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Acute and sub acute studies of catechol derivatives from *Semecarpus anacardium*

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ABSTRACT

The present study was aimed at evaluating the acute and subacute toxicity of catechol derivatives (I–IV, isolated from *Semecarpus anacardium* nuts) in Wistar Albino rats. In acute study (14 days), catechol derivatives I–IV 800 mg/kg caused no behavioral adverse effects and mortality. Fifty percent (LD_{50}) of mortality was observed in catechol derivatives I–III (1600 mg/kg b.wt) and catechol derivative IV (1250 mg/kg b.wt). In subacute study, daily oral administration of catechol derivatives I–IV (300 mg/kg b.wt) for 30 days did not result in death or significant changes in the body weight and organ weight, In hematological and some biochemical analysis showed few beneficial effects particularly in catechol derivatives I and IV treated rats that is transient rise in WBC count and HDL cholesterol and decrease in LDL, plasma and tissue lipid profile. These results indicate the impact of catechol derivatives in boosting the immune system and reducing cardiovascular risk factors and thereby they possess cardio protective and immunopotentiating effect. Further, histopathological examination of liver and kidney showed normal architecture that suggests no morphological disturbances. Based on the results obtained, it may be concluded that the catechol derivatives are potentially toxic but therapeutically effective.

1. Introduction

Conventional use of plant basis medications for treatment of various ailments is widely experienced in both developed and developing countries. It has been estimated that around 60% of the world's population relies on plants for medications. This quantity elevate to more than 80% due to the increase of populations in developing world, easy access and increasing drug expenses [1,2]. Thus, plants remain the chief provider of active drugs from natural sources [3]. Flora contain pharmacologically active components which are quite safe and often considered to be less toxic and free from side effects than synthetic ones [4]. Plants derived components play a vital role in world health and have long been known to have biological activity [5]. Thirty percent of all recent drugs are derived from plants [6]. According to the World Health Organization about 80% of the world's population living in developing countries relies basically on plants for primary health care [7]

Most repeatedly, these herbal medication methods are used in most disease conditions over a long period of time without proper dosage monitoring and consequently toxic effects maybe produced from such prolonged traditional practice. The danger associated with the potential toxicity of such herbal therapies used over a long period of time imposes in keeping abreast reported occurrences of renal and hepatic toxicities, consequential from intake of these medicinal herbs [8]. Thus, in modern medicine, animal toxicity studies are also required to establish the potential adverse effect of newly plant derived drugs [9]. Therefore, the present study is intended to investigate the basic toxic evaluation of four catechol derivatives (isolated from *Semecarpus anacardium* seeds) for establishing the safety of each drug.

2. Materials and methods

2.1. Plant material

Semecarpus anacardium seeds were purchased from K.R. Vasan Traditional & Herbal Medicine shop, Parris, Chennai, Tamil Nadu, India. The identity of the plant was confirmed by Prof. Raman, plant taxonomist, Centre for Advanced Studies in Botany, University of

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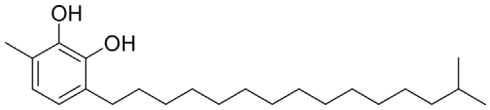

Fig. 1. Isolation and characterization of catechol derivatives from *Semecarpus anacardium* seeds. Catechol derivative 1.

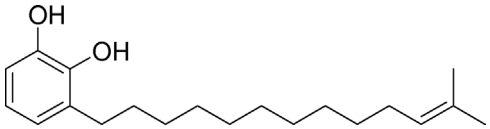

Fig. 2. Isolation and characterization of catechol derivatives from *Semecarpus anacardium* seeds. Catechol derivative 2.

Madras, Guindy Campus, Chennai-600025. A voucher specimen (MUCASB- H105) was preserved in the Department herbarium for future reference.

2.2. Extraction and isolation

In our previous study, we have explained the isolation and characterization of catechol derivatives I, II, III and IV from *Semecarpus anacardium* seeds and their antibacterial property against gram positive and gram negative bacteria [10]. The chemical structure of catechol derivatives are given in Figs. 1–4.

