

# Impact of Polyherbal Extract (*HAMACK*) On Anti-Oxidative Markers in Benign Prostatic Hyperplasia Induced Rats

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## Abstract

The effects of a polyherbal extract, *HAMACK*, on antioxidant defences were assessed in with male albino rats with testosterone propionate-induced BPH. Thirty rats (148–156g) were acclimatized and grouped into 6. Group one served as the normal control (2 ml/kg distilled water), while BPH was induced in Group two. Group three received finasteride (5 mg/kg), Groups 4 and 5 were administered with 350 and 700 mg/kg *HAMACK* respectively, while Group 6 was administered 700 mg/kg alone. Antioxidant status was assessed by measuring reduced glutathione (GSH), glutathione peroxidase, superoxide dismutase, catalase, and glutathione S-transferase (GST). In addition, malondialdehyde (MDA) was determined as a marker of lipid peroxidation. BPH induction significantly ( $P < 0.0001$ ) reduced antioxidative markers, with a concurrent increase in MDA, confirming oxidative stress. Treatment with finasteride and polyherbal extract significantly ( $P < 0.0001$ ) restored antioxidant parameters and reduced MDA levels dose-dependently. Additionally, group administered with 700 mg/kg *HAMACK* alone exhibited the highest antioxidant activity, characterized by elevated antioxidant enzymes alongside reduced MDA. In summary, the polyherbal extract effectively ameliorates oxidative stress associated with BPH by enhancing enzymatic and non-enzymatic antioxidant defences and reducing lipid peroxidation. Its efficacy suggests strong potential therapy for oxidative stress-mediated prostate conditions.

**Keywords:** Benign Prostatic Hyperplasia; Antioxidant; Oxidative stress; Polyherbal extract; lipid peroxidation.

## INTRODUCTION

Benign prostatic hyperplasia (BPH) is an age-related benign disorder characterized by prostate enlargement and resulting to lower urinary tract manifestations. Although androgen-dependent mechanisms have been associated in prostatic growth and development, there has been an increase attention directed toward the contribution of redox imbalance in the pathogenesis of BPH (Song *et al.*, 2025). Excessive generation of reactive oxygen species coupled with weakened antioxidant defences can disrupt cellular homeostasis and promote inflammatory responses, abnormal cell proliferation, and tissue within the prostate (Del Rio *et al.*, 2005; Han *et al.*, 2020). Antioxidant enzymes like as superoxide dismutase, catalase, and glutathione peroxidase are essential in protecting cells from oxidative damage by through the maintenance of redox homeostasis. Kaltsas *et al* reported that altered activity or expression of these enzymes is associated with hyperplastic changes in prostate tissue, indicating compromised antioxidant capacity during disease progression. Redox imbalance results from an imbalance between the production of reactive oxygen species (ROS)

and the ability of endogenous antioxidant defense systems to detoxify them. In BPH, increased ROS generation has been associated with lipid peroxidation, protein oxidation, and DNA damage within prostatic tissues (Yusuf *et al.*, 2021). These oxidative alterations can disrupt cellular signaling pathways, promote chronic inflammation, and enhance cell proliferation while inhibiting apoptosis, thereby contributing to prostate enlargement (Kalinina *et al.*, 2022). Key enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), together non-enzymatic antioxidants like reduced glutathione (GSH), play important function in maintaining cellular redox balance. A reduction in the activity or levels of these antioxidants has been reported in BPH, further exacerbating oxidative damage (Wu *et al.*, 2004).

In recent years, attention has shifted toward plant-derived bioactive compounds as promising natural remedy for oxidative stress-related conditions. Natural products derived from medicinal plants are particularly attractive due to their bioavailability, relative safety, and diverse biochemical activities. Polyherbal extracts, which combine two or more medicinal plants, are believed to exert enhanced therapeutic effects through synergistic

interactions among their bioactive constituents including terpenoids, phenolic acids, flavonoids, and alkaloids. These bioactive compounds have been shown to neutralise reactive oxygen species, increase endogenous antioxidant enzyme capability, and regulate redox-sensitive signaling pathways at the biochemical and molecular levels (Sadiq, 2023; Kang & Kim, 2023). Measuring antioxidant enzyme activities and oxidative stress markers in BPH-induced rats allows for a better understanding of the mechanisms by which polyherbal extracts may protect against oxidative damage and prostatic tissue alteration. Assessment of antioxidative markers in prostatic tissue and systemic circulation offers insight into the molecular mechanisms through which polyherbal extracts may give protective effects against oxidative damage and hyperplastic changes.

The present study focuses on a polyherbal formulation designated as HAMACK, which is composed of six medicinal plants: *Hunteria umbellata*, *Annona muricata*, *Mimosa pudica*, *Alchornea cordifolia*, *Corchorus olitorius*, and *Kalanchoe pinnata*. Each of these plants is known for its significant medicinal properties, particularly its antioxidant potential.

