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SPERMATOGENIC AND LIBIDO ENHANCING EFFECT OF ETHANOL EXTRACT OF *KIGELIA AFRICANA* IN Δ^9 TETRAHYDROCANNABINOL INDUCED ERECTILE DYSFUNCTION IN MALE WISTAR RATS

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ABSTRACT: *Erectile dysfunction has remained one of the major global health issues for the past two decades. Since the discovery of phosphodiesterase type 5 inhibitors, a significant number of patients have solved the issue of erectile dysfunction. However, the wide distribution of phosphodiesterase type 5 enzymes at various sites of the body led phosphodiesterase type 5 inhibitors to cause various unnecessary outcomes. Hence, it is vital to look for optional agents that could solve these limitations. In this present work, erectile dysfunction was induced by administering 30 mg/kgbwt THC for 3 days. Treatment given was as follows: A - Normal Control, B - Std control (THC+Viagra), C - Negative control (THC only), D - THC + 200 mg/Kgbwt ethanol leaf extract of Kigelia africana (200 mg/Kgbwt), E - THC + 400 mg/Kgbwt ethanol leaf extract of Kigelia africana for a succession of 14 days. Sexual behaviour parameters was monitored in the male rats on Days 1, 7 and 14 respectively after administration by pairing with a receptive female (1:1); thereafter, rats were sacrificed and serum was collected for some biochemical parameters using standard method.Cage side observation on the animals reve aled prospective behaviours by the receptive female rats and precopulatory be haviours by the ethanol extract K.africana treated male rats.The extract at 2 00 and 400 mg/kg body weight significantly (P<0.05) increased the frequencie s of mount and intromission.In addition, the ejaculation latency was significan tly (P< 0.05) prolonged.The latencies of mount and intromission were reduced significantly (P<0.05) whereas ejaculation frequency increased.The extract also reduced the post-ejaculatory interval of the Wistar rats. Computed percentages of index of libido, mounted, intromitted, ejaculated and copulatory efficiency were significantly (p<0.05) higher in the extract-treated animals in a dosage dependent manner than the control whereas the inter copulatory interval decreased significantly. The extract also significantly (p<0.05) increased the serum testosterone, FSH and LH concentration but significantly (p<0.05) reduced serum oestrogen, prolactin and progesterone of the treated groups when compared with the control. The extract also significantly (p<0.05) increased the sperm motility, total sperm count, and sperm viability but produced a significant (p<0.05) decrease in serum immobility when compared with the THC control. It can be inferred from this work that an extract of K. africana may elicit spermatogenic, androgenic and libido enhancing activities in THC induced erectile dysfunction in a dosage dependent manner.*

KEYWORDS: Androgenic, androgen binding protein, *K. africana*, reproductive hormones, spermatogenesis, THC.

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INTRODUCTION

Male erectile dysfunction (ED) or impotence refers to inability to reach and retain adequate penile tumescence for sexual intercourse. Over 152 million men globally suffer from ED (Eliazu *et al*., 2017). The global issue of ED is anticipated to affect around 322 million of males by 2025 (Yovwin *et al*., 2015; Pallangyo *et al*., 2016; Dasofunjo *et al.,* 2020). Incompetence in accomplishing normal penile erection leads to depression, loss of self-confidence, socialization, and communication with the family (Oyelade *et al.*, 2016). Also, ED leads to conflict in the relationships that negatively influence the well-being of couples (Muneer *et al*., 2014). There is an increasing focus on the use of medicinal plants and their bioactive agents in drug design and development in recent decades (Ubon *et al*., 2017; Dasofunjo *et al.,* 2024).

The incidence of sexual inadequacy in males has led to the development of a number of available treatment options. Therefore, successful treatment of sexual dysfunction will improve reproduction, self-esteem and provide increased relationship satisfaction (Neeruganti *et al*., 2017). The remedies for male sexual dysfunction in modern medicine are limited. Allopathic drugs such as sildenafil citrate, tadalafil citrate, vardenafil, avanafil, alprostadil, and papaverin have been developed for the management of erectile dysfunction, but have produced side effects like sudden hypotension, hypersensitivity reaction, abnormal vision, urethral burning, bleeding, suicidal tendencies and mental disorders, and these limit their utility (Alok *et al*., 2017; Joe *et al*., 2017).

