutase:

Superoxide dismutase scavenges the superoxide radical (O● 2) and thus provides a first line defence against free radical damage. Superoxide dismutase is an endogenous enzymatic antioxidant which catalyzes the dismutation of superoxide free radical. This method is based on the inhibition of the spontaneous oxidation of the adrenaline to adrenochrome by the enzyme superoxide dismutase. Superoxide anion (O2 -) interacts with peroxide to form hydroxyl radical (OH•) which causes damage in the absence of superoxide dismutase activity (R•)

Procedure

SOD was estimated as per the procedure described by Kakkaret al[22].

Liver homogenate (0.5 ml) was diluted with 0.5 ml of distilled water. To this, 0.25 ml ethanol and 0.15 ml of chloroform, all reagents chilled, were added. The mixture was shaken for 1 minute and centrifuged at 2000 rpm. The enzyme in the supernatant was determined. To 0.5 ml of the supernatant, 1.5 ml of buffer was added. The reaction was initiated by the addition of 0.4 ml epinephrine and change in optical density per minute was measured at 480 nm in a double beam UV-VIS spectrophotometer (UV 1700, Szhimadzhu)

SOD activity was expressed as U/mg.

Change in optical density per minute at 50% inhibition to adrenochrome transition by the enzyme is taken as one enzyme unit.

2. Determination of catalase:

Procedure

The catalase activity was assayed by the method of Sinha (1972).[23] Liver homogenate (0.1 ml) was taken, to which 1.0 ml of phosphate buffer and hydrogen peroxide were added. The reaction was arrested by the addition of 0.2 ml dichromate acetic acid reagent. Standard hydrogen peroxide in the range of 4 to 20 µl were taken and treated similarly. The tubes were heated in a boiling water bath for 10 min. The green color developed was read at 570 nm in a Double beam UVVIS spectrophotometer (UV 1700, Szhimadzhu). Catalase activity was expressed as U/mg.

3. Determination of glutathione peroxidase:

Procedure

EDTA (0.2 ml each), sodium azide, reduced glutathione, H2O2; 0.4 ml of buffer and 0.1 ml of enzyme (liver homogenate) were mixed and incubated at 37°C for 10 min. The reaction was arrested by the addition of 0.5 ml of TCA and the tubes were centrifuged. To 0.5 ml of supernatant, 3.ml of sodium hydrogen phosphate and 1 ml of DTNB were added and the color developed was read at 412 nm immediately in a Double beam UV-VIS spectrophotometer (UV 1700, Szhimadzhu.)

Glutathione peroxidase activity, in serum is expressed as µg/mg.

Determination of reduced glutathione:

Procedure

Reduced Glutathione was estimated by Ellman's procedure[24].

To 250 µL of tissue homogenate taken in 2 ml eppendroff tube, 1 mL of 5% TCA was added and the above solution was centrifuged at 3000 g for 10

min at room temperature. To 250 µL of the above supernatant, 1.5 ml of 0.2 M phosphate buffer was added and mixed well. 250 µL of 0.6 mM of Ellman's reagent (DTNB solution) was added to the above mixture and the absorbance was measured at 412 nm within 10 min. A standard graph was plotted using glutathione reduced solution (1 mg/ml) and GSH content present in the tissue homogenates was calculated by interpolation. Amount of glutathione expressed as µg/mg protein.

Determination of lipid peroxidation:

Procedure

Lipid peroxidation was estimated by the method of Okhawaet al., (1979)[25] One ml of liver homogenate was mixed with 0.2 ml 4 % (w/v) sodium dodecyl sulfate, 1.5 ml 20% acetic acid in 0.27 M hydrochloric acid (pH 3.5) and 15 ml of 0.8% thiobarbituric acid (TBA, pH 7.4). The mixture was heated in a hot water bath at 85˚C for 1 h. The intensity of the pink colour developed was read against a reagent blank at 532 nm following centrifugation at 1200 g for 10 min. The concentration was expressed as n moles of MDA per mg of protein using 1,1,3,3,- tetra-ethoxypropane as the standard.

Histophatological Techiniques

Histopathology is the microscopical study of tissues for pathological alterations. This involves collection of morbid tissues from biopsy or necropsy, fixation, preparation of sections, staining and microscopical examination.

1) Collection of materials

Thin pieces of 3 to 5 mm, thickness were collected from tissues showing gross morbid changes along with normal tissue.

2) Fixation:

Kept the tissue in fixative for 24-48 hours at room temperature The fixation was useful in the following way

a. Serves to harden the tissues by coagulating the cell protein,
b. Prevents autolysis,
c. Preserves the structure of the tissue, and
d. Prevents shrinkage

Common Fixatives: 10% Formalin

3) Haematoxylin and eosin method of staining:

Deparaffinise the section by xylol 5 to 10 minutes and remove xylol by absolute alcohol. Then cleaned the section in tap water and stained with haematoxylin for 3-4 minutes and again cleaned under tap water. Allow the sections in tap water for few minutes and counter stained with 0.5% eosin until section appears light pink 15 to 30seconds), and then washed in tap water. Blotted and dehydrated in alcohol and cleared with xylol(15 to 30 seconds). Mounted on a Canada balsam or DPX Moutant and kept the slide dry and remove air bubbles.

STATISTICAL ANALYSIS

Statistical analysis was performed using GraphPad Prism version 7 for Windows (GraphPad Software, San Diego, CA, USA) and Microsoft Excel 2013. Raw data obtained from different wound models are expressed as mean ± SEM. Values less than 0.03 were considered to be statistically significant. The data were analyzed using GraphPad Prism version 7 for Windows and differences among groups were compared by one-way ANOVA followed by Dunnett's test.

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