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Original Research Article

Biochemical and Histological Evaluation of Sub-Chronic Administration of *Canscora decussate* Leaf Extract on Liver and Heart of Wistar Rats

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ABSRTACT

Plants have been used as food and medicine since the beginning of recorded human history. *Canscora decussate* is traditionally believed to relieve cardiovascular and hepatic disorder. The aim of this study is to evaluate the biochemical and histological effect of sub-chronic administration of ethanol leaf extract of *Canscora decussate* on liver and heart of wistar rats. Twenty four male adult rats were used for this work. Group 1 received distilled water (10 ml/kg), while groups 2, 3, and 4 received 100, 200, and 400 mg/kg of *Canscora decussate*, respectively. The animals were housed in conventional cages for 28 days, with oral access to the extract provided before they were weighed and euthanized. A heart puncture was used to take blood, which was then promptly submitted for chemopathological investigation. Phytochemical analysis revealed the presence of secondary metabolite such as tannin, reduced sugar, flavanoids and saponins. There was significant decrease ($P \leq 0.05$) in serum ALB at 200 and 400 mg/kg dose, while there was no significant change ($P \leq 0.05$) in ALT and ALP when compared to the control group. There was significant increase ($P \leq 0.05$) in level of CHOL at 200 mg/kg dose when compared to the control. There was significant ($P \leq 0.05$) increase in serum HDL at 400 mg/kg dose. LDL and TRI value remain unchangeSlight lymphocyte hyperplasia with normal heart and liver histology architecture observed at all doses and the control (10 ml/kg). *Canscora decussate* is relatively safe for use and may be of benefit in cardiovascular and hepatic conditions.

Key words:*Canscora decussate*, Blood, Rats, Liver, Heart

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Introduction

The liver is a crucial metabolic organ found only in vertebrates that performs various critical biological processes such as detoxification and protein and biochemical synthesis necessary for digestion and growth[1]. In humans, it is located in the right upper quadrant of the belly, beneath the diaphragm, and is mostly protected by the lower right rib cage. Carbohydrate metabolism, hormone production, nutrition conversion and storage such as glucose and glycogen, and red blood cell breakdown are all metabolic processes[2,3]. The liver also serves as an accessory digestive organ, producing bile, an alkaline fluid rich in cholesterol and bile acids that emulsifies and aids in the digestion of dietary fat. The gallbladder is a tiny hollow pouch found directly beneath the right lobe of the liver that collects and concentrates bile before it is discharged into the duodenum to help digestion[4,5].

The human heart is located in the middle mediastinum between thoracic vertebrae T5 and T8[6]. Ackroff*et al.* [7] define the pericardium as a double-membranous sac that surrounds and attaches to the heart. The three major blood arteries that link to the top region of the heart are the vena cavae, aorta, and pulmonary trunk. On the third level of costal cartilage, the upper half of the heart is placed. The apex of the heart is located to the left of the sternum (8 to 9 cm from the midsternal line) at the point where the fourth and fifth ribs meet the costal cartilages[3].

Atherosclerosis is a condition in which plaque accumulates in the artery walls. This buildup narrows the arteries and makes blood flow more difficult[8]. A blood clot can impede blood flow when it forms. This can cause a heart attack or stroke. Appropriate heart failure management requires not just maximizing pharmacotherapy as recommended by published national guidelines, but also implementing appropriate nonpharmacologic approaches[9].

*Canscora decussate*is cultivated in the gardens as ornamental plant for its flowers[10]. This is an erect annual herb with 4-winged stem and half a meter in length with decussate branches. It grows well in moist conditions. Leaves are sessile, 2.5-4 cm in length, lanceolate, decussate with 3 prominent vertical lines; flowers are axillary, solitary, and white or yellowish in color. The entire plant, as well as fresh juice, is used in the traditional medicine for the treatment of insanity, epilepsy, and nervous debility. This plant contains bitter substances and an oleoresin. It is also found to contain triterpines, alkaloids, and xanthones[11]. It is also a natural source of pentaoxygenated, hexaoxygenated, and dimericxanthones. It is traditionally used in cerebral abnormalities, epilepsy, insomnia, burning sensation, liver, cardiovascular, kidney disease, GIT disorder, edema, urinary disorders, snake-bites, and diseases caused by evil spirits. It is traditionally believed to be a good tonic for brain and nerves and has also been recommended for sexual and seminal debilities[12-14]. No study has been done to assess the subchronic potential of this plant. Hence, The aim of this study is to evaluate the biochemical and histological effect of sub-chronic administration of ethanol leaf extract of *Canscora decussate* on liver and heart of wistar rats.

