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Review

Potential health benefits and scientific review of ginger

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Ginger has been known for its several scientific properties and valued for the last 2500 years in different parts of the globe. Ginger has rich phytochemistry and several health promoting perspectives. In ginger family, *Zingiber officinalis* is one of most widely used species and it is found in several foods and beverages. Ginger has been used commonly to treat diarrhea, stomach upset, indigestion and nausea. It also has anti-inflammatory and antioxidant properties. Ginger constituents are 80% moisture, 2% protein, 2% fiber, 1% mineral, 0.9% fat, and 12% carbohydrate. The chemistry of ginger is well documented with the respect to the oleoresin and volatile oil. It is concluded that, ginger has potential to treat numerous disorders including cancer due to its anti-inflammatory and anti-oxidant properties. It is also useful in controlling the process of aging. This scientific review favors ginger due to its rich phytochemistry; however, due to some ambiguities, it is recommended to conduct clinical trials of ginger with sound protocol design before claiming its efficacy.

Key words: Ginger, *Zingiber officinalis*, anti-inflammatory, anti-oxidant.

INTRODUCTION

The rhizome of ginger plant has been used as a spice since several years across the globe. It was found that, ginger was one of wildly used herbs in traditional Chinese, Ayurveda, Europe and America (Duke and Ayensu, 1985; Langner et al., 1998; Avato et al., 2000; Duke and Ayensu, 1985; Kapil et al., 1990; Qureshi et al., 1989; Blumenthal et al., 1997; Kamtchouing et al., 2000; Afzal et al., 2011; Grzanna et al., 2005).

The mode of administration of ginger is oral, intra muscular (IM) and topically (Barnes et al., 2002; Yang and Chang, 1988; Chrubasik et al., 2005; Shukla and Singh, 2007). Historically, it has been used to treat nausea, vomiting, rheumatism, baldness, respiratory diseases and bleeding disorders (Young et al., 2006; Suekawa et al., 1984; Newall et al. 1996; Srivastava, 1984; Kim et al., 2005; Kelly et al., 2009).

PROPERTIES OF GINGER

1. Potency: spicy
2. Taste: bitter
3. Properties: light, adhesive and thick

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In 13th century, ginger culinary properties were discovered and soon it was widespread across the globe including Europe and was indicated for several diseases including travel sickness and flatulence. It is cultivated from Asia to Africa and used everywhere as a cooking spice. It is also useful in case of chills. In India, it is widely consumed in dose of 8-10 g as a flavouring agent (Kelly et al., 2009; al-Yahya et al., 1989; Gong et al., 1989; Stewart et al., 1991; Yamahara et al., 1985; Yamahara et al., 1990).

BIOCHEMISTRY OF GINGER

Ginger standards have been well documented in USP (United State Pharmacopoeia) and National formulary. The chemistry of ginger is well documented with the respect to the oleoresin and volatile oil. There is stringent criteria for the usage of medical grade (should contain 1.5% or more volatile oil).

The studies have identified more than 400 different compounds in ginger and major constituents are as follows:

1. Carbohydrates- about 70%
2. Lipid- about 8% which includes free fatty acids.
3. Volatile oils- about 3% consist mainly of the sesquiterpenes, beta-bisabolene
4. In addition, raw fibres, vitamins and minerals are also present in ginger.

Ginger also contains amadaldehyde, paradole, gingerdiols, gingerdiacetates, gingerenones, 6-gingersulfonic acid, diterpense, gingerglycolipids A, B and C (Qian and Liu 1992; Huang et al., 1991; Pecoraro et al., 1998; Anonymous 1997; Frisch et al., 1995).

MATERIALS AND METHODS

The review article was written with help from secondary data analysis. Information on searching databases, various journals, books, articles and key words were used during writing of therapeutic properties of ginger.

THERAPEUTIC PROPERTIES OF GINGER

Cardiovascular effects

Large number of studies showed that the important constituents of ginger namely gingerol and shogaol classes of compounds might have many therapeutic effects including anti-inflammatory, antioxidant, and hypo-cholesterolemic effects.

Ginger enhances blood circulation throughout the body by stimulation of the heart muscle and by diluting circulating blood. This enhances cellular metabolism and helps to relief cramp and tension (Gong et al., 1989; Pecoraro et al., 1998; Frisch et al., 1995; Yamahara et al., 1989; Ernst and Pittler, 2000; Chaiyakunapruk et al., 2006).

Hypotensive effect

There are many studies which prove hypotensive effect of ginger when it was given at 0.3-3 mg/kg. It helps to reduce atrial blood pressure by blocking calcium channel or by acting on muscarinic receptor (Ernst and Pittler, 2004; Portoni et al., 2003; Ozgoli and Goli, 2009; Vutyavanich et al., 2001).

