# Blood Urea Reducing Effects of Ethanolic Extracts of Yellow Monkey Kola Fruit (Cola *Lepidota*) Seeds on Ibuprofen-Induced Hyperuremia in Albino Rats.

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***Abstract-*** ***Plants are the richest sources of drugs used in traditional medicine, modern medicines, nutraceuticals, food supplements, pharmaceutical intermediates, and chemical entities for synthetic drugs. There has been a problem over the years in obtaining a stable treatment and management regimens for renal diseases using traditional medicines. Blood urea-reducing effects of yellow Monkey kola (Cola lepidota) seed ethanolic extract on ibuprofen-induced hyperuremic rats were studied. Albino rats weighing between 200 to 206 g were investigated in groups using 200 - 800 mg/kg weight of yellow Monkey kola seed extract and the sample was examined for serum urea using Randox diagnostic kits and statistically analyzed using statistical package for social science (SPSS) windows, version 20.0. The results were expressed as the Mean ± SD. The results for the serum urea concentrations of untreated diabetic rats, and treated rats showed a significant ($P < 0.05$) progressive decrease from 200 - 800 mg/kg when compared to the control rats. This study confirms the hypouremic effects of yellow Monkey kola (Cola lepidota) seed extract. The reduced serum urea concentration could be attributed to the nephroprotective activities of the rich flavonoids content in yellow Monkey kola seed extract (Vargas et al., 2018) and also due to the high fiber and low carbohydrate contents in yellow Monkey kola seed extract. Based on this, it is recommended that further studies be conducted to authenticate the pharmacodynamic pathways by which yellow Monkey kola seed extract reduces urea levels.***

***Indexed Terms-*** ***Uremia, Hyperuremia, Yellow Monkey Kola, Renal Diseases, Ibuprofen.***

## I. INTRODUCTION

One of the clinical conditions associated with renal dysfunction is uremia. It is the term for high levels of urea above 40 mg/dl, leading to renal failure [1]. Urea is one of the major chemical substances found in urine and it is formed via the urea cycle from ammonia [4]. It is the end product of protein metabolism. In clinical practice, one of the indicators of renal function is blood urea and its normal level ranges from 20 to 40mg/dl [11, 22]. Hyperuremia occurs when renal function is compromised. Serum urea is increased in all forms of kidney diseases, most especially in acute glomerulonephritis, chronic nephrosis, and chronic pyelonephritis. One of the causes of increased blood urea is the intake of excess or overdose of nonsteroidal anti-inflammatory drugs (NSAIDs) like ibuprofen [22]. NSAIDs have been observed to impede prostanoid-regulated mechanisms that affect the blood vessels within the nephrons of the kidney, hence lowering the glomerular filtration rate. Ibuprofen toxicity may increase the risk of acute kidney injury due to decreased renal blood flow [17].

Uremia is associated with serious alterations in fluid, electrolyte, and hormonal imbalances and metabolic disorders, which develop with a high risk of renal dysfunction [22]. Some of the common symptoms of uremia as stated by Meyer and Hostetter [10] and Zemaitis et al. [22] are nausea, vomiting, fatigue, anorexia, muscle cramps, pruritus, coma, oxidative stress, seizures, and others. Among the metabolic effects of uremia, insulin resistance, and oxidative stress are the most common. Insulin resistance is a key contributor to progressive vascular disease, which is a major cause of death in patients with kidney failure [10, 16, 18].

Monkey kola is a common name used to identify some minor relatives of the Cola species that produce ripe juicy fruits [7,13]. Yellow Monkey kola fruit (Cola lepidota) is mostly consumed by native people of southern Nigeria and the Cameron, as well as some wild primate animals especially monkeys, baboons, and other species [2, 9, 13]. The medicinal importance of the seed of Monkey kola (*Cola lepidota*) is based mainly on the phytochemical components of the plants such as tannins, terpenoids, flavonoids, phenols, coumarins, and anthocyanins [14], out of which flavonoids have been observed earlier to be the most abundant [6]. The high fiber and low carbohydrate obtained in Monkey kola can play a key role in the diets of diabetic and hypertensive patients [6]. Monkey kola seed has been reported to have substantial amounts of minerals like iron, zinc, and copper; B vitamins, and vitamin C [6]. The seed of yellow Monkey kola fruit (Cola lepidota) has been observed to have hypolipidemic effects [5].

There is no or insufficient knowledge about blood urea-reducing effects of ethanolic extracts of yellow Monkey kola fruit (Cola lepidota) seeds on ibuprofen-induced acute uremia in albino rats, hence the aim of the study is to ascertain the antiuremic effects of ethanolic extracts of yellow Monkey kola fruit (Cola lepidota) seeds on ibuprofen-induced acute uremia in albino rats.

## II. MATERIALS AND METHODS

### 2.1. Laboratory Animals

Sixty male 10 - 15 weeks old albino wistar rats with a weight range between 200 to 206 g were purchased from the Animal house of the University of Port Harcourt, Nigeria. The animals were kept in cages to acclimatize at temperatures between 25˚C - 27˚C and adequate ventilation was given for three weeks and fed with their normal feeds and clean water ad libitum. They were handled in line with the university's ethics on animal handling.

