INTRODUCTION

Plants, either as traditional preparations or pure active principles, have always been among the common sources of medicines [1]. Over 5000 plants are known to be used for medicinal purposes in Africa, but only a few have been studied [2]. A great number of Nigerian higher plants are traditionally noted for their medicinal properties, but regrettably only few have so far been studied for their active constituents. The use of herbal remedies can be attributed to their perceived efficacy and the fact that they are a cheap source of medicines [3].

There is an assumption that that the use of plants in traditional medical practice for treatment of various ailments is harmless and safe because they are derived from natural sources [4]. This assumption is based on the common belief that herbs are by nature safer and gentler than orthodox drugs and plant-based medicine have been used in the treatment of diseases over many centuries [5]. However, herbal preparations assumed to be safe may contain contaminants such as pathogenic microbes, heavy metals and aflatoxins due to the manner in which they are prepared [6]. Moreover, many studies have reported various toxic effects of herbal medicines, such as hepatotoxicity [7] and nephrotoxicity [8].

*Cinnamonum verum*, called "true cinnamon", Ceylon cinnamon or Sri Lanka cinnamon is a small evergreen tree belonging to the family Lauraceae, native to Sri Lanka. Among other species, its inner bark...
Cinnamon’s unique healing abilities come from three basic types of components in the essential oils found in its bark. These oils contain active components called cinnamaldehyde, cinnamyl acetate, and cinnamyl alcohol, plus a wide range of other volatile substances [10]. Cinnamomum verum reported to possess Anti-Microbial Activity [11], hypoglycemic activity [12], Cinnamon’s Scent Boosts Brain Function [13] and Antioxidant [14]. In addition to the active components in its essential oils and its nutrient composition, cinnamon has also been valued in energy-based medical systems, such as Traditional Chinese Medicine, for its warming qualities. In these traditions, cinnamon has been used to provide relief when faced with the onset of a cold or flu, especially when mixed in a tea with some fresh ginger [15].

Therefore, the current study was aimed at investigating the phytochemical composition, and determining the acute (LD₅₀) and sub-chronic toxicity of the aqueous stem bark extract of Cinnamomum verum in albino rats.

MATERIALS AND METHODS
Collection and preparation of plant material
Cinnamomum verum bark was bought from Kurmi market Kano. It was made into powder and 500 g was soaked in 5 litres of distilled water, and vigorously shaken, for 48 hours, at room temperature. The mixture was filtered with muslin cloth and later with Whatman Number 1 Filter Paper. The filtrate (extract) was concentrated to dryness in an oven at 45°C. Percentage yield was calculated, and the extract was stored in a plastic container until required. The dried extract was reconstituted in distilled water; the volume administered to each rat was calculated according to Muhammad et al [16].

Phytochemical screening
Phytochemical tests were carried out by using the standard methods of Harborne [17], Sofowora [18], Trease and Evans [19], Kokate [20], Rasal [21] and Savithramma et al [22].

Animals
Twenty eight wistar albino rats of both sexes, weighing 100-150 g, were obtained from Department of Physiology, Bayero University Kano, Nigeria. They were kept, at room temperature, in wire-mesh cages, to acclimatise for 1 week. They were fed with animal feeds (Vitalised Feeds, Jos, Nigeria), and tap water ad libitum.

Lethal mean dose (LD₅₀) determination
Twenty eight rats were used in this study, thirteen for acute toxicity test and fifteen for sub chronic toxicity. The acute toxicity study was done in two phases; in phase I, nine rats were divided into three groups of three rats each and were administered the aqueous bark extract of Cinnamomum verum at different doses of 10, 100 and 1000mg/kg body weight orally. The rats were observed for mortality and general behaviour for 24hrs. In phase II, four rats were administered with aqueous bark extract of Cinnamomum verum at higher doses of 1500, 2500, 3500 and 5000mg/kg and were observed for mortality and other signs of toxicity for 24hrs.

Sub-chronic toxicity studies
For the sub chronic toxicity experiment, fifteen rats were divided into five groups of three rats each. Group I was the control group, groups II to V were orally administered 50, 100, 150 and 200mg/kg of aqueous bark extract of Cinnamomum verum, respectively for four weeks. On the 29th day, weight was taken, and the rats were humanely sacrificed. Blood samples were taken in plane containers, for biochemical analysis. Analysis was performed on sera obtained after centrifugation of the whole blood. Standardized diagnostic kits (Labkit®) (Randox) and Teco diagnostic kits were used for spectrophotometric determination of biochemical parameters.