Anti-hypercholesteraemic effect

Ginger extracts interfers with cholesterol biosynthesis leading to decreasing cholesterol levels. Ginger extracts have antilipidemic effects, by reducing thermogenesis and high lipids levels. It also helps to increase serum HDL-cholesterol (Ernst and Pittler, 2004; Portoni et al., 2003; Ozgoli and Goli, 2009; Vutyavanich et al., 2001; Al-Awwadi, 2010; 2013).

Gastrointestinal effect of ginger

Ginger is very useful in the treatment of several gastrointestinal diseases including peptic and duodenal ulcer. Ulcer is generally caused due to imbalance between defensive and offensive factors like acid, pepsin and *Helicobacter pylori*; and in this case, ginger is useful due to its anti-inflammatory properties. Ginger acts and protects gastric mucosa against several ulcerogenic agents. Ginger is also very useful in cases of ulcerogenesis due to its antioxidant activities (Lumb, 1994; Gull et al., 2012; Dugasani et al., 2010; Halvorsen et al., 2002).

Antiemetic effect of ginger

Ginger shows strong antiemetic property by enhancing intestinal motility and inhibiting serotonin receptors. It stimulates peripheral anti-cholinergic and ant-histaminic receptors and antagonises 5- hydroxytreptamine receptors in the GIT (Lumb, 1994; Gull et al., 2012; Dugasani et al., 2010; Halvorsen et al., 2002).

Ginger anti-nausea effect due to chemotherapy

Chemotherapy is known to cause severe nausea and vomiting. It has been proved that ginger is effective in

preventing nausea and vomiting caused by chemotherapy. Gingerols the key ingredients responsible for the activity have shown pharmacological effect.

It is also used to treat nausea after surgery and same has been proved in several randomised clinical trials. This effect is seen due to its action on the 5-HT3 receptor (Ajith et al., 2007; Krim et al., 2013; Waggas, 2009; Sabina et al., 2011; Ahmed et al., 2008).

Morning sickness

FDA classifies ginger as safe for the treatment of morning sickness and it is widely used during early pregnancy. It reduces symptoms of morning sickness if same is taken in the recommended amount. The German Commission and Europe does not consider it as safe due to lack of published data (El-Sharaky et al., 2009; Nasri et al., 2013; Ajith et al., 2008 ; El-Abhar et al., 2008; Kyung et al., 2006).

Hematologic (platelets) effects of ginger

Scientific evidence is still pending; however it was found that ginger is having anti-thrombotic and strong anti-inflammatory effect due to increased fibrinolytic activity when same has been taken at about 5 g. It was found that Gingerols and Paradol have good anti-platelet and COX-I inhibitor properties (Mehdizadeh et al., 2012; Jagetia et al., 2004; Jagetia et al., 2003). The effect of the ginger is different if it is consumed dry or fresh.

Regulation of blood glucose and lipid levels

Ginger is very effective in lowering blood glucose level when same has been taken in dried form. It also decreases cholesterol and triglyceride level. Long term usage helps to increase high-density lipoprotein cholesterol concentrations (Duke and Ayensu, 1985; Afzal et al., 2011; Kim et al., 2007; Li et al., 2012).

Rheumatologic effect of ginger

Ginger exerts its anti-inflammatory effects by the mechanisms which explain the role of inhibition of pre-inflammatory factor like prostaglandin and leukotriene biosynthesis which can decline pain associated with rheumatoid and osteoarthritis. It is having proven history of treatment of rheumatic conditions (Duke and Ayensu, 1985; Avato et al., 2000; Afzal et al., 2011; Ha et al., 2012).

Headache

Ginger is used for the treatment of headache and having good effect on reducing symptoms of pain. This effect is due to reduction in prostaglandin synthesis. It also has been reported that ginger suppresses leukotriene biosynthesis by inhibiting 5- lipoxyganse (Ernst and Pittler, 2004; Nasri et al., 2013; Tjendraputra et al., 2001).

Anti- Inflammatory effect

Ginger is showing anti-inflammatory effect by suppression of PG synthesis and also interference in cytokine signalling (Duke and Ayensu, 1985; Uz et al., 2009; Mahmoud et al., 2012).

Antimicrobial

Due to phenolic compounds, ginger has shown excellent antimicrobial properties and effective in controlling virus, bacteria, fungal disease. In many countries, ginger is used to preserve food (Ernst and Pittler, 2004; Liao et al., 2012; Chen et al., 2009).

Antiviral

Ginger has shown antiviral effect; however, more published literature is needed to prove efficacy (Gong et al., 1989; Ernst and Pittler, 2004; Anonymous, 1997; Ha et al., 2012; Lantz et al., 2007).

Antibacterial

Ginger has shown good antimicrobial effect against both Gram positive and negative bacteria; however, severally, this effect is reduced due to heating (Jagetia et al., 2004; Ha et al., 2012; Tjendraputra et al., 2001; Kubra et al., 2013).