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Materials and methods

Study area

This study was conducted at the University of Uyo, AkwaIbom, UyoState, Nigeria. Between March 11, 2022 and April 29, 2022.Uyo, Nigeria is in the Nigerian National Urban Areas category with GPS coordinates of 5° 2' 20.2668" N and 7° 54' 34.0920" E on the day of arrival.Uyo has a summer season, a rainy season, and a hot, dry climate; Annual temperatures range from 69°F to 87°F.[15](Figure 1).

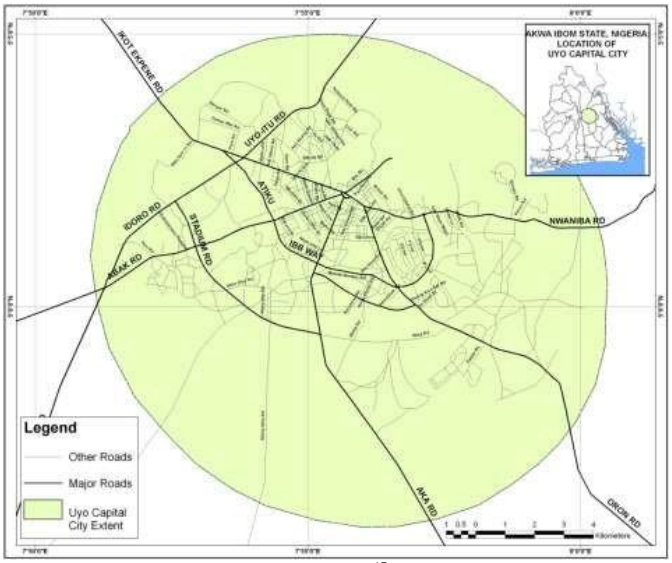

Fig. 1:Figure 1. Map of the research area[15].

Plant collection

Canscora decussate was acquired at a conservative medicinal garden in Uyo, Akwa Ibom State, Nigeria on 28th of February 2022. The plants were verified by the Department of Botany at the University of Uyo in AkwaIbom State, Nigeria. The voucher specimens were stored in the herbarium department (No: 276).

Animals

Male Wistar rats were obtained from the University of Uyo Animal House. They were fed animal pellets purchased from Grand Cereals Limited and given unlimited water. Rats (n = 6) were placed in different treatment groups. Animal studies were conducted under similar conditions. Care and handling of animals in accordance with public health guidelines in the Guide for the Care and Use of Animals (2011).

*Plant*extraction

Theplant leaves were shade dried for two weeks. The dried plant material was then crushed into coarse powder. The powdered sample (200 g) was extracted by percolation in 70% ethanol (1 L) at room temperature. The extract was filtered and the filtrate was evaporated to dryness in vacuo at 40°C using a rotary evaporator. The extract was kept at -4°C until it was needed.

Animalstudy

Twenty-four rats (weighing 182-256g) of either sex were chosen at random and divided into four groups of six rats each. Groups 2, 3, and 4 received 100, 200, and 400 mg/kg of *Canscora decussate* extract, respectively, while group 1 served as the control group, receiving normal saline (10ml/kg). The weights of the rats were recorded at the start of the experiment and once a week thereafter.

Sample collection

A heart puncture was used to collect blood samples. Blood samples were collected in plain bottles for biochemical analysis. Allowing the blood in the plain container to coagulate, it was centrifuged at 3500rpm for 10 minutes before being split into labelled containers.

Qualitative phytochemical screening

The test was carried out according to the procedures outlined by Lv[13] and Kalantar-Zadeh et al [12]. Ten percent (10%) preparation of the extract in distilled water was considered as the test samples. Distilled water was used as a negative control throughout the phytochemical tests.

