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Age-related Effects of *Momordica charantia* Leaf (Tea) Extract on Prostate Gland Health in Male Wistar Rats

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ABSTRACT: Prostate disorders are age-related issues that are known to be influenced by sex hormones, diet, and lifestyle and stress. With increasing dissatisfaction with orthodox treatment methods, host of alternative therapies including medicinal plants are currently being employed. The present study investigated the effect of oral administration of aqueous extract of *Momordica charantia* leaf tea on prostate gland health. Rats were grouped into three age groups (young, adult, and old), each with control fed normal rat pellets and water only, and treated groups received 140 mg/kg body weight of *M. charantia* leaf extract daily for 40 days via the oral route. The animals were sacrificed on the last day and blood samples collected were analyzed for testosterone, prolactin, dehydroepiandrosterone level, catalase and superoxide dismutase activities, lipid peroxidation and weights of prostate glands were also recorded. The extract produced no significant increase in body weight of the rats, increased testosterone in all the age groups, decreased prolactin concentration in the young and old age-groups while dehydroepiandrosterone level of the young age-rats significantly increased, those of the old-age rats decreased significantly. The extract significantly increased catalase and superoxide dismutase activities of rats and significantly decreased lipid peroxidase activity of the rats in the three age groups. The marginal positive effects on total body and prostate gland health recorded in this study suggest the usage and intake of *M. charantia* tea as a preventive measure against prostate disorders for a long period.

Keywords: *Momordica charantia*, Prostate gland disorders, Diabetes mellitus, Liver enzymes

Introduction

The use of secondary metabolites from plant origin as therapeutic agents is at an all-time peak. Many patients are in search of 'natural' alternatives or complements to conventional drug therapy. Herbal pharmaceuticals are generally promoted as being effective for chronic diseases and devoid of adverse effects (Tulunay *et al*., 2015; Mahomoodally, 2013). Herbal preparations have been used for centuries by people all over the world to treat disease and promote health. Both the west and the east have spent considerable time, research and energy developing the theories and applications within the field of herbal medicine. Herbs are generally easy to administer and cost-effective and when properly prescribed and used, have the advantage of being relatively free

of side effects when compared to western pharmaceutical medicines. Recently, the World Health Organization estimated that 85 % of people worldwide rely on herbal medicines for some aspect of their primary healthcare (Jamshidi *et al*., 2018). Administration of herbal preparations has a long history. WHO define traditional medicine as the sum `of the knowledge, skill, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement, or treatment of physical and mental illness (WHO, 2013). The emphasis on the use of medicinal plants had hitherto been placed on the treatment rather than prevention of diseases. However, there exists in the literature considerable report in recent times, research work on the use of medicinal plants and their constituents in disease prevention. A World Health Organization (WHO) Expert Group defined Traditional Medicine as the sum of all knowledge and practices, whether explicable or not, used in diagnosis, prevention, and elimination of physical, mental, or social imbalance and relying exclusively on practical experience and observation handed down from generation to generation, whether verbally or in writing (Sawadogo *et al*., 2012).

Diabetes is the most common of the endocrine disorders. It is estimated that in the year 2010 more than 200 million people world-wide had diabetes mellitus and 300 million people will subsequently have the disease in 2025 (Liu *et al*., 2021; Garau *et al*., 2003). The pantropical herbaceous vine *Momordica charantia (Cucurbitaceae)* is used in a traditional medicine wherever it is found. *Momordica charantia* is the most common plant used in alternate medicines used as anti-diabetic (Ahmad *et al*., 2016). Of the many hormonal, dietary and genetic factors that have been investigated, several meta-analyses indicate that diabetes mellitus is associated with a 9–16 % decreased risk of prostate disorders although there is considerable heterogeneity, estimates suggesting possible differential effects of diabetes on prostate cancer subtypes. Some studies suggest that recent-onset diabetes increases prostate cancer risk, but that long-standing diabetes lowers risk (Turner *et al.*, 2011). Interest in and use of complementary and alternative therapies, is high in prostate disease. These therapies have shown potential in benign prostatic hyperplasia (BPH), prostatitis, and prostate cancer. Some have produced results equal to or better than pharmaceuticals currently prescribed for BPH. In category III prostatitis, some nutraceuticals may offer relief to patients who get little from standard therapy. Because it is becoming apparent that inflammation may play a role in the progression of BPH and development of prostate cancer, nutraceuticals, which commonly have anti-inflammatory properties, may play a role. These therapies have also shown potential in prostate cancer treatment and prevention, especially those that also reduce cardiovascular events or risk. Nevertheless, uses of some nutraceuticals in prostate disease have had less, desirable consequences, showing lack of efficacy, adulteration, and/or severe side effects or drug interactions. By ensuring that these therapies undergo careful study for effectiveness, quality, and safety, urologists can look forward to adding them to their evidence-based armamentarium for prostate disease (Curtis *et al*., 2008).

Momordica charantia leaves are consumed as tea across the globe, especially by the ageing population for diabetic conditions despite the paucity of knowledge on its effects on the intact prostate gland (Jia *et al*., 2017). Bitter gourd leaf is used for making tea and can also be cooked and eaten as leafy vegetables. In some countries, the tea or decoction prepared from bitter gourd leaves is used as aphrodisiac and taken by women as a measure for birth control. The leaf of the plant has anti-diabetic, anti-hyperglycemic, anthelminthic, antioxidant, anti-microbial, emetic, purgative, anti-hepatotoxic, anti-ulcerogenic and antiviral properties against chicken pox and measles (Jia *et al*., 2017).