3. Acute toxicity study

3.1. Animals

Wistar albino rats of either sex weighing 100 ± 20 g were secured from Central Animal House, Institute of Basic Medical Sciences, University of Madras, Taramani Campus, Chennai, India. The rats were housed in clean, sterile and polypropylene cages under standard conditions 12 h light/12 h dark cycle and constant temperature (25 ± 2 °C) with free access to standard commercial rat chow and water. The study has got the approval from the Institutional Animal Ethical Committee (IAEC No.01/03/08) of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA).

3.2. Experimental study design for acute toxicity study

The single dose of acute oral toxicity study was evaluated following the recommendations by OECD/OCDE [11]. The animals were randomly divided into twenty nine groups of four animals in each group. After overnight fasting, four catechol derivatives were separately dissolved in 1 ml of olive oil and administered only once/per day orally to experimental groups through gastric intubation at doses of 50, 100, 200, 400, 800, 1600, and 2000 mg/kg b.wt, and control group received 1 ml of olive oil (vehicle) alone. Group II–VIII received catechol I at above mentioned doses individually. Likewise, Group IX–XV received catechol II, Group XVI–XXII received catechol III and Group XXIII–XXIX received catechol IV, respectively. Feeding was restarted 4 h after dosing All animals were observed for clinical signs including mortality and morbidity, immediately after dosing at 1, 2, 4, 8 and 12 h, then twice daily until 14 days. Abnormal findings were observed with the

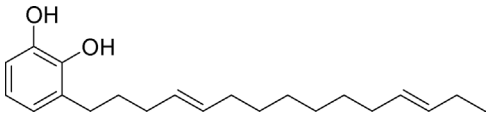

Fig. 3. Isolation and characterization of catechol derivatives from *Semecarpus anacardium* seeds. Catechol derivative 3.

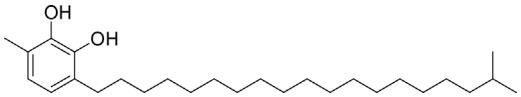

Fig. 4. Isolation and characterization of catechol derivatives from *Semecarpus anacardium* seeds. Catechol derivative 4.

time of onset and disappearance. Body weights and food consumption were measured on day 0, 1, 3, 5, 7, 10 and 14. On the 14th day, all animals were sacrificed and all organs and tissues were observed macroscopically. The abnormal organs were placed in 10% formalin and observed by pathological examination.

3.3. Experimental design

Groups	Treatment
Group I	Served as vehicle treated normal control
Group II	Animals received single dose of catechol I (50 mg/kg b.w orally) dissolved in 1 ml of olive oil for only one day
Group III	Animals received single dose of catechol I (100 mg/kg b.w orally) dissolved in 1 ml of olive oil for only one day
Group IV	Animals received single dose of catechol I (200 mg/kg b.w orally) dissolved in 1 ml of olive oil for only one day
Group V	Animals received single dose of catechol I (400 mg/kg b.w) dissolved in 1 ml of olive oil for only one day
Group VI	Animals received single dose of catechol I (800 mg/kg b.w orally) dissolved in 1 ml of olive oil for only one day
Group VII	Animals received single dose of catechol I (1600 mg/kg b.w orally) dissolved in 1 ml of olive oil for only one day
Group VIII	Animals received single dose of catechol I (2000 mg/kg b.w orally) dissolved in 1 ml of olive oil for only one day
Group IX	Animals received single dose of catechol II (50 mg/kg b.w orally) dissolved in 1 ml of olive oil for only one day
Group X	Animals received single dose of catechol II (100 mg/kg b.w orally) dissolved in 1 ml of olive oil for only one day
Group XI	Animals received single dose of catechol II (200 mg/kg b.w orally) dissolved in 1 ml of olive oil for only one day
Group XII	Animals received single dose of catechol II (400 mg/kg b.w orally) dissolved in 1 ml of olive oil for only one day
Group XIII	Animals received single dose of catechol II (800 mg/kg b.w orally) dissolved in 1 ml of olive oil for only one day
Group XIV	Animals received single dose of catechol II (1600 mg/kg b.w orally) dissolved in 1 ml of olive oil for only one day
Group XV	Animals received single dose of catechol II (2000 mg/kg b.w orally) dissolved in 1 ml of olive oil for only one day
Group XVI	Animals received single dose of catechol III (50 mg/kg b.w orally) dissolved in 1 ml of olive oil for only one day
Group XVII	Animals received single dose of catechol III (100 mg/kg b.w orally) dissolved in 1 ml of olive oil for only one day