*Hunteria umbellata* (Hunter's tree) is a tropical medicinal plant of the *Apocynaceae* family, native to West and Central Africa. It is a small tree or shrub known locally in Nigeria as "Osu" (Yoruba), "Erokoto" (Igbo), and other regional names. Traditionally, it is used in ethnomedicine for a variety of therapeutic purposes, particularly in the management of metabolic, infectious, reproductive, and gastrointestinal disorders. It is traditionally used in West African medicine for treating diabetes, hypertension, and infections. Its bioactive compounds possess antioxidant and anti-inflammatory activities that can contribute to the reduction of oxidative stress (Akinmoladun *et al.*, 2021).

*Annona muricata*, widely known as soursop or graviola, is a tropical fruit-bearing tree that belongs to the *Annonaceae* family. Indigenous to the tropical regions of the Americas, the plant is commonly distributed in Africa, Southeast Asia, and the Caribbean. Its various parts including leaves, fruit, seeds, and bark have long been used in traditional medicine for the treatment of ailments such as fever, infections, hypertension, and cancer. It has been reported to exhibit antiproliferative, antioxidant, and anti-inflammatory effects, which are relevant in the context of BPH (Bourdy *et al.*, 2022).

*Mimosa pudica* *Mimosa pudica*, commonly referred to as the "sensitive plant," "touch-me-not," or "shame plant," is a creeping annual or perennial herb which belongs to the family *Fabaceae*. Native to South and Central America, it is now seen in many tropical and subtropical regions in the world, including Asia and Africa. The plant is characterized by its rapid leaf-folding response to touch or other stimuli, a phenomenon known as thigmonasty, which helps deter herbivores. It contains

various secondary metabolites that have demonstrated free radical scavenging and anti-inflammatory capabilities in preclinical models (Aliyu *et al.*, 2020). Research has shown that its antioxidant and antimicrobial components facilitate tissue regeneration and prevent infection (Suthar *et al.*, 2020).

*Alchornea cordifolia* (Christmas bush) is a fast-growing, evergreen shrub or small tree that is linked to the *Euphorbiaceae* family. It is native to tropical Africa and widely distributed across West, Central, and parts of East Africa. Known locally by different names such as "Ewe-ipon" in Yoruba and "Ubulu inu" in Igbo it plays a significant role in traditional African medicine. It is used for treating wounds, respiratory infections, and gastrointestinal disorders. Its leaves and roots are rich in polyphenols and flavonoids that exhibit antioxidant and immunomodulatory effects (Oruka, & Achuba 2023).

*Corchorus olitorius*, commonly known as jute mallow or "ewedu" in Nigeria, is a tropical leafy vegetable cultivated widely in Africa, Asia, and the Middle East. Beyond its nutritional value, the plant has long been recognized for its medicinal importance in traditional systems of medicine. The therapeutic potential of *C. olitorius* is largely due to its diverse array of bioactive constituents, such as flavonoids, alkaloids, saponins, tannins, cardiac glycosides, antioxidant vitamins (A, C, E), and essential minerals such as calcium, magnesium, and iron (Mokgalaboni, & Phoswa 2023)

Finally, *Kalanchoe pinnata*, widely known as "miracle leaf," or "Bryophyllum pinnatum," is a juicy plant commonly seen in tropical and subtropical areas. It has earned a significant place in traditional medicine due to its extensive therapeutic potential. Used in Ayurvedic, African, Caribbean, and Chinese traditional medicine, this plant is famous for combating anti-inflammatory, antimicrobial, antioxidant, antiulcer, hepatoprotective, nephroprotective, antidiabetic, and anticancer activities (Dogra *et al.*, 2022).

Therefore, this research work aims to evaluate the impact of this polyherbal extract on antioxidative markers in benign prostatic hyperplasia-induced rats. By evaluating key biochemical markers of oxidative stress and antioxidant defences, this study provides insight into the potential role of polyherbal formulations in the management of benign prostatic hyperplasia.

## MATERIALS AND METHOD

### Plant Materials

The leaves of *Kalanchoe pinnata*, *Annona muricata*, *Corchorusolitorius*, *Mimosa pudica*, *Hunteria umbellate*, and *Alchornea cordifolia* were used for this research to evaluate the effect of the extract on antioxidative markers.

### Experimental Animals

Thirty male albino rats were used for this study.

### Standard Drugs

Finasteride and Testosterone Propionate were Standard Drugs used.

### Methods

#### Collection of Plant Materials

The plant materials (*H. umbellate*, *A. muricata*, *M. pudica*, *A. cordifolia*, *C. oclitorius*, and *K. pinnata*) were collected from the humid forest the Forestry Research Institute of Nigeria and Ahia Eke, Umuahia, Abia State. The respective leaves were properly identified and authenticated by taxonomist at the herbarium unit of the Department of Forestry and Environmental Management, College of Natural Resources and Environment, Michael Okpara University of Agriculture, Umudike.

