

Full length Research Article

# ***Mucuna pruriens* Seed Repeals the Hypothalamic-Pituitary-Testicular Axis Disruption following Carbamazepine Treatment in Male Wistar Rats**

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**Summary:** This study examined the potential effects of *Mucuna pruriens* (MP) seed powder on the disruptions of the hypothalamic-pituitary-testicular axis caused by the carbamazepine (CBZ) treatment in male Wistar rats. A total of 35 male Wistar rats were randomized into 5 groups (n=7). The animal in group 1 received normal saline (0.2 ml) orally, while groups 2-5 received carbamazepine (CBZ) 25 mg/kg per oral. Groups 1, and 2 were fed with standard rats' chow, while groups 3-5 rats were supplied with a diet containing MP seed powder at 2.25 g, 1.5 g, and 0.75 g respectively. The serum levels of male reproductive hormones [gonadotropic releasing hormone (GnRH), follicle-stimulating hormone (FSH), testosterone, and estradiol] were determined using enzyme-linked immunosorbent assay; seminal profile was evaluated by determining the sperm count, morphology, and viability; the testicular tissue lipid peroxidation was delineated by conventional spectrophotometric assay; while the histomorphology of the hypothalamus, pituitary, and testis was delineated using conventional hematoxylin and eosin staining technique. Descriptive and inferential statistics were used to analyze the result. There was a marked decrease in the testicular weight, FSH, testosterone concentration, and normal sperm cells in the CBZ, and CBZ + MP (2.25 g) treatment groups. There was a marked increase in the testicular tissue lipid peroxidation in the CBZ, and CBZ + MP (2.25 g) treated rats in addition to various morphological alterations in the hypothalamus, pituitary, and testis. These anomalies receded in the CBZ + MP (1.5 g), and CBZ + MP (0.75 g) treatment groups. Consumption of MP (1.5 g, and 0.75 g) may alleviate the injurious effects of CBZ treatment on the hypothalamic-pituitary-testicular functions.

**Keywords:** *Mucuna pruriens*; Carbamazepine; Hypothalamic-pituitary-testicular axis

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## **INTRODUCTION**

Epilepsy is one of the most serious neurological disorders that affects around 46 million people worldwide (Beghi, 2020). The pathophysiology of seizure is characterized by an occurrence of anomalous neuronal firing due to disequilibrium in the excitation and inhibition mechanisms in the brain (Stafstrom and Carmant, 2015). Carbamazepine, a sodium-gated channel blocker is one of the most popular anticonvulsant drugs; it is often required for long-term treatment of epilepsy because it only recedes the symptoms of epilepsy (seizure), not epilepsy which is a chronic disorder.

Accumulating shreds of evidence have shown that epilepsy is a debilitating disorder while its treatment is with attendant abnormal sexual function (Atif *et al.*, 2016; Nikoobakht *et al.*, 2017; Mazdeh *et al.*, 2020). Both clinical and experimental investigations showed that the hypothalamic-pituitary-testicular axis disruption remains a

pivot of reproductive dysfunctions with eventual manifestations of poor sexual performances, loss of libido, and ultimately, infertility (Semet *et al.*, 2017; Zhao *et al.*, 2019; Osuntokun *et al.*, 2020).

Among other indigenous plants consumed as herbal formulations to cure some male reproductive disorders in some developing countries e.g., Nigeria is *Mucuna pruriens* (M.P) (Sofowora 1982); Ashidi *et al.*, 2019). It is popularly called velvet bean/ devil bean and also referred to as 'werepe', 'agbada/ Agboloko', and 'karara' among the Yoruba, Igbo, and Hausa tribes of Nigeria respectively. M.P plant belongs to a Fabaceae and it is common in South Western Nigeria (Vadivel and Janardhanan, 2000). Studies on the phytochemical screening of *Mucuna pruriens* seed showed a high concentration of cardiac glycosides, phenols, flavonoids, terpenoids, alkaloids, and coumarins (Ravikumar and Ramachandra, 2020). As a result of the presence of L-3,4-dihydroxyphenylalanine (L-DOPA) in the seed of MP as its active compound, findings from human

and animal models have revealed how *Mucuna pruriens* seed improves reproductive performances (Ahmad *et al.*, 2008; Mutwedu *et al.*, 2019).

