



Effects of Antimalarial Herbal Mixture (Abc – 123) on the Liver of Rats

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ABSTRACT

Antimalarial herbal mixture coded ABC – 123 has been used as herbal remedy in Nigeria for years and is claimed to cure malaria without producing any serious adverse effects. The aim of this study was to investigate the effects of antimalarial herbal mixture on the liver of rats. Twenty adult Wistar albino rats (apparently healthy) were divided into four groups of five rats each. ABC – 123 was administered at the dose of 0.5, 1.0 and 2.0 ml/100 g (orally) to groups 1, 2 and 3 respectively, while group 4 was administered 0.5 ml/100 g distilled water. All treatments were once daily for 21 days. On the 22nd day, blood samples were collected for liver enzyme evaluation and the rats were then sacrificed, the livers were collected for histopathological investigation. There was a significant elevation of all the liver enzymes after 21 days of administration. The histopathological investigation revealed a number of toxic effects, including intracytoplasmic vacuolization, intraparenchymal hemorrhage and hepatic necrosis, which are signs of hepatotoxicity in rats. Antimalarial herbal mixture caused a dose dependent hepatotoxicity and is therefore necessary that it should be brought under stringent control by drug regulatory authorities in Nigeria in order to ascertain their effectiveness and safety.

KEYWORDS: Antimalarial herbal mixture, Hepatotoxicity, Rats

INTRODUCTION

Herbal remedy is the major component of traditional medicine that can be subjected to scientific investigation and adaptation [1]. It is through the scientific investigation that many of the first generation plant drugs came to existence [1]. These were usually simple botanicals employed in their more or less crude form and sometimes as food supplements [2]. Several effective medicines used in their natural state such as cinchona, opium, belladonna and aloe were selected as therapeutic agents based on empirical evidence of their clinical application by traditional societies.

The use of ABC – 123 and other herbal remedies for the self treatment of malaria and a wide range of diseases has been increasing progressively all over the world [2]. ABC – 123 consists of dry leaves of two natural herbs namely *Mangifera indica* and *Nuclearlatifolia*, crushed and mixed with water. It is used orally in the treatment of various ailments such as malaria, typhoid and gastrointestinal disturbances. *Mangifera indica* and

Nuclearlatifolia have been traditionally used orally for years for the treatment of malaria, diarrhea or dysentery [3]. The aqueous extract of leaves of *N. latifolia* has been used as remedy for diabetes mellitus in northern Nigeria [4].

ABC – 123, a proprietary product, is one of the numerous non – clinically endorsed herbal remedies in the market and is widely used in Nigeria for a number of diseases particularly claimed to cure malaria without producing any serious adverse effects. Despite this wide spread use and claims, there is no scientific evidence of the effectiveness or safety of ABC – 123 for medicinal purposes. This study reports on acute toxicity studies and the effects of orally administered ABC – 123 on the liver of rats.

MATERIALS AND METHODS

Adult wistar rats of both sexes weighing between 110 – 155 g obtained from the Department of Pharmacology, Animal House, University of Jos,



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were used. The rats were kept in metabolic cages under normal laboratory conditions of 12 hour day – night cycle and temperature of 28 – 32°C to acclimatize to the environment. The rats were fed with standard commercial animal feeds and drank clean water *ad libitum*.

All the animals were handled in this study according to International and Institutional guidelines for animal experimentation and permission for conducting this study was obtained from the Research and Ethical Committee, Department of Pharmacology, University of Jos.

ABC – 123 was obtained from herbalist in Jos, and is said to contain the dry and powdered leaves of *Mangifera indica* and *Nuclear latifolia* mixed with water (identification of the plant materials was by a taxonomist at the Herbarium section in Department of Botany, University of Jos, where voucher specimens were deposited for future reference).

The doses of the herbal mixture administered to rats were calculated using the recommended dose of the herbalist, namely; 350 – 1050 ml daily either once or in two to three divided doses for adult humans. The presumptive human adult weight was taken as 70 kg and the doses to be administered to the rats were calculated using this weight and the mean weight of the rats (100 g).