Bitter gourd leaves contain many bioactive constituents, full of medicinal properties. The leaves are used for treatment of wide variety of ailments such as diabetes, dysentery, rheumatism and gout, viral diseases, respiratory ailments etc. from time immemorial. Studies have shown hypoglycemic activity of bitter gourd leaves comparable to that of tolbutamide (first-generation potassium channel blocker oral hypoglycemic drug of sulfonylurea class) (Aeri and Raj, 2020). Bitter melon grows as a fast-growing climbing vine with thin stem and soft tendrils. The vine can reach six feet or more but requires support. It is a relative of cucumber, gourds, squashes, and melon and requires similar growing habits. Bitter gourd plant leaves are also edible. In some countries leaves and young shoots are used as flavoring agents (Aeri and Raj, 2020).

The aim of the study is to observe and document the effects, if any, of the aqueous leaf extracts of *Momordica charantia* on the normal prostate gland health via prostate weight changes, serum testosterone, prolactin and dehydroepiandrosterone (DHEA) and its sulfated analogue (DHEA-S) changes between the normal and treated animals within each group and across the age groups.

Materials and methods

Study area: The study was carried out in June and December, 2020 in the Department of Medical Physiology, Olabisi Onabanjo University, Ikenne Campus, Nigeria.

Plant material: Momordica charantia leaves were obtained from a colleague's farm where they were being nurtured in the wild. Forest Research Institute, Ibadan, Nigeria confirmed its authenticity, where the leaf was assigned voucher no; FRI 109921, a voucher specimen was deposited in the Forest Herbarium, Ibadan. The leaves collected were well-rinsed under running tap water to rid them of impurities. They were then spread on absorbent surface in a well-ventilated room for ten days, with enough attention of removing individual leaves that appeared darkish. Regular turning over of the leaves was done to ensure uniform drying. The leaves were then transferred to the oven, set at 40±2 °C. They were left in the oven for another seven days with regular inspection in order to make them crisp enough to enhance their shelf life for proper storage. The dry matter was ground Kenstar electric mill (Kitchen Appliances Indian Ltd, India) into powder. This was then stored till time for use.

Plant sample preparation: The aqueous extract (tea) was prepared daily as previously described (Nakagawa *et al.*, 2002; Fiorino *et al*., 2012) by adding 10 gm of powdered *Momordica charantia* leaves to 1000 ml of hot water at 80 °C for 8 min before putting into water bath (temperature accuracy ± 1°C) and stirred continuously with a glass rod (Nakagawa *et al*., 2002). The solution was filtered using Whatman No 1 filter, then allowed to cool to room temperature in the covered state. It was then strained into another container for storage. The resulting solution was 21.8 % by weight of *Momordica charantia* leaves.

$$\textbf{Percentage of dissolved substances} = \frac{\mathbf{A} - \mathbf{B}}{\mathbf{A}} \times \mathbf{100}$$

where: Initial weight of powdered *Momordica charantia* leaves = A

Dry weight of resulting residue after filtration = B

Experimental animals: Sixty male albino Wistar rats were obtained from the animal house of the Department of Medical Physiology, Olabisi Onabanjo University, Ikenne Campus, Nigeria. They were acclimated for two weeks before the experiments. They were placed in designed sterile polypropylene cages in the department animal holding room whose temperature ranged between 25-30 °C with relative humidity of 60±5 %. The cages had their wooden shavings that served as beddings that were changed on daily basis. Food and clean water were served *ad libitum*. They were maintained on standard livestock feed.

The Wistar rats used for the experiment were in according to the National Institutes of Health Guide for the care and use of laboratory animals (NRF, 1996)

At the start of the experiment the rats were separated into treated and control groups. Three groups of animals differentiated by age were involved in the study. Each age-group consisted of 20 animals, subdivided into 2 units of 10 each as Control (Normal) and Experimental (Herbal)

Group A: Old; 450 days old (retired old breeders) with average weight of 445 g.

Group B: Adult; 185 – 200 days old with average weight of 310 g.

Group C: Young; 65 – 70 days old with average weight of 200 g.

Feeding protocol: The rats were fed as follows: Control groups were fed only normal rat pellets and drinking water; while the test groups, in addition were given (140 mg/kg body weight according to Adedeji and Ojulari, 2014) concentration of the leaf extract daily for 40 days via the oral route by gastric gavage once daily. All rats were allowed free access to drinking water.

Collection of blood samples: At the end of the forty (40) day treatment period, after an overnight-fast, all the sixty animals were sacrificed. The animals were made unconscious with chloroform inhalation (cotton wool soaked in 3.5 % chloroform) and blood was collected via cardiac puncture using a 5-ml syringe attached to a needle (0.813 mm); the blood was collected into plain tubes.

The samples in plain tubes had their serum separated from each blood sample after centrifugation into clean labeled tubes and used for analysis. Sera collected were stored immediately in portable coolers filled with ice cubes for onward transportation to the laboratory refrigerator for the estimation of biochemical parameters. All biochemical Parameters were determined by using respective kits.

Relative organ weight: After the end of the experiment period, animals were weighed, anesthetized by diethyl ether, and prostate were obtained and weighed immediately with sensitive balance (an electronic weighing balance, model DT 1000 England with a capacity of 0.1 to 1000) after being cleaned from the accessory connective and adipose tissues, washed with normal saline and dried with gauze strip.

The prostate weight to body weight ratio was calculated according to the following equation:

$$\textit{Relative organ weight} = \frac{\textit{Absolute prostate organ weight } (g)}{\textit{Body weight of rat on sacrifice day } (g)} \times \mathbf{100\%}$$

Hematological parameters: Blood samples were analyzed using an automated cell counter (Coulter Electronics, Luton, Bedfordshire, UK) with standard calibration, according to the manufacturer's instructions for packed cell volume (PCV), white blood cell (WBC) count, erythrocyte sedimentation rate (ESR).