#### Extraction And Formulation of A Polyherbal Extract

Fresh leaves of *H. umbellate*, *A. muricata*, *M. pudica*, *C. oclitorius*, *A. cordifolia* and *K. pinnata* were air dried and pulverized in the grinder to obtain coarse powder. 200g of each of the powdered sample was macerated in 6.5 litres of 70% ethanol for 72 hours before undergoing filtration using muslin cloth and whatmann filter paper placed in a funnel. The filtrate was then concentrated into a semi-solid paste with water bath at 65°C. The resulting extract after concentration was called the HAMACK-extract and used for the experiment.

### Experimental Animals

Thirty-six (36) male albino rats weighing 100-200g were purchased from the animal house, Department of zoology and environmental Sciences, Faculty of biological sciences, University of Nigeria Nsukka, Nigeria.

### Experimental Design

Thirty-six (36) male albino rats with average body weight (148–156g) were used for the experiment. They were grouped as follows after acclimatization:

- Group one = Normal control (2 ml/kg injection water)
- Group two = BPH control (Testosterone propionate only)
- Group three = BPH + Finasteride (5 mg/kg),
- Group four = BPH + 350 mg/kg HAMACK
- Group five = BPH + 700 mg/kg HAMACK;
- Group six = 700 mg/kg HAMACK only.

Testosterone propionate injection (25 mg/ml) was immersed in 1 ml of injection water. Each of the rats was administered 0.4 ml of the resultant solution equivalent to 5 mg/kg testosterone propionate via intraperitoneal route for 28 days consecutively. The administration with either Finasteride or HAMACK was through oral route 30 minutes after the administration of the testosterone propionate throughout the study. The rats fasted overnight on the 28th day of the study and were

sacrificed by euthanasia with chloroform and blood samples were taken for biochemical analyses via cardiac puncture.

### Acute Toxicity (LD<sub>50</sub>) Of Extract

The lethal dose study was conducted in accordance with Lorke's method (Lorke's, 1983). This study was conducted in two phases using a total of 18 male Wistar albino mice. In phase I, nine mice were divided into 3 groups of 3 mice each. Groups 1, 2 and 3 animals were given 10, 100 and 500 mg/kg body weight of the extract respectively to possibly establish the range of doses producing any toxic effect.

In the phase II, further specific doses of 1000, 2900 and 5000 mg/kg body weight of the extract were administered to nine mice (three rat per dose) to further determine the correct LD<sub>50</sub> value. The extract was dissolved in distilled water and given via oral route. All animals were observed frequently on the day of treatment and were monitored daily for 2 weeks for signs of acute toxicity.

### Determination of Antioxidant Properties of Polyherbal Extract (Hamack).

#### Estimation of superoxide dismutase (SOD)

Superoxide dismutase activity was carried out using Arthur and Boyne (1985) method as contained in Randox kit. To 0.05ml diluted sample in a test tube was added 1.7ml mixed substrate solution and mixed xanthine oxidase (0.25ml) was added and the initial absorbance taken after 30 seconds. The final absorbance was taken after 3 minutes and units of SOD per gram haemoglobin were extrapolated from a standard curve.

#### Catalase Estimation

Catalase activity was assayed by the method of Sinha (1972). 0.9ml of distilled water and 0.1ml of plasma in a test tube were added 2ml of H<sub>2</sub>O<sub>2</sub> and 2ml phosphate buffer. The reaction was initiated by addition of 2ml of dichromate acetic acid reagent into mixture. Absorbance of the reaction was taken in 30 seconds interval for 2 minutes. The activity of catalase was expressed as μmol of plasma (micro-moles of H<sub>2</sub>O<sub>2</sub> utilized per second).

#### Glutathione Peroxidase Estimation

This was carried out according to the method described by Paglia and Valentine (1967). A known volume, 0.05ml of heparinised whole blood was diluted with 2ml of diluting reagent. This mixture was used for the assay. A volume, 50ml of dilute sample was mixed with 1ml of phosphate buffer + EDTA, glutathione + glutathione reduce + NADPH and cumene hydroperoxide respectively. The initial absorbance of both blank and test were read after per minute. The absorbances were read again after 1 and 2 minutes intervals at 340nm. The glutathione peroxidase activity was calculated as follows:

$$U/L \text{ of haemolysate} = 8H12 \times DA \text{ 340nm} / \text{minute}$$

### Estimation of reduced glutathione

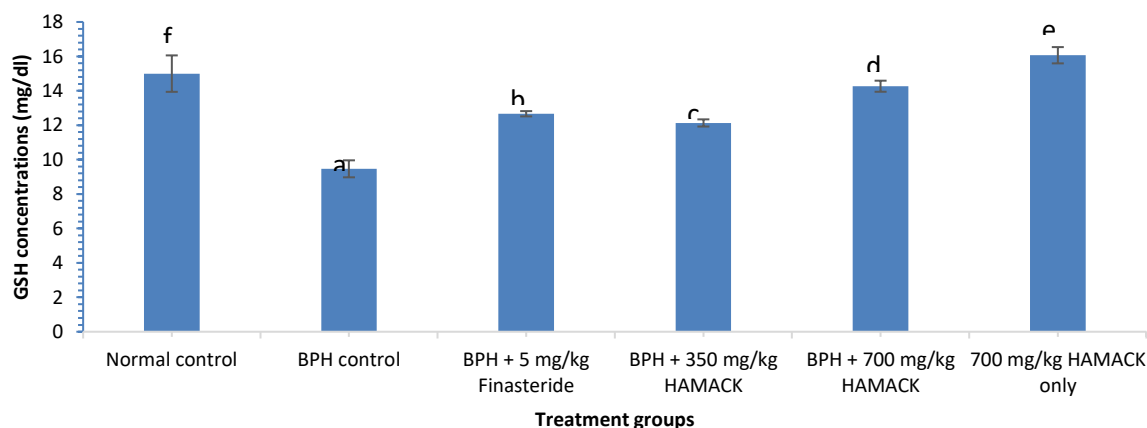
The reduced glutathione concentration was determined by the method of Exner *et al* (2000). The reagents are as follows:

1. 0.3M disodium salt of EDTA
2. 0.1% disodium salt of EDTA
3. **Precipitating agent:** 1.67g of metaphosphoric acid, 0.2g of EDTA disodium salt, 30g of sodium chloride in 1 litre of distilled water.
4. **5, 5-dithio-bis-2-nitrobenzoic (DTNB) reagent:** 40mg of DTNB in 100ml of 1% sodium citrate.
5. **Standard solution:** 10mg of reduced glutathione in 100ml distilled water.

A volume (0.2ml) of sample was mixed with 1.8ml of EDTA solution. To this 3.0ml of precipitating reagent was added, mixed thoroughly and kept for 5 minutes before centrifugation. To 2ml of the supernatant, 4ml of 0.3m disodium hydrogen phosphate solution and 1ml of DTNB reagent were added and the colour developed was read at 412nm in spectrophotometer. A set of standard solutions containing 20-100mg of reduced glutathione was treated similarly. The values were expressed as mg/dl for plasma.

### Statistical analysis

One-way analysis of variance (ANOVA) and a Duncan multiple range comparison tests were carried out on the data generated, with a statistical significance difference attained at a 95 % confidence level ( $P < 0.05$ ). Statistical Products and Service Solutions (SPSS) version 22 was used for the data analysis.



Bars are plotted as mean  $\pm$  standard deviation, and bars with different letters are significantly ( $P < 0.0001$ ) different from each other.

**Figure 1.** Glutathione (GSH) concentrations of BPH induced rats.

### Superoxide Dismutase (SOD) Activity of Bph Induced Rats

Significant ( $P < 0.0001$ ) decrease was observed SOD concentration of BPH control compared to normal control. Groups administered with finasteride (5 mg/kg),

## RESULTS

### Acute toxicity effect of HAMACK on rats

The acute toxicity results of HAMACK in table 1 and 2 revealed that the polyherbal extract is relatively non-toxic as no death or a sign of adverse reactions or toxicity was observed.

**Table 1.** Phase 1 and phase 2 LD<sub>50</sub> results of Hamack on rats.

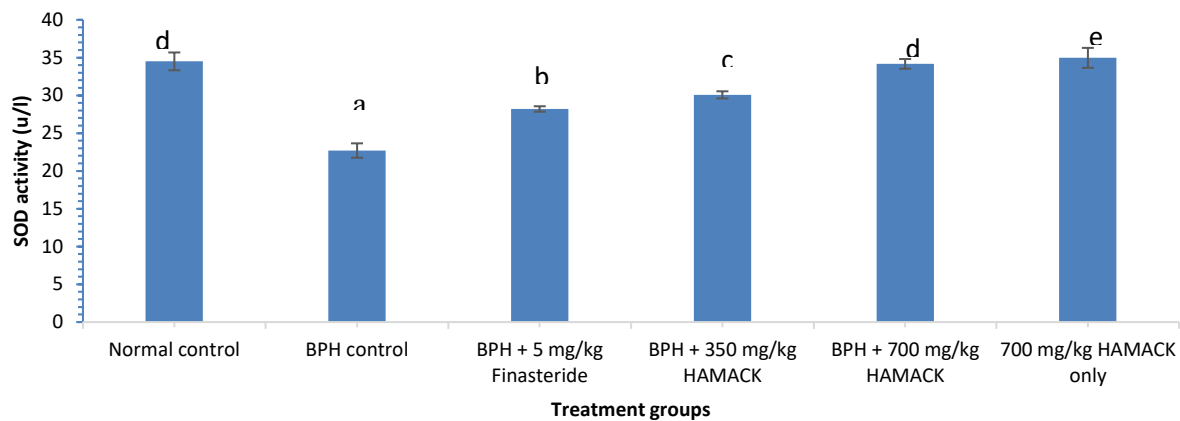
Groups	Dosage mg/kg body weight	
Phase I	Dose (mg/kg)	
Group 1	10	0/3
Group 2	100	0/3
Group 3	1000	0/3
Phase II		
Group 4	1600	0/3
Group 5	2900	0/3
Group 6	5000	0/3