In the sub acute toxicity studies to determine the effects of ABC – 123 on the liver of rats, twenty rats were divided into 4 groups of 5 rats each. Three groups were administered three different doses (0.5, 1.0 and 2.0 ml/100 g respectively) of ABC – 123 (orally by gastric intubation) once daily for 21 days, which were the equivalents of the minimum recommended dose, maximum recommended dose and double the maximum recommended dose. One of the groups served as control and was administered 0.5 ml distilled water (orally by gastric intubation) once daily for 21 days. At the end of 21 days, blood samples of 5 ml each were collected via cardiac puncture for liver enzyme evaluation. All the rats were then sacrificed by chloroform anesthesia and the livers were collected for histopathological investigation.

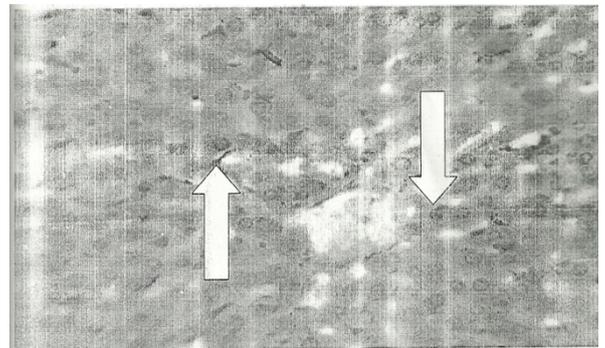
The livers were harvested and stored in 10 % formaldehyde solution. The tissue specimens were dehydrated in alcohol series, processed in xylene and embedded in paraffin. Sections from each specimen were stained with haematoxylin – eosin. All sections were evaluated with Olympus CX21 Binocular light microscope consisting of 4x, 10x, 40x, 100x oil objectives and WF 10x eyepieces at x40 magnification and photomicrographs taken.

The blood samples were collected in plain chemistry bottles, centrifuged and analyzed for the liver enzymes alkaline phosphatase (ALP), aspartate transaminase (AST) and alanine transaminase (ALT), using the acurex chemistry analyzer.

Statistical analysis was by the student t – test, where $P < 0.05$ was considered to be statistically significant. Values were expressed as mean \pm standard error of mean.

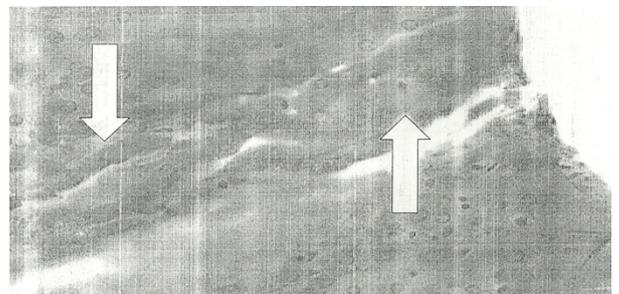
RESULTS

Liver specimens of control group (Figure I showed normal arrangement of hepatocytes) but with the dose of 0.5 ml/100 g ABC – 123 once daily (Figure II showed enlarged nuclei and wider sinusoid), 4 (80 %) had moderate portal triditis and 1 (20 %) did not show any evidence of hepatotoxicity. With the 1.0 ml/100 g once daily (Figure III showed extensive degenerative change of the hepatocytes), 1 (20 %) had portal triditis and 4 (80 %) had extensive hepatic necrosis. With the 2 ml/100 g once daily (Figure IV showed swelling, cytoplasmic granularity and vacuolization), 1 (20 %) had extensive hepatic necrosis and 4 (80 %) had intracytoplasmic



vacuolization.

Figure I: Photomicrograph of liver tissue showing



normal arrangement of hepatocytes

Figure II: Photomicrograph of liver tissue showing enlarged nuclei and wider sinusoid

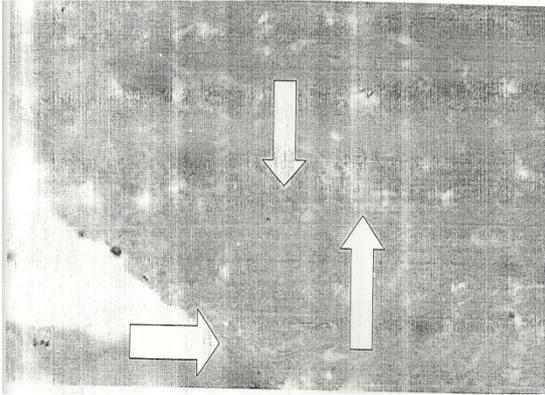


Figure III: Photomicrograph of liver tissue showing extensive degenerative change of the hepatocytes

