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ORIGINAL ARTICLE

Antihepatotoxicity of *Tagetes erecta* (Mexican marigold) against indomethacin-induced Antihepatotoxicity in Sprague Dawley rats

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ABSTRACT
This research finds the Antihepatotoxicity and in vivo cell antioxidant activities of Tagetes erecta *(Mexican marigold). From the start, an intense Antihepatotoxicity study was made on Sprague Dawley rats by giving basic, watery, n-hexane, chloroform, ethyl acetic acid derivation, and n-butanol portions 180-220 mg/kg/day for one day. Liver capacity tests were completed. Antihepatotoxicity induced by indomethacin (330-3600 mg/kg) orally. All liver capacity tests, liver peroxidation tests like malondialdehyde, glutathione, and histopathological examination of the liver were performed. In antihepatotoxicity, the ethyl acetic acid derivation portion indicated a significant reduction in serum proteins' degree. Peroxidation levels in the ethyl acetic acid derivation treated group in liver homogenates reduce in malondialdehyde while decreased glutathione level increased. This investigation shows that* Tagetes erecta *has Antihepatotoxicity and antioxidant impacts.*
Keywords: Antihepatotoxicity; *Tagetes erecta*; Sprague Dawley rats; antioxidant

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INTRODUCTION

Day to day increase in exposure to chemicals has resulted in more incidences of hepatotoxicity and other liver disorders; therefore, it is necessary to find out new drugs from natural sources to protect against liver diseases [1]. There are some plants which have the Antihepatotoxicity effect i.e., *Ruta montana* [2], *Artocarpus lakoocha* [3], *Ceriops decandra* [4], *Alhagi maurorum* [5], *Meconopsis integrifolia* [6]. *Tagetes erecta*, the Mexican marigold, is native to Mexico and found in Central America countries: it can be found in Asian countries as an introduced species [7]. Its flowers show solitary inflorescences and are liguladas of yellow colors to red [8]. This plant has been used for medicinal purposes. A pigment called lutein is associated with the prevention of cataracts and macular degeneration [9]. Some studies indicate the latter's effectiveness in preventing coronary artery disease, heart attacks, immune response, old age, and cancer [10]. Antioxidant activity has been discovered in this plant's essential oil [11].
The present study focused on identifying the *in vivo* Antihepatotoxicity properties against indomethacin-induced Antihepatotoxicity in Sprague Dawley rats.

MATERIAL AND METHODS

Plant material collection and extraction

The plant was collected and dried under shade and powdered the whole herb. This powdered herb dipped in commercial methanol for one week, filtered, and evaporated using an evaporator. After extraction, fractionation was done using different solvents according to polarization. The active fraction was separated by using small column chromatography. Spots were visualized using UV radiation and by spraying with 10-12 % hydrogen sulfate, tracked by heating with a heat gun [12].

Animals

Sprague Dawley rats of either sex (190-220 g) were used as an animal model. These animals were fed on a diet with free water access under managed states of temperature 21 ± 5°C, humidity, and light. All animals give a standard diet and overnight fasting before slaughtering. Animals randomly group, as usual, indomethacin group, silymarin group, and treated groups. At the end of the study, animals slaughtered with placid ethyl ether as an analgesic.

Experimental design

According to the method described elsewhere, the Antihepatotoxicity activities of all derived fractions studied using the indomethacin-induced liver injury model [13]. After an adaptation period, rats were divided randomly into nine groups of 6 animals each. Treatments then carried.

Acute hepatoprotective study*:* Group 1: Normal control group, which received distilled water only; Group 2: Received indomethacin only (1.25 g/kg); Group 3: Received the standard drug silymarin (90 mg/kg/day); Group 4: Received the total methanolic extract (450 mg/kg per day); Groups 5–9: Received the aqueous, ***n***-hexane, chloroform, ethyl acetate, ***n***-butanol fractions (400 mg/ kg/day) respectively. Rats of Group 3-9 received indomethacin (80mg/kg/day) after 120 minutes of the treatment.

Chronic hepatoprotective study*:* Group 1: Normal control group, which received the distilled water only; Group 2: Received indomethacin (250 mg/kg); Group 3: Received the standard drug silymarin (45 mg/kg/day); Group 4: Received ethyl acetate fraction (250 mg/kg/day). Group 3 and Group 4 received indomethacin (80 mg/kg/day) 120 minutes after giving silymarin (Group 3) and ethyl acetate (Group 4). For liver injury induction, each group except the control group gave an indomethacin dose of 1.25 g/kg after half-hour administration of a standard drug and plant extract fractions. ALT, AST, alkaline phosphatase, and total bilirubin carried on each group's blood sample [14]. After this acute study, a chronic study was conducted on the ethyl acetate fraction for 14 days; on the day 15, blood samples collected to determine enzyme serum level, and livers were taken for histopathology and ***in vivo*** antioxidant studies.

Biochemical study

All the animals anesthetized with mild ether after indomethacin intoxication, and blood collected by cardiac puncture method. Using Randox laboratory kits, liver function tests (serum transaminase, alkaline phosphatase, and total bilirubin) were analyzed [15]. For ***in vivo*** antioxidant activity, rats' liver homogenates were used to measure superoxide dismutase and reduced glutathione [16].

Statistical analysis

Results were presented as mean ± SEM. ANOVA followed by Tukey post-hock test during statistical analysis of data. A value of $p<0.05$ was considered significant.