Serum enzymes activities: Acid phosphatase (ACP), alkaline phosphatase (ALP), and alanine aminotransferase (ALT) activities were determined using spectrophotometric method, following the procedure outlined in the diagnostic kits from Randox Laboratories Ltd., UK.

Serum hormonal levels: Serum testosterone, serum prolactin and serum dehydroepiandrosterone sulphate levels

were determined by using enzyme-linked immunosorbent assay (ELISA) for quantitative determination of testosterone, prolactin and dehydroepiandrosterone sulphate concentrations following the procedure outlined in the diagnostic kits from Biotec Laboratories Ltd., UK.

Catalase activity: Catalase (CAT) was measured in the haemolysate where the rate of decomposition of hydrogen peroxide by catalase was measured spectrophotometrically. Catalase activity was determined according to the previously described method (Sinha, 1972).

Superoxide dismutase activity: Superoxide dismutase (SOD) activity was measured in haemolysate. SOD activity was determined using the commercial kit from Jiancheng Biological Engineering Institute (Nanjing, China) following the protocol provided by the manufacturer. Data were expressed as SOD U/mg protein. The observed absorbance of the reaction was read at 420 nm and the enzyme activity was calculated as mg/g protein. The protein content was measured as previously described with bovine serum albumin as a standard (Lowry *et al*., 1951).

Lipid peroxidation: The level of peroxidation product viz. malondialdehyde (MDA) was measured in blood where the reaction depends on the formation of a coloured complex between malondialdehyde (MDA) and thiobarbituric acid (TBA) having an absorption maximum at 532 nm. Lipid peroxidation was estimated spectrophotometrically by the thiobarbituric acid reactive substance (TBARS) method as described by Varshney and Kale (1990) and malondialdehyde (MDA) was quantified using a molar extinction coefficient of 1.56 $x10^5$/M/cm by the method of Buege and Aust (1978).

Statistical analysis: This research work used a completely randomized design (CRD) model. The results were expressed as mean of 10 replicates ± standard error of mean (SEM). Results were analyzed using Graph Pad Prism 8.0 software. Results were subjected to one way analysis of variance (ANOVA) (non-parametric test) to test the effect on the parameter under investigation at 95 % level of confidence. The Tukey Test was conducted for the pair-wise mean comparisons of all columns, to determine the significant treatment at 95 % level of confidence. Values were considered statistically significant at $p<0.05$.

Results

General observation: The present study was an attempt to know about any effect of *Momordica charantia* leaf-tea consumption on normal prostate function. The enquiry is necessitated by extensive consumption of the tea by Type-2 diabetic, most being geriatric patients seeking solution in alternative therapy. They reported amelioration of the nuisance of frequent urination habit. Co-morbidity in this age-group amongst others are prostate disorders. The study was designed to cover all age groups - the young, adult, and old - for better understanding since prostate disorders have lengthy gestation period. The old usually would have been tainted with varying levels of metabolic syndrome.

The use of *Momordica charantia* leaf tea is becoming common among the elderly because they are likely to have other illnesses that are age-related. Men using alternative medicine tended to have higher incomes, more education with predilection for active lifestyle. The average age of men who use alternative treatments is becoming lower. Along with being more educated and reporting poorer health status, most alternative medicine users appear to be doing so not so much as a result of being dissatisfied with conventional medicine but largely because they find these health care alternatives to be more congruent with their own values, beliefs, and philosophical orientations toward health and life.

Physical observation: There was no untoward clinical sign observed in the rats following oral administration of *Momordica charantia* leaf tea, at the dose level tested. There were no changes in stool, urine, and eye colour of all the animals. No mortality was recorded in the different groups of rats. No lethality was observed throughout the period of experimental protocol, but mild sedative effects were clearly perceptible in the experimental animals. Progressive increase in the body masses of the rats in all six groups was observed as initial and final body weights of each animal were recorded.

Table1: Body weights of rats

Group*	**Initial Body Weight (g)**	**Final Body Weight (g)**
Young Control (YC)	200 ± 15.95	225 ± 14.50
Young Treated (YT)	198 ± 20.66	216 ± 13.50
Adult Control (AC)	300 ± 18.70	321 ± 10.25
Adult Treated (AT)	305 ± 25.45	320 ± 16.60
Old Control (OC)	445 ± 51.50	456 ± 22 00
Old Treated (OT)	450 ± 45.70	458 ± 30.50

*n=10 in each group

Organ to body weight ratio

Table 2. Relative organ weights of rats (g/100g body weight)

Group	Young	Adult	Old
Control	0.128±0.07	0.149±0.03	0.281±0.08
Treated	0.135±0.05	0.188±0.03	0.368±0.02

Values are mean ±SEM (n=10). Different levels of significant difference, when the mean of each group is compared with the mean of every other group are as follows at (ANOVA)

Hematological parameters: Figure 1 showed the differences in each age group when the herbal group (treated group) is compared with the control group. There was significant decrease in Packed Cell Volume (PCV) at $P \leq 0.0001$ of the herbal groups of both adult and old but no appreciable difference in that of young group. Across the ages as in Figure 1, there was a progressive increase in the PCV from the young to the old the control group, while in the herbal group (treated group) a reduction in PCV in the adult and old animal when compared to the young animal was recorded. However young herbal was significantly different at $P \leq 0.0001$ from adult herbal.