A significant number of men living with epilepsy experience sexual dysfunction (Nikoobakht *et al.*, 2007; Zhao *et al.*, 2019), while the attendant adverse effects of anticonvulsant drugs stem from erectile dysfunction, reduction in sexual desire to alterations of ejaculation (Yang and Wang, 2016). Additionally, traditional anticonvulsant drugs such as sodium valproate, carbamazepine, phenytoin, etc. have been associated with impairment of the hypothalamic-pituitary-testicular axis (Osuntokun *et al.*, 2017; Osuntokun *et al.*, 2020). However, the management of epilepsy or its co-morbidity (e.g., reproductive disorder) using orthodox medicine is neither easily assessable nor effortlessly affordable by citizens of many developing countries (Birbeck 2010; Ashidi *et al.*, 2019); it is, therefore, imperative to investigate the scientific mechanism of actions of some of the natural plants with acclaimed fertility enhancement on the deranged hypothalamic-pituitary-testicular axis following chronic treatment with an anticonvulsant drug hence, this study.

## MATERIALS AND METHODS

**Seed collection and preparation:** The procurement of the seeds of *Mucuna pruriens* (L.) DC, Var, leaf identification, authenticated, and extraction has been reported in our previous study Osuntokun *et al.* (2021), while Ashidi *et al.* (2019) also reported the phytochemical composition of the seed powder.

**Experimental Animal:** A total of 35 male Wistar rats procured from the animal house of the College of Health Sciences, Osun State University, Osogbo, Nigeria was randomly assigned into 5 groups (n=7). Group 1 received normal saline (0.2 ml) orally, while groups 2-5 received carbamazepine (CBZ) 25 mg/kg per oral. Groups 1, and 2 were fed with standard rats' chow, while groups 3-5 rats were fed with diets containing MP seed powder at 2.25 g, 1.5 g, and 0.75 g respectively (Ashidi *et al.*, 2019). This study was carried out in agreement with the provisions established by the Health Research Ethics Committee (HREC) of the Osun State University, Osogbo, Nigeria in line with the Guidelines for Proper Experimental Animal care (National Research Council (US) Committee for the Update of the Guide for the Care and Use of Laboratory Animals (2011).

**Seminal analysis:** Epididymal sperm were collected from the caudal epididymis immediately after the rats were sacrificed. Sperm progressive motility, morphology, count, and viability were determined using conventional methods as described in our previous study (Osuntokun *et al.*, 2020). Briefly, The number of motile spermatozoa was calculated per unit area and expressed as percentage motility. Sperm were counted using a counting chamber and the results were expressed as million sperm/ml suspension. Sperm viability was investigated by ensuring uniform spermatozoa smear on slides with eosin/nigrosine stain, while hundred of sperm cells were counted per slide to obtain the percentage of life/death ratio.

**Hormone Assay:** The releasing hormone from the hypothalamus (gonadotrophic releasing hormone- GnRH), a stimulatory hormone from the anterior pituitary (follicle-stimulating hormone-FSH), and luteinizing hormone- LH), the testicular hormone testosterone, and serum concentration of estradiol were determined using the enzyme-linked immunosorbent assay method as described in our previous study (Osuntokun *et al.*, 2020b).

**Assessment of the markers of lipid peroxidation in the hypothalamus, pituitary, and testicular tissues:** The activities of reduced glutathione and concentration of the product of lipid peroxidation, malondialdehyde (MDA) were evaluated in the supernatant of the hypothalamic, pituitary, and testicular tissues spectrophotometrically (Osuntokun *et al.*, 2021).

