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RESEARCH PAPER

# THE HEPATO-PROTECTIVE POTENTIALS OF AQUEOUS LEAF EXTRACT OF *CASSIA OCCIDENTALIS* AGAINST PARACETAMOL INDUCED HEPATOTOXICITY IN ADULT WISTAR RATS

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## ABSTRACT

This study investigates the hepato-protective potentials of aqueous leaf extract of *Cassia occidentalis* on paracetamol-induced hepatotoxicity in adult Wistar rats. Twenty adult rats weighing between 150 – 300g were used for this study. They were randomly divided into four groups (A, B, C, and D), whereby group A served as the control, while groups B, C and D served as test groups. Hepatotoxicity was induced in the test groups via oral administration of paracetamol (800mg/kg bw). However, while groups C and D were treated for 21 days with 250mg/kg and 500mg/kg/BW of *Cassia occidentalis* leaf extract respectively, group B was left untreated and served as the test control. Using standard laboratory procedures, the livers were harvested, histologically processed, and examined. Microscopy revealed normal histological hepatocytes in the control animals while those of test control were severe vascular congestion, periportal infiltrates of chronic inflammatory cells and periportal oedema. However, hepatic sections from groups C and D presented a dose dependent healing actions compared to the features observed for group B (untreated hepatotoxic group). Judging by these findings therefore, one can assert that aqueous leaves extract of *Cassia occidentalis* may be hepato-protective against hepatotoxicity.

**Keywords:** ***Cassia occidentalis, Hepatotoxicity, Paracetamol, Liver*.**

## INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used in the treatment of pain, fever, and inflammation (Ozbakis Dengiz et al., 2007). Common amongst this class of drugs is Acetaminophen, also known as paracetamol, which has been reported to induce hepatic injury (Schnellman et al., 1999; Bessems and Vermeulen, 2001; Vermeulen et al., 1992). Certainly, the effect of paracetamol is not unexpected considering the fact that metabolism of chemicals occur largely in the liver (Kaplowitz, 1996), which surely may account for the organ's susceptibility to metabolite-dependent/drug-induced injury. Worrisome however, is the fact that modern medicines have little to offer as regards alleviating hepatic diseases and the alternative, plant-based preparations are largely employed (Brattin et al., 1985). In line with this fact, Ayurvedic medicine is essentially promotive and preventive in therapeutic approach for treating liver disorders and as such, search for crude drugs of plant origin has become a central focus of study of hepatic protection (Ven kumar and Latha, 2002).

Available literature show that the drugs offered by modern medicine for the treatment of liver diseases such as corticosteroids and immuno-supressants, are said to provide only symptomatic relief; mostly without influencing the disease, and their use is associated with the risk of relapse and danger of side effects (Ram and Goel, 1999). However, in recent times, there has been a resurgence of interest in herbal medicine in many parts of the world in view of the acclaimed therapeutic efficacy of many herbal preparations (Kolawole et al., 2006). In fact, Nuhu and Aliyu (2008) asserts that most rural dwellers rely on traditional medicine for the treatment of various ailments, and it

is now generally believed that herbal medicine does not only agree with cultural and socio-economic peculiarities, but also symbolizes safety in contrast to conventional drugs (Taiwo et al., 2012). Hence, herbal medicine is becoming a focus for a wider coverage of primary health care delivery in Nigeria, Africa, India, China, and possibly, the rest of the world.

Of particular interest, is therapeutic potentials of *Cassia occidentalis*, which is commonly called '*Dora rai*' in Hausa, '*Akidi ogbara*' in Igbo, '*Abo rere*' in Yoruba and '*Coffee senna*' in English. It is said to belong to the family *Leguminosae*, sub family *Caesalpinoidae*, and botanically classified as both *Cassia occidentalis* and *Senna occidentalis* according to Egharevba et al. (2010). Extract of several parts of this plant has been widely reported for its pharmacological activities, which ranges from antibacterial, anti -histamine release, antiplatelet aggregation, memory protection and neuroprotection (Kim *et al.*, 2007; Kitanaka *et al.*, 1998; Sung *et al.*, 2004). For example, the various classes of *Cassia* roots, flowers, seeds and leaves have been employed in herbal medicine for purposes such as laxatives, expectorants, antimalarias (Tons et al., 2001), relaxants (Ajagbonna et al., 2001), anti-inflammatory (Sadique et al., 1987), wound healing (Sheeba et al., 2009), and hepatoprotective potentials (Bhakta *et al.*, 2001; Jafri *et al.*, 1999; Usha et al., 2007).