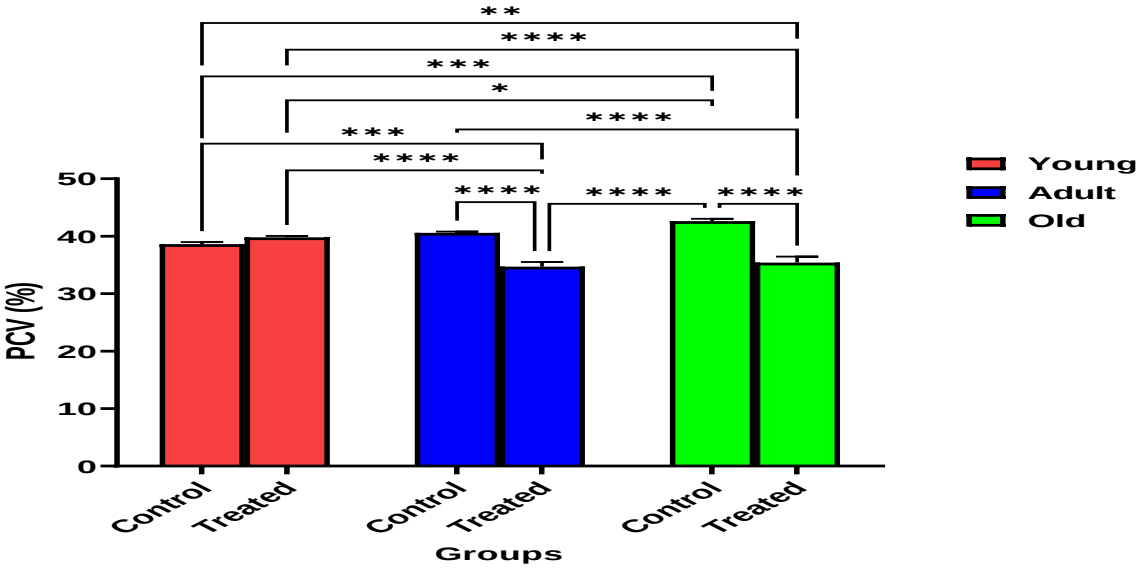

Figure 1: Effect of *Momordica charantia* leaf tea on Packed Cell Volume (PCV). Bars and error bars are displayed by mean and SEM, respectively.

Serum Hormonal Levels

Testosterone concentration: Figure 2 showed significant increase in serum testosterone concentration in the treated group of old and adult rats when compared to the control group.

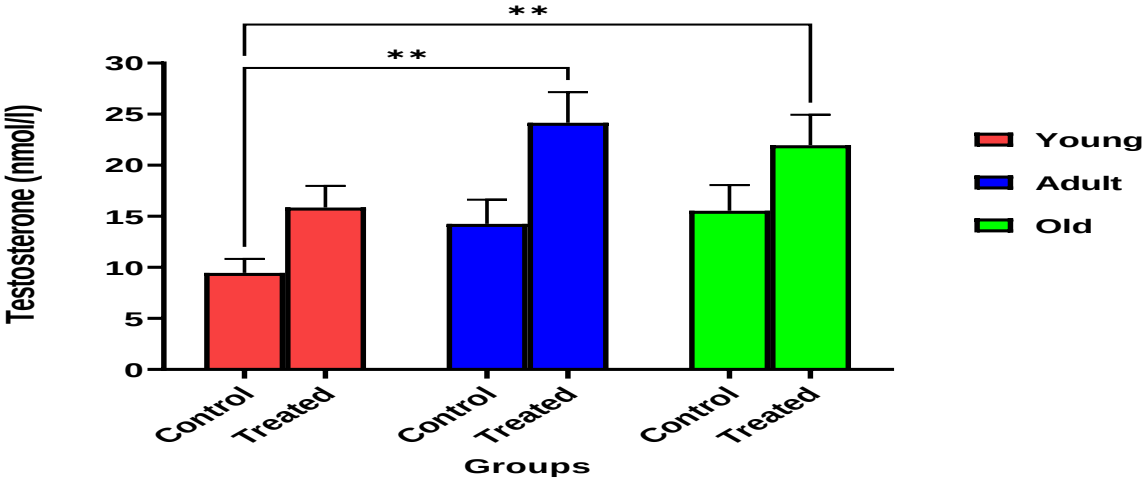

Fig. 2: Effect of *Momordica charantia* leaf tea on serum testosterone. Bars and error bars are displayed by mean and SEM, respectively.

Prolactin concentration: Figure 3 showed a decrease in serum prolactin level in the old rats of the control group when compared with the young rats of the treated group, and both control and treated group of adult rats. The figure also displayed differences among the control and treated group of old rats

