

# Effect of The Dry Aqueous Leaf Extract Of *Cnidoscopus* *Aconitifolius* On Blood Alcohol Clearance In Rabbits

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## Abstract

Herbal therapy or plant based drugs might be useful in the management of alcohol-related complications, hence the influence of various substances on alcohol “affects” are being investigated in a search for a substance which could scavenge radicals produced during ethanol metabolism and accelerate ethanol clearance to reduce blood ethanol levels. Oral administration of *Cnidoscopus aconitifolius* leaf extract increased blood ethanol clearance rate in a dose dependent manner. The ingestion of 0.55 g ethanol/kg body weight produced a peak blood alcohol level (BAL) of 0.121% and 0.156%. The administration of 0.5 g/kg of the extract produced a peak blood alcohol level (pBAL) of 0.112% as against 0.121% by ethanol alone. Also, the administration of 1 g/kg of the extract produced a peak blood alcohol level (pBAL) of 0.127% as against 0.156% by ethanol only. The 0.5 g/kg and 1 g/kg of the extract also reduced the intoxication time (i.e. time to zero BAL) from 146min to 137min and 160min to 128min respectively. Results from this study revealed that *Cnidoscopus aconitifolius* leaf extract might have amethystic property as locally claimed but further investigations is required to show the mechanism on how the extract accelerates ethanol clearance.

**Keyword:** *Cnidoscopus aconitifolius*, alcohol, and Blood alcohol level (BAL)

## 1. Introduction

Ethanol is not only a pharmacological substance, but one of the few nutrients that are profoundly toxic (Preedy *et al.*, 1999). Thus, excessive ethanol ingestion disturbs the metabolism of most nutrients and tissues in the body (Forsander, 1998; Bunout, 1999). Excessive ethanol consumption has been reported to initiate a wide range of enormous problems (Odebunmi, 1994; Edeaghe and Agwubike, 2004) that culminate in the death of alcohol addicts. Although there are no accurate data to describe the frequency of such deaths in Nigeria, speculations indicates a high percentage (Obot, 2009). The alterations in cytosolic and mitochondrial NAD<sup>+</sup>/NADH ratios initiate the metabolic disturbances associated with alcohol consumption (Peters and Preedy, 1998; Edenberg, 2007). These metabolic changes in turn elicit series of cascade-like biochemical events that culminate in the diverse health problems common among alcoholics.

In spite of the health risk associated with heavy alcohol consumption, alcohol abuse and addiction have continued to grow posing serious problems to many societies. Therefore, the search for anti-intoxicating substances capable of ameliorating the associated metabolic disturbances and reversing the effects of alcohol in the body would be of interest in Africa, particularly in the Delta regions of Nigeria where alcohol consumption is known to be very high (Edeaghe and Agwubike, 2004). It is on this note that the treatment value of some supportive agents that could enhance the elimination of alcohol from bloodstream was investigated. Available evidence (Kalant and Khanna, 1987) suggests that the use of amantadine, naloxone, benzodiazepine receptor inverse agonist, Ro 15-4513, and gelatin - containing 50 mg methylene blue have not yielded beneficial results in humans (Vonlanthen *et al.*, 2000). Oral fructose has been demonstrated to enhance the metabolic clearance of ingested alcohol (Mascord *et al.*, 1992; Berman *et al.*, 2003; Onyesom and Anosike, 2004a), but its use has remained a contentious issue. It is on this note that the treatment value of some supportive agents that could enhance the elimination of alcohol from bloodstream was investigated.

*Cnidoscopus aconitifolius* has been claimed traditionally to possess medicinal properties such as strengthening of finger nails and darkening of gray hair, treating alcoholism, insomnia, gout, scorpion sting, brain and vision improvement (Jensen 1997; Atuahene *et al.*, 1999; Awoyinka *et al.*, 2007). The plant has also been claimed to be used in the management of diabetes, obesity, kidney stones, hemorrhoids, acne, and eye problems (Diaz-Bolio, 1975; Oyagbemi and Odetola, 2010). *Cnidoscopus aconitifolius* shoots and leaves have been taken as a laxative, diuretic, circulation stimulant; to improve digestion, stimulate lactation (Rowe, 1994), while the aqueous leaf extract has also been recommended as a female contraceptive (Yakubu *et al.*, 2008).

Interestingly, *Cnidoscopus aconitifolius* has been acclaimed to have anti-intoxicating property in folk medicine of Nigeria but this claim have not been substantiated with scientific data. Hence, this present research therefore attempts to investigate the effect of the aqueous leaf extract of *Cnidoscopus aconitifolius* on blood alcohol

clearance.