### 2.2. Preparation of Ethanolic Extract of Yellow Monkey kola seeds

Fresh Yellow Monkey (Cola lepidota) fruits (6 kg) were purchased from Oil mill market, Aba road, Port Harcourt, Rivers State, Nigeria. The extraction methods used were the modified method of Sofowora [19]. In the ethanolic seed extraction process, the fleshy mesocarp of yellow monkey kola was removed, exposing the seed. The seed was removed, washed, cut into pieces, and air dried for about 24 hrs at 30˚C room temperature. The dried seed pellets were ground to a fine powder using an electric blender and sieved with a 10-um sieve. 100 g of the powder was soaked in 150 ml of 96% ethanol for three days in a clean and sterilized 200 ml conical flask. The flask was shaken vigorously from time to time and then left to stand at room temperature for 72 hours. The resultant mixture was then filtered with Whiteman's No. 1 filter paper and sterile cotton wool to remove tiny particles. The solution was then dried at 65˚C using the water bath. The semisolid concentrations of the extracts were collected in sterile pre-weighed screw-capped bottles and labeled accordingly and refrigerated at 4˚C to avoid degradation when the extract was not used immediately, following the procedures stated by Parekhi et al. [15].

Figure 1. Monkey kola fruit – yellow type (Cola lepidota)

### 2.3. Induction of Acute Uremia

Ibuprofen was purchased from Qualikems Laboratory Reagents, Saint Louis, USA. A single dose of freshly prepared ibuprofen dissolved in 2.5 ml of distilled water was injected intra-peritoneally at a dose of 50 mg/kg body weight into eighty rats. After 72 hrs, a blood sample was collected by tail vein tapping, and blood urea was monitored. Rats that had blood urea levels above 40 mg/dl were considered hyperuremic and selected for the study.

### 2.4. Experimental Animal Grouping

Fifty rats that have blood urea concentration levels above 30 mg/kg body were selected and divided into six groups of 10 rats in addition to the normal rats (control) as follows:

1) Group one consisted of normal rats (control) that received their normal feeds and water ad libitum.
2) Group two consisted of untreated uremic rats that received their normal feeds and water ad libitum.
3) Group three consisted of uremic rats treated with 200 mg/kg weight of yellow Monkey kola seed extract.
4) Group four consisted of uremic rats treated with 400 mg/kg weight of yellow Monkey kola seed extract.
5) Group five consisted of uremic rats treated with 600 mg/kg weight of yellow Monkey kola seed extract.
6) Group six consisted of uremic rats treated with 800 mg/kg weight of yellow Monkey kola seed extract.

2.5. Sample Collection

After the administration of the last dose of the yellow Monkey kola (Cola lepidota) seed extracts, rats were fasted overnight and anesthetized with ethyl ether, and sacrificed. Whole blood was collected by cardiac puncture into plain centrifuge tubes and was allowed to clot and then centrifuged at 3000 rpm for 5 minutes to obtain the serum that was used for the estimation of blood urea.

2.6. Sample Estimation

Estimation of blood urea was in line with Ochei and Kolhatkar's [12] methods using Randox diagnostic kits.

2.7. Statistical Analysis

Statistical analysis was performed on the statistical package for social science (SPSS) windows, version 20.0 test of significance was determined using the student "t" test, and the statistical significance was set at $P < 0.05$. The results were expressed as the Mean ± SD.3. Results

## III. RESULTS

Table 1. Groups of rats and concentrations of blood urea

| Group of rats | Blood Urea (mg/dl) |
|---|---|
| Controls | 18.40 ± 0.31 |
| Untreated uremic rats | 42.02 ± 0.31 |
| 200 mg/kg body weight of rats | 38.28 ± 1.44 |
| 400 mg/kg body weight of rats | 36.03 ± 1.62 |
| 600 mg/kg body weight of rats | 32.22 ± 2.01 |
| 800 mg/kg body weight of rats | 29.77 ± 1.58 |

The results presented in Table 1, showed that there was a progressive decrease in the urea concentrations in a dose-dependent manner. There was a progressive decrease in the urea concentrations of treated uremic rats with increased concentrations of the yellow monkey kola seed extracts compared to the controls and the untreated uremic rats respectively. The higher the dosage, the higher the decrease in serum urea concentrations.

## IV. DISCUSSION

The serum urea concentration of treated uremic rats was significantly reduced ($P > 0.05$) compared to the serum urea concentration of untreated uremic rats and that of the controls. The reduced serum urea concentration could be attributed to the nephroprotective activities of the rich flavonoids content in yellow monkey kola seed extract [20]. The reduced blood urea concentration may be due to the high fiber and low carbohydrate reported to be present in monkey kola by Ene-Obong et al. [6], which can play a significant role in the diets of diabetic and hypertensive patients.

MacDonald et al. [8] and Cheng et al. [3] independently pointed out that high dietary fibre and low carbohydrates have a significant effect on mucosal insulin binding receptors, hence decreasing insulin resistance through a complex biochemical mechanism. This implies that the ethanolic extract of Cola lepidota seed caused the reduction of the metabolic effect of urea, which is the progressive decrease in insulin resistance, leading to improved kidney function.

## CONCLUSION

C. lepidota seed could serve as a drug and food to both man and animals since it contains rich nutrients and

high phenolics. The result of the study revealed that there is a significant decrease in urea concentrations in rats treated with yellow monkey kola seed extract, confirming the hypouremic activities of yellow monkey kola seed extract and its potency to protect the kidney. In search for non-conventional oral hypouremic agents that will not only restore normal urea levels but also reduce the extent of complication associated with the traditional drugs, the yellow monkey kola (Cola lepidota) seed extract should be an alternative.

It is therefore, recommendable that further studies are required to authenticate the pharmacodynamics pathway by which yellow monkey kola seed extract reduces urea levels.

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