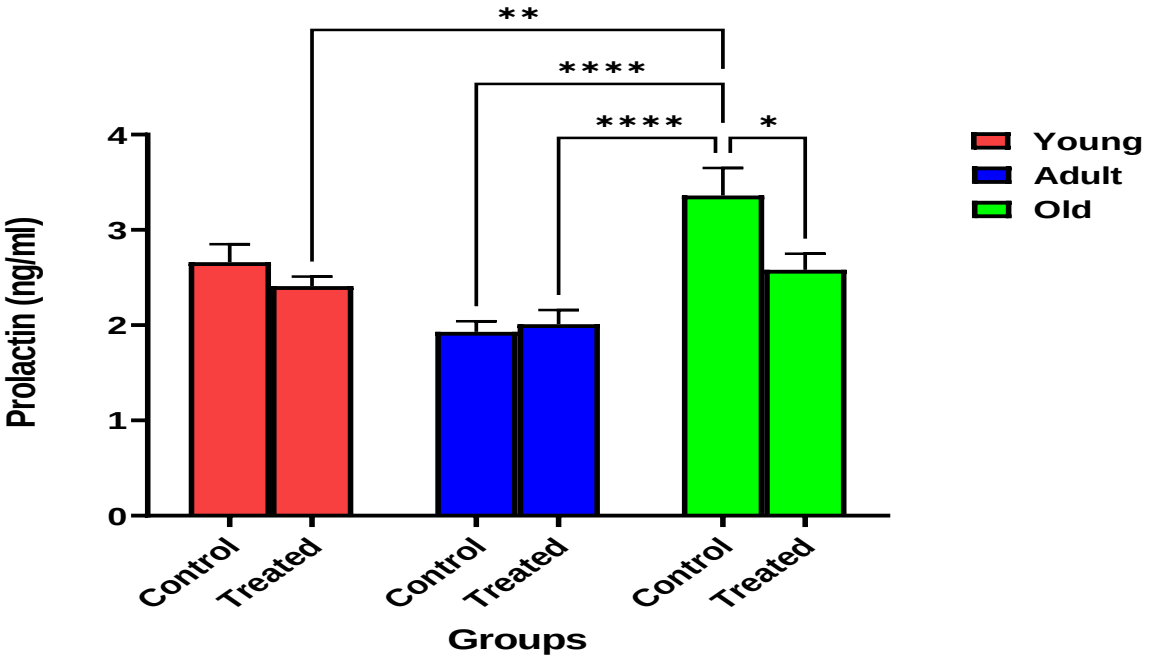

Fig. 3: Effect of *Momordica charantia* leaf tea on serum prolactin concentration. Bars and error bars are displayed by mean and SEM, respectively. Asterisks indicate significant difference.

Dehydroepiandrosterone concentration: Figure 4 showed serum level of dehydroepiandrosterone was significantly reduced in old rats of the treated group when compared with control and treated groups of both young and adult rats.

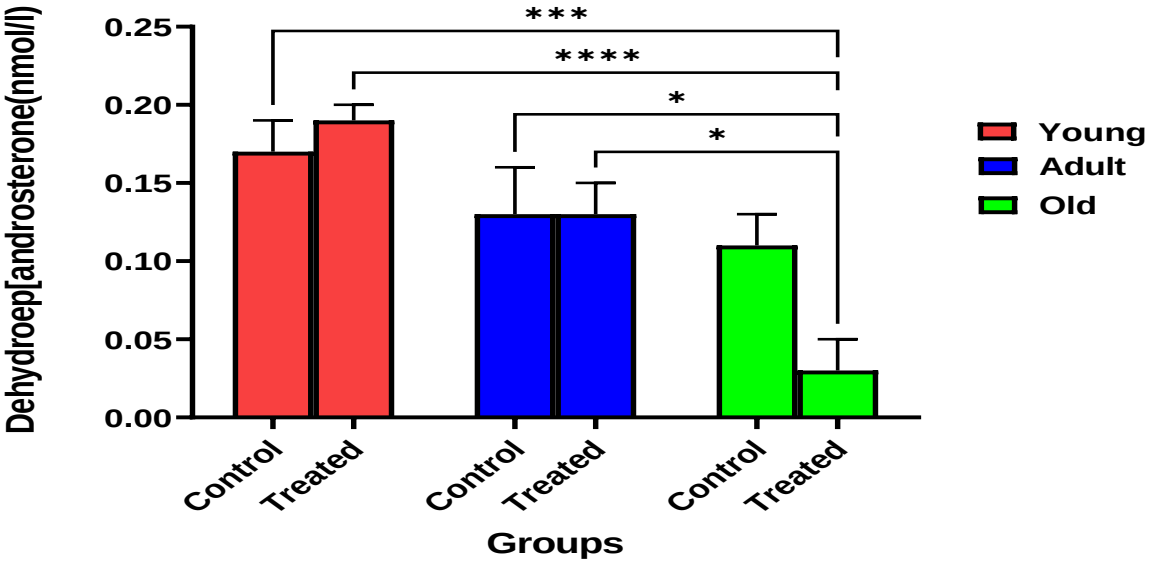

Fig. 4: Effect of *Momordica charantia* leaf tea on serum Dehydroepiandrosterone Concentration. Bars and error bars are displayed by mean and SEM, respectively. Asterisks indicate significant difference.

Serum Enzymes Activities

Blood catalase activity: Figure 5 showed patterned increase in the enzymatic activity when young rats of the treated group was compared with the adult rat of control and treated group and old rats of the control group.

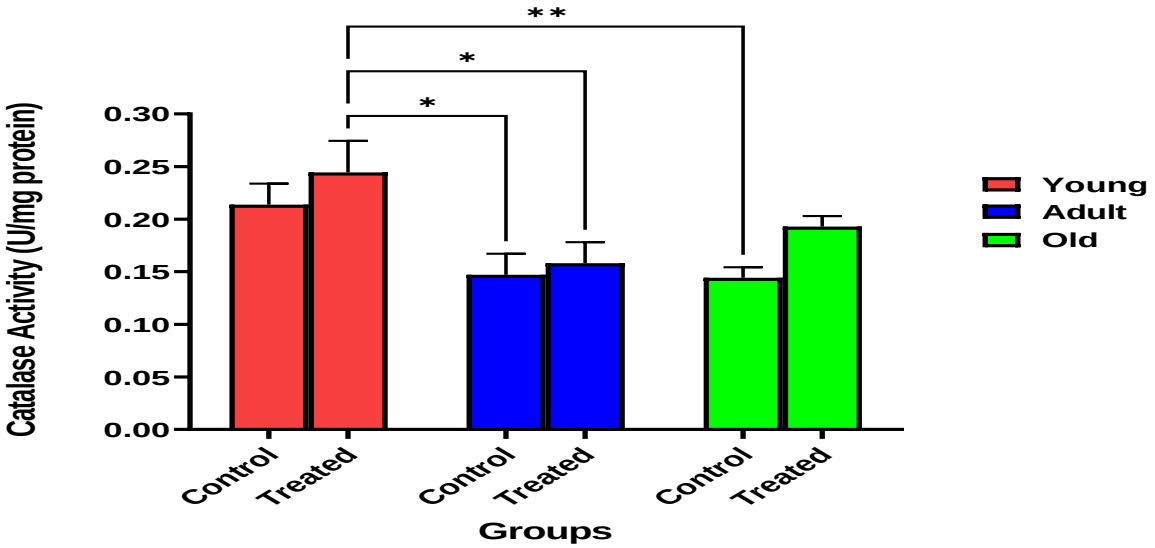

Fig. 5: Effect of *Momordica charantia* leaf tea on Blood Catalase Activity (A) between each age group and (B) across the three age groups. Bars and error bars are displayed by mean and SEM, respectively. Asterisks indicate significant difference.