## 2. Materials and Methods

### 2.1 Plant Collection and identification

Fresh samples of *Cnidoscolus aconitifolius* were collected from an uncultivated farmland at the University of Benin, Edo state, Nigeria. Botanical identification was carried out at the herbarium unit of Forestry Research Institute of Nigeria (FRIN), Ibadan Oyo State. The voucher number obtained was FHI.108788.

### 2.2 Preparation of the Aqueous plant Extract

The plant material was sundried and macerated into uniform powder using Thomas Contact Mill (Pyeunicam, Cambridge, England). Approximately 218g of this powder was extracted with 500ml distilled water using soxhlet apparatus and concentrated by rotator evaporator 50°C. This was transferred into a suitable container and lyophilized (freeze dried). The yield of the crude aqueous plant extract was 8.75g. The dried extract was stored in desiccators until required for use. The extract was dissolved in appropriate volume of distilled water to the desired concentration.

### 2.3 Animals and Experimental Designs

Ten rabbits (1.5kg – 2.5kg) used for this study were purchased from the Animal Unit, College of Medicine, Ambrose Ali University, Ekpoma, Edo state Nigeria. They were divided into two experimental groups of five rabbits per group. Members of each group were housed in a standard rabbit cage and allowed to acclimatize to laboratory condition for one week. All rats were then allowed free access to drinking water and rat feed (chow) – product of Edo Feeds and Flour Mill (EFFM), Ewu Edo state, Nigeria.

### 2.4 Determination of *Cnidoscolus aconitifolius* on blood alcohol level

After 3 hours of feeding; five rabbits (group A) were given a moderate dose of 0.55 g (20% ethanol/ kg body weight) (Onyesom *et al.*, 2005) via the oral route on two different occasions. During the first occasion, alcohol alone was consumed, but during the second occasion 0.5 g extract/kg body weight (Oyagbemi and Odetola, 2010) was administered orally after 20 minutes of ingesting the alcohol. Blood alcohol level (BAL) was determined every 20 minutes for 120 minutes using 0.5ml whole blood obtained from the ear vein of the animals. This was repeated using 1 g extract/kg with the same dose of alcohol for rabbits as above. The equivalent volume of 0.55 g ethanol/kg body weight ingested was determined using the relationship: Volume (ml) = Amount (g ethanol/kg body weight) x body weight (kg)/ % of ethanol (as a decimal) x density of ethanol

### 2.5 Biochemical Assay

Blood alcohol level (BAL) was quantified using the alcohol dehydrogenase method as described by Busher and Redetzki, 1951.

### 2.5 Statistical Analysis

Values obtained from a standard alcohol calibration curve were expressed as mean  $\pm$  SD

## 3. Results and Discussion

The stimulatory effect of aqueous leaf extract of *Cnidoscolus aconitifolius* on ethanol clearance (disappearance) rate has been a traditional way in the handling of ethanol intoxication in some part of Nigeria. But pieces of scientific evidences to substantiate this achieved claims has not yet being documented. Previous studies have shown the use of certain compounds such as fructose (Onyesom, 2006); methylene blue (Vonlanthen *et al.*, 2000) to stimulate the disappearance rate of ethanol, but this has recorded little success in the management of alcoholism.

The peak blood alcohol level (pBAL) was reduced from 0.121% to 0.112% on administration of 0.5g/kg body weight *Cnidoscolus aconitifolius* extract (table 1) and from 0.156% to 0.127% on administration of 1g/kg extract (table 2). The higher the peak BAL, the more intoxicated an individual is, and this bears no relationship to behavioral disorder (Jones and Jones, 1976). From this study, it appears that the extract might be implicated in the reduced peak BAL observed in tables 1 and 2. The intoxication time (i.e. time to zero BAL) was reduced on

co-administration of ethanol with 0.5 g/kg of the aqueous extract by 7% (from 146 minutes to 137 minutes) (table 1), which was reduced further upon 1 g/kg extract administration by 25% (from 160 minutes to 128 minutes) (table 2). This therefore implies that the lesser the time the faster the ethanol clearance rate and hence increase metabolism (Onyesom, 2006). The most likely reason for this reduced intoxication time as observed in tables 1 and 2 might be the ability of the extract at doses of 0.5 g/kg and 1 g/kg, to enhance alcohol clearance from the system, hence increasing alcohol metabolism in the subject. However, in the presence of the extract, remarkable changes were observed in the kinetics of ethanol metabolism. From this investigation, the blood ethanol disappearance rate,  $\beta_0$ , (the gradient of the descending limb) and ethanol elimination rate, BEER, upon administration of 0.5 g/kg extract were found to be 0.088%/h and 241.10 mg/kg/h respectively (Table 1), while for 1 g/kg dose extract was 0.090%/h and 268.10 mg/kg/h (Table 2). The administration of 1 g/kg showed a faster disappearance rate compared with the ethanol treatment alone.

