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TOXICOPATHOLOGICAL INVESTIGATION OF THE EFFECTS OF ETHANOL CORM EXTRACT OF *ZYGOTRITONIA CROCEA* ON THE LIVER OF WISTAR ALBINO RATS

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ABSTRACT: *Toxicity and histopathological effects of ethanol corm extract of Zygotritonia crocea traditionally used for treatment of intestinal disorder associated with typhoid, diarrhoea and dysentery in South-west, Nigeria was studied on the liver of Wistar albino rats. Rats were randomly distributed into groups A, B and C (n=7). Groups B and C received 100 and 200 mg/kg body weight extract respectively per day through oral cannula for 21 days while group A (control) received 0.3 ml normal saline for the same period. Then, the liver was collected for histopathological examinations. The mortality rate of treated rats was 42.86% for both doses on the 7th and 14th day while 57.14% was recorded on the 21st day for rats treated with 200 mg/kg compared with the untreated rats (control). Histopathatological findings showed that the liver sections of the treated rats have clear evidence of degenerative changes and cyto-architectural distortions of the hepatic parenchyma which was more severe with the higher dose. These findings show that Z. crocea is toxic at the doses investigated and therefore, will need some caution in its consumption.*

KEY WORDS: *Zygotritonia crocea*, toxicology, histopathology, ethanolic extract, wistar rats.

INTRODUCTION

The liver is a large organ that sits on the right side of the belly. It is reddish-brown in color, protected by the rib cage and has two large sections, called the right and the left lobes. The liver and other organs such as gallbladder, pancreas and intestine work together to digest, absorb, and metabolize food. Its major job is to detoxify chemicals and metabolizes drugs (webMD, 2014). In the cause of carrying out this important function, exposure to chemicals or drugs can cause liver damage that is, drug-induced liver injury (Cano-Paniagua *et al*., 2019). Injury to the liver or impairment of its functions may constitute health complications, one of the serious public health challenges which is often presented with distortion of the metabolic functions (Udom *et al*., 2018). Drug-induced liver injury (DILI) is the most common cause of acute liver failure and accounts for the majority of regulatory actions on drugs such as withdrawal of drug from the pharmaceutical market (Benesic and Gerbes, 2015;

Andrade *et al*., 2007). The incidence of DILI in developed world is 1/600 to 1/3500 of all hospital admissions, with 2%–3% hospitalizations for jaundice, 10% for acute hepatitis (>40% inpatients aged >50 years), and 15%–30% for fulminant hepatic failure (Larrey, 2002).

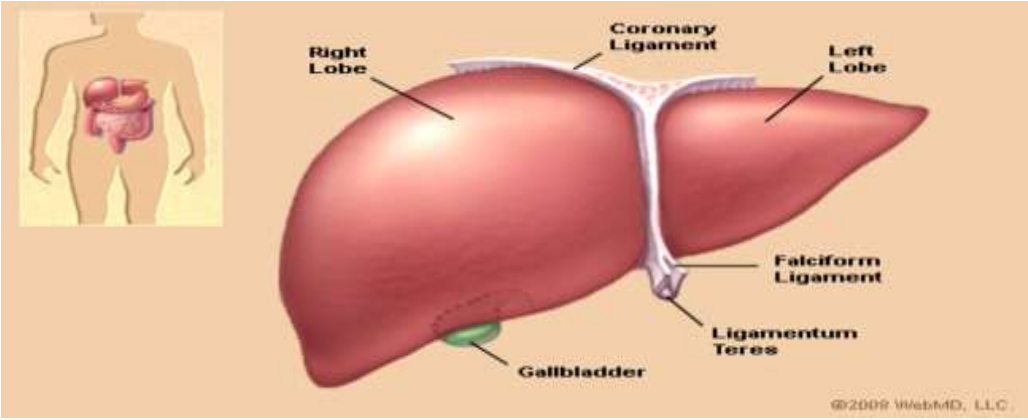

Figure 1: The anatomy of the liver (webMD, 2014)

Herbal or medicinal plants have been used to cure or prevent diseases from time immemorial. In Africa, majority of the people use herbal plants in one form or the other to manage health related problems as a result of poverty, low cost, easy access, and perceived belief that medicinal herbs, due to its natural nature, are safe and free from undesirable side effects while still acting as an effective medicine (Capasso *et al*., 2000). However, herbs may interact with medications that could result in adverse effect which may cause other unforeseen medical complications. Despite several researches into the efficacy of herbal remedies, medicinal plants are not really understood because of lack of systemic nomenclature, good quality control and safety, and/or toxicity information on herbs (Fugh-Berman, 2000; Ashafa and Kazeem, 2015). Therefore, it is immensely important to put medicinal plants and its bioactive components through thorough safety and toxicity tests.