LD_{50} determination

Lorke[11] approach was used to perform an acute toxicity, LD_{50} test. In two phases, a total of 13 rats weighing 100-120 g were employed.
The animals were separated into three groups of three mice each in the first stage, and the extract was supplied at three dose levels (10, 100, and 1000 mg/kg) body weight. The animals were kept under constant observation for 24 hours. Due to the lack of deaths in the first phase, extract doses of 2000, 3000, 4000, and 5000 mg/kg were used for four groups of one animal each. The animals were inspected again after 24 hours. The number of deaths (s) for each group was recorded, and the LD50 was determined as follows;
$LD_{50} = \sqrt{(D_0 \times D_{100})}$.
Where: D_0 = Highest dose that gave no mortality
D_{100} = Lowest dose that produced mortality.

Biochemical study

Atlas medical diagnostic kits (Germany) was used for this analysis, the levels of lipid profile (LDL, HDL, Cholesterol and triglyceride) and liver indices (ALT, ALP, AST,ALB, BILT and BILD) were measured as indicators of heart and liver functions. The University of Jos Teaching Hospital's Chemical Pathology Department determined the aforementioned parameters. The heart and liver were carefully removed and stored in 10% formal saline solution before being processed, sectioned, and stained with hematoxylin and eosin (H&E) according to standard procedures.

Histological study

Liver and heart organs were removed and stored in buffered formalin for 12 h before histological examination. Histopathological examination was performed using a Leica Microsystems (Nigeria) light microscope. A histopathologist was blind to the coded treatment group and reviewed the slides. Hematoxylin and eosin staining technique was used in this study.

Statistical analysis

The data were expressed using the mean and standard error of the mean (SEM). Before Dunnett's post hoc test for multiple comparisons between the control and treated groups, one-way ANOVA was performed to statistically examine the data. $P \leq 0.05$ was considered significant.

Result and Discussion

Phytochemical screening of Canscora decussate

Phytochemical test was carried out on the whole ethanol extract as well as the. The results are shown in Table 1. Phytochemical screening of all the crude extract of *Canscoradecussate*extract showed the presence of various chemical constitutions mostly Alkaloid, flavonoid, cardiac glycoside, saponins, tannins, terpenes, reducing sugar, carbohydrate.

Acute toxicity

There was no death after 24 hours of administration of *Canscora decussate* (10, 100 and 1000 mg/kg body weight) of the ethanol extract of *Canscora decussate*. In the second stage, there was also no

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death noted after 24 hours. Thus LD_{50} it is estimated that LD_{50} of *Canscora decussate* is ≥ 5000 mg/kg b.wt. in mice. It is can considered as safe.

Effect of Canscora decussateon relative organ to body weight ratio in rats.

Rats receiving 200 mg/kg of the ethanol extract of *Canscora decussate*were found to have slightly larger value liver and heart when compared to the control group. There was no significant ($p<0.05$) difference at higher doses of 100 and 400 mg/kg (Table 2).

Effect of 28 days oral administration of ethanol extract of *Canscora decussate* on lipid profile in Wistar rats.

Significant ($p<0.05$) increases were observed in total cholesterol and HDL levels at 100 and 400 mg/kg dose level of *Canscora decussate* respectfully when comparedto the control. The extract did not produce significant changes in all other parameters (LDL, TRIG levels) studied when compared to the control (Table 4)

Table 1: Results of Phytochemical Analysis of ethanol fruit extract of *Durantaerecta*

	Phytochemical	Crude extract
1	Tannins	+
2	Alkaloids	+
3	Reducing Sugars	+
4	Flavonoids	+
5	cardiac Glycosides	+
7	Saponins	+
8	reducing sugar	+
9	Terpene	+
10	cardiac glycoside	+
11	Acidic compounds	_
12	carbohydrate	+

Key + = level of availability

Table 2: Effect of 28 daysadministration of *Canscoradecussate*on relative organ to body weight ratio in rats.

Relative Organ To Body weight Ratio%		
Treatment(mg/kg))	HEART	LIVER
DW(10 ml/kg)	0.37±0.11	2.51±0.23
100 mg/kg	0.38±0.23	2.61±0.36
200 mg/kg	0.34±0.345	2.55±0.77*
400 mg/kg	0.36±0.51	2.67±0.73

*Significantly different from the distilled water (DW) control at $p<0.05$.CD=*Canscora decussate*

Effect of Canscora decussate on liver function

There was significant decrease ($P\leq0.05$) in serum ALB at 200 and 400 mg/kg dose, while there was no significant change ($P \leq 0.05$) in ALT and ALP when compared to the control group. (Table 5 and figure 2).