**Assessment of the morphological profile of the hypothalamus, pituitary, and testis:** The brain, epididymis, and testis were preserved in either neutral buffered formalin or Boin's fluid followed by routine laboratory procedures. After staining with hematoxylin and eosin, sections (5  $\mu$ ) of the processed hypothalamus, pituitary, and testis were viewed under the Leica DM 750 microscope for any signs of morphological aberrations (Osuntokun *et al.*, 2020a).

**Statistical analysis:** Descriptive and inferential statistics were carried out with the aid of a graph pad prism software, while Student–Newman–Keul's test was employed for the post hoc analysis where appropriate. The level of significance was set at  $p < 0.05$ .

## RESULTS

**The weight of reproductive and accessory organs:** There was a significant ( $p = 0.0001$ ) decrease in the testicular weights of CBZ, and CBZ + MP (2.25 g) treated rats compared with the control (Table 1).

**Table 4.1**

The weight of reproductive and accessory organs

Treatment Group	Testicular weight (g)	Epididymal weight (g)	Seminal vesicle (g)
Control	1.32 $\pm$ 0.04	0.30 $\pm$ 0.01	0.82 $\pm$ 0.14
CBZ	0.94 $\pm$ 0.04 <sup>a</sup>	0.28 $\pm$ 0.01	0.59 $\pm$ 0.08
CBZ + MP (2.25 g)	1.16 $\pm$ 0.03 <sup>ab</sup>	0.31 $\pm$ 0.04	0.47 $\pm$ 0.11
CBZ + MP (1.5 g)	1.25 $\pm$ 0.08 <sup>b</sup>	0.29 $\pm$ 0.05	0.45 $\pm$ 0.04
CBZ + MP (0.75 g)	1.38 $\pm$ 0.03 <sup>b</sup>	0.32 $\pm$ 0.01	0.70 $\pm$ 0.11

*a:* decrease compared with the control ( $p = 0.0001$ )

*b:* increase compared with CBZ ( $p = 0.0006$ )

**The hypothalamic, pituitary, and testicular hormones concentration:** The serum concentration of gonadotropic-releasing hormone (GnRH) increased significantly ( $p = 0.0180$ ) in the CBZ + MP (0.75 g) treatment group. There was a significant ( $p = 0.0001$ ) decrease in the serum concentration of follicle-stimulating hormone (FSH) following CBZ treatment, while this hormone significantly ( $p = 0.0003$ ) increased in the CBZ + MP treatment groups relative to CBZ-treated rats. The luteinizing hormone (LH)

concentration increased markedly ( $p = 0.0055$ ) in the CBZ + MP (0.75 g). The serum concentration decreased significantly ( $p = 0.0001$ ) in the CBZ treatment. However, testosterone concentration increased significantly ( $p = 0.0008$ ) across the CBZ + MP treatment groups compared with the CBZ-treated rats (Table 2).

**The serum concentration of estradiol:** There was a significant increase ( $p = 0.0003$ ) in the concentration of estradiol in the CBZ treatment groups, while the estradiol concentration decreased significantly ( $p = 0.0015$ ) compared with CBZ treated rats (Figure 1).

**Table 2**

The hypothalamic, pituitary, and testicular hormones concentration

Treatment Group	GnRH	FSH	LH	Testosterone
Control	43.90 ± 0.93	0.41 ± 0.01	0.34 ± 0.03	0.36 ± 0.03
CBZ	41.64 ± 5.72	0.29 ± 0.02 <sup>a</sup>	0.34 ± 0.01	0.20 ± 0.01 <sup>a</sup>
CBZ + MP (2.25 g)	44.60 ± 4.03	0.44 ± 0.03 <sup>δ</sup>	0.38 ± 0.03	0.38 ± 0.02 <sup>δ</sup>
CBZ + MP (1.5 g)	45.03 ± 4.40	0.40 ± 0.04 <sup>δ</sup>	0.36 ± 0.05	0.36 ± 0.04 <sup>δ</sup>
CBZ + MP (0.75 g)	49.91 ± 1.80 <sup>βδ</sup>	0.52 ± 0.04 <sup>βδ</sup>	0.45 ± 0.02 <sup>βδ</sup>	0.43 ± 0.05 <sup>δ</sup>