Blood superoxide dismutase activity: Figure 6 showed increase activity of the enzyme across the age groups of the control and treated. The figure showed increase in the enzymes activity in only the treated group of adult animal as compared to both young and old in the control group as well as the herbal group (treated).

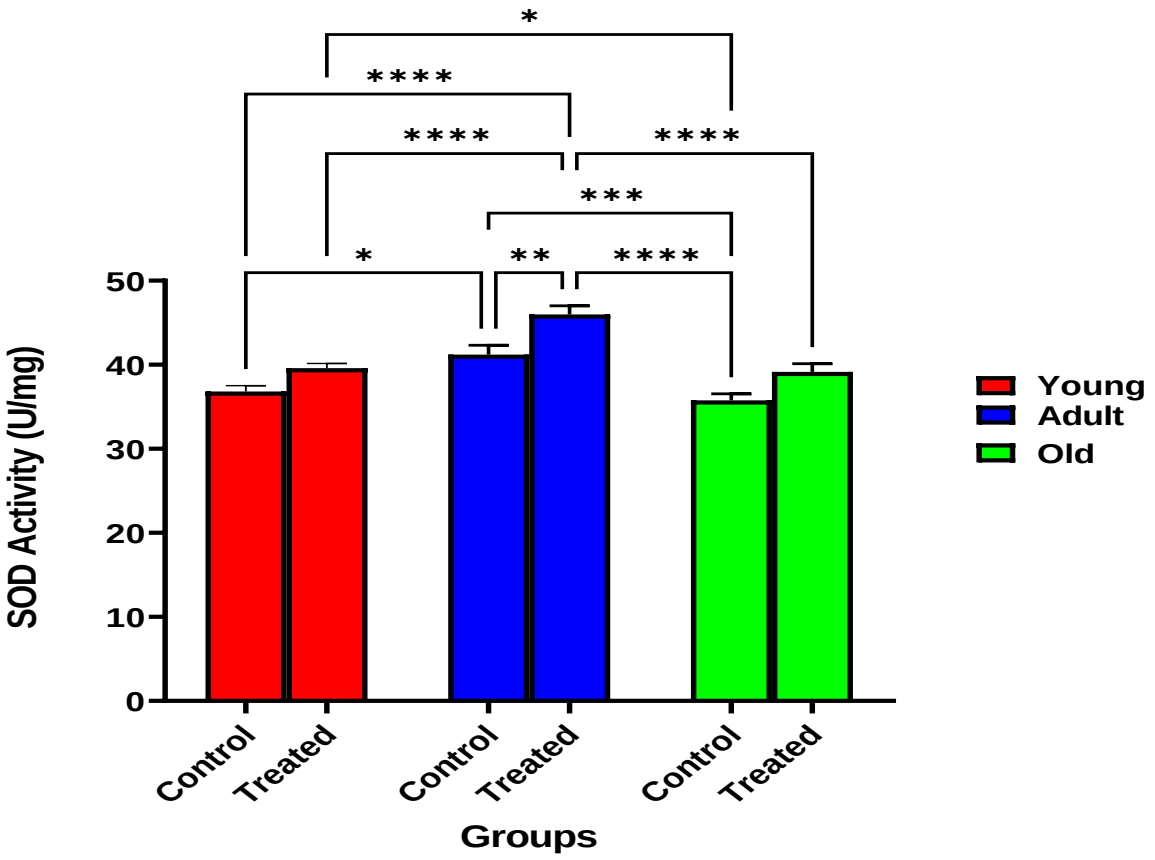

Fig. 6: Effect of *Momordica charantia* leaf tea on blood superoxide dismutase activity. Bars and error bars are displayed by mean and SEM, respectively. Asterisks indicate significant difference.

Blood lipid peroxidation: Figure 7 showed significant decrease in the blood lipid peroxidation measurement in both the groups of adult and old rats when compared with both the control and treated group of the young rats respectively