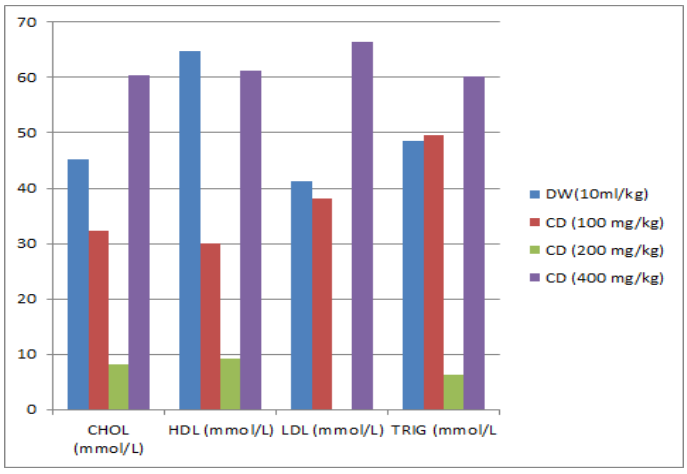

Figure 2: Effects of 28 days oral administration of *Canscora decussate* extract on liver parameters

Effect of Canscora decussate on cardiovascular parameters

There was significant increase ($P \leq 0.05$) in level of CHOL at 200 mg/kg dose when compared to the control. There was significant ($P \leq 0.05$) increase in serum HDL at 400 mg/kg dose. LDL and TRI value remain unchange Slight lymphocyte hyperplasia with normal heart and liver histology architecture observed at all doses and the control (Table 6 and figure 3).

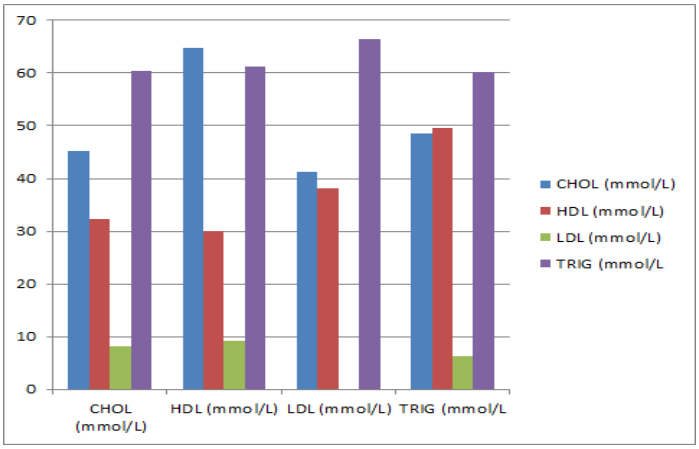

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Figure 3: Effects of 28 days oral administration of *Canscoradecussate*extract on cardiovascular parameters

Effect of leaf extract of Canscora decussateon histology of rat

There was no alteration in the histological integrity of the structure of the rat's kidney and stomach. Histological characteristics remained unchanged at all doses when compared to the control (Figure 4 and 5). The LD_{50} of *Canscora decussate* rats is more than 5000 mg/kg. This indicates that no significant incident occurred. No animal deaths were recorded within 24 hours. The plant *Canscora decussate* was studied to see how it altered vascular and cardiac functions. Serum ALB levels decreased compared to controls at the middle and highest doses, while ALP, ALP, and AST levels were unchanged at all doses. At higher doses, there was a slight increase in BILT levels compared to controls. Additionally, there was no significant difference in BILD compared to the control group. The fact that enzyme levels in the blood do not increase indicates that *Canscora decussate* will not harm the liver. Joseph *et al*.[16] define liver function tests as blood tests that provide information about the patient's liver. These include ALB, ALP, AST, SGOT, activated partial albumin, bilirubin (direct and indirect) and more. (Liver transaminases) Aspartate aminotransferase (AST or SGOT) and alanine aminotransferase (ALT or SGPT) are good markers of liver damage in patients with liver dysfunction[17]. Most liver diseases cause minor liver damage. Symptoms may be present initially but should be noticed as soon as possible. This test involves testing the patient's blood. Some tests measure activity (e.g. albumin), some measure cell integrity (e.g. transaminases), and some bile tests (gamma-glutamyltransferase and alkaline phosphatase). Because some of these tests do not measure function, it is more accurate to call them liver chemistry or liver tests rather than liver function tests[18]. Various biochemical tests may be performed to evaluate and treat patients with liver damage. These tests can detect liver disease[19].

