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# The role of Gongronema latifolium in Attenuation of chloroquine induced nephrotoxicity and hepatoxicity

**Nnodim Johnkennedy., Uduji Helen Ifeoma and Uduji Godwin Obinna**

*Dept of medical laboratory science, faculty of health science, Imo State University owerri, Imo State, Nigeria and Department of public Health Federal University of Technology Owerri,Imo State Nigeria*

**ABSTRACT**

**Objective**: The attenuated effect of *Gongronema latifolium* against chloroquine induced nephrotoxicity and hepatoxicity was investigated in wistar rats. **Methods**: Twenty wistar rats were divided into 4 groups of 5 rats per group. Animal in group one served as control while animal in group 2, 3 and 4 received single oral administration of chloroquine (970mg/kg body weight). However experimental group 3 and 4 were additionally treated with 250mg /kg and 500mg/kg body weight of leaf extract of *Gongronema latifolium* respectively. The treatment lasted for 14days. **RESULTS:** The results obtained showed that the serum urea and creatinine significantly increased in group 2 than in group 1, but significantly reduced in group 3 and 4 when compared with group 2 ($P<0.05$). On the other hand, serum bilirubin, AST, ALT, and ALP levels were significantly increased in group 2, when compared with the control. However, the level of serum bilirubin, AST, ALT, and ALP levels dropped marginally in group 3 and 4. **Conclusion**: This observation probably implies that the leaf extract of *Gongronema latifolium* attenuated the nephrotoxicity and hepatoxicity induced by chloroquine. Hence the use *Gongronema latifolium* could be helpful to patients with liver and kidney derangement.

***Key words:*** chloroquine, nephrotoxicity,hepatoxicity, *Gongronema latifolium*

## Introduction

Chloroquine is a member of an important series of chemically related anti malarial agents, the quinolone derivatives. Being a 4-aminoquinoline, it is a rapidly acting blood schizontocide with some gametocytocidal activity(Ekanem *et al*, 1990). It is a synthetic drug for effective treatment of malaria and the anti malarial drug of choice for many years in most parts of the world. In malaria endemic regions like south eastern part of Nigeria, where *Plasmodium falciparum* is sensitive to chloroquine, the drug is still useful for the treatment and prophylaxis of the infection, in spite of increasing prevalence of resistance of the parasite to the drug (Sowunmi *et al*, 2000; Pari and Amali, 2005 ). However, chloroquine treatment is often accompanied by serious side effect such as headache and visual disturbances. It has been reported to cause hepatic damage (Pari and Murugavel, 2006). The free radicals have been implicated in many diseases including nephrotoxicity and hepatotoxicity (Nnodim *et al*, 2010). Experimental, clinical and epidemiological studies have provided evidence in support of the role of free radicals in the etiology of hepatotoxicity by anti malaria drugs (Ali *et al*, 2001; Nnodim *et al,* 2012a). When produced in excess, free radicals cause tissue injury. However, the natural antioxidants defense mechanisms can be inadequate and therefore some herbal plant can be of great importance. One of such plants is *Gongronema latifolium* This plant *Gongronema latifolium* is locally called "utazi by Igbos, "arokeke" by Yorubas, and Utasi" by the Efiks and Ibiobios in Nigeria*. Gongronema latifolium* belongs to the family of Asclepiadacae. It is an edible rainforest plant native to the South East part of Nigeria and has widely used in folk medicine (Nnodim *et al,* 2012b). It is a herbaceous shrub with yellow flowers and the stem that yields characteristic milky exudates when cut. Some phytochemicals such as β – sistosterol, lupenyl esters, Pregnance ester, glucosides, essential oils and saponins are associated with parts of this herb (Edet *et al*, 2009). Gongronema latifolium which has been used in traditional medicine for treating diabetes, malaria, hypertension and as laxative. Also used as a spice and vegetable (Morebise *et al*, 2002; Ugochukwu *et al*, 2003).

Since this plant has been described to be beneficial, the present study investigates the protective attenuation role of G latifolium in chloroquine induced nephrotoxicity and hepatotoxicity as there have been relatively few studies on this model.

## Materials and Methods

*Plant materials*. The *Gongronema latifolium* leaves were obtained from Ekeonunwa market in Owerri Nigeria. The botanical identification and authentication was confirmed by Dr. C. Okere (Head of Department of Plant Science and Biotechnology, Imo State University,Owerri). The plant material was sun dried for seven days.The dried leaves of *Gongronema latifolium* were milled to get a fine powder. The appropriate

**Corresponding Author:** Nnodim Johnkennedy, Dept of Medical Laboratory Science, faculty of health science, Imo State University Owerri, Imo State, Nigeria
E-mail: johnkennedy23@yahoo.com Tel:+2348034237000

concentrations of the extract were made in distilled water for the experiment. Hence,the following concentrations: 250mg and 500mg were prepared.

*Drugs:*

Chloroquine (Emzor) was purchased from a standard pharmacy shop in Owerri, Imo State Nigeria. The tablets were dissolved in distilled water according to the required concentrations required for administration to the Wistar rats on the basis of their body weight.