Following suggestions on the protective potentials of *Cassia occidentalis* (Nadkarni, 1976), this study was designed therefore, to investigate the hepato-protective potentials of aqueous leaf extract of *Cassia occidentalis* in rats exposed to paracetamol induced liver injury.

## MATERIALS AND METHODS

**Collection Plant Material:** *Cassia occidentalis* plants were harvested from bushes around Benin City. It was taken for identification at the Herbarium in the Department of Pharmacognosy, Faculty of Pharmacy, University of Benin, Benin City, Edo, Nigeria.

**Experimental animals and grouping:** Twenty adult Wistar strain rats (150 – 300g body weight) were used for this study. They were obtained and maintained at the Animal house of the Department of Anatomy, University of Benin. They were kept in four separate wooden cages (60x45x45cm each) under standard laboratory conditions and fed on a standard diet (Grower's mesh). The four cages were labeled A to D. Animals in group A served as the control, while those in group B served as the test control (untreated). On the other hand, animals in group C and D served as test groups treated with varying concentrations of the plant extract.

**Preparation of plant:** The plant leaves were sundried for four days and taken to the oven to remove moisture content. After drying, the leaves were grinded into fine powder using an electric blender in the Department of Pharmacognosy, University of Benin, Edo, Nigeria.

The fine powdered form of the plant material was then soaked into distilled water for 48 hours at room temperature and the mixture filtered into conical flask using Watman filter paper. The filtrate was dried at temperature of 30$^{o}$C for 10 hours to produce a gel-like extract.

Appropriate concentration of the extract was then subsequently made by dilution with distilled water into 250mg/kg and 500mg/kg/body weight. All preparations were performed at the Department of Pharmacognosy, Faculty of Pharmacy, University of Benin, Edo, Nigeria.

**Paracetamol induced hepatotoxicity and treatment mode:** Hepatotoxicity was induced in rats by administrating 800mg/kg body weight of paracetamol using an orogastric tube.

The treatment regimens are as follows: Group A served as normal control. Group B served as text control in which hepatotoxicity was induced with 800mg/Kg/ body weight of paracetamol and left untreated for twenty one days. Group C served as test I in which hepatotoxicity was induced with 800mg/Kg/ body weight of paracetamol and then treated with 250mg/kg/body weight of *Cassia occidentalis* leaves extract for twenty one days. Group D served as test II in which hepatotoxicity was induced with 800mg/Kg/ body weight of paracetamol and then treated with 500mg/kg/body weight of *Cassia occidentalis* leaves extract for twenty one days.

**Histopathological technique:** Histological examination was done using a binocular microscope at x100 and x400 magnification.

## RESULTS

**Histological examination:** The histological findings (H&E) showed normal histological features in the liver section of the control (group A) (see figure 1), while that of the hepatotoxic control (group B) presented severe vascular congestion (A), periportal infiltrates of chronic inflammatory cells (B) and moderate periportal oedema (*See* figures 2).

On the other hand, liver features of the treated groups (C and D) showed moderate vascular congestion (A) and periportal infiltrates of chronic inflammatory cells (B) for the 250mg/kg *Cassia occidentalis* extract treated rats (see figure 3), while the 500mg/kg *Cassia occidentalis* extract treated rats showed milder vascular congestion (A) and focal periportal infiltrates of chronic inflammatory cells (B) (*See* figures 4).

The hepatoprotective effects of *Cassia occidentalis* leave extract was confirmed by the comparative histopathological changes presented by the treated groups (C and D) in relation to the features presented by those group A (control) and group B (untreated) (*See* figures 1, 2, 3 & 4). Also, the observed efficacy of Cassia occidentalis leave extract in the treatment groups was dosage dependent (*See* figures 3 & 4).