Canscora decussate did not cause significant changes in cholesterol or low-density lipoprotein compared to the control group, but did cause an increase in high-density lipoprotein in the blood. This means that the herb can improve heart parameters, thus explaining its traditional use in the prevention and control of heart problems. A lipid test is a blood test that measures the amount of lipids in the blood. LDL cholesterol is called "bad cholesterol" because it causes plaque buildup in the arteries and heart disease. Therefore, LDL cholesterol should be kept as low as possible. HDL cholesterol is also called "good cholesterol" because it helps remove LDL cholesterol and prevent its accumulation[20]. Total cholesterol is the sum of all types of cholesterol in the body, including LDL, VLDL, and HDL. Excess calories are converted by the body into triglycerides and stored as body fat. High triglyceride levels cause heart disease, liver disease and stroke[21,22].

Phytochemical analysis of *Canscora decussate* revealed proteins, carbohydrate flavonoids, glycosides, triterpenesaponins, tannins, flavonoids. The antioxidant capacity of plant molecules such as saponins, tannins and triterpenoids can reduce tissue necrosis in studied organisms[23,24]. Additionally, *Canscora decussate* extract can improve wound healing through three main mechanisms: contraction, tissue matrix deposition, and epithelialization[25]. Open wound healing by contraction; The interaction between cells and matrix causes tissue to migrate to the wound site[26]. The process of binding collagen, proteoglycans, and proteins to form a new extracellular matrix is called matrix deposition[27]. Epithelialization is the process by which epithelial cells around the wound or in remaining skin appendages, such as hair follicles and sebaceous glands, lose contact inhibition and begin to migrate toward the wound. As migration progresses, underlying cells continue to proliferate, giving rise to more epithelial cells[28,29].

Table 3: Effect of ethanol leaf extract of *Canscoradecussate*on liver indices

		Treatment (mg/kg)		
Hepatic indices	**DW(10ml/kg)**	**CD (100)**	**CD (200)**	**CD (400)**
ALB (g/L)	43.12±2.21	45.11±2.32	35.20±1.78*	28.12±2.67*
ALP (IU/L)	100.23±8.05	112.00±8.69	92.22±6.15	85.15±4.23
ALT (IU/L)	67.12±4.52	71.23±8.23	64.34±5.21	55.11±4.65
AST (IU/L)	195.12±9.43	201.21±7.00	171.88±5.17	131.13±8.43*
BILD (mol/L)	0.42±0.02	0.37±0.23	0.51±0.23*	0.66±0.37
BILT (mol/L)	3.43±0.43	3.62±0.11	3.49±0.08	3.76±0.21

Table 4: Effect of 28 days oral administration of *Canscora decussate*on serum lipid profile in rats.

		Treatment (mg/kg)		
Lipid profiles	**DW(10ml/kg)**	**CD (100 mg/kg)**	**CD (200 mg/kg)**	**CD (400 mg/kg)**
CHOL (mmol/L)	45.20±4.42	64.80±6.25*	41.23±6.00	48.62±5.26
HDL (mmol/L)	32.34±3.24	30.00±3.29	38.21±3.55	49.65±2.11*
LDL (mmol/L)	8.11±2.10	9.18±4.11	8..16±2.99	6.41±5.12
TRIG (mmol/L	60.45±2.44	61.13±3.23	66.52±3.26	60.23±3.11

*Significantly different from the distilled water (DW) control at $p<0.05$. (CHOL = total cholesterol, HDL = high density lipoprotein, LDL = low density lipoprotein, TRIG = triglycerides).