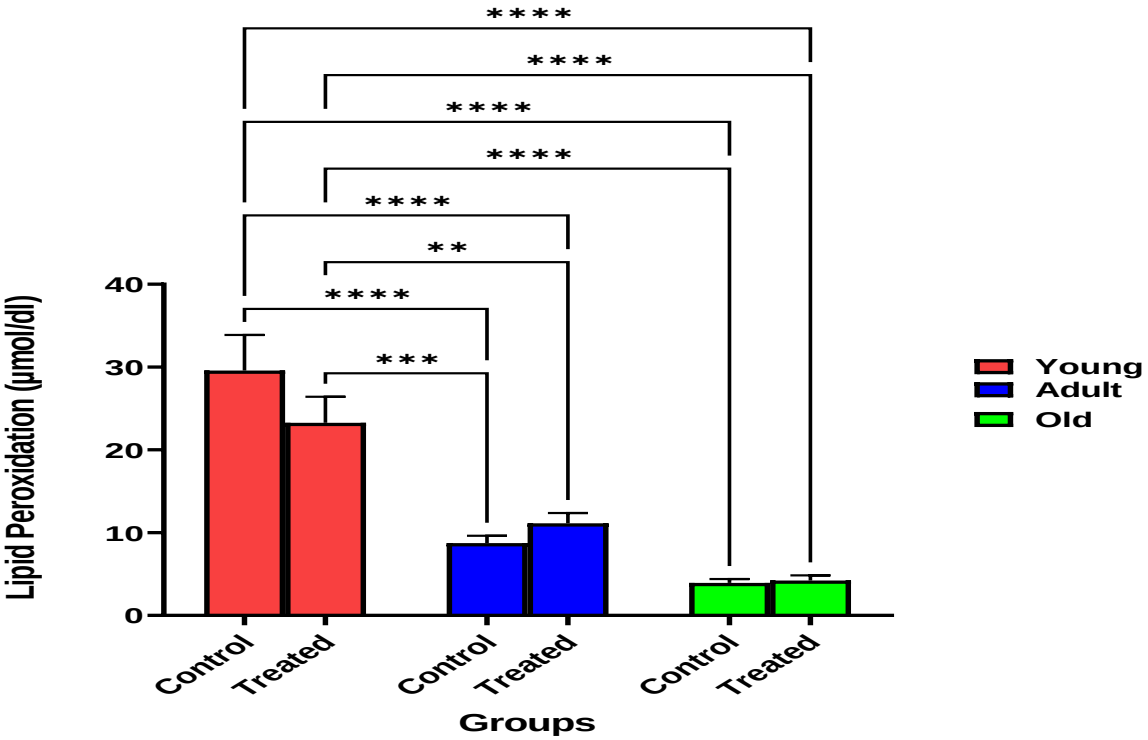

Fig. 7: Effect of *Momordica charantia* leaf tea on Blood Lipid Peroxidation (A) between each age group and (B) across the three age groups. Bars and error bars are displayed by mean and SEM, respectively. Asterisks indicate significant difference.

Discussion

General observation: *Momordica charantia* leaves have been used for thousands of years for their medicinal properties (Lalèyè *et al*., 2015). In Nigeria, the main methods of preparation of this plant were hot water extract (tisanes), long-term boiled extract (decoctions), cold infusion (maceration) and mixing component materials thoroughly (trituration).

Accessibility to this form of treatment is another factor as products are readily obtainable both in shops and online. *M. charantia* leaf tea otherwise known as Gohyah or bitter melon tea whole leaf (80 g) are imported from Vietnam and Dalgety Caribbean Cerassie. The tea bags advertised contains 100 % pure and natural dried Cerassie leaves with no artificially additives or flavorings naturally. Association between diabetes mellitus and prostate disorders is yet to be well defined. Some prospective studies and a hospital-based case–control study have found a reduced risk of prostate disorders associated with type II diabetes mellitus (Feng *et al*., 2020). The cohort studies suggest that risk of prostate disorders decreases with increasing time since diabetes diagnosis.

The cause of prostate disorders is not fully known, but hormonal, genetic, environmental, and dietary factors are thought to play roles. Among the risk factors linked with development of these conditions, age appears to have a strong correlation between increasing age and development of all forms of prostate disorders.

The triads of prostatitis, benign prostatic hyperplasia (BPH) and prostate cancer make up the body of prostate disorders (Kim *et al*., 2021). Prostatitis is the least important condition of the prostate. Prostatitis can affect men of any age and it is estimated that 50 percent of men experience the disorder during their lifetime. In addition to causing impaired quality of life, men who have a history of prostatitis have increased rates of benign prostatic hyperplasia, lower urinary tract symptoms and prostate cancer (Mishra *et al*., 2016).

The prevalence of BPH is about 10 percent for men in their thirties and 20 percent for men in their forties (Park *et al*., 2009). Enlarged prostate is common in older men and more likely to develop with advancing age, particularly after age 40. It rises as high as 60 percent for men in their sixties, and up to 80 to 90 percent for men in their seventies and eighties, according to the 2005 report (Park *et al*., 2009).

In 2010, BPH affected 210 million men worldwide, or about 6 % of the male population (GDB, 2015). About 1 man in 7 will be diagnosed with prostate cancer during his lifetime. Prostate cancer develops mainly in older men. About 6 cases in 10 are diagnosed in men aged 65 or older, and it is rare before 40 years (Häggström *et al*., 2017). The average age at the time of diagnosis is about 66 years (Feng *et al*., 2020).

Our findings demonstrated that *M. charantia* leaf tea has the potential to increase body weight, which is consistent with previous study (Phimarn *et al*., 2018).

Nutritional status of an individual is dependent on dietary intake and effectiveness of metabolic processes. These can be determined by either or combinations of clinical, anthropometric, biochemical, or dietary methods. The first worthy statement about the study is that none of the animal died either naturally or due to feed ingestion. The values obtained from compared favorably with each other, indicating that the rats in both groups were placed on the same amount of nutrients quantitatively and therefore whatever differences that are noticed might be due to the differences in the quality of the nutrients in these diets or their bioavailability when consumed.

Hematological Parameters: The packed cell volume (PCV) is the volume percentage (%) of red blood cells in blood. It is otherwise known as hematocrit or erythrocyte volume fraction (EVF). The packed cell volumes of the control group rats were within acceptable range as previously reported (Lalèyè *et al*., 2015; Temitope, 2014). As PCV is the percentage of red blood cells in circulating blood, a suggestion of adequate nutritional status is thereby noted for all groups of rats.

Odewusi *et al*. (2010) noted a significant difference between the mean PCV of the adult control group and the adult herbal (test) groups when treated with *Momordica charantia*. Temitope *et al*. (2014) showed a highly significant decrease in the test group as the dose decreases with aqueous extract.

In contrast, Lalèyè *et al*. (2015) observed no significant increase in the packed cell volume when control group and test groups, corresponding to our adult category, fed with aqueous or ethanolic extract of *Momordica charantia* leaf are compared. However, with methanolic extract recorded an initial increase with increasing dosage followed by gradual decrease (Hsu *et al*., 2012).