STATISTICAL ANALYSIS
Results were expressed as mean ± standard error. The data collected were subjected to one-way Analysis of Variance (ANOVA) using Graphad Instat, Version 3.02, Benferoni, (San Diego, USA) [23].

RESULTS
Various phytochemical constituents from aqueous bark extract of Cinnamomum verum such as saponins, reducing sugars, alkaloids, tannins, flavonoids, steriods, coumarins, resin were detected as shown in table1. The Quantitative analysis showed that the extract has high concentration of saponins (1.998±0.04) followed by reducing sugars (1.099±0.01) then cardiac glycosides (0.646±0.06 ), tannins (0.200±0.03) and flavonoids (0.094±0.01).
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Table-1: Phytochemical Screening of aqueous bark extract of Cinnamomum verum

<table>
<thead>
<tr>
<th>Constituents</th>
<th>Inference</th>
<th>Content (g%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saponins</td>
<td>+</td>
<td>1.998±0.04</td>
</tr>
<tr>
<td>Flavonoids</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Flavonoids</td>
<td>+</td>
<td>0.094±0.01</td>
</tr>
<tr>
<td>Reducing Sugars</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Resins</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Coumarins</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Tannins</td>
<td>+</td>
<td>0.200±0.03</td>
</tr>
<tr>
<td>Steroids</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

Key: (+) = Present (-) = Absent

Acute Toxicity Test

In the initial phase of the determination of acute toxicity, mortality and toxic symptoms were not observed when the aqueous bark extract of *Cinnamomum verum* was administered orally to the experimental rats (Table 2a). In the second phase, no mortality was observed although some rats exhibited symptoms of weakness (Table 2b).

Table-2a: Phase I LD<sub>50</sub> (oral, rat) of the aqueous bark extract of *Cinnamomum verum*

<table>
<thead>
<tr>
<th>Doses (mg/kg)</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>0/3</td>
</tr>
<tr>
<td>100</td>
<td>0/3</td>
</tr>
<tr>
<td>1000</td>
<td>0/3</td>
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</tbody>
</table>

Table-2b: Phase II LD<sub>50</sub> (oral, rat) of the aqueous bark extract of *Cinnamomum verum*

<table>
<thead>
<tr>
<th>Doses (mg/kg)</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1500</td>
<td>0/1</td>
</tr>
<tr>
<td>2500</td>
<td>0/1</td>
</tr>
<tr>
<td>3500</td>
<td>0/1</td>
</tr>
<tr>
<td>5000</td>
<td>0/1</td>
</tr>
</tbody>
</table>

Sub chronic toxicity studies

Table 3 present liver function indices of rats administered with aqueous extract of *Cinnamomum verum*. The Mean serum Alkaline phosphatase (ALP), Alanine amino transferase (ALT), Aspartate amino transferase (AST) and Total protein (TP) activities of the rats administered with the aqueous bark extract of *Cinnamomum verum* were found to decrease significantly (p<0.05) (table 4), while serum Total Bilirubin and Albumin increased significantly (p<0.05) with respect to control group.

Table 3: Mean Serum Liver Enzymes, Bilirubin, Albumin and Total Proteins of rats administered with aqueous bark extract of *Cinnamomum verum* for 4 weeks.