LD<sub>50</sub> > 5000 mg/kg body weight

### Glutathione (GSH) concentrations of BPH induced rats

There was a significant ( $P < 0.0001$ ) decrease in the GSH concentration in BPH control compared to normal control. However, compared to BPH-control, there was significant ( $P < 0.0001$ ) increase in GSH concentration in BPH treated groups' not-dose dependently. In addition, there was a significant ( $P < 0.0001$ ) increase in GSH compared to normal control in group treated with 700 mg/kg HAMACK only.

350mg/kg and 700mg/kg HAMACK, revealed a statistically significant ( $P < 0.0001$ ) increase compared to BPH control. Notably, the rat administered 700 mg/kg HAMACK only show a statistically significant ( $P < 0.0001$ ) increase compared to normal control.



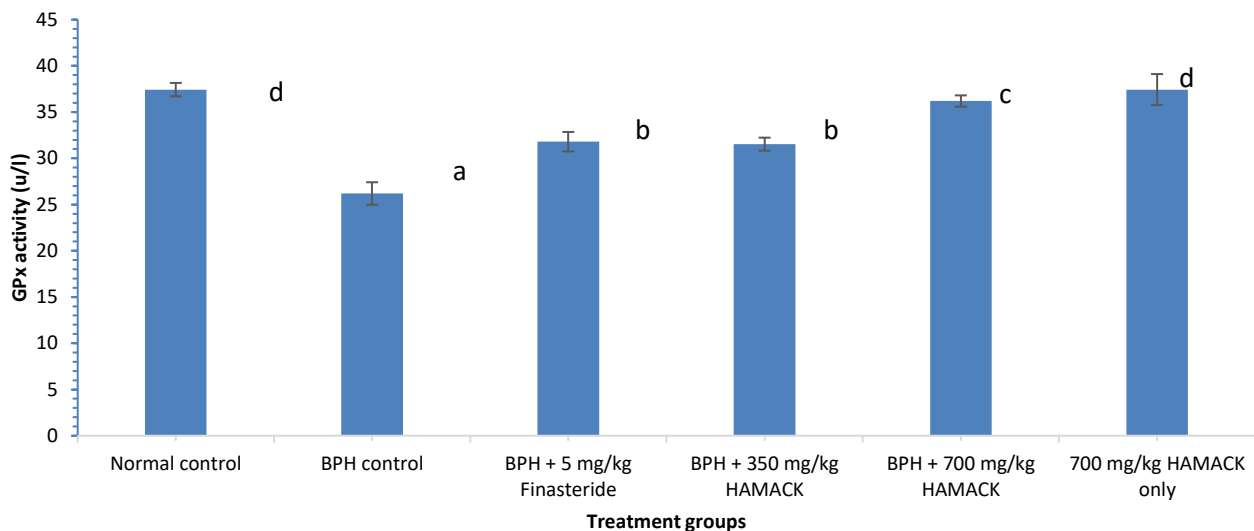
Bars are plotted as mean  $\pm$  standard deviation, and bars with different letters are significantly ( $P < 0.0001$ ) different from each other.

**Figure 2.** Superoxide dismutase (SOD) activity of BPH induced rats.

### Glutathione peroxidase (GPx) activity of BPH induced rats

In respect to GPx, a significant ( $P < 0.0001$ ) decrease was seen in BPH control compared to normal rats. However, the rats administered 700 mg/kg HAMACK only show a

non-significant ( $P < 0.0001$ ) rise when compared to normal control. In addition, significant ( $P < 0.0001$ ) increase was observed in BPH treated groups compared to BPH control.