Serum hormonal levels: The study shows gradual elevation of testosterone level in the blood of control animals with increasing age that was consistent with previous reports (Kim *et al*., 2014) and those for the age group of animals (Heywood, 1980; Oyekunle *et al*., 2010). Administration of *Momordica charantia* was reported to have reduced serum testosterone of rats which are at variance with the results that indicate increase in concentration (Yama *et al*., 2011; Osonuga *et al*., 2014; Tumkiratiwong *et al*., 2014).

Prolactin concentration: It has been reported pituitary prolactin content decreased with age in male rats with concentrations in 12-and 18-month-old male rats being 54 and 31% of those in 6-month-old male rats as previously reported by Takahashi *et al*. (2014). The 12- and 18-month-old male rats fall in the adult group of this study.

Dehydroepiandrosterone concentration: The result of dehydroepiandrosterone concentration agreed with previous report (Mizin *et al*., 2017), that reported an age-related sensitivity of dehydroepiandrosterone sulfate. They found the old to be lower by 91 % relative to young and 87 % lower in comparison with the adult.

Treatment with *Momordica charantia* leaf tea has caused a significantly increased serum testosterone concentration compared to control in the old, while there is no difference in serum DHEA concentration in the adult group, and a non-significant increase in the young group.

Serum enzymes activities: Catalase enzyme exists in all aerobic cells. It is a hemeprotein that acts as a catalyst for the conversion of hydrogen peroxide to oxygen and water. Catalase is an important antioxidant enzyme responsible for the scavenging of free radical generated in tissue, thereby protecting the cells from the damaging effect of hydrogen peroxide that is present intra-cellularly.

The results of the control groups agree with previous reports (Thenmozhi and Subramanian, 2011; Tripathi and Chandra, 2009) when age or weight of the rats in various studies are considered. This reinforces the confidence in the state of good health of the subjects.

In comparing the control with the treated in each age group, no significant effect at $P<0.05$ was recorded, despite increased enzymatic activities in the treated. The results are corroborated in previous reports (Thenmozhi and Subramanian, 2011; Sagor *et al*., 2015) even at various concentrations.

During the investigation of the antioxidant activities of the *Momordica charantia*, previous research reported varying levels of significant increases, which depended not only on dosage also on the material – leaves or fruits (Thenmozhi and Subramanian, 2011; Sagor *et al*., 2015). Hence *Momordica charantia* plant offers protective influence against reactive oxygen species (ROS) that damage cells.

Blood lipid peroxidation: Lipid peroxidation (LPO) is one of the main events induced by oxidative stress. It is simply oxidative degradation of lipids. It is the process in which free radicals "steal" electrons from the lipids in cell membranes, resulting in cell damage. This process proceeds by a free radical chain reaction mechanism attacking lipids containing carbon-carbon double bond(s), especially polyunsaturated fatty acids (PUFAs).

Currently, lipid peroxidation is considered as the main molecular mechanisms involved in the oxidative damage to cell structures and it is the toxicity process that leads to cell death. This study shows different effects in the age groups however the result of the adult group that identifies with age/weight of male rats in earlier reports showed a slight increase that is not significant at $P \leq 0.05$ in the treated ((Thenmozhi and Subramanian, 2011; Abiola *et al*., 2017).

Conclusion

This study has demonstrated that administration of the water extract of *Momordica charantia* leaves in young, adult and old rats showed that it has no untoward clinical sign in the treated rats in all the age groups, but for the insignificant increased body weight when compared with their respective controls.
Catalase showed patterned increase in the enzymatic activity when comparing the treated group with the control group. The young and the old had higher units of measurement than their respective controls while being marginal in the case in the adult group. Superoxide dismutase showed increase activity of the enzyme in all the age groups of the treated group when compared with the control group. Lipid peroxidation (LPO) showed gradual reduction in the lipid peroxidation from the young to old in both the control and the treated groups. None of the enzymatic activity differences was significant at $P \leq 0.05$.
Serum testosterone concentration showed a steady increase in the treated group when compared to the control group with aging. Blood prolactin levels in the old rats of the treated group decreased when compared with the control group while no difference was observed in blood prolactin levels in the treated young and adult animals. Blood level of dehydroepiandrosterone showed gradual reduction as the age increases for both the control and treated groups but when the treated are compared with the control group; the old is significantly increased, the young is not significantly increased and the adult virtually the same.

Compliance with ethical guidelines

This study abided by the ethical principles governing the use of laboratory animals as set by the Olabisi Onabanjo University, Ago-Iwoye, Nigeria and the Ethics Committee on Medical and Scientific Research. Also, the current internationally accepted principles of care for and using laboratory animals as contained in the Canadian Council on Animal Care Guidelines and Protocol Review were duly observed.

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Authors' contributions

Designed the study, wrote the protocol and supervised the experiments: Gbolahan O. Idowu, Mutiu A. Alabi and Emmanuel O. Ajani; Carried out all of the laboratory work and performed the statistical analyses: Gbolahan O. Idowu, Mutiu A. Alabi and Fatai A. Kareem; Managed the data analyses: Gbolahan O. Idowu, Asiat Na'Allah and Taoheed A. Abdulsalam; Wrote the first draft of the manuscript: Gbolahan O. Idowu, Mutiu A. Alabi and Emmanuel O. Ajani; Managed the literature search and edited the various drafts of the manuscript: Gbolahan O. Idowu and Mutiu A. Alabi. All authors read and approved the final manuscript prior to submission.

Conflict of interest

The authors declare no conflict of interests in conducting this study with any internal or external entity.

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Ethical Approval

The Ethics Committee of the Olabisi Onabanjo University, Ago-Iwoye, Nigeria, approved the study design and protocol upon several expert reviews (registered code OOU/REC/2019/051).

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