$\beta$ : increase compared with control ( $p = 0.0180$ )

$a$ : decrease compared with control ( $p = 0.0001$ )

$\delta$ : increase compared with CBZ ( $p = 0.0003$ )

**The semen parameters:** The percentage of sperm motility declined ( $p = 0.0001$ ) across the treatment group compared with the control. Also, the percentage of sperm viability decreased markedly ( $p = 0.0001$ ) across the treatment group except for the CBZ + MP (0.75 g) treatment group. The sperm count of the CBZ treated rats decreased significantly ( $p = 0.0044$ ). The percentage normal morphology decreased

**Table 3**

The semen parameters

Treatment Group	% Motility	% Viability	Sperm count (10 <sup>6</sup> X ml)	% Normal morphology
Control	86.60 ± 2.29	97.00 ± 0.55	112.40 ± 7.74	88.60 ± 1.36
CBZ	19.00 ± 5.57 <sup>a</sup>	25.00 ± 2.04 <sup>a</sup>	69.80 ± 10.20 <sup>a</sup>	18.00 ± 0.71 <sup>a</sup>
CBZ + MP (2.25 g)	12.50 ± 1.44 <sup>a</sup>	37.00 ± 5.15 <sup>a</sup>	93.20 ± 13.95	68.00 ± 6.77 <sup>aβ</sup>
CBZ + MP (1.5 g)	52.50 ± 13.31 <sup>aβδ</sup>	61.75 ± 13.80 <sup>aβ</sup>	97.20 ± 6.19	75.60 ± 7.76 <sup>β</sup>
CBZ + MP (0.75 g)	72.00 ± 3.39 <sup>aβδ</sup>	81.25 ± 1.25 <sup>βδ</sup>	129.60 ± 8.51 <sup>β</sup>	78.60 ± 3.01 <sup>β</sup>

$a$ : decrease compared with control ( $p = 0.0001$ )

$\beta$ : increase compared with CBZ ( $p = 0.0001$ )

$\delta$ : increase compared with CBZ + MP (2.25 g) ( $p = 0.0006$ )

**Table 4**

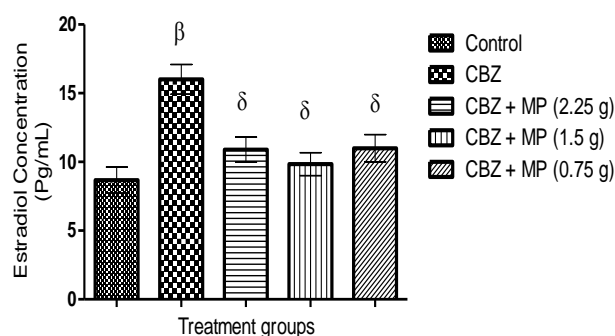
Effects of dietary meal supplemented with *Mucuna pruriens* seed powder on the characteristics of carbamazepine-induced sperm morphological alteration in male Wistar rats.

Morphological Parameters	Control	CBZ	CBZ + MP (2.25 g)	CBZ + MP (1.5 g)	CBZ + MP (0.75 g)
Head defect	1.80 ± 0.20	2.60 ± 0.24 <sup>β</sup>	2.60 ± 0.24 <sup>β</sup>	1.80 ± 0.20	2.00 ± 0.41
Midpiece defect	2.80 ± 0.37	3.60 ± 0.51	3.40 ± 0.40	2.60 ± 0.24	2.00 ± 0.41
Tail defect	3.80 ± 0.37	13.60 ± 0.68 <sup>β</sup>	12.60 ± 1.12 <sup>β</sup>	13.00 ± 0.71 <sup>β</sup>	10.20 ± 0.92 <sup>βμ</sup>
Head only	1.80 ± 0.37	8.40 ± 0.40 <sup>β</sup>	6.25 ± 0.95 <sup>β</sup>	3.40 ± 1.03	1.80 ± 0.66
Headless	1.40 ± 0.51	6.60 ± 0.24 <sup>β</sup>	7.25 ± 0.95 <sup>β</sup>	1.60 ± 0.68	1.80 ± 0.49

$\beta$ : increase compared with control ( $p = 0.0001$ )

$\mu$ : decrease compared with CBZ ( $p = 0.0175$ )

markedly (0.0001) in the CBZ and CBZ + MP (2.25 g) treatment group. (Table 3).