Kigelia africana is locally used to manage diseases including leprosy, impetigo and worm infestations in blood, dermal complaints and infections, such as whitlows, cysts, ache and boils (Dasofunjo *et al.,* 2020) .The bark of *Kigelia africana* has anti-inflammatory, analgesic, anti-microbial, anti-anaemic, anti-hypertensive and anti-cancer properties (Palmer *et al*., 2002; Asuk *et al*., 2021;). This present research work is designed to assess the aphrodisiac effect of *Kigelia africana* leaf extract *in* Δ^9 tetrahydrocannabinol *induced* erectile dysfunction in male Wistar rats.

MATERIALS AND METHODS

Plant Material

Kigelia africana was collected from the University of Cross River State (UNICROSS) community, Nigeria. The plant was identified at the Department of Botany, University of Calabar, Calabar. The leaves were air dried until constant weight was obtained. The dried leaves were pulverized after which 200 g was desolved in I000 ml (1:5 w/v) of 70% ethanol for 72 hours with constant shaking using the electric shaker. This was later filtered using Whatman No. 1 filter paper. The filtrate was then concentrated in a water bath at 45ºC. The resulting slurry was weighed and reconstituted in distilled water to give the required dose.

Experimental Animals

Thirty-five (35) male and female Wistar rats (200-250 g) were obtained from the Animal Holding Unit of the Medical Biochemistry Department, UNICROSS, Okuku Campus. The animals were allowed to undergo acclimatization for seven days. The rats were housed in a plastic cage. The animal house was well ventilated and kept at room temperature and relative

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humidity of 29±2ºC and 70% respectively with 12 hours of natural light-dark cycle. Each rat was allowed free access to food and water *ad libitum*. Good hygiene was maintained by constant cleaning and removal of faeces and spilled feeds from cages daily. Oral route of administration was employed throughout the experimental period.

Methods

Phytochemical analysis was determined by the method of Trease and Evans (1996). The male sexual behaviour test was carried out by the methods of Ratnasonriva and Dhamasiri (2000), as modified by Dasofunjo *et al.* (2013). Serum testosterone, luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels of extract-treated male rats was estimated using the method of Ismail (1986); sperm profile was determined by standard methods.

Experimental Design

Erectile dysfunction was induced by administering 30 mg/kgbwt of THC for 3 days. Treatment given was as follows: A - Normal Control, B - Std control (THC + Viagra), C - Negative control (THC only), D - THC + 200 mg/Kgbwt ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), E - THC + 400 mg/Kgbwt ethanol leaf extract of *Kigelia africana* for a succession of 14 days.

RESULT

Thirty-five (35) female proceptive and male precopulatory behaviour parameters were observed from the cage side when the extract-treated male rats were introduced to the receptive female rats. The proceptive behaviour displayed by the female rats included ear-wiggling characterized by a rapid antero posterior vibration of the ears, a short run where they suddenly stop and present their posterior to the male rats (darting) and a short jump with stiff legs followed by immobility and presentation (hopping).

The male rats, upon introduction, responded with immediate advances toward the females and displayed precopulatory behaviour such as chasing and anogenital sniffing which eventually culminated into mounting. The extract produced no sedative effect on the male rats since none of the animals showed any evidence of tiredness throughout the observatory period. Similarly, dot receptivity was not displayed by any of the female rats used in the study.

The effect of the extract of K. *africana* on sperm profile in THC induced erectile dysfunction in male Wistar rats. The extract significantly raised the pH of the spermatozoa of all the treated groups to neutral pH range when compared with the normal control (Fig. 1). The extract also significantly ($p<0.05$) increased the sperm motility, total sperm count, and sperm viability but produced a significant ($p<0.05$) decrease in serum immobility when compared with the THC control (Fig. 2-5).

The sexual behaviour parameters (MF, IF, EF, ML, IL, EL and PEI) were monitored for both the controlled and *K. africana* treated groups but were observed to have varying latency and frequency (Fig. 6-26).

At Day 1, the control group showed a decrease in IF, ML and increase in MF and PEI but no significant impact was observed in the other days (Day 7 and Day 14) compared to the extract-

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treated group. The extract-treated group at 200 and 400 mg/kg body weight showed a significant effect on the parameters in which IF and EF increased significantly ($p<0.05$) while ML and PEI decreased ($p<0.05$) significantly at the days of observation compared to the controlled group and standard control (Fig. 6-26).