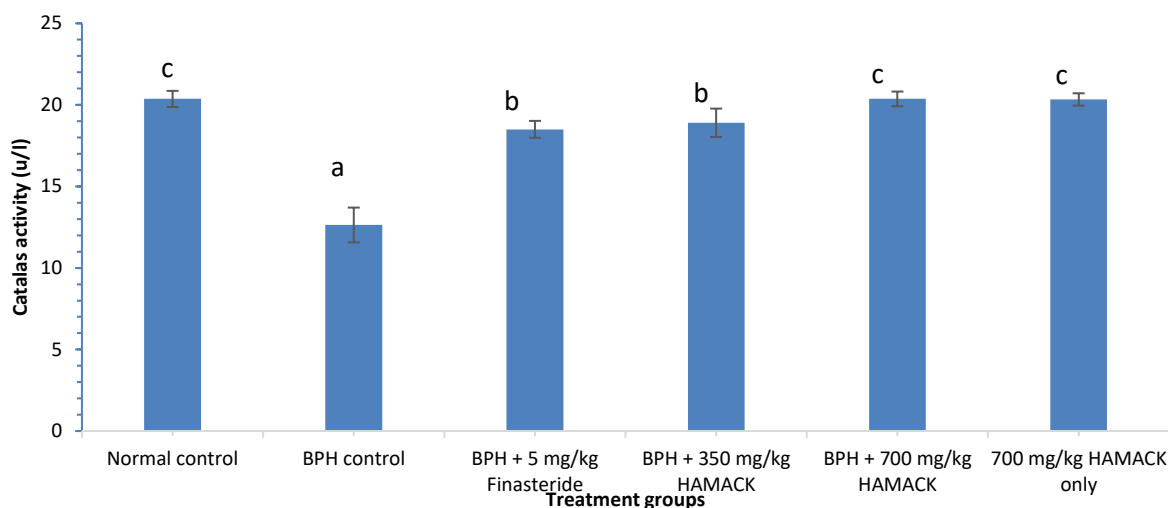
Bars are plotted as mean  $\pm$  standard deviation, and bars with different letters are significantly ( $P < 0.0001$ ) different from each other.

**Figure 3.** Glutathione peroxidase (GPx) activity of BPH induced rats.

### Catalase (CAT) activity of BPH induced rats

Compared to normal control, a significant ( $P < 0.0001$ ) decrease was observed in the CAT concentration in BPH-control, while groups administered with 5 mg/kg

finasteride, 350 mg/kg HAMACK and 700 mg/kg HAMACK showed significant ( $P < 0.0001$ ) increase in CAT concentration compared with of BPH-control.



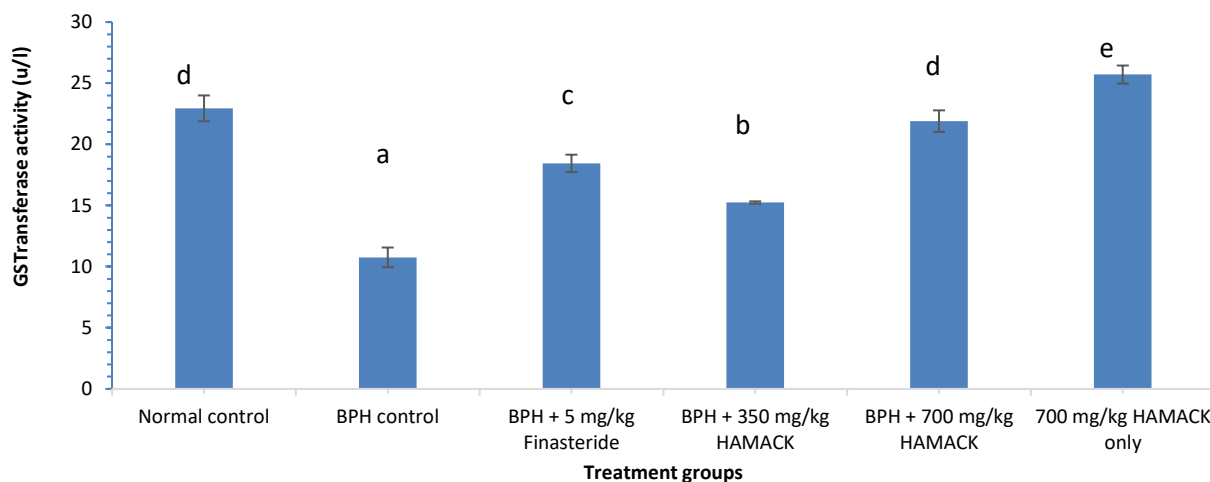
Bars are plotted as mean  $\pm$  standard deviation, and bars with different letters are significantly ( $P < 0.0001$ ) different from each other.

**Figure 4.** Catalase (CAT) activity of BPH induced rats.

#### Glutathione S-transferase (GST) activity of BPH induced rats.

There was a significant ( $P < 0.0001$ ) decrease in the GST concentration in BPH-control compared to normal rats. However, groups treated with 5 mg/kg finasteride, 350 mg/kg HAMACK and 700 mg/kg HAMACK revealed

significant ( $P < 0.0001$ ) increase in GST compared to BPH-control though not dose dependent. Group administered 700 mg/kg HAMACK only revealed a significant ( $P < 0.0001$ ) increase in GST compared to normal rats.