RESULTS

The number of serum enzymes increased in indomethacin-induced Antihepatotoxicity. Levels of alanine transaminase, aspartate transaminase, alkaline phosphatase, and total bilirubin in ethyl acetate-treated group were given in Table 1. In a chronic study, serum enzyme levels in the ethyl acetate-treated group in comparison to silymarin are given below. After the chronic study, all rats were slaughtered, and the liver was saved for ***in vivo*** antioxidant activity. Malondialdehyde and glutathione were performed on rats' liver homogenate (Table 2).

Table 1: Effect of different derivations of *Tagetes erecta* (Mexican marigold) on serum enzyme levels in acute Antihepatotoxicity rat

Treatment	ALT (IU/L)	AST (IU/L)	ALP (IU/L)	Total bilirubin (mg/dL)
Normal	52.6± 4.5	71.1 ± 7.2	103.9± 2.7	0.6 ± 0.1
Indomethacin	1601.7± 27.1	1779.6± 22.6	221.0 ± 42.2	0.6 ± 0.2
Silymarin plus Indomethacin	82.2 ± 8.2	102.8± 11.6	126.6 ± 20.9	0.6 ± 0.0
Methanol plus Indomethacin	448.1± 64.8	246.8± 60.2	164.6 ± 17.0	0.6 ± 0.0
Aqueous plus Indomethacin	702.7± 72.9	270.0± 24.1	174.7 ± 11.2	0.8 ± 0.0
n-Hexane plus Indomethacin	221.6± 22.1	292.0± 26.7	208.1 ± 18.7	0.8 ± 0.0
Chloroform plus Indomethacin	262.7± 26.2	196.2± 21.1	182.2 ± 24.2	0.8 ± 0.0
Ethyl acetate plus Indomethacin	178.8 ± 21.8	97.6± 10.7	140.0 ± 16.9	0.8 ± 0.0
n-Butanol plus Indomethacin	266± 62.6	222.1± 76.7	166.0 ± 14.7	0.6 ± 0.0

Table 2: Effect of different derivations of *Tagetes erecta* (Mexican marigold) on serum enzyme levels in chronic Antihepatotoxicity rat

Treatment	ALT (IU/L)	AST (IU/L)	ALP (IU/L)	Total bilirubin (mg/dL)	MDA (nmol/g)	GSH (µmol/g)
Normal	52.6± 4.5	71.1 ± 7.2	103.9± 2.7	0.6 ± 0.1	24.9 ± 1.4	104.2± 6.6
Indomethacin	267.0 ± 64.2	224.6 ± 26.9	271.0 ± 17.2	0.6 ± 0.0	71.2 ± 2.9	62.6± 4.0
Silymarin + Indomethacin	117.0 ± 17.0	97.0 ± 6.6	126.6 ± 20.9	0.6 ± 0.0	24.4 ± 1.9	107.9 ± 2.7
Ethyl acetate + Indomethacin	96.6 ± 9.1	101.0 ± 12.6	147.2 ± 11.1	0.6 ± 0.0	42.6 ± 9.1	106.6 ± 0.9

DISCUSSION

Antihepatotoxicity activities of *Tagetes erecta* (Mexican marigold) **are** reported in this research study. The safe use of plant extracts in the treatment of various diseases can be proved through various ***in vitro*** cytotoxic assays [17]. Our findings verified the safe use of *Tagetes erecta* (Mexican marigold) fractions. In acute and chronic hepatotoxicity, ethyl acetate fraction is showing the significant result.

The presence of phenolic compounds indicated its antioxidant activity, scavenging of free radical, and reducing extracts' power may provide DNA protection. Treatment with *Tagetes erecta* (Mexican marigold) extracts normalized serum enzymes' elevated levels is a clear manifestation of its Antihepatotoxicity effect. Stabilization of the plasma membrane is one of the leading causes to reconsider the Antihepatotoxicity effects of various plants ([18]. Active constituents of plant extract responsible for the inhibition of lipid peroxidation; this factor is also involved in hepatoprotection [19]. Liver injury is the result of oxidative stress induced by hepatotoxicity agents.

In our study, the ethyl acetate fraction showed reduced serum enzymes' reduced elevated levels (alanine transaminase, aspartate transaminase, alkaline phosphatase, and total bilirubin) compared to indomethacin-induced Antihepatotoxicity. The presence of various phytochemicals constituents in plant extracts may also be related to that plant's Antihepatotoxicity effect [20].

An increase in liver glutathione activity in drug treated rats, as observed in this study, indicates the hepatic cell protection. Malondialdehyde is another cytotoxic product [21]. In treatment, a reduced level of malondialdehyde indicated that it prevents lipid peroxidation by indomethacin-induced hepatotoxicity. The maximum amount of phenolics was evaluated in a plant (*M. majus*) is a close relevant specie of *Tagetes erecta* [22]. The hepatoprotective effect of *Tagetes erecta* was closely relevant to silymarin [23]. These results helped to find out the exact reason how the hepatocytes maintained the membranous integrity against indomethacin Antihepatotoxicity [24]. It can be supposed that pretreatment with ethyl acetate fraction reduced the lipid peroxidation induced by indomethacin due to natural antioxidants [25].

CONCLUSION

Tagetes erecta (Mexican marigold) has hepatoprotective and antioxidant effects.

CONFLICT OF INTEREST

Authors have no conflict of interest

AUTHOR'S ROLE

Usman Abid presented the plan and helps in methodology and lab work, Nuzhat Sial manages all research work, Sobia Abid is corresponding author and helps in lab work and results assemblage, Abdul Rasheed helps in lab work and managing animals, Sadia Khalid helps in paper writing while Waseem Akram helps in managing work plan and paper writing.

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