The computed male rat's sexual behaviour parameters which include percentage (%) index of libido, mounted, intromitted, ejaculated and copulatory efficiency were significantly ($p<0.05$) higher in the *K. africana* extract-treated animals when compared to the control group (Fig. 27-32).

The ethanol extract of *K. africana* showed a significant ($p<0.05$) dosage increase in serum FSH, LH and testosterone but a significant decrease in prolactin, progesterone and oestrogen at 200 and 400 mg/kg body weight when compared with the control (Fig 33-38). The phytochemical screening also revealed the presence of flavonoids, tannins, steroids, phlobatannins, saponins triterpenoids glycosides and alkaloids at varying concentrations (Table 1).

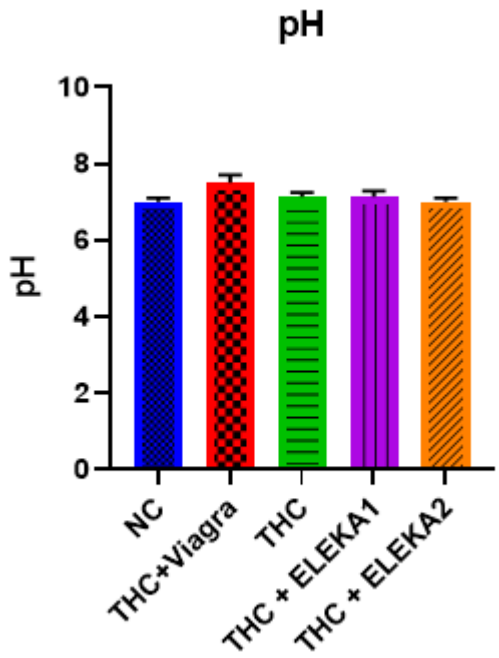

Fig. 1: The effect of *K. africana* extract on sperm pH profile following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

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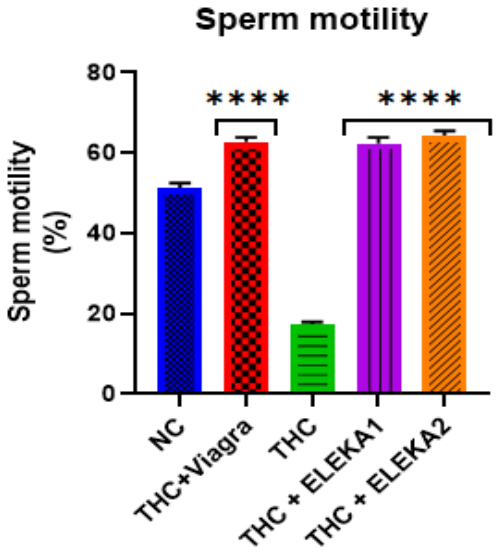

Fig. 2: The effect of *K. africana* extract on sperm motility following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

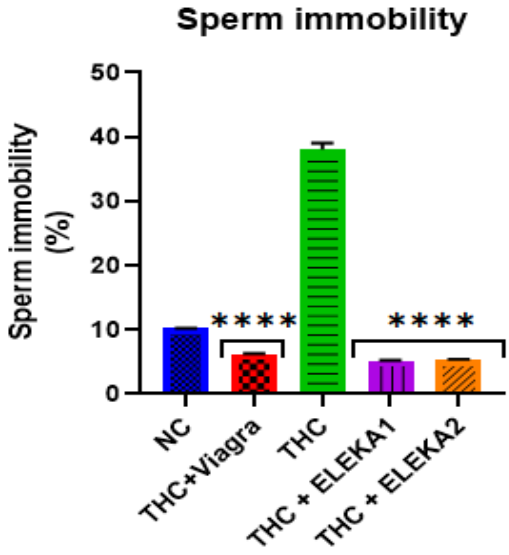

Fig. 3: The effect of *K. africana* extract on sperm immobility following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