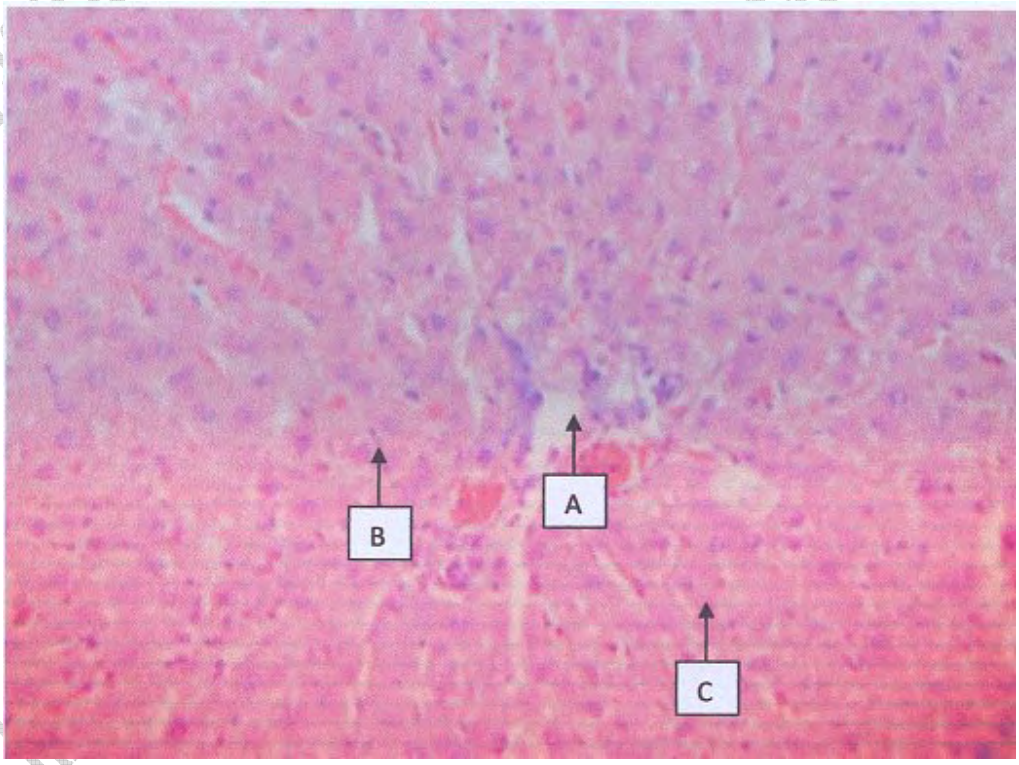


Figure 1: Control liver section (group A; H&E x100) showing normal cytoarchitectural features

## DISCUSSION

Paracetamol is a common antipyretic agent which is safe in therapeutic doses but can produce fatal hepatic necrosis in toxic doses. Paracetamol (acetaminophen) induced hepatic injury has been reported by several studies (Schnellman, 2001; Bessems and Vermeule, 2001; Plevris et al., 1998) and this was justified in view of the hepatocytotoxic indications observed in the liver sections of group B (figure 2) in this study. The hepatotoxic mechanism of paracetamol is said to be mediated through direct liver toxicity of the parent drug or it metabolites (Pham et al., 1997), increase peroxidation (Schnellman, 2001; Bessems and Vermeule, 2001; Plevris et al., 1998), and formation of toxic metabolite; N-acetyl-p-benzoquinoneimine (Lee and Marks, 2007; Jafri et al., 1999).