The mechanism by which the aqueous extract of *Cnidioscolus aconitifolius* accelerates alcohol metabolism is uncertain, it is suggested that the extract might have delayed gastric emptying and hence reduces alcohol absorption. This allows increased first-pass metabolism which decreases alcohol bioavailability (Crabb, 1997; Mascord *et al.*, 2001). In the presence of the aqueous extract of *Cnidioscolus aconitifolius*, remarkable changes were observed in the kinetics of ethanol metabolism. From this investigation, the blood ethanol disappearance rate,  $\beta_0$ , and the ethanol elimination rate, BEER, obtained on administration of the aqueous extract at doses of 0.5 g/kg and 1 g/kg with ethanol (Tables 1 and 2) revealed a faster disappearance rate. Although, the mechanism by which *Cnidioscolus aconitifolius* accelerates alcohol metabolism is uncertain and hence needs further investigations, this current research further supports the traditional claim of using the aqueous *Cnidioscolus aconitifolius* extract on ethanol as an amethystic agent.

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**Table 1: The kinetics of alcohol metabolism induced by oral administration of 0.5g/kg of *Cnidoscopus aconitifolius* extract in male albino rabbits**

Subjects	BAL After 20min (%)	BAL After 40min (%)	BAL After 60min (%)	BAL After 80min (%)	BAL After 100min (%)	BAL After 120min (%)	Peak BAL (%)	Time to Peak BAL (Min)	Time to Zero BAL (Min)	$\beta$ 60 (%/h)	BEER (mg/kg/h)
Mean $\pm$ SD Alcohol metabolism in male rabbits	0.055 $\pm$ 0.01	0.102 $\pm$ 0.02	0.125 $\pm$ 0.02	0.098 $\pm$ 0.01	0.067 $\pm$ 0.02	0.038 $\pm$ 0.01	0.121 $\pm$ 0.02	58.5 $\pm$ 1.90	145.5 $\pm$ 7.20	0.082 $\pm$ 0.01	227.21 $\pm$ 11.30
Mean $\pm$ SD Alcohol metabolism induced by 0.5g/kg of <i>C.a.</i> extract	0.048 $\pm$ 0.01	0.087 $\pm$ 0.02	0.110 $\pm$ 0.02	0.085 $\pm$ 0.02	0.055 $\pm$ 0.01	0.026 $\pm$ 0.01	0.112 $\pm$ 0.02	55.75 $\pm$ 1.92	137.0 $\pm$ 3.46	0.088 $\pm$ 0.01	241.10 $\pm$ 6.55

n= 5, values are expressed as mean  $\pm$  SD

BAL= Blood Alcohol Level,  $\beta$ 60= Blood Alcohol disappearance rate (%/h), BEER= Blood Ethanol Elimination Rate (mg/kg/h), *C. a.* = *Cnidoscopus aconitifolius*.

**Table 2: The kinetics of alcohol metabolism induced by oral administration of 1g/kg of *Cnidoscolus aconitifolius* extract in male albino rabbits**

Subjects	BAL After 20m in (%)	BAL After 40m in (%)	BAL After 60m in (%)	BAL After 80m in (%)	BAL After 100m in (%)	BAL After 120m in (%)	Peak BAL (%)	Time to Peak BAL (Min)	Time to Zero BAL (Min)	$\beta 60$ (%/h)	BEER (mg/kg/h)
Mean $\pm$ SD	0.05 6	0.11 6	0.15 5	0.12 9	0.094 $\pm 0.02$	0.061 $\pm 0.01$	0.15 5	59.0 $\pm 1.2$	160 $\pm 5.9$	0.05 8	209.21 $\pm 7.87$
Alcohol metabolism in male rabbits	$\pm 0.0$ 1	$\pm 0.0$ 2	$\pm 0.0$ 2	$\pm 0.0$ 2			$\pm 0.0$ 2	0 0	0 0	$\pm 0.0$ 1	
Mean $\pm$ SD	0.06 0	0.11 0	0.12 7	0.09 3	0.061 $\pm 0.01$	0.029 $\pm 0.01$	0.12 7	57.5 $\pm 1.9$	128. 0	0.09 0	268.10 $\pm 12.84$
alcohol metabolism induced by 1g/kg of <i>C.a.</i> extract	$\pm 0.0$ 1	$\pm 0.0$ 2	$\pm 0.0$ 1	$\pm 0.0$ 2			$\pm 0.0$ 2	2 2	$\pm 6.3$ 3	$\pm 0.0$ 1	

n= 5, values are expressed as mean  $\pm$  SD

BAL= Blood Alcohol Level,  $\beta 60$ = Blood Alcohol disappearance rate (%/h), BEER= Blood Ethanol Elimination Rate (mg/kg/h), *C. a.* = *Cnidoscolus aconitifolius*.

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