Antifungal

Gingerols and Gingerdiol are the main anti-fungal principles and extract of ginger powder is effective against several antifungal diseases (Ernst and Pittler, 2004; Ramkissoon et al., 2012; Mallikarjuna et al., 2008; Nasri et al., 2013).

Antiparasitic action

Ginger acts as anti-parasitic; study shows the *in vivo* potential of methanolic extract of *Zingiber officinale* in the treatment of trypanosomiasis (Halvorsen et al., 2002; Jagetia et al., 2003; Kubra et al., 2013; Duarte, 2016; Kumar et al., 2015; Choi et al., 2013; Saraswat, 2010; Pushpanathan, 2008).

Antineoplastic

Ginger is a powerful antineoplastic agent. In several studies, extracts of ginger suppress cell proliferation and act against resistance of cancerous cells (Barnes et al., 2002; Newall et al. 1996; Ernst and Pittler, 2000; Nasri et al., 2013; Kumar et al., 2015; Saraswat, 2010).

Antioxidant

Ginger is having powerful antioxidant activity due to its oil which has protective effect on DNA damage. They have demonstrated this effect in many cell culture (Chaiyakunapruk et al., 2006; Ramkissoon et al., 2012; Kabuto et al., 2005; Mahmoud et al., 2012; Al-Awwadi,2010; 2013).

Ginger is a scavenger of free radicals

Ginger oil has scavenging effects due to volatile oils and same has been proved in many studies (Duke and Ayensu, 1985; Avato et al., 2000; Kamtchouing et al., 2000; Kumar et al., 2015; Pushpanathan, 2008).

Lipid peroxidation

Ginger has preventive effect on lipid peroxidation and it inhibits or breaks its chain (Duke and Ayensu, 1985; Afzal et al., 2011; Verma et al., 1993).

Insulin

Studies have suggested that ginger may improve insulin sensitivity in body. The mineral element of ginger is effective for the same (El-Sharaky et al., 2009; El-Abhar et al., 2008; Jagetia et al., 2004; Choi et al., 2013 ; Pushpanathan, 2008).

Anti-ulcerogenic effect of ginger

This has both many benefits and drawbacks. Prostaglandin has been shown to have housekeeping and gastro-protective function by maintaining gastric mucosal integrity (Duke and Ayensu, 1985; Qureshi et al., 1989; El-Sharaky et al., 2009; Ajith et al., 2008; Duarte, 2016).

Modulation of biological activities by ginger

Ginger modulates genetic pathway, acts on tumour suppression of genes and modulates biological Activities (Duke and Ayensu, 1985; Jagetia et al., 2004; Ha et al., 2012; Duarte, 2016).

Therapeutic effects of Zingiber officinale in HCV (hepatitis C virus*)*

Ginger has powerful antiviral effect. It is effective in hepatitis C virus (HCV) infection where viral clearance is affected (Newall et al. 1996; Chaiyakunapruk et al., 2006; Verma et al., 1993; Kubra et al., 2013).

Menstrual cramps (dysmennorhea)

The powerful anti-inflammatory action on prostaglandin synthesis help in menstrual cramps (Halvorsen et al., 2002; Mallikarjuna et al., 2008; Mahmoud et al., 2012; Kubra et al., 2013).

CONCLUSION

This review article is based on current and past research done on the therapeutic effect of ginger for the various indications. It was found that ginger is useful in many acute and chronic conditions such as nausea, vomiting, menstrual cramp, reducing gas, joint pain, asthma, congestive conditions, and as an aphrodisiac.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

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Full Length Research Paper

Assessment of the effect of aqueous leaf extract of cassava (*Mannihot esculenta*) on adult Wistar rats

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This study aimed to explore the effect of aqueous leaf extract of *Mannihot esculenta* on the morphology and histology of the kidney of adult Wistar rats. Three groups of Wistar rats were used. Group A served as the control treated with 0.3 ml of normal saline, while groups B and C served as the experimental groups. Group B and C were treated with aqueous extract of *M. esculenta* orally at 0.2 and 0.5 ml, respectively for 14 days. At the end, the animals were sacrificed and the kidneys were processed for routine histology. From the results obtained, significant decrease in body weight of the rats treated with 0.5 ml and significant increase in the weight of the rats treated with 0.2 ml of the extract as compared to the control group was observed. The kidney section from the control group revealed normal kidney architecture. Low dose group showed hypertrophy of the tubular cells, occlusion of the Bowman's space and edematous glomerulus. High dose group animals revealed dilated convoluted tubules, occluded Bowman's space and glomerular derangement indicating adverse effect of the extract. From the results of this study, it may be concluded that the administration of aqueous extract of *M. esculenta* leaf is toxic to Wistar rats.

Key words: Cassava, Wistar Rat, kidney, Bowmans space.