Zygotritonia crocea is a medicinal plant widely known in Southwest, Nigeria as 'Baka'. It is a member of the Iridaceae family (Gbile, 1984). The plant is known as famine food as a result of the corms and fruits being eaten during times of famine (http://zipcode, 2009; Adeniyi *et al*., 2010). Abo *et al*., 1999 reported the presence of alkaloids as the only phytochemical constituent of the plant. Traditional medicine practitioners claimed that *Zygotritonia crocea* is useful for the treatment of intestinal disorders particularly those associated with typhoid, diarrhoea and dysentery. It could also been use as components of traditional anti-tuberculosis recipes [Ashidi *et al*., 1997]. One of the few published works on the plant reported its antimicrobial potential, that it exhibited a significant anti-fungal activity using the corms methanolic extract of the plant. Our previous study on the plant showed that the ethanolic extract of the plant significantly reduce plasma glucose and protein levels, the enzyme activities of AST, ALT and ALP while the cholesterol level was increased significantly (Adeniyi *et al*., 2010). However, the role of medicinal herbs in the

treatment and prevention of diseases do not guaranty their safety for uncontrolled use by an uninformed public [Ofusori *et al*., 2008; Matthews *et al*., 1999).

As a result of our observation of the lowering effect of the plant on the liver function enzymes, we designed this study to investigate the possible effect of *Zygotritonia crocea* on the histology of the liver of wistar albino rats.

MATERIALS AND METHODS

Plant material

Z. crocea fresh corms were bought from Obantoko Market, Abeokuta, Ogun State, Nigeria, identified and authenticated at Forest Research Institute of Nigeria (FRIN), Ibadan, Nigeria. A specimen was deposited at the herbarium of the Institute.

Preparation of extract

200 g of fresh corms was peeled, sliced, washed and oven dried at 60^{o}C. Weighed 50 g of dried sample was ground to fine powder and macerated in 250 ml ethanol for 3 days. This was decanted and filtrate oven-dried at 60^{o}C and weighed. The extract was reconstituted in normal saline to give two concentrations of 100 and 200 mg/ml

Animal grouping and treatment

Twenty-one female albino rats of wistar strain weighing 170 ± 10.2 g were obtained from the Animal House of College of Veterinary Medicine (COLVET), University of Agriculture (UNAAB), Abeokuta, Ogun State, Nigeria. They were maintained under standard laboratory condition, fed freely with pellets and water *ad libitum*. The animals were randomly distributed into groups A, B and C (n=7). Groups B and C received 100 and 200 mg/kg body weight extract respectively per day through oral cannula for 21 days while group A (control) received 0.3 ml normal saline for the same period of days. The rats were handled in accordance with international principles guiding the Use and Handling of laboratory animals (USNIH, 1985). The rats were observed for signs of toxicity such as behavioural changes and death throughout the period of the experiment.

Histopathological studies of rat livers

At the end of the animal treatment, the rats were sacrificed and post-mortem was performed. The livers were identified and carefully removed. Specimens were taken from each organ and rinsed in normal saline. The tissue was fixed in 10% (v/v) formaline. It was then processed to go through alcohol concentrations in ascending order (70%, 90%, 95% and 100%), xylene to remove alcohol and embedded in paraffin wax. It was then sectioned into 5 µm thick and stained with haematoxylin and eosin (H & E) and observed under a photomicroscope (Ajayi *et al*., 2019).

RESULTS

Toxicity

Z. crocea ethanolic extract at the doses applied (100 and 200 mg/kg) induced behavioural signs like depression, loss of appetite, partial paralysis and death

(42.86%) within few days of the commencement of the experiment compared with group A rats, the control (Table 1). More death (57.14%) was recorded in rats treated with 200 mg/kg of extract at 21 days of the experiment as shown in Table 1 and Figure 1.