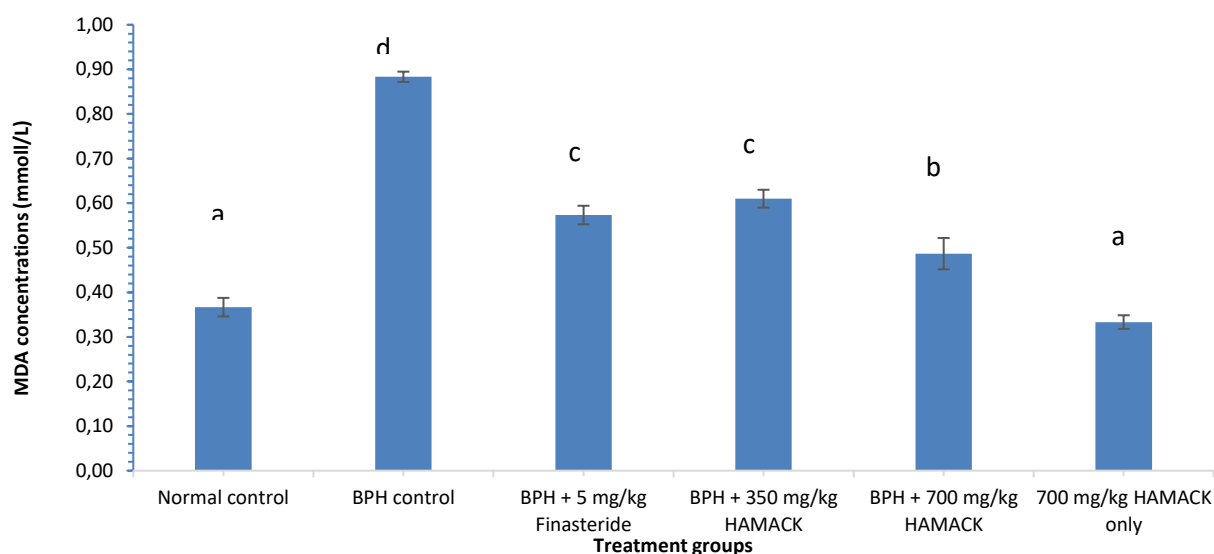
Bars are plotted as mean  $\pm$  standard deviation, and bars with different letters are significantly ( $P < 0.0001$ ) different from each other.

**Figure 5.** Glutathione S-transferase (GST) activity of BPH induced rats.

#### Malondialdehyde (MDA) concentration in BPH induced rats

There was a significant ( $P < 0.0001$ ) increment in MDA concentration in BPH-control compared to normal control. However, significant ( $P < 0.0001$ ) reduction in

MDA level was seen in BPH-treated groups, though not dose dependent compared to BPH control. While, there is non significant difference in group that received 700 mg/kg HAMACK only compared to normal control.



Bars are plotted as mean  $\pm$  standard deviation, and bars with different letters are significantly ( $P < 0.0001$ ) different from each other.

**Figure 6.** Malondialdehyde (MDA) concentration in BPH induced rats.

## DISCUSSION

The acute toxicity study of the hydro-alcoholic mixture of *Annona muricata*, *Alchornea cordifolia*, *Kalanchoe pinnata*, *Mimosa pudica*, *Hunteria umbellata*, and *Corchorus olitorius* (HAMACK) was carried out to determine its safety profile. The findings indicated that oral administration of HAMACK up to 5000 mg/kg body weight did not cause mortality in rats during the 14-day observation period in Phase 1. In Phase 2, rats administered 1600 mg/kg and 2900 mg/kg doses remained largely stable, although transient physical inactivity was observed at 2900 mg/kg for about 25 minutes. However, rats treated with 5000 mg/kg exhibited mild sedation and reduced locomotor activity for approximately 2 hours but subsequently recovered and remained physically stable throughout the study period. The observed transient inactivity at very high doses may reflect mild central nervous system (CNS) depressant effects, as some constituent plants within HAMACK such as *Annona muricata* and *Hunteria umbellata* contain alkaloids, flavonoids, and acetogenins known to modulate neurotransmitter systems (Ezekwesili *et al.*, 2022). However, this effect was reversible and did not progress to toxicity or mortality, indicating that such responses may not be of toxicological concern at lower therapeutic doses.

In this study, SOD activity was significantly ( $P < 0.0001$ ) reduced in BPH control rats compared to the normal control group, reflecting impaired antioxidant enzymatic defense in the hyperplastic prostate. This is consistent with reports that oxidative stress downregulates antioxidant enzyme activity in prostate tissue, further aggravating cellular injury (Mishra *et al.*, 2018; Ogunlakin *et al.*, 2023). Treatment with

HAMACK significantly ( $P < 0.0001$ ) elevated SOD activity, indicating restoration of antioxidant balance. The effect was dose-dependent, with the higher dose showing greater efficacy. The observed increase may be attributed to the presence of bioactive phytochemicals such as flavonoids and phenolic compounds in HAMACK constituents, which have been reported to enhance SOD activity through both direct radical scavenging and upregulation of antioxidant enzyme expression (Ogunlakin *et al.*, 2023).