INTRODUCTION

Medicinal plants have been identified and used from prehistoric times. Plants make many chemical compounds for biological functions, including defense against insects, fungi and herbivorous mammals. Over 12,000 active compounds are known to science. These chemicals work on the human body in exactly the same way as pharmaceutical drugs, so herbal medicines can be beneficial and have harmful side effects just like conventional drugs. However, since a single plant may contain many substances, the effects of taking a plant as medicine can be complex (Atanasov et al., 2015). The compounds found in plants are of many kinds, but most are in four major biochemical classes: the alkaloids, glycosides, polyphenols and terpenes.

Manihot esculenta Crantz is a dicotyledonous plant which belongs to the family, Euphorbiaceae (Madukosiri et al., 2010). Cassava is a vital food crop for more than 600 million people worldwide. It thrives on marginal

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lands, especially in semi-arid tropical and sub-tropical lands that could be the most severely impacted by climate change. Cassava makes up nearly 50% of the diet in parts of sub-Saharan Africa, where populations are projected to increase by more than 120% in the next 30 years (Amanda et al., 2016). Africa produces more than half of the world's cassava-about 86 million tons from over 10 million hectares (International Institute of Tropical Agriculture, 2017). Cassava leaves have been reported to contain alkaloids, flavonoids, tannins, anthraquinones, phlobatinnins, saponins, reducing sugars and anthrocyanosides. Cyanogenic glycosides, lotaustralin and linamarin have been isolated from the fresh leaves of cassava (Ebuehi et al., 2005). The three cyanogenicglucosides, linamarin (2-Dglucopyranosyloxy-2-ethylpropanenitrile), lotaustralin (2R)-2-D-lucopyranosyloxy-2-methylbutyronitrile] and lataustralin (2D)-D-lucopyranosyloxy-2-methylbutyronitrile were derived from valine and isoleucine, respectively (Krieger, 2004; Koch et al., 1992). Studies showed that cassava leaves contain alphacarotene and vitamin C (Miladiyah et al., 2016). *M. esculenta* extract has been used as analgesic (Miladiyah et al., 2016), antihemorrhoid, anti-inflammatory, anti-pyretic, anti-diarrhea and antimicrobial (Popoola et al., 2007) antioxidant and antihelmintic (Jayasri et al., 2011).

The kidneys are two reddish brown organs situated high up on the posterior abdominal wall, one on each side of the vertebral column. Functionally, the kidney affects the formation and secretion of urine, production and secretion of erythropoietin, the hormone responsible for controlling the rate of formation of red blood cells, the hormone responsible for controlling renin, an important enzyme in the control of blood pressure (Gannon, 2014). They also function in the removal of waste products of metabolism and excess of water and salts from the blood and maintain its pH (Guyton and Hall, 2011).

Chronic kidney disease (CKD) is a global health burden with a high economic cost to health systems and is an independent risk factor for cardiovascular disease (CVD) (Nathan et al., 2016). Ten percent of the population worldwide is affected by chronic kidney disease (CKD), and millions die each year because they do not have access to affordable treatment, according to the 2010 Global Burden of Disease Study, chronic kidney disease was ranked 27th in the list of causes of total number of deaths worldwide in 1990, but rose to 18th in 2010 (Jha et al., 2013).

This study aimed to explore the effect of aqueous leaf extract of *M. esculenta* on the morphology and histology of the kidney of adult Wistar rats.

MATERIALS AND METHODS

Experimental animals

Twelve adult Wistar rats weighing about 110 to 150 g were bought from the animal house of the Department of Anatomy, Cross River University of Technology (CRUTECH). The animals were allowed to acclimatize for a period of two weeks before commencement of the treatment. They were housed in cages under standard conditions with 12 h light/12 h dark cycle throughout the duration of the experiment. They were fed with rat chow from Agro Feed Mill Nigeria Ltd and water was provided *ad libitum*.

Extract preparation

Fresh cassava leaves were harvested from Okuku community of Yala Local Government Area of Cross River State, Nigeria. The leaves were verified and authenticated in the Herbarium Unit of Botany Department, University of Calabar. They were plucked and air-dried at a room temperature (27°C for 3 weeks). They were blended to a fine powder using a local mortar and pestle. The blended sample was weighed using digital weighing balance and was 250 g. The aqueous extract was done using water bath extractor. The weight of the extract was 28.7 g. The extract, 28.7 g obtained was stored in the refrigerator for preservation.

Experimental protocol

Then, from the yield of 28.7 g of leaf extract, the stock solution was prepared by dissolving 2 g of the extract in 10 ml of distilled water. The different dosages were calculated based on the body weight of the animals. Every 0.5 ml of the extract administered contained 10 mg/ml of the extract for the high dose, while the 0.2 ml of it contained 4 mg/ml for the low dose. The animals were divided into three groups as follows: Group 1 served as the control group and were fed with distilled water. Group 2 served as the low dose group administered with 0.2 ml of the extract, while group 3 served as the high dose group administered with 0.5 ml of the extract. The extract was administered using the oral route. After 14 days of daily administration of the extract, the animals were sacrificed, kidney harvested and processed for histological observation.