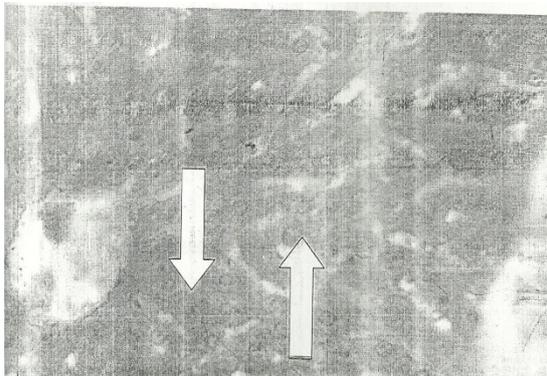


Figure IV: Photomicrograph of liver tissue showing swelling, cytoplasmic granularity and vacuolization

The results of the liver enzyme analysis are summarized in Table I. The table indicates the levels of AST, ALT and ALP at the 3 different dose levels for the 21 days administration of ABC – 123 in rats as being compared with levels of these enzymes in the control group.

Table I: Liver enzyme values of rats administered ABC – 123

Dose of ABC – 123 (ml/100 g)	ALT (IU/L)	AST (IU/L)	ALP (IU/L)
Control	52.88 ± 1.86	27.00 ± 2.31	203.50 ± 4.48
0.5	71.68 ± 12.77*	33.00 ± 14.00	458.25 ± 78.01*
1.0	73.10 ± 10.20*	61.75 ± 12.27*	576.00 ± 19.67*
2.0	86.73 ± 7.14*	89.00 ± 19.63*	740.00 ± 104.00*

(P < 0.05)* is statistically significant when compared with the control

The elevation of liver enzymes among the groups administered ABC – 123 were significantly different from the control group after 21 days at all the three doses except 0.5 ml/100 g for AST level. It is noteworthy that graded increase in all the liver enzymes was observed in all the treated groups as the dose increased.

DISCUSSION

The study demonstrated that ABC – 123 can induce hepatotoxicity, which was evidenced by both elevated liver enzymes in blood and histopathological changes in the liver. Analysis of the liver enzyme levels is the most common method of estimating liver damage. Several enzymes can be used, however, the AST, ALT or ALP are those usually employed.

Alkaline phosphatase is secreted into the bile of the liver, and its serum concentration increase substantially with mild intra hepatic or extra hepatic biliary obstruction but in normal liver, serum concentration is low [5]. AST serum levels are used to diagnose and assess the prognosis of liver damage resulting from hepatocellular damage but it is not specific to the liver. ALT are enzymes present in the hepatocytes and are said to be parallel to AST in liver damage but ALT is more specific to the liver than AST. Elevation of ALT levels often suggests the existence of other medical problems such as viral hepatitis, liver damage and biliary duct problems [5].

In the current study, liver enzymes (ALT, AST and ALP) were elevated following the administration of ABC – 123 at all 3 doses. This elevation occurred in a dose – dependent manner for all the liver enzymes. The continued rise in liver enzyme levels may be due to portal triditis induced by the mixture or bile duct dilation which is known to cause cholestasis [6]. Similarly, the development of hepatic necrosis can lead to liver failure [6]. Hepatic necrosis is possibly due to pro – oxidant effect of ABC – 123.

The mechanism of toxicity might, therefore, be due to induction of oxidative stress [7], thus the need to test for anti – oxidant effect of this mixture, although some studies have shown that anti – oxidant like vitamin E has opposing effects at different concentrations [8].

ABC – 123 caused a statistically significant elevation of liver enzymes which was dose dependent for ALP, AST and ALT. Mild to moderate hepatotoxic effects without liver damage such as portal triditis were common and severe

hepatotoxicity characterized by hepatic necrosis appears to occur in a dose dependent manner.

CONCLUSIONS

Based on the observed toxic effects on the liver of rats, it is necessary that this antimalarial herbal mixture should be brought under stringent control by drug regulatory authorities in Nigeria in order to ascertain their effectiveness and safety.

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