<table>
<thead>
<tr>
<th>Grouping/Dose</th>
<th>AST(U/L)</th>
<th>ALP(U/L)</th>
<th>ALT(U/L)</th>
<th>TB(U/L)</th>
<th>ALB(g/dl)</th>
<th>TP(g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1(Normal)</td>
<td>88.50±1.23&lt;sup&gt;a&lt;/sup&gt;</td>
<td>90.46±6.13&lt;sup&gt;b&lt;/sup&gt;</td>
<td>25.91±0.70&lt;sup&gt;c&lt;/sup&gt;</td>
<td>15.70±1.05&lt;sup&gt;d&lt;/sup&gt;</td>
<td>2.89±0.07&lt;sup&gt;e&lt;/sup&gt;</td>
<td>5.49±0.14&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>G1I (50mg)</td>
<td>87.47±1.27&lt;sup&gt;c&lt;/sup&gt;</td>
<td>89.93±5.22&lt;sup&gt;b&lt;/sup&gt;</td>
<td>21.43±0.07&lt;sup&gt;d&lt;/sup&gt;</td>
<td>18.27±0.53&lt;sup&gt;c&lt;/sup&gt;</td>
<td>3.67±0.29&lt;sup&gt;d&lt;/sup&gt;</td>
<td>4.40±1.04&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>G1II (100mg)</td>
<td>84.87±5.45&lt;sup&gt;c&lt;/sup&gt;</td>
<td>85.13±2.93&lt;sup&gt;b&lt;/sup&gt;</td>
<td>21.08±1.99&lt;sup&gt;d&lt;/sup&gt;</td>
<td>19.23±3.64&lt;sup&gt;c&lt;/sup&gt;</td>
<td>4.13±0.20&lt;sup&gt;d&lt;/sup&gt;</td>
<td>4.37±0.25&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>G1III (150mg)</td>
<td>84.53±5.37&lt;sup&gt;c&lt;/sup&gt;</td>
<td>83.57±4.13&lt;sup&gt;c&lt;/sup&gt;</td>
<td>17.23±0.45&lt;sup&gt;d&lt;/sup&gt;</td>
<td>19.76±0.31&lt;sup&gt;c&lt;/sup&gt;</td>
<td>4.63±0.60&lt;sup&gt;d&lt;/sup&gt;</td>
<td>4.03±0.17&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>G1IV (200mg)</td>
<td>67.8±3.37&lt;sup&gt;c&lt;/sup&gt;</td>
<td>71.23±2.05&lt;sup&gt;c&lt;/sup&gt;</td>
<td>15.83±1.11&lt;sup&gt;d&lt;/sup&gt;</td>
<td>20.77±0.69&lt;sup&gt;d&lt;/sup&gt;</td>
<td>4.53±0.76&lt;sup&gt;c&lt;/sup&gt;</td>
<td>3.37±0.41&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD, n=5. Values with similar superscript on the same column are significant (p < 0.05).

Key: AST= Aspartate amino Transferase, ALP= Alkaline phosphatase, ALT= Alanine amino Transferase, TB= Total Bilirubin, ALB= Albumin, TP= Total protein.

The mean serum levels of sodium (Na<sup>+</sup>), potassium (K<sup>+</sup>), chloride (Cl<sup>-</sup>), Creatinine and Urea of the rats administered aqueous bark extract of *Cinnamomum verum* significantly decreased (p<0.05) when compared to the control group while bicarbonate (HCO<sub>3</sub>–) increased significantly (p < 0.05) (table 4).
ng toxins, which may be cytotoxic or
and ALT) are involved in amino acid metabolism.
enzymes, aspartate and alanine aminotransferases (AST
metabolism of some of the toxic phytochemicals found
many metabolic processes of not
functions in the body, and its disorders are numerous
metabolism, detoxification, and secretory
regulation, inter and intra
studies which reported decreased activity of
sub
higher the activities of both enzymes [32]. The result of
and the greater the degree of the liver damage the
AST are alw
cardiac muscle, and skeletal muscle. Serum ALT and
Large amounts of AST are present in the liver, kidney,
cardiac muscle, and skeletal muscle. Serum ALT and
and uric acid can be used to evaluate the functional
capacity of the nephrons of study animals and are
considered as good indicators of kidney function.
Similarly, the serum concentrations of electrolytes, uric
acid and creatinine could give an insight into the effect
of plant extract on the tubular and or glomerular part of
the kidney. The significant decrease in serum Na⁺, K⁺,
creatinine and urea with significant increase in
serum HCO₃⁻ indicates the beneficial effect of the
extract on kidney which is in accordance with the work of
Rabiatul et al [35].

CONCLUSION
According to the findings of this study, Cinnamomum verum aqueous stem bark extract is rich
in phytochemicals that may be responsible for the
reported pharmacological activities of this plant. It is
also shown that aqueous bark extract of Cinnamomum verum is practically non-toxic, evidenced by high LD₅₀ value with no lethality. It may be considered that the
extract is safe at the tested sub-chronic doses, and well
tolerated for the 28 days study period. Thus, have
potential for safe use as herbal medicine.

REFERENCES
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organs of rats administered subchronic doses of
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