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The chronic toxic effect of *Teucrium polium* aqueous extract on some blood parameters in rat

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ABSTRACT

T.Polium is consumed by many Algerians and other people in the Mediterranean countries for the treatment of several ailments and since there is no detailed information on the liver status after the consumption of the plant, the chronic oral toxicity of Teucrium Polium was evaluated in Wistar rats. Therefore, the LD 50 of this plant was estimated to be more than 3000 mg/kg. In the repeated dose 90-day oral toxicity study, the administration of 800 mg/kg, 1600 mg/kg, and 2500 mg/kg/day of Teucrium Polium extract per body weight revealed significant difference (P> 0.05) and biochemical parameters, relative organ weights, compared to the control group.

Key words: Teucrium Polium, liver function, Kidney Function, , chronic toxicity, rats

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INTRODUCTION

Teucrium Polium is a traditional plant commonly used in folk medicine for various types of pathological conditions. Some biological and therapeutic effects have been reported such as anti –inflammatory[1],anti-oxidant[2][3] antipyretic and antibacterial actions[4], anti –gastric ulcer[5] and hypolipidemic effect[6]hypoglycemic effect[7][8], cardiovascular effects[9] and. Anticancer activity[10].

The purpose of the present study was carried out to examine the chronic effects treatment with T. Polium on the biochemical composition of the blood effects of albino Wistar rat.

MATERIALS AND METHODS

Plants material

The aerial parts of Teucrium Polium were collected from the region of Bejaia. The plant materiel was rinsed from dust with tap water and dried under shade at room temperature for one week. The plant was identified by Pr. Laouar of Setif University of (Algeria) and the sample of the plant was deposited at the herbarium of the laboratory of toxicology and pharmacology, university of Algiers (Voucher specimen N° BK01).

Finally, the aerial plant was ground and the powder was kept in a closed container at 4°C.

Animals

Experiments were performed on Wistars rats (40males and 40 females). They were obtained from Mentouri University weighing 140 -180. They were housed randomly in stainless steel wire cages and kept on a 12 h light/dark cycle at 22+3°C and constant humidity. Rats in all cages had free access to food and water.
All animals were kept for two weeks before experimentation.

The study protocol was approved by the Scientific Council of the Institute of Veterinary Sciences (University of Constantine), Algeria and conforms to the guidelines of animal care and used in research and teaching.

Experimental protocol

Determination of leathal dose of *T. polium*

The acute toxicity study of aqueous *T Polium* was conducted following Lorkes Method [11]the male albino Wistar rats were divided into six groups of five weight-matched animals. The different groups received 500, 2000, 3000,4000,5000,6000 mg/kg of aqueous *T Polium.* Body weight, signs of toxicity and mortality were observed for 24h.

Chronic toxicity

Chronic toxicity testing was conducted according to World Health Organization and Organization for Economic Co-operation and Development guidelines.[12] The rats were divided into four groups of 10 weight-matched animals each. In the present study, the toxicity of the plant was studied by preparing three different concentrations of the extract 800mg/kg, 1600mg/kg and 2500mg/kg/day which represents 25%, 50% and 75% of a LD_{50} (3333 mg /Kg) and administered orally to three groups of animals daily for 90 days. The fourth group was taken as a control and given 1ml normal saline.

The symptoms of toxicity such as asthenia, hypo activity (motor activity), anorexia, diarrhoea and syncope were checked. Survival animals were kept under observation for 90 days.

At the end of the experimental period, the animals were scarified by decapitation

Immediately after decapitation, blood samples were obtained directly from the neck for haematological analysis and serum chemistry. By thoracic abdominal longitudinal incision, the animal's abdomen was opened and the liver and left kidney were removed and the weights were recorded

Statistical analysis

Data were expressed as mean ± SEM. Statistical differences between normal, treated, and control groups were determined using one-way repeated measures analysis of variance (ANOVA) followed by Duncan's multiple range as post hoc test. The differences between the groups were considered significantly different when Pvalue was less than 0.05

RESULTS AND DISCUSSION

Considering the different therapeutic potentials of Teucrium Polium as an alternative medicine effective for a wide range of illnesses and infections, as reported in a number of scientific reports [13], it is only pertinent that a safety profile of the plant be established as a guide for the management of its applications and usage in herbal preparations. This should serve to prevent exposing human subjects to potential toxicity-related health risks while using Teucrium Polium. Toxicity studies in appropriate animal models are commonly used to assess potential health risks in humans. Such toxicity studies assess the danger and determine the risk level by addressing the probability of exposure to that particular danger at certain doses.

The Level of Liver Function Enzyme and Kidney Function Parameters.

Hepatorenal toxicity was studied by measurement of some biochemical parameters of the kidney and liver.