*Experimental Animals:*

The Wistar albino rats weighing between 170 and 220g, ages (8-10 weeks) were used in the study. These animals were obtained from the Animal House of College of Medicine and Health Sciences, Imo State University, Owerri Nigeria. They were kept under standard laboratory conditions, fed with commercial growers mash, product of Tops Feeds Ltd, Sapele, Nigeria. Water and feed were provided *ad libitum.* The animals were left for two weeks to acclimatize and then divided into groups for experimentation.

*Experimental Design:*

The animals were randomly assigned to four experimental groups (n = 5 x 4group). The first group of animals which served as control was given distilled water. Group II, III and 1V were given chloroquine (970mg/kg body weights), chloroquine and G latifolium extract (250mg/kg body weight), chloroquine and G latiolium extract (500mg/ kg body weight) respectively for 14 days. In all groups the drug was administered through oral route using a feeding tube attached to a 5ml syringe. All animals were allowed free access to food and water throughout the experiment.

*Blood Collection:*

Twenty four hours after the last doses were administered, the animals were anaesthetized with chloroform vapor, quickly brought out of the jar and sacrificed. Whole blood was collected by cardiac puncture from each animal into clean dry test tubes. The blood was allowed to stand for about 15 minutes to clot and further spun in a Westerfuge centrifuge (model1384) at 10,000g for 5 minutes. Serum was separated from the clot with Pasteur pipette into sterile sample tubes for the measurement of the biochemical parameters.

*Biochemical Analysis:*

Serum urea and creatinine were measured using standard method(Cheesbrough,2000).Serum AST and ALT were assayed by the method of Reitman and Frankel(1957). ALP was determined by the method of king and king (1954). Also, serum bilirubin was determined by the method of Jendrassik and Groff(1938).

*Statistical analysis:*

The results were expressed as mean ± standard deviation. The statistical evaluation of data was performed by using one-way ANOVA (Analysis of variance) followed by Duncan's multiple range test [16].

*Results:*

**Table 1:** Effect of G. latifolium on chloroquine induced nephrotoxicity

| Group | Treatment | urea(mg/dl) | creatinine(mg/dl) |
|---|---|---|---|
| 1 | Control | 19.2 ±4.1 | 0.6 ±0.02 |
| 2 | Chloroquine | 39.97 ±4.7 * | 1.8 ±0.03* |
| 3 | Chloroquine+G.L250mg | 27.43±6.2 * | 1.41±0.03* |
| 4 | Chloroquine+G.L500mg | 22.59±6.0* | 1.10±0.02* |

*Significantly different from control (P<0.05)

**Table 2:** Effect of G. latifolium on chloroquine induced hepatoxicity

| Group | Treatment | AST(iu/l) | ALT(iu/l) | ALP(iu/l) | Bilirubin(mg/dl) |
|---|---|---|---|---|---|
| 1 | Control | 14.2 ±2.1 | 13.11±2.8 | 66.22±9.02 | 0.6± 0.02 |
| 2 | Chloroquine | 33.27±3.1* | 24.31± 2.9 | 93.8 ±8.73* | 1.9 ±0.02 * |
| 3 | Chloroquine+G.L250mg | 24.93±3.6* | 21.42 ± 3.4* | 85.71±8.03* | 1.42±0.04 * |
| 4 | Chloroquine+G.L500mg | 20.37±3.0* | 17.51± 3.0 | 79.43±6.10* | 1.20±0.04* |

*Significantly different from control (P<0.05)

*Discussion:*

The commonest biochemical parameters regarded as indicators of liver damages are AST, ALT, ALP and bilirubin while urea and creatinine are important renal indicator for kidney damage. The damage to the hepatocelluar cells and renal cells resulted in the increase in these biochemical parameters (Nwanjo *et al*, 2007; Nnodim *et al*, 2012c). In this study, chloroquine administration in the dose of 970mg/kg body weight of rats results in increase serum bilirubin,AST, ALT, ALP and activities as well as urea and creatinine. The increase is roughly proportional to the extent of liver enzymes in serum following anti malaria administration as has been earlier reported (Nwanjo and Oze, 2009). The liver and renal cell damage may be associated with the generation of reactive oxygen species(ROS) by chloroquine overdose which are also partly responsible for their anti malaria effects, hence the harmful effects were considered to be caused by ROS produced during peroxide formation (Valko *et al*, 2007; Nnodim *et al,* 2012d). The level of hydroxyl and peroxide radical induced by chloroquine treatment may be responsible for the hepatic and renal impairment in Wistar rats (Iniaghe, *et al*, 2008). The observed increased in enzyme activities may be probably due to a leakage of cytoplasmic enzyme into circulation as a result of inflammation of the liver cells. However, the simultaneous administration of G. latifolium along with CQ significantly reduced the effect of chloroquine by lowering bilirubin,AST, ALT and ALP activities as well as urea and creatinine. In the same vein, significantly increased serum bilirubin concentration in group 2 was significantly reduced on the administration of G latifolium when compared. This result suggests that G latifolium offer attenuation effect by preserving the structural integrity of renal and hepatocelluar membrane against chloroquine.

In conclusion the present investigation indicates that Gongronema latifolium exerted significant protection against chloroquine induced nephrotoxicity and hepatoxicity

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