Histological procedure

The harvested rat kidneys were preserved in 5% formaldehyde for 48 h. Then, dehydrated through ascending grades of alcohol, 2 changes of 70, 90%, and absolute alcohol for 1 h in each change. After dehydration, the tissues were cleared in xylene with 3 changes, 1 h in each. The tissues were placed in 2 changes of molten paraffin wax for 20 min each. They were embedded in molten paraffin wax inside the L-shape Leuckhart mould. The blocks were trimmed and mounted on wooden blocks. Serial sections were cut using a rotary microtome at 5 µ thickness. Sections were floated in a water bath to spread out and later picked on albuminized slides and dried on at 52°C. To stain, slides were put in staining racks and placed in staining wells containing xylene to dewax, then they were rehydrated in descending grades of alcohol, absolute alcohol (2 changes, 70% alcohol and then water for 5 min after which they were stained with haematoxyline for 5 min. Excess haematoxylin was washed off with water and differentiated with 1% acid alcohol. Sections were counter stained with 1% eosin and washed off with water. They were dehydrated with 70, 90% and absolute alcohol and finally cleared in xylene to remove water. A drop of mountant was placed on the surface of the slides and covered with a 22 by 22 mm cover slip.

RESULTS

Effects of extracts on the body weight

The mean body weights of the groups of the animals

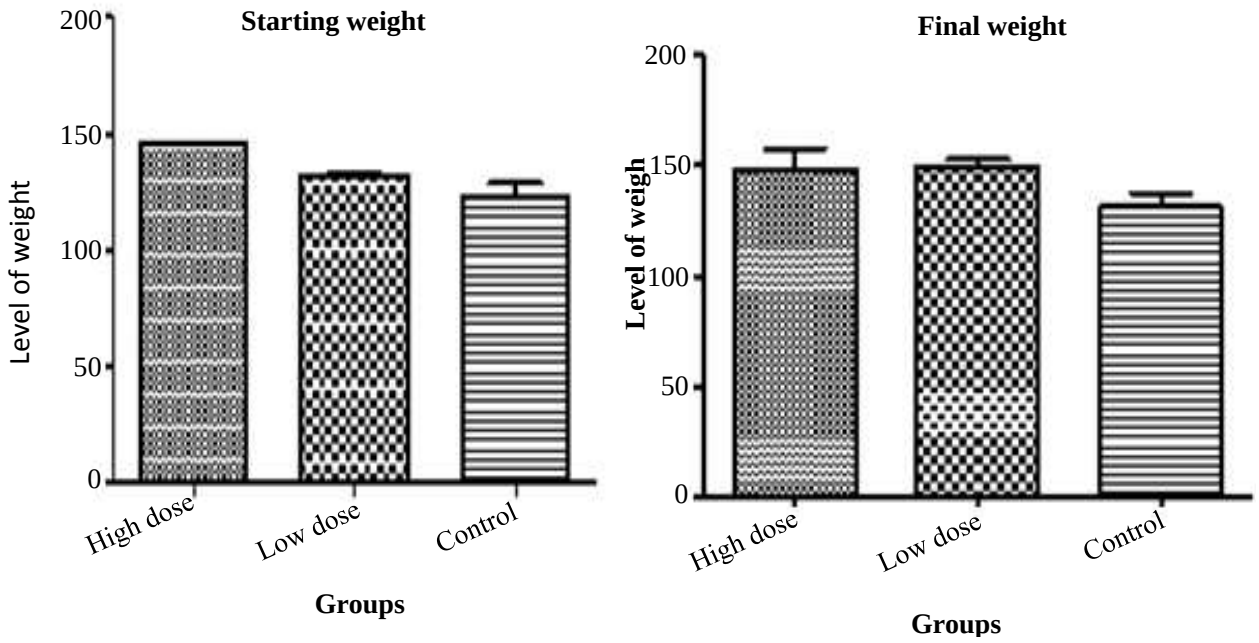

Figure 1. Comparison of initial and final mean body weights in the different experimental groups. Values are mean ±SEM.

administered the extract before and at the end of the experimental periods are shown in Figure 1. It was observed that the final mean weights of the groups showed 131± 6.6 g for the control group as against its initial mean body weight of 122 ± 6.3 g. While the groups 2 (Low dose) and 3 (high dose) showed 150 ± 3.1 g and 148 ± 9.4 g as their final mean body weight, as against their initial mean body weights of 132 ± 1.0 g and 145 ± 0.8 g, respectively. There was weight gained in the control and low dose animals. However, the animals in the high dose lost weight.