**Figure 1**

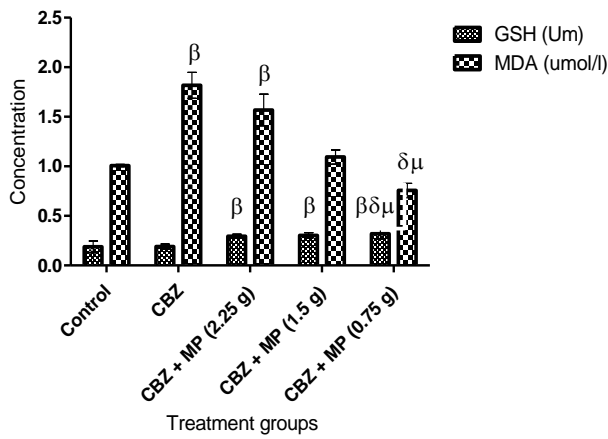
The serum concentration of estradiol

$\beta$ : increase compared with the control ( $p = 0.0001$ )

$\delta$ : decrease compared with CBZ ( $p = 0.0031$ )

**Percentage of sperm morphological alterations:** The number of spermatozoa with the observable feature of head defect increased significantly in the CBZ and CBZ + MP (2.25 g) treatment groups. The number of sperm cells with tail defect increased significantly ( $p = 0.0001$ ) across the treatment group except for CBZ + MP (0.75 g) treated rats. Moreover, the number of sperm with the head only increased significantly ( $p = 0.0001$ ) in the CBZ, and CBZ + MP (2.25 g) treated a headless body which increased significantly ( $p = 0.0001$ ) in the CBZ, and CBZ + MP (2.25 g) (Table 4).

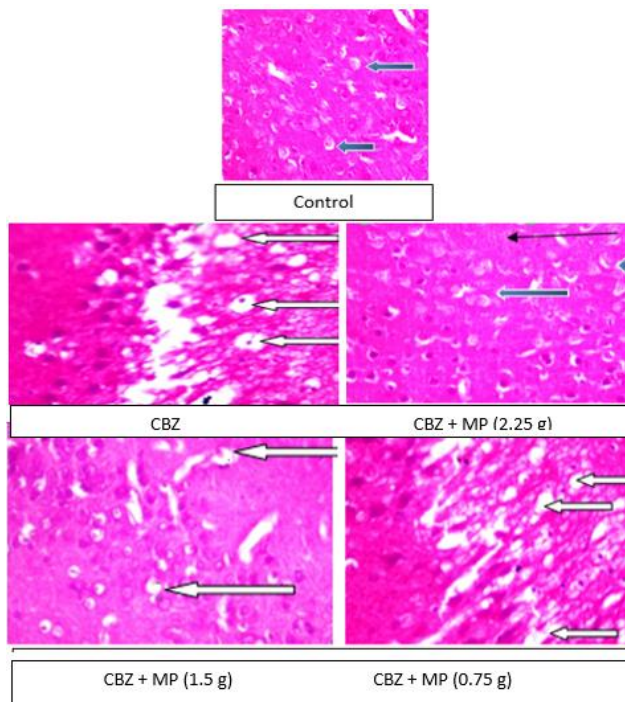
**The markers of oxidative stress in the testis:** This study shows a significant ( $p = 0.0001$ ) increase in the activities of reduced glutathione in the testicular tissue of all the treatment groups except the CBZ-treated rats. However, the testicular concentration of MDA increased significantly ( $p = 0.0001$ ) in the CBZ, and CBZ + MP (2.25 g) (Figure 2).