CAT activity was significantly ( $P < 0.0001$ ) reduced in BPH control rats compared to normal controls. Reduced CAT activity indicates accumulation of hydrogen peroxide and enhanced oxidative burden within prostatic tissues. Administration of HAMACK significantly ( $P < 0.0001$ ) increased CAT activity in BPH rats, suggesting effective detoxification of peroxides and strengthening of enzymatic antioxidant defenses. This result corroborates findings from (Ojo *et al.* 2021), who demonstrated that *Alchornea cordifolia* extract restored CAT activity in oxidative stress-induced models. Similarly, flavonoid-rich plants such as *Kalanchoe pinnata* have been reported to enhance catalase activity by modulating endogenous antioxidant enzyme expression (Singh *et al.*, 2022). Thus, the improvement in CAT levels observed in HAMACK-treated groups highlights its synergistic effect in neutralizing hydrogen peroxide and reducing oxidative insults in prostatic tissue.

GSH concentrations in this study were significantly ( $P < 0.0001$ ) lower in the BPH control group compared to normal controls, indicating depletion of antioxidant reserves due to persistent oxidative stress. Treatment with HAMACK significantly ( $P < 0.0001$ ) restored GSH levels in BPH-induced rats, with higher doses producing

effects comparable to normal control levels. This suggests that HAMACK may either directly replenish GSH levels through its phytochemicals or stimulate the activity of  $\gamma$ -glutamylcysteine synthetase, the rate-limiting enzyme in GSH synthesis (Nwachukwu *et al.*, 2021).

Notably, *Annona muricata* has been shown to increase GSH concentration and protect against oxidative damage in experimental models (Adeyemi *et al.*, 2020), while *Corchorus olitorius* is reported to enhance intracellular GSH content due to its high vitamin C and carotenoid content (Chikezie *et al.*, 2021). Together, these findings suggest that HAMACK exerts its protective role partly by sustaining glutathione homeostasis.

Malondialdehyde (MDA) is a well-established biomarker of lipid peroxidation and oxidative damage to cell membranes. MDA levels were significantly ( $P < 0.0001$ ) elevated in BPH control rats compared to the normal control group, confirming heightened lipid peroxidation and oxidative tissue injury in BPH. HAMACK administration significantly ( $P < 0.0001$ ) reduced MDA levels in a dose-dependent manner, reflecting inhibition of lipid peroxidation and stabilization of cellular membranes. These results are consistent with reports that phytochemical-rich plants suppress MDA formation and protect against oxidative stress-induced cell damage (Ogunyemi *et al.*, 2022). In particular, *Mimosa pudica* and *Hunteria umbellata* have been associated with strong lipid peroxidation inhibitory activity, attributed to their rich content of alkaloids and polyphenols (Ezekwesili *et al.*, 2022). This suggests that HAMACK mitigates membrane damage by limiting peroxidation cascades and preserving cell integrity.

The antioxidant effects of HAMACK are likely attributable to the combined and synergistic actions of its constituent plants. Polyherbal formulations are increasingly recognized for their superior efficacy compared to single plant extracts, as they target multiple biochemical pathways simultaneously (Abubakar *et al.*, 2021). HAMACK likely acted through three complementary mechanisms such as direct scavenging of free radicals via polyphenolic compounds, upregulation of endogenous antioxidant enzymes such as SOD, CAT, and GPx, and prevention of lipid peroxidation through stabilization of cell membranes. Additionally, recent studies suggest that phytochemicals can activate nuclear factor erythroid 2-related factor 2 (Nrf2), a transcription factor that regulates antioxidant response elements (AREs) and promotes the expression of detoxifying and antioxidant enzymes (Zhang *et al.*, 2020). Therefore, it is plausible that HAMACK exerts its effects partly via Nrf2-mediated signaling, enhancing cellular resilience against oxidative stress and preventing further damage to prostatic tissue.

## CONCLUSION

The findings of this study have important clinical implications. Conventional treatment for BPH, such as finasteride, primarily targets androgenic pathways but does not address oxidative stress, which is a significant driver of disease progression. Moreover, synthetic antioxidants have shown limited clinical application due to potential toxicity upon long-term use (Halliwell, 2012). In contrast, plant-derived antioxidants are generally safer, more tolerable, and possess multiple protective effects. The ability of HAMACK to significantly ( $P < 0.0001$ ) improve antioxidant status and reduce oxidative damage suggests its potential role as an alternative therapy in the management of BPH.

**Author's Contribution:** CLA is the principal investigator of this research work. ACL and RIU were included in preparing the concept and design. ACL, RIU, and SMU revised the manuscript and critically evaluated the intellectual contents.

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**Competing Interest:** Authors have declared that no competing interests exist

**Availability of Data and Material:** The data analysed used during the current study are available from the corresponding author on reasonable request

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