Histological observation

Control group

Sections showed normal histological features of the kidney. This shows the renal corpuscles (RC) of the cortex composed of the glomerulus (G) within the Bowman's capsule. The Bowman's capsule is lined by thin layer of single squamous cells. The proximal (PCT) and distal convoluted tubules (DCT) are lined by single layer of cuboidal epithelium. The Bowman's space (BS) is also present as shown in Plate 1.

Group 2 (Low dose)

Plate 2 represents photomicrograph of section of kidney from the group of animals which received the low dose of the leaf extract 0.2 ml showed hypertrophy of the tubular cells and the glomerulus appearing edematous.

Group 3 (high dose)

Plate 3 is a photomicrograph of a section of the kidney tissue from the animals treated with 0.5 ml of leaf extract showing the glomerulus with larger urinary space.

DISCUSSION

The kidneys play an essential role in regulating the amount of several important inorganic ions in the body, including sodium, potassium, chloride, bicarbonate, hydrogen, calcium and phosphate. They contribute to the maintenance of organic ion balance, eliminate metabolic waste and maintain pH balance (Arroyo, 2008).

From the results obtained, the administration of aqueous leaf extract of *M. esculenta* revealed significant decrease in body weight of the rats treated with 0.5 ml and significant increase in the weight of the rats treated with 0.2 ml of the extract and that of the control group. This result is not in agreement with the work of Awe and Kolawale (2013) which reported significant ($P<0.05$) body weight loss during four weeks treatment period. The kidney section from the control group revealed normal kidney architecture, darker stained cortex and the pale stained medullar, the renal corpuscles appearing as dense rounded structure and the glomerula being surrounded by narrow Bowmans space.

Low dose group (0.2 ml) administered rats showed hypertrophy of the tubular cells, occlusion of the Bowman's space and edematous glomerulus. This indicates that the extract administered has affected the renal histology and functions which may consequently

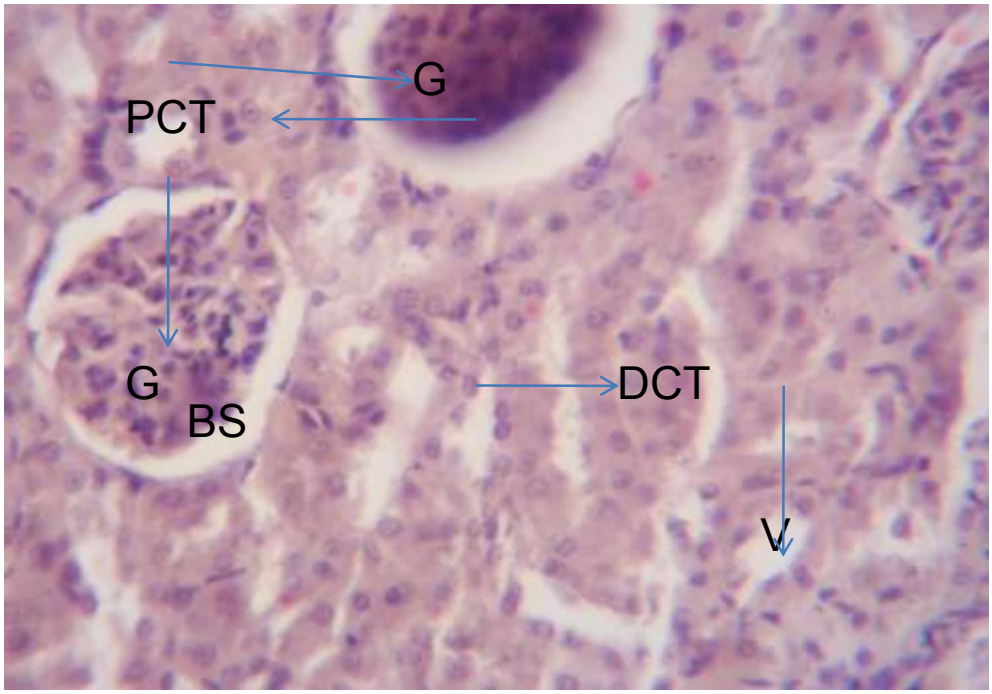

Plate 1. Photomicrograph of the control kidney (cortex and medulla).