Table 1. Number of survival and mortality rate (%) of rats treated orally with ethanolic extract of *Z. crocea*.

Group	**Treatment**	**Number of rat survival**				**Mortality (%)**
		0 day	7 days	14 days	21 days	
A	0.3 ml nornal saline, OC	7	7	7	7	0
B	100 mg/kg b. wt. ZC, OC	7	4	4	4	42.86
C	200 mg/kg b. wt. ZC, OC	7	4	4	3	57.14

ZC = *Zygotritonia crocea*
OC = oral cannula
b.wt. = body weight

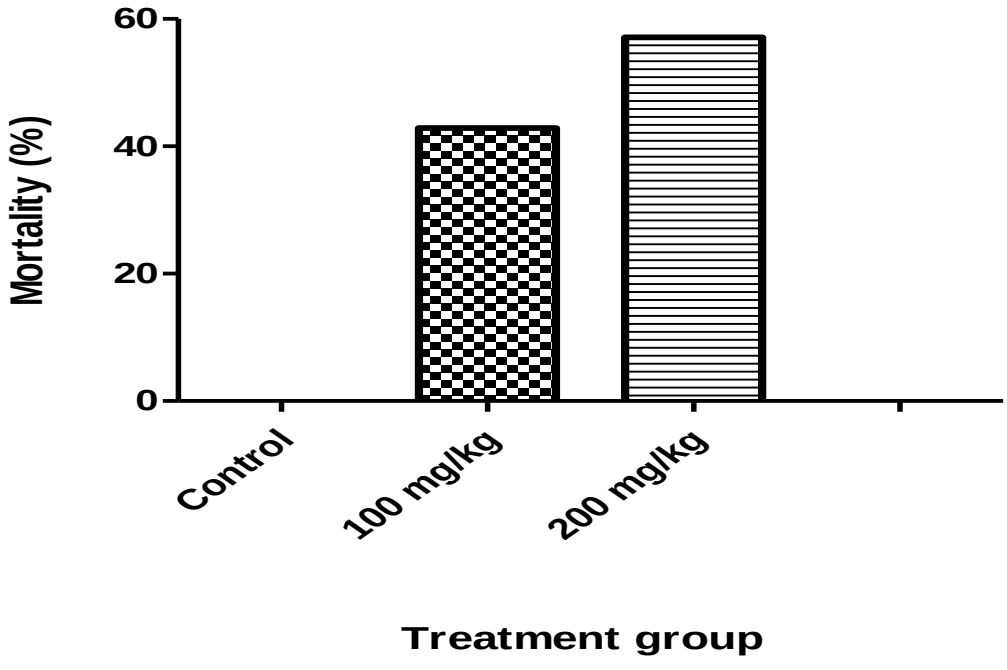

Figure 2: Percentage mortality of rats after oral administration of ethanol corm extract of *Z. crocea* for 21 days.

Histopathological studies

There is no gross changes observed in the group A, control rats while the liver was pale, larger and fatty in the treated rats. Pathological lesions in group C rats were marked and pronounced, while group B rats showed mild pathological changes. The liver sections of the extract treated rats produced multiple areas with bile duct proliferations while no adverse lesion was noticed in the control rats. The lesions caused by the doses 100 and 200 mg/kg were similar but more severe in the higher dose. These include haemorrhages, dilated liver sinusoid congestion and severe central hepatic vein necrosis (Figures 3, 4 & 5).