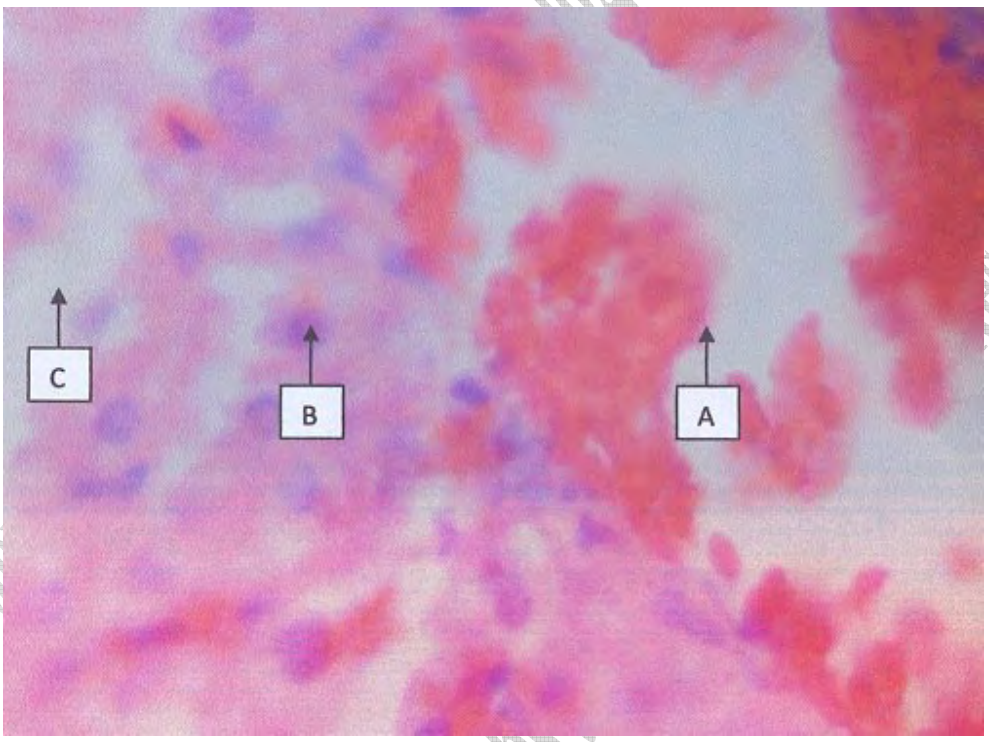


Figure 2: Liver section (Test group B; H&E x400) of rats treated with 800mg paracetamol showing severe vascular congestion (A), periportal infiltrates of chronic inflammatory cells (B) and moderate periportal oedema (C).

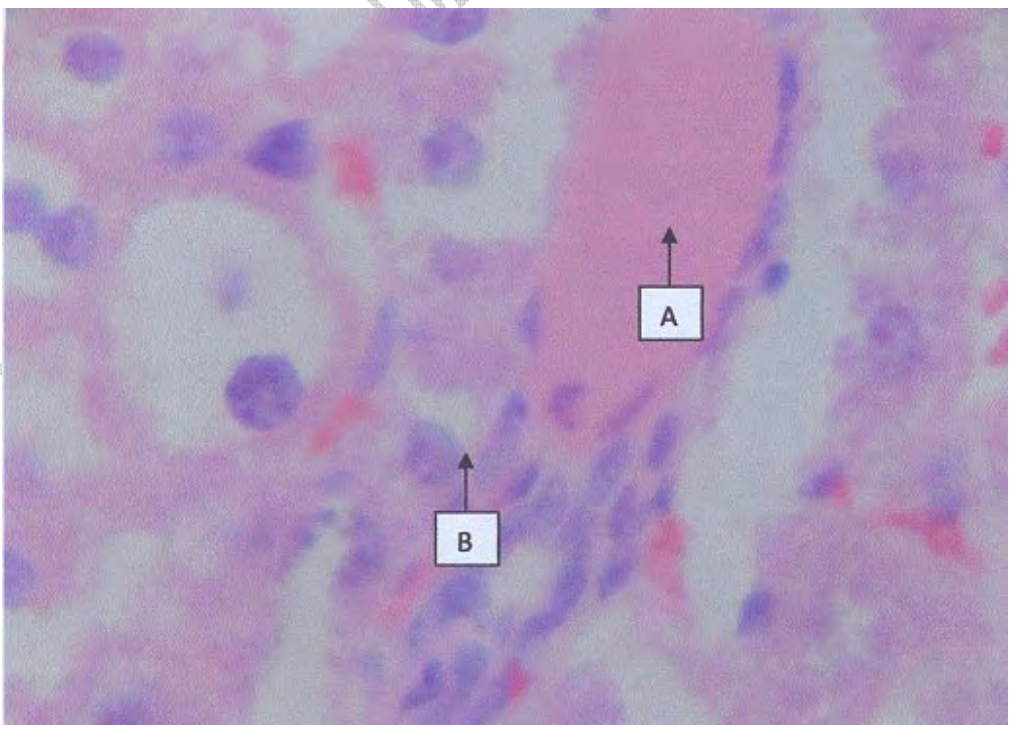


Figure 3: Liver section (Test group C; H&E x400) of rats treated with 800mg paracetamol and 250ml *Cassia occidentalis* showing mild vascular congestion (A) and periportal infiltrates of chronic inflammatory cells (B).