The result of the SGOT, SGPT, urea, creatinine level was showed in table.1 and table .2

Table 1: The mean level of ast, alt, urea, and creatinine of males after 90 days treatment to *Teucrium Polium*

	Control Males	800 mg/kg	1600 mg/kg	2500 mg/kg
AST UI/L	122,26±2,57	111,80*±10,30	108,3*±10,86	150,2*±4,46
ALT UI/L	55±3,91	57±3,80	55±3,91	91,66*±4,62
Uréa mg/l	0,35±0,02	0,294*±0,02	0,35±0,03	0,41*± 0,03
Créatinine mg /L	5,17 ±0,10	5,08 ±0,06	5,39*±0,43	7,05*±0,71

Data are given as percent of organ weight /body weight a:Mean (SEM)10 Animals: Significantly different from control at p<0, 05*

Table 2: The mean level of ast, alt, urea, creatinine of females after 90 days treatment to *Teucrium Polium*

	Control Females	800 mg/kg	1600 mg/kg	2500 mg/kg
AST UI/L	124,7±6,32	119,1*±11,1	99,8*±3,88	150,6*±18,31
ALT UI/L	66,10±6,47	69,5±2,79	63,1±4,53	83,20*±10,29
Urea mg/L	0,35±0,03	0,24*±0,02	0,42*±0,04	0,50*±0,05

Data are given as percent of organ weight /body weight a: Mean (SEM) 10 Animals: Significantly different from control at p<0, 05*

Hepatorenal toxicity was studied by measurement of some biochemical parameters of the kidney and liver. Significant increases in the levels of AST in the group treated with800, 1600 and 1000 mg/kg in the male group andin the group treated whit2500mg/kgin the female group. This result agree with Vahidi and all (14) and krache and all (15)

Increased Urea and creatinine levels were also observed in the groups treated with 1600 and 2500 mg/kg compared with the control group ($p < 0.05$). These results were previously observed by Benoudah and all (16)and Iriadam and all (17).

Table 3: Effect of chronic toxicity of teucrium polium on organ weight of rats

Animal group	Females	Males	Females	Males
	Liver %	Kidney %	Kidney %	Liver %
Control	9,10±0,29	2,27*±0,15	2,71*±0,13	8,85*±0,27
800mg /Kg	8,70*±0,34	2,11*±0,06	2,47*±0,13	8,39*±0,04
1600mg/Kg	7,68*±0,38	1,63*±0,17	2,24*±0,12	7,69*±0,43
2500mg/Kg	6,71*±0,38	1,16*±0,14	1,87*±0,11	7,14*±0,52

Data are given as percent of organ weight /body weight a: Mean (SEM) 10 Animals: Significantly different from control at p<0, 05*

The analysis of the relative organ weights studied (Table 3) showed a significant decrease in liver($p < 0.05$) and kidney ($p < 0.05$).Weight at a dose of 2500mg / kg. The liver weight changes may suggest treatment-related changes. It appears from this analysis that the liver was certainly affected by the aqueous extract of Teucrium Polium at a dose of 2500 mg / kg.

Effects of Oral Administration of Teucrium Polium Extract on General Behavior In the chronic toxicity study. Both the male and female rats administered with 800 mg/kg of Teucrium Polium extract did not exhibit symptoms of toxicity. However, the male rats that received 1600 mg/kg of the extract showed signs of lethargy, and weakness. The symptoms of toxicity started manifesting around days 28–30 and days 36–37, respectively, in the groups treated with the 1600 and 2500 mg/kg doses. Mortality and changes in respiratory rhythm and fur patterns were observed at day80 experimental periods in the aforementioned groups. However, in the female rats, physical manifestation of toxicity symptoms occurred on days70, 74 and days 85–86, respectively, in the groups receiving 1600 and 2500 mg/kg of the extract. The toxic symptoms observed included lethargy, self-isolation, heavy breathing, changes in fur patterns, and abnormally slow motor and reflex activities. Overall, the toxic symptoms were most pronounced in the male group treated with the highest dose; while 2deaths were recorded in females groups treated whit 2500mg/kg.

The deaths of two female rats indicate gender sensitivity of the toxic effect. However, this result previous findings by Rasehh and all (18)

CONCLUSION

This study validated the toxic effects of Teucrium Polium extract at the doses of 2500 mg/kg with prolonged use. The toxic effects comprised changes in the biochemical composition. Both the male and female groups treated with 800 mg/kg did not display signs of toxicity. The death of the two female rats in the high dose group may indicate that the female rats are more sensitive to Teucrium Polium toxic effects than the male rats. Therefore, caution and safety measures should be taken before oral ingestion of Teucrium Polium for therapeutic purposes or for other uses; and prolonged use should be discouraged because the toxicity of medicinal plants was underestimated due to the perception that herbal medicines are absolutely safe and many people use them for self-medication and few know about the pharmacology and toxicology of the most common remedies.

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