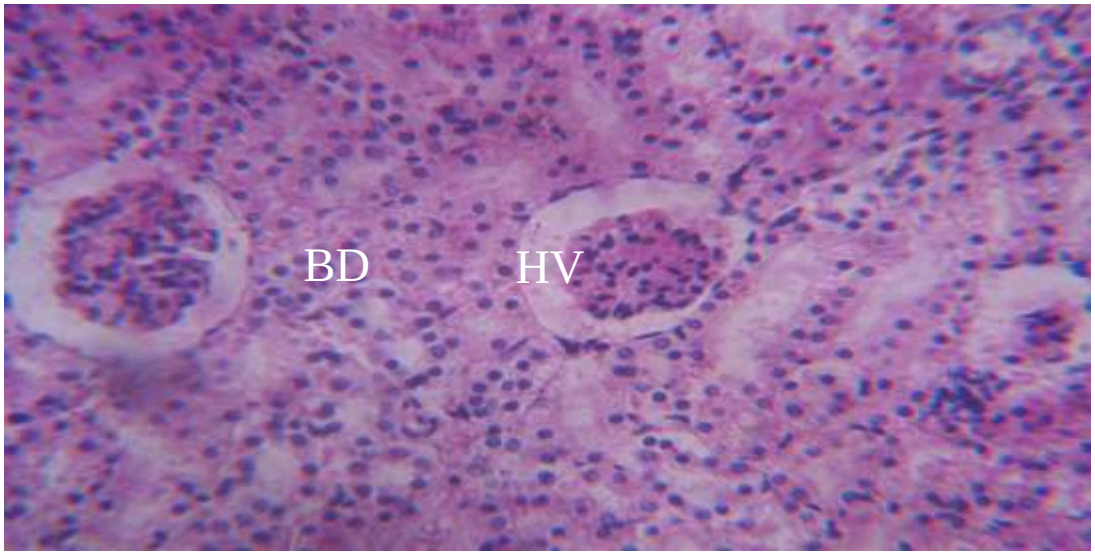

Figure 3: Group A (control) liver showing no visible lesion in bile ducts (BD) and hepatic vein (HV). H and E X350

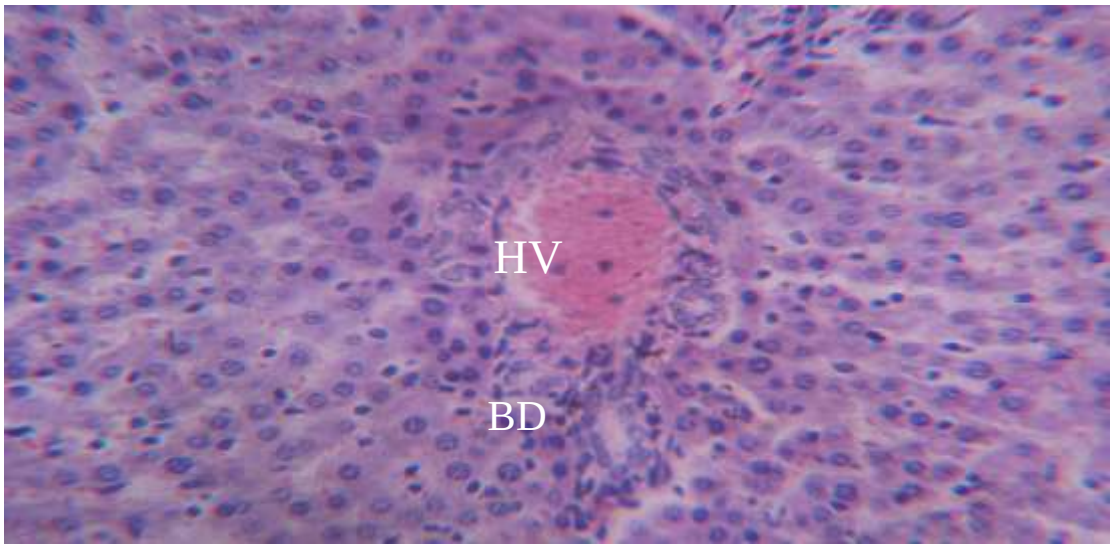

Figure 4: Group B liver showing multiple areas with bile duct (BD) proliferation and hepatic vein (HV) congestion. H and E X350