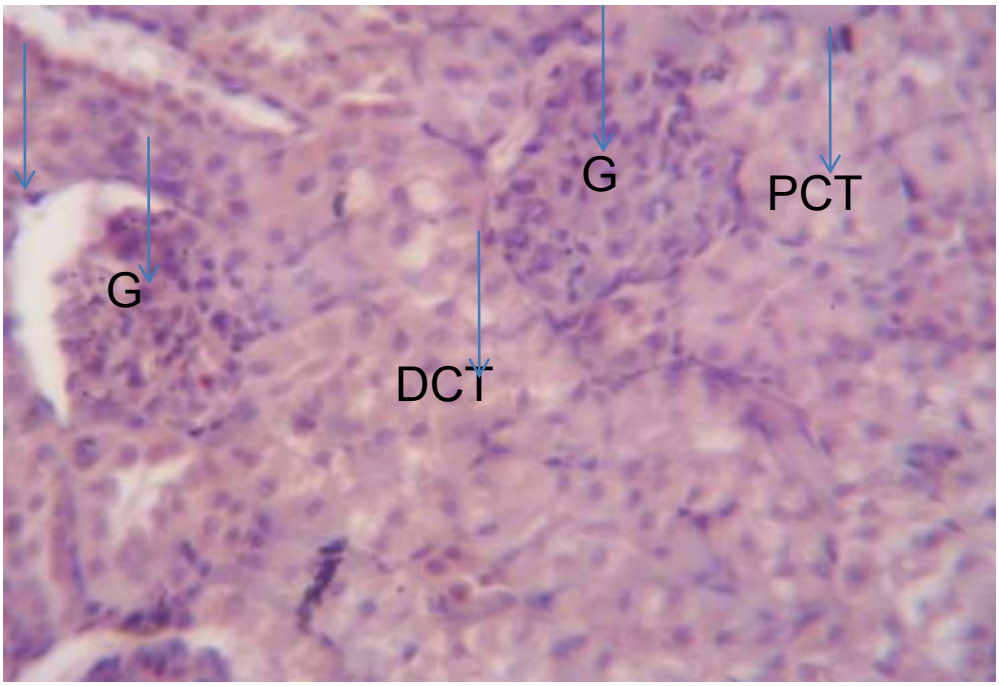

Plate 2. Photomicrograph of kidney (cortex and medulla) of rat administered with 0.2 ml of leaf extract of (Me) showing hypertrophy of the tubular cells and edematous glomerulus and occluded bowman space (low dose group); ×400 H&E stain.

result in renal failure and can lead to severe reduction in glomerular filtration leading to acute diffuse proliferative glomerulonephnitis (Morris, 2012).

High dose group (0.5 ml) treated animals revealed dilated convoluted tubules, occluded Bowman's space and glomerular derangement indicating adverse effect of

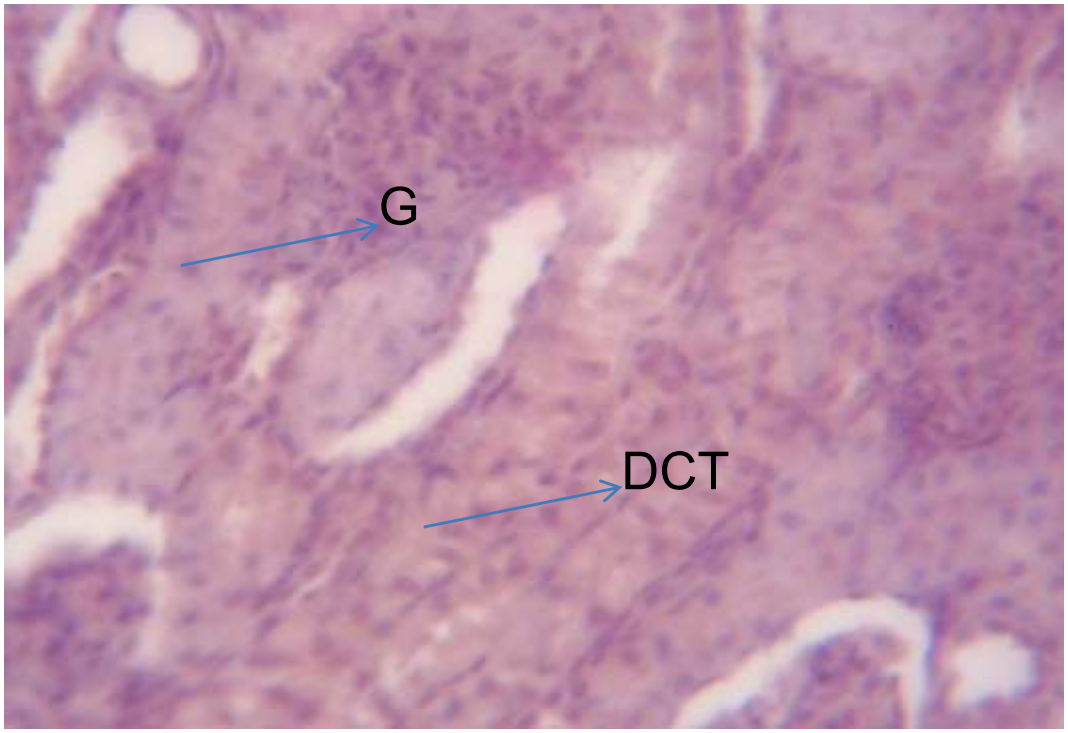

Plate 3. Photomicrograph of kidney (cortex and medulla) of rat administered 0.5ml of leaf extract of *M. esculenta*, showing dilated distal convoluted tubules, occluded bowman space and also showing glomerular dearangement; ×400 H&E.

the extract on the cells and tissues of the kidney which may consequently result in diuresis. This result differ from previous studies that have reported the presence of biologically active compounds in *M. esculenta* in particular alkaloids which have been documented to have many pharmacological properties capable of protecting tissues and cells from toxic effects (Prawat et al., 1995; Ebuchi et al., 2005).