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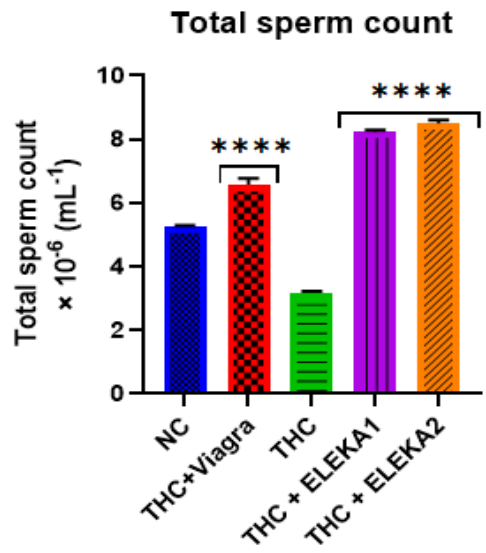

Fig. 4: The effect of *K. africana* extract on total sperm count following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

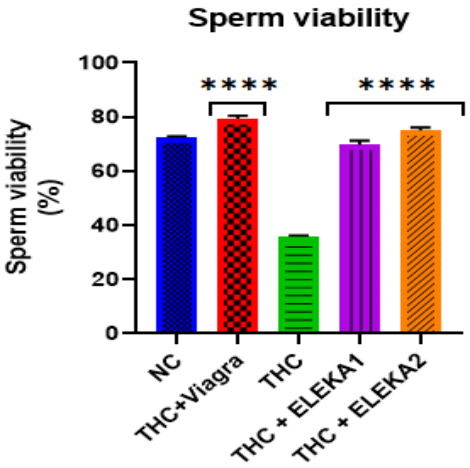

Fig. 5: The effect of *K. africana* extract on sperm viability following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

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The Effect of *K. africana* Leaf Extract on Some Sexual Behaviours Following THC Induced Erectile Dysfunction in Male Wistar Rats on Day 1

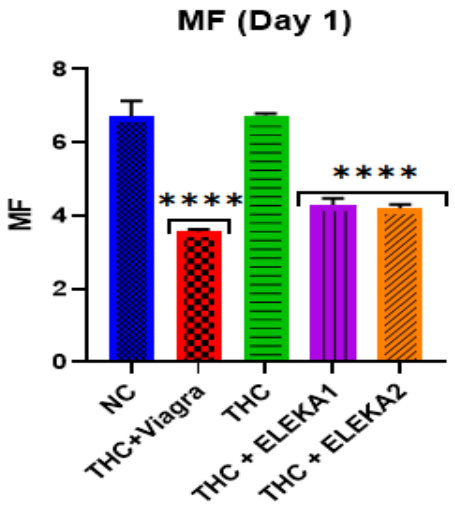

Fig. 6: The effect of *K. africana* extract on mount frequency following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol ol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

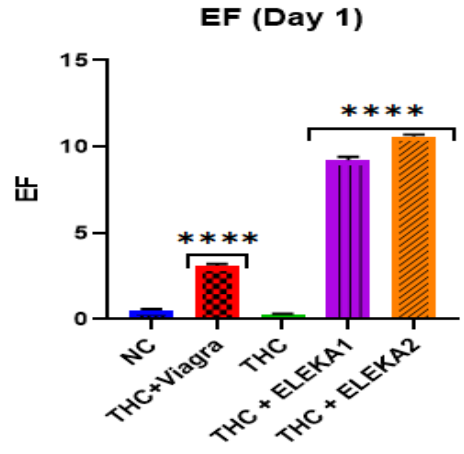

Fig. 7: The effect of *K. africana* extract on ejaculation frequency following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

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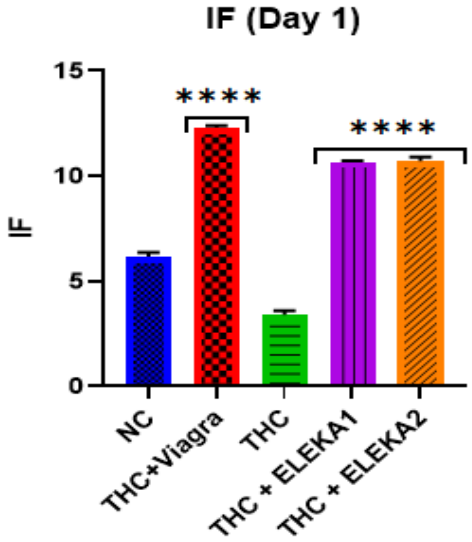

Fig. 8: The effect of *K. africana* extract on intromission frequency following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

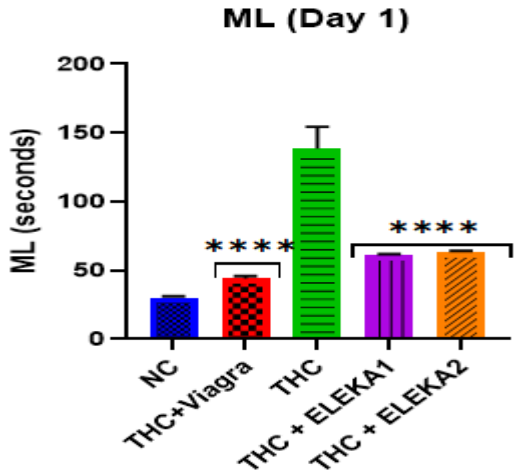

Fig. 9: The effect of *K. africana* extract on mount latency following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

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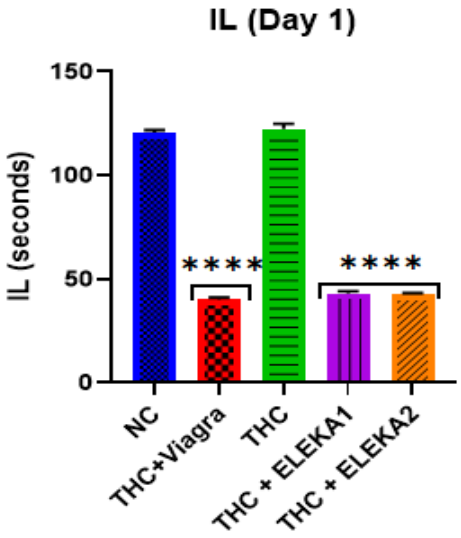

Fig. 10: The effect of *K. africana* extract on intromission latency following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

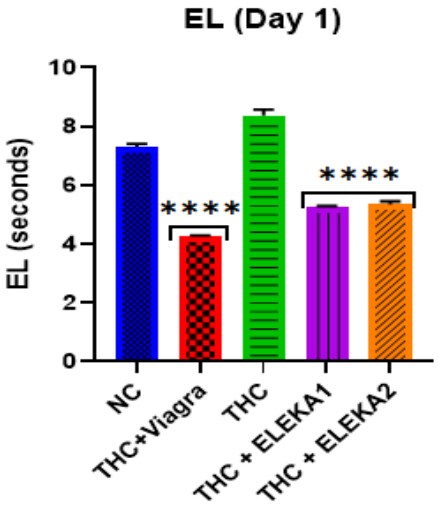

Fig. 11: The effect of *K. africana* extract on ejaculation latency following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

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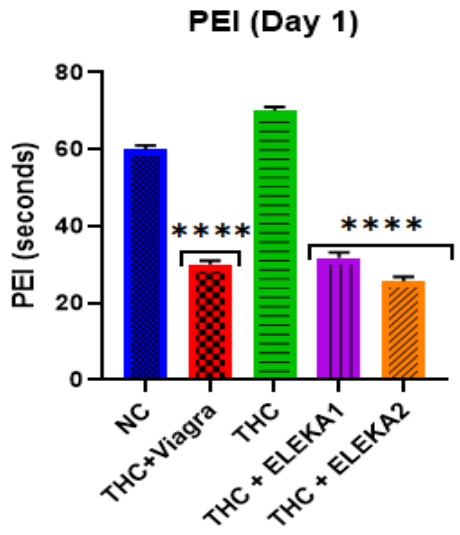

Fig. 12: The effect of *K. africana* extract on post ejaculation interval following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

The Effect of *K. africana* Leaf Extract on Some Sexual Behaviours Following THC Induced Erectile Dysfunction in Male Wistar Rats on Day 7

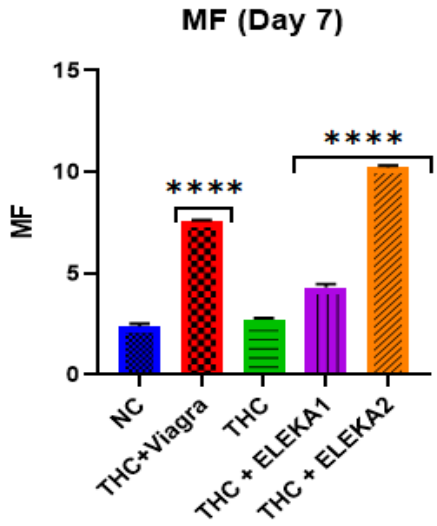

Fig. 13: The effect of *K. africana* extract on mount frequency following THC induced erectile dysfunction in male Wistar rats

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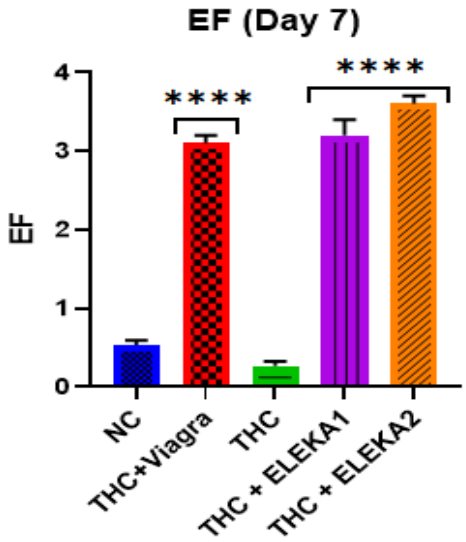

Fig. 14: The effect of *K. africana* extract on ejaculation frequency following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

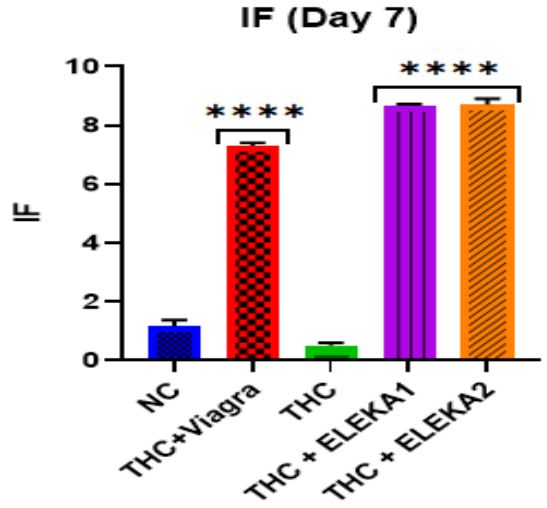

Fig. 15: The effect of *K. africana* extract on intromission frequency following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

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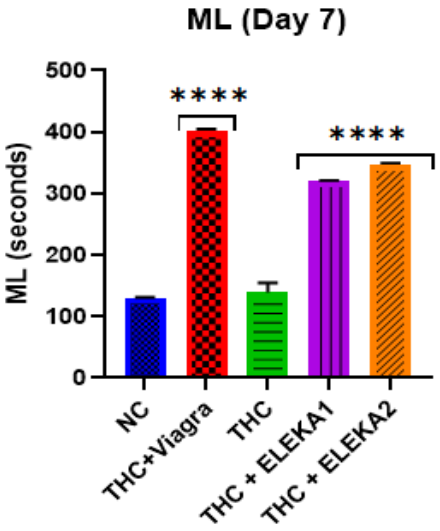

Fig. 16: The effect of *K. africana* extract on mount latency following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

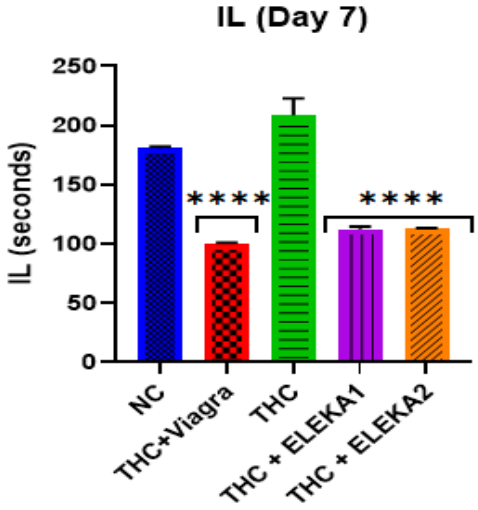

Fig. 17: The effect of *K. africana* extract on intromission latency following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt)

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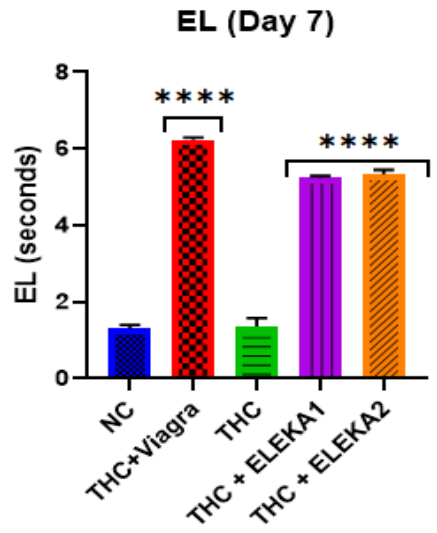

Fig. 18: The effect of *K. africana* extract on ejaculation latency following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

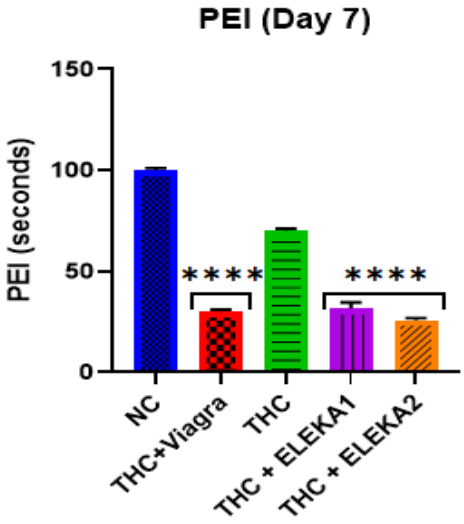

Fig. 19: The effect of *K. africana* extract on post ejaculation interval following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

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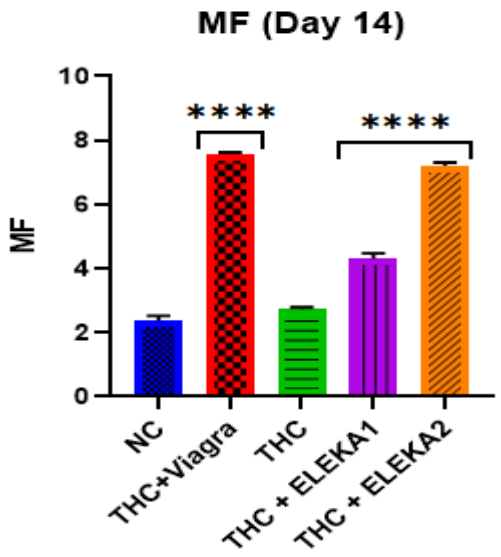

Fig. 20: The effect of *K. africana* extract on mount frequency following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

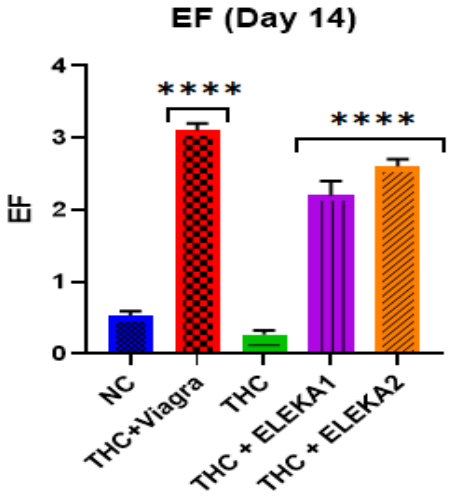

Fig. 21: The effect of *K. africana* extract on Ejaculation frequency following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

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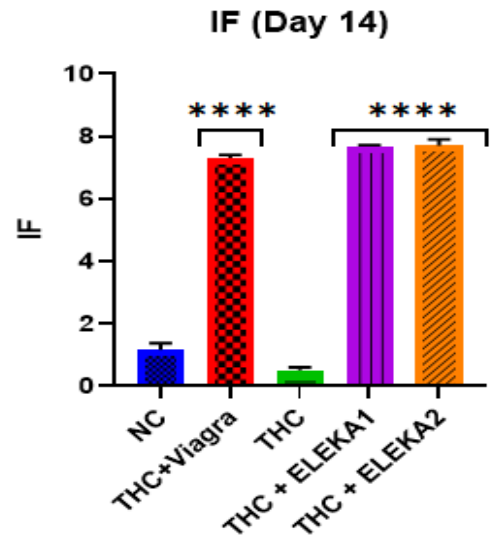