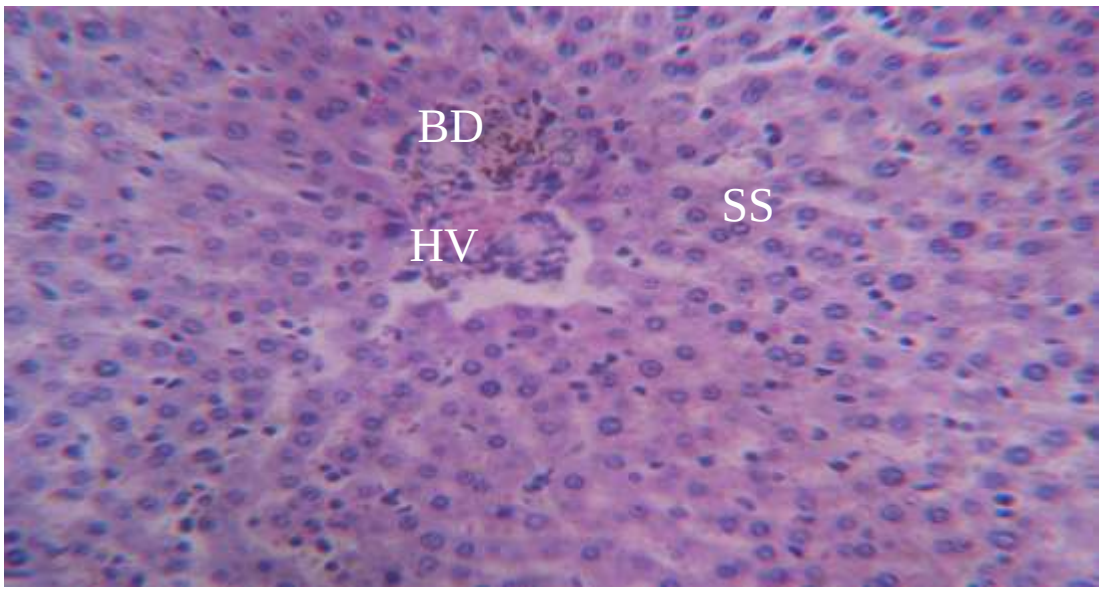

Figure 5: Group C liver showing multiple bile duct (BD) proliferation, severe hepatic vein (HV) necrosis and sinusoid (SS) congestions. H and E X350

DISCUSSION

The present study was designed to evaluate the level of toxicity and the effect of ethanol extract of *Z. crocea* corm on the liver of rats. Liver is a very important organ that performs vital functions for the healthy survival of the body. Such functions of the liver include detoxification of harmful substances, secretion of bile into intestine, synthesis and storage of important molecules, among other things (Wurochekke *et al*., 2008; Ofusori *et al*., 2008; Heath *et al*., 1999).

As there are many medicinal plants used in the treatment of liver diseases, so also are many that can cause injury to the liver after intake of herbals including those already advertised for treatment of liver diseases. There are reports also that those herbs which usually cause liver damage normally contain compounds such as pyrrolizidine alkaloids, kava, atractylis gummifera and senna alkaloids (Wurochekke *et al*., 2008; Adeniyi *et al*., 2010). In his own report, Abo et al, (1999) reported the presence of alkaloids as the only phytochemical component in *Z. crocea*. The degenerative changes with the bile ducts proliferation and severe hepatic vein congestion of the liver recorded in this study may be as a result of the alkaloids present in the plant.

There was a high mortality rate of 42.86% and 57.14% recorded in rats treated with 100 and 200 mg/kg of the ethanolic extract respectively at the end of 21 days treatment. It was also noticed that the 7th and 14th day treatment of rats with the two different doses of 100 and 200 mg/kg of the extract recorded a high mortality rate of 42.86%. This is an indication that the ethanolic extract of the plant using the doses of 100 and 200 mg/kg body weight is highly toxic.

There is contradiction noticed between our previous study and this one. In our previous work on this plant, we postulated the hepatoprotective effect of *Z. crocea* as

a result of the reduced values of liver enzyme activities such as ALT, AST and ALP recorded after treatment of rats with doses of 100 and 200 mg/kg compared with the control rats. Serum enzyme measurement has been noted to be a valuable tool in clinical diagnosis, providing information on the effect and nature of pathological damage to any tissue, and damage to structural integrity of tissues is always reflected by increase in some of these enzymes in the serum (Afolayan *et al*., 2009). This contradiction needs to be further investigated.

Our present findings have clearly shown that ethanolic extract of *Zygotritonia crocea* is not safe at the doses investigated as it has a damaging effect on the liver which is a major organ for detoxification. However, effort has started to further investigate in detail the toxicity of the plant.

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