**Figure 2**  
Oxidative stress in the testis  
β: increase compared with the control ( $p = 0.0001$ )  
δ: decrease compared with CBZ ( $p = 0.0013$ )  
μ: decrease compared with CBZ + MP (2.25 g) ( $p = 0.0061$ )

**The histomorphology of the hypothalamus**

Carbamazepine chronic treatment induced neuronal necrosis (White arrow) which was attenuated following MP (2.25 g) treatment (Blue arrow) (Plate 1).



**Plate 1**  
**The histomorphology of the hypothalamus**  
Blue arrow: Normal neuron; Slender arrow: normal stroma; White arrow neuronal necrosis; magnification: 400

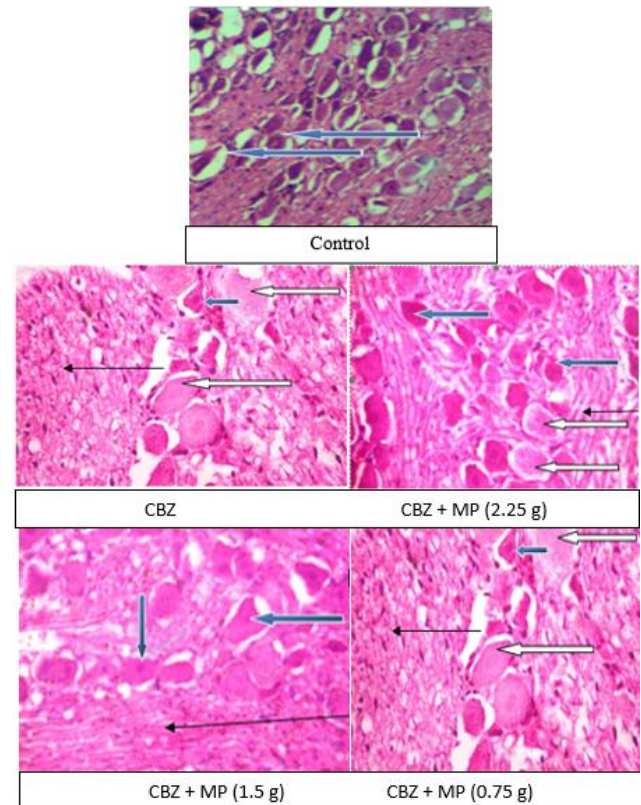
**The histomorphology of the pituitary**

There was marked neuronal vacuolation in the CBZ treated group. However, MP (2.25 g), and MP (1.5 g) alleviated this (blue arrow) (Plate 2).

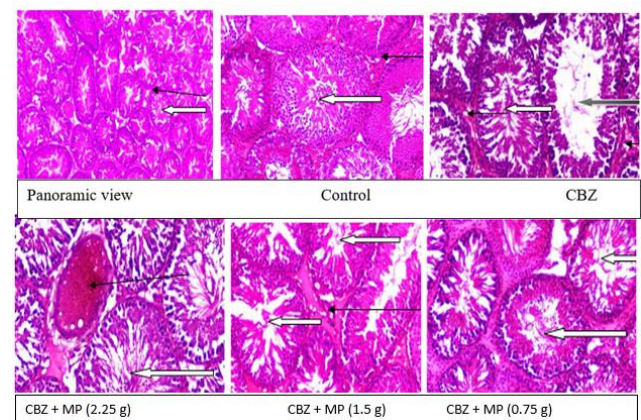
**The histomorphology of the testis**

Plate 3 below is the photomicrograph of the testicular section. there was normal histoarchitecture in the testis of the normal saline-treated rats. This was evident with the appearance of the normal seminiferous tubule containing

mature spermatozoa within their lumen (white arrow). Several tubules in the CBZ-treated rat are seen with maturation arrest (black arrow), and congested interstitium (slender arrow). The interstitial spaces of the CBZ + MP (2.25 g), and CBZ + MP (1.5 g) showed normal Leydig cells, but with vascular congestion (slender arrow). However, there was no difference in the morphology of the testis of the CBZ + MP (0.75 g) and the normal saline (control) treatment group.