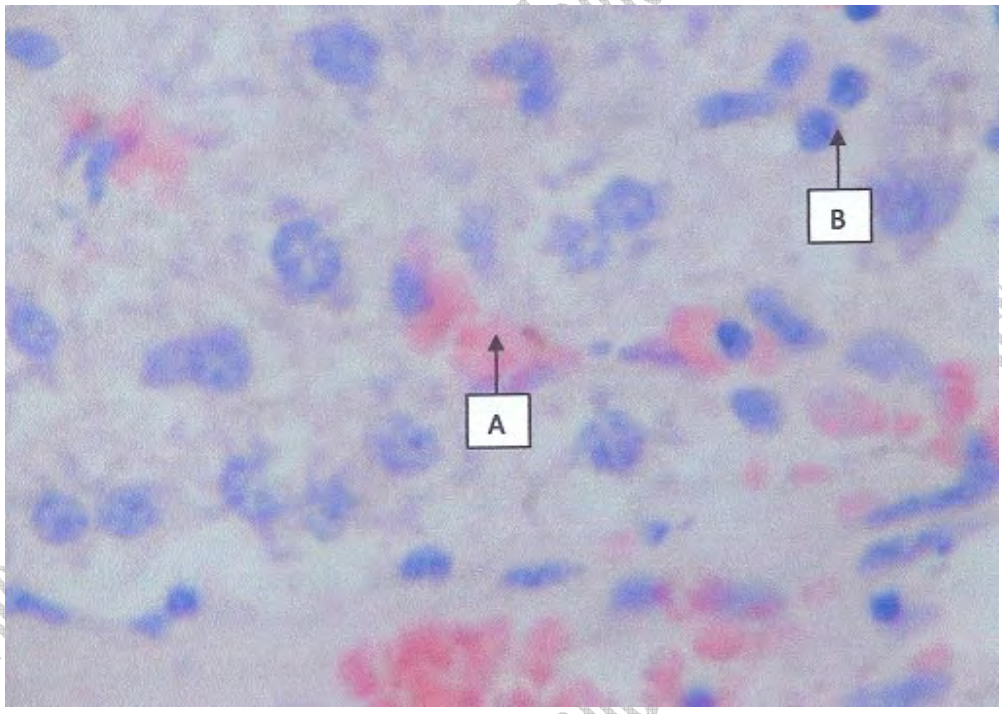


Figure 4: Liver section (Test group D; H&E x400) of rats treated with 800mg paracetamol and 500ml *Cassia occidentalis* showing milder vascular congestion (A) and focal periportal infiltrates of chronic inflammatory cells (B)

However, on the effect of *Cassia occidentalis* extracts on paracetamol induced hepatotoxicity, this study shows that the paracetamol induced hepatotoxic indications were to some degree reduced after 21 days of treatment with *Cassia occidentalis* leaves extract in a dose dependent manner. These lessened hepatic damage by the administration of *Cassia occidentalis* leaf extracts in group C and D compared to that of group B, indicates recovery from paracetamol hepatic damage and suggests its healing potentials as well. This finding is in line with other studies in which different species of *Cassia* extracts have showed hepatoprotective activity against paracetamol, ethyl alcohol and diethylnitrosamine (Bhakta *et al.*, 2001; Jafri *et al.*, 1999; Parthasarathy and Prasanth, 2009; Rani et al., 2010; Sastry et al., 2011).

Although the reported hepatotoxic healing potential of *Cassia occidentalis* leaves extract in this study is based on histological observation, extracts of its various parts have as well been documented to be hepatoprotective biochemically (Rani et al., 2010; Sastry et al., 2011). Specifically, the hepatoprotective effect of aqueous extract of *Cassia occidentalis* on liver damage induced by paracetamol has been shown by parameters of oxidative stress, antioxidants capacity, and liver enzymes such as ALP, ALT, AST, SGPT, SGOT, alkaline phosphate, and total bilirubin (Sherlock and Dooley, 2002; Rani et al., 2010; Sastry et al., 2011). For this reason, the hepatoprotective/ healing potential of *Cassia occidentalis* extracts may be attributed to its chemical constituents considering the several chemical active constituents isolated from the plant.

The assertion that the active components of *Cassia occidentalis* extracts are responsible for its hepatoprotective/healing potentials is justifiable when one considers that oxidative stress plays a critical role in the initiation and progression of a variety of liver disorders (Medina and Moreno-Otero, 2005). Moreover, many natural antioxidants have been used to prevent oxidative-stress-mediated liver injury (Nwozo and Oyinloye, 2011; Skinner and Rangasami, 2002). However, according to Pari and Murugan (2004), the protective effect of *Cassia occidentalis* is said to be the result of stabilization of plasma membrane therapy protecting the structural integrity of cells, as well as repair of paracitamol induced hepatic tissue damage.

Irrespective of the mechanism involved in the hepatoprotective/ healing activities of *Cassia occidentalis* extracts, the findings of this study and studies before, at least, points towards the pharmacological potential of *Cassia*

*occidentalis* against liver damage. It is therefore recommended, that researchers should begin to deduce the overall clinical significance of *Cassia occidentalis*.

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**AUTHORS' CONTRIBUTIONS**

Uzzi H.O. and Grillo, D.B. were actively involved in this study and in the presentation of this manuscript.