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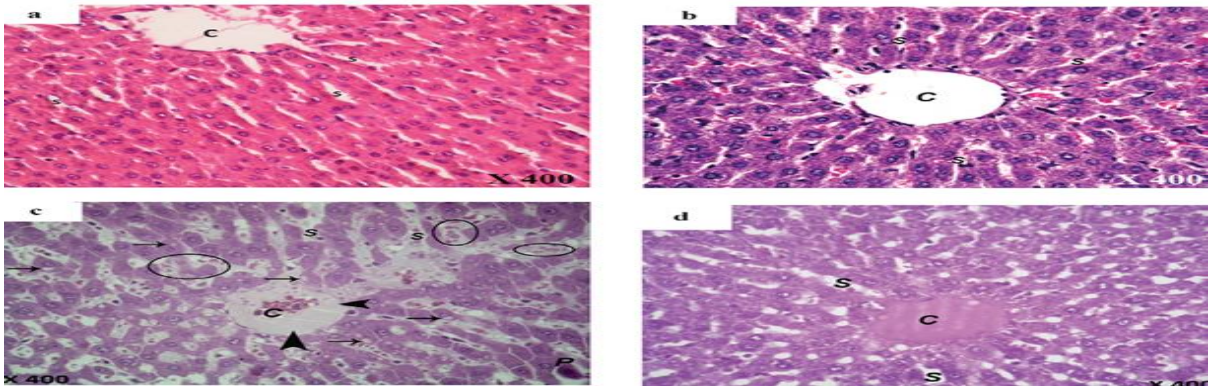

Figure 4: figure of the heart (Hematoxylin and eosin. H and E ×100). (1) Control group, Shows normal neurons (N). (2) 100 mg/kg. (3) 200 mg/kg (4) 400 mg/kg of ethanol leaf extract of *Canscora decussate*

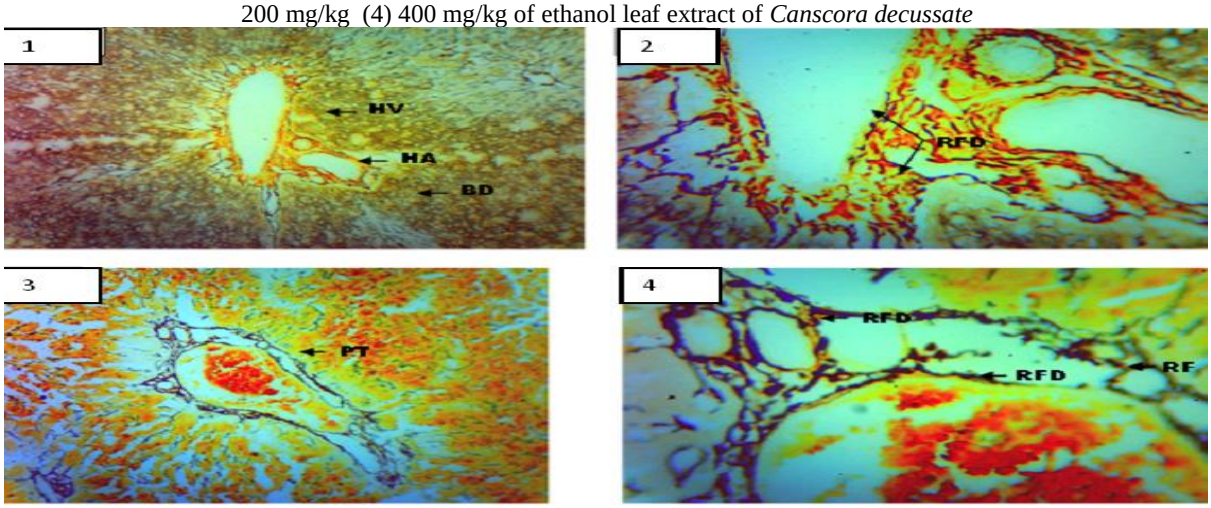

Figure 5:figure of the liver (Hematoxylin and eosin. H and E ×100). (1) Control group, Shows normal neurons (N). (2) 100 mg/kg. (3) 200 mg/kg (4) 400 mg/kg of ethanol leaf extract of *Canscora decussate*

Conclusion

*Canscora decussate*is a plant with many different traditional application in different culture. When used for a sustained period of time, *Canscora decussate has shown to be relatively safe* may also be useful in preventing and managing hepatic and cardiovascular issues.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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