Conclusion

The histological observations suggests that aqueous leaf extracts of *M. esculenta* is toxic to the kidney at the doses given since its administration causes morphological changes and histological damage of the cellular integrity of the kidney. The administration of aqueous leaf extract showed some toxicity to the kidney cells in the Wistar rats. The full potentials of this plant have not been fully exploited. Hence, this review will stimulate further scientific research into the biological activities, with the view to discovering novel or lead pharmaceutical agents.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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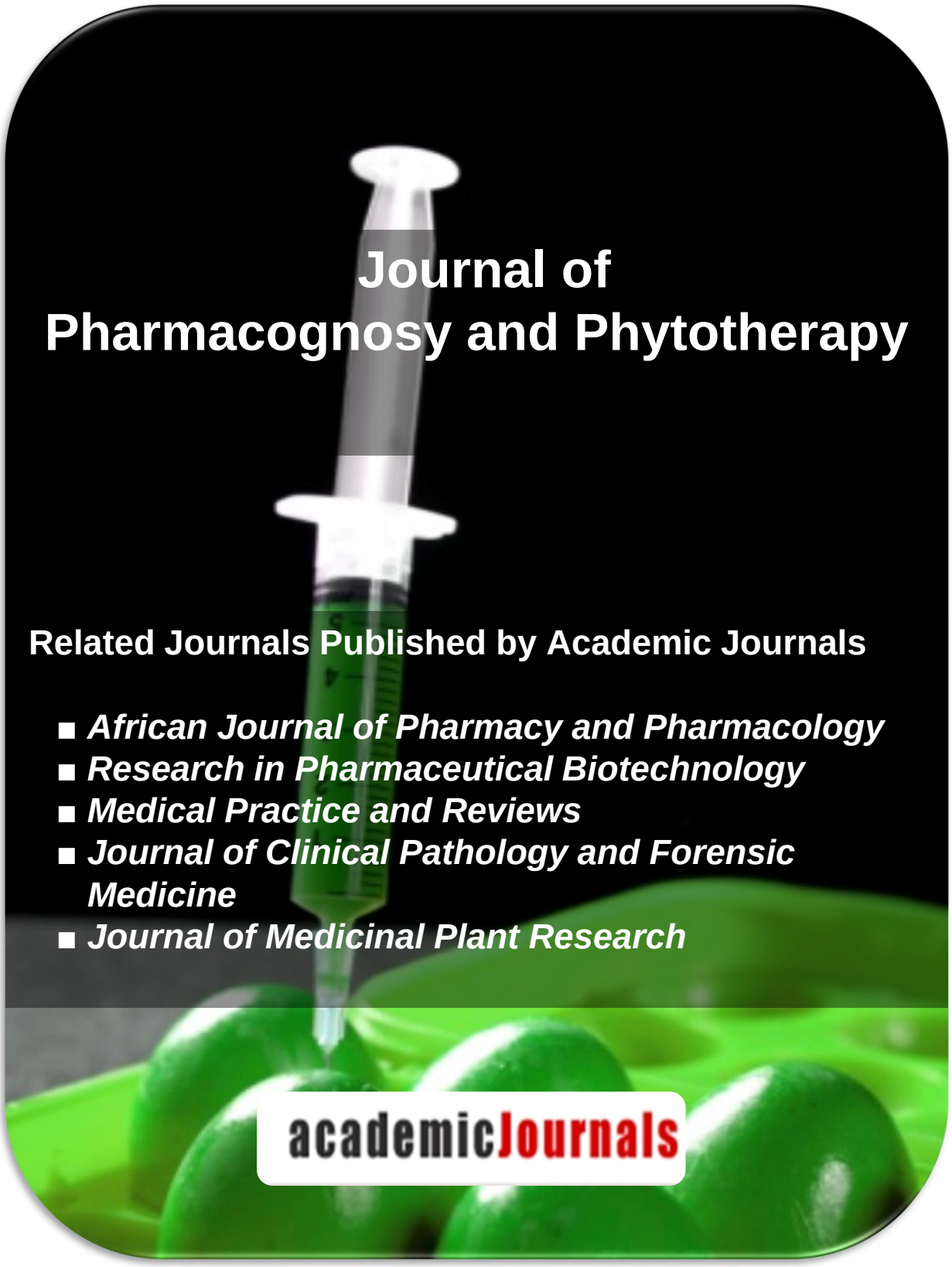

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