**Plate 2**  
Effects of carbamazepine on the histomorphology of the pituitary gland in male Wistar rats fed dietary meal supplemented with *Mucuna pruriens* seed powder.  
White arrow: neuronal: Neuronal vacuolation; Slender arrow: Normal stroma; Blue arrow: normal neuron; magnification: 400



**Plate 3**  
Effects of carbamazepine on the histomorphology of the testis in male Wistar rats fed dietary meal supplemented with *Mucuna pruriens* seed powder.  
Magnification: X400; Stain: Haematoxylin and eosin

## DISCUSSION

While there are different levels of reproductive toxicity as a response to diverse classes of anticonvulsant drugs, previous studies have shown that the worse sexual function scores were seen in patients or animals treated with sodium valproate, CBZ, phenytoin, etc. compared to some newer anticonvulsant agents like levetiracetam (Mazdeh *et al.*, 2020; Osuntokun *et al.*, 2020a&b); which are not better off than the former in terms of efficacy (Li *et al.*, 2014; Suresh *et al.*, 2015). Therefore, since the treatment with some conventional anticonvulsant drugs remains the mainstay in chronic epilepsy, despite their untoward adverse effects, there is a need to investigate the therapeutic effects of some medicinal plants such as *Mucuna pruriens* seed as adjunctive treatment with carbamazepine.

In this present study, neither seminal vesicle nor epididymal weight was affected by the CBZ treatment. However, a significant decrease in testicular weight recorded against CBZ treatment could not be receded completely by the MP (2.25 g) in contrast to what is obtainable in the CBZ + MP (1.5 g), and CBZ + MP (0.75 g) groups. This may serve as potential evidence that the compounds of MP seed at the highest dose (2.25 g) may cause some biological effects which might have interfered with the efficacy of the result. This finding is consistent with our result obtained from the concentration of GnRH analysis, where the lowest dose of MP (0.75 g) tends to be efficacious compared to the other treatment groups.

In this present study, however, although CBZ had no significant effect on the reproductive hypothalamic hormone, an increase in the secretion of GnRH induced by the MP (0.75 g) treatment had a direct and positive influence on the serum concentration of the FSH (despite the adverse effect of CBZ), and LH; while an increase in the serum concentration of testosterone is another suggestive potential evidence that the influence of MP is gonadotropic.

It is a known fact that L-3,4-dihydroxyphenylalanine (L-DOPA) is an active substance of *Mucuna pruriens* seed with levels ranging up to 13% (Deli *et al.*, 2021). Meanwhile, this substance (L-DOPA) has been implicated as a potent secretagogue of GnRH, with consequential stimulation of the FSH and LH secretion from the anterior portion of the pituitary gland, and eventual testosterone production (Singh *et al.*, 2013; Marques *et al.*, 2018). This could serve as an evidential (scientific) justification for the aphrodisiac properties of the *Mucuna pruriens* seed as reported by several authors (Ahmad *et al.*, 2008; Mutwedu *et al.*, 2019). However, despite a high concentration of L-DOPA in the 2.25 g of MP consumed by the CBZ-treated rats, there was no significant difference in the concentration of GnRH between the CBZ and CBZ + MP (2.25 g) treated rats; a suggestive indication that MP (2.25 g) might have posed additional toxicity to the CBZ-treated. Moreover, it is worthy of note that the concentration of L-DOPA in *Mucuna pruriens* at 0.75 g, an equivalent of 1 seed of M.P (Ashidi *et al.*, 2019) appears adequate in the induction of GnRH secretion from the hypothalamus and sufficient to attenuate the inhibitory influence of CBZ on the FSH, LH and testosterone secretion.