Fig. 22: The effect of *K. africana* extract on intromission frequency following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

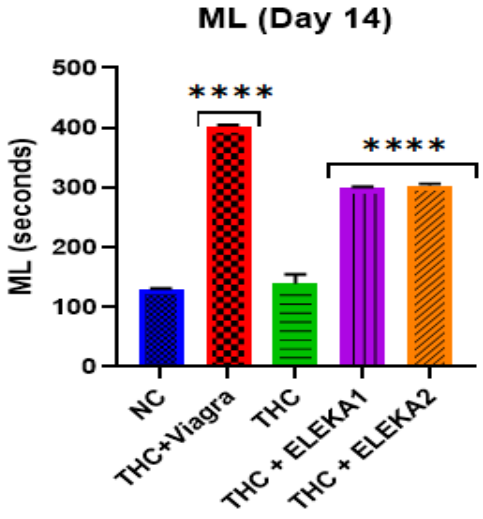

Fig. 23: The effect of *K. africana* extract on mount latency following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

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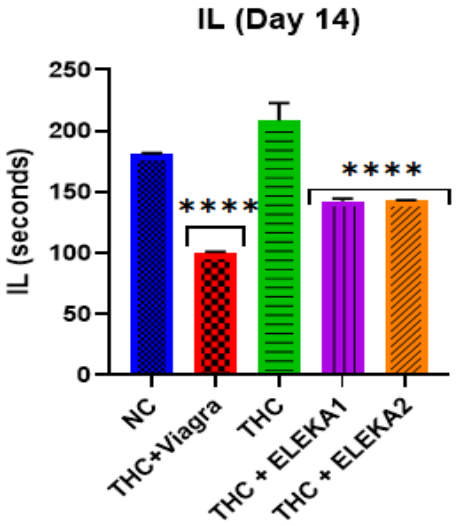

Fig. 24: The effect of *K. africana* extract on intromission latency following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

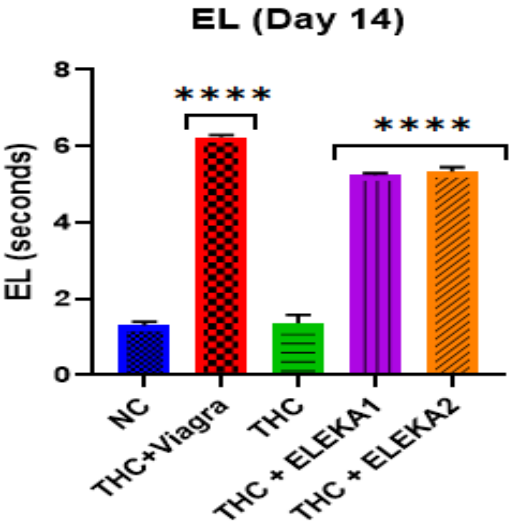

Fig. 25: The effect of *K. africana* extract on ejaculation latency following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

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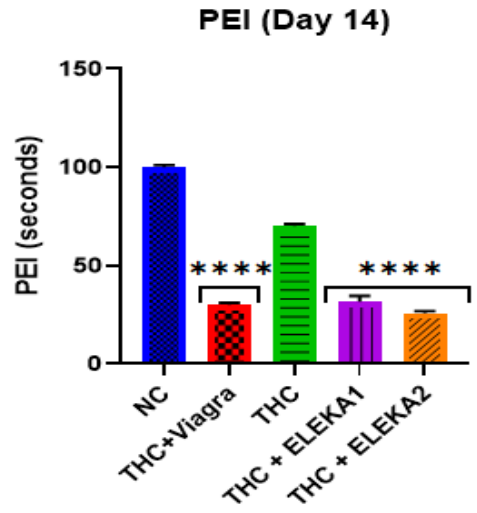

Fig. 26: The effect of *K. africana* extract on post ejaculation interval following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

The Effect of *K. africana* Leaf Extracts on Some Computed Parameters of the Sexual Behaviours of Male Wistar Rats