Our finding shows a decrease in the serum concentration of testosterone and an increased level of estradiol in the CBZ-treated rats; this is an assertion of the involvement of

CBZ in the induction of enzyme aromatase, an enzyme whose activities convert androgens to estrogens (Jacobsen *et al.*, 2008). Additionally, it is evident from this study that MP is a potential therapeutic agent that could attenuate the activities of the enzyme aromatase in the conversion of testosterone to estradiol. This may not be unrelated to a high concentration of alkaloids, tannins anthraquinones, saponins, flavonoids, and cardiac glycosides (Vadivel and Janardhanan, 2000). This finding is consistent with the report of Golan *et al.*, (2008) that the phytochemicals, including steroidal saponins and flavonoids Tarigan *et al.*, 2016), attenuate estrogen production by inhibiting the action of aromatase.

Our result on the sperm parameters (percentage motility, viability, morphology, and sperm count) reflects the spermicidal effects of CBZ (tables 3 and 4). However, MP supplement in the CBZ + MP (1.5 g) treatment group averted the CBZ-toxicity on the seminal profile, while these adverse effects not only receded in the CBZ + MP (0.75 g) but the indices of normal seminal profile increased significantly compared to the control. While it remains undoubted that the compounds in MP seed increased the testosterone level through hypothalamic-pituitary-testicular axis stimulation; the highest treatment dose in this study (CBZ + MP (2.25 g) posed a deleterious effect, worse than what is obtainable in the CBZ alone treatment group.

An increase in the concentration of malondialdehyde in the testicular tissue of CBZ-treated rats recorded in this present study is a pointer to the potential toxicity posed by CBZ treatment. Despite an increase in the activities of reduced glutathione in the testicular tissue of the CBZ + MP (2.25 g) treatment group, the concentration of malondialdehyde remains very high; suggestive evidence of (1) innate adaptive mechanism of the tissue to oxidative stress posed by the CBZ, and/ (2) the potential toxicity of the MP (2.25 g) which may have been heightened by the CBZ + MP (2.25 mg/kg) combination. However, MP (1.5 g), and MP (0.75 g) doses are more tolerated and therapeutic than the highest dose MP (2.25 g).

The neuronal necrosis and vacuolation observed in the hypothalamus and pituitary of the CBZ treatment group may be partly contributed to a decrease in the FSH, and LH secretions. Therefore, it could be posited that a decrease in the serum concentration of testosterone recorded in the CBZ-treated rat in this study is indirectly caused by damage to the hypothalamus and or the anterior pituitary gland. Apparently, this damage is ameliorated in the CBZ + MP (2.25 g), CBZ + MP (1.5 g), and CBZ + MP (0.75 g) treatment groups in descending order, a factor substantiating the potential toxicity of MP (2.25 g). Moreover, maturation arrest and interstitial space/vascular congestion, a sign of testicular toxicity following CBZ administration in this present study are consistent with our previous findings (Osuntokun *et al.*, 2017; Osuntokun *et al.*, 2020). Additionally, Ashidi *et al.* (2019) reported a possibility of alteration in the spermatogenesis of male rats fed with 2.25 g (3 seeds) of M.P seed. This is therefore an assertion that M.P (2.25 g) may not ameliorate the damaging effects posed by CBZ but rather compound it. However, it is worthy of note, that CBZ + MP (1.5 g), and CBZ + MP (0.75 g) treatment groups had relatively normal testicular histoarchitecture, which was devoid of morphological

aberrations in contrast to what was found in the CBZ and CBZ + M.P (2.25 g) treated groups.

In conclusion, this study revealed that the hypothalamic-pituitary-testicular axis derangement induced by carbamazepine toxicity may be attenuated by a moderate or low quantity of *Mucuna pruriens* seed supplement. MP seed enhanced the indices of reproductive function in male Wistar rats by increasing the GnRH, FSH, and LH; and decreasing the serum concentrations of estradiol due to the presence of L-DOPA. The M.P seed also repealed the disruption of the CBZ-induced seminal profile, and histomorphology of the hypothalamus, pituitary, and testis due to its antioxidative mechanism as evident in the activities of the reduced glutathione. However, it is expedient in our future studies to examine the effects of MP on the immunohistochemistry of the hypothalamic-pituitary-testicular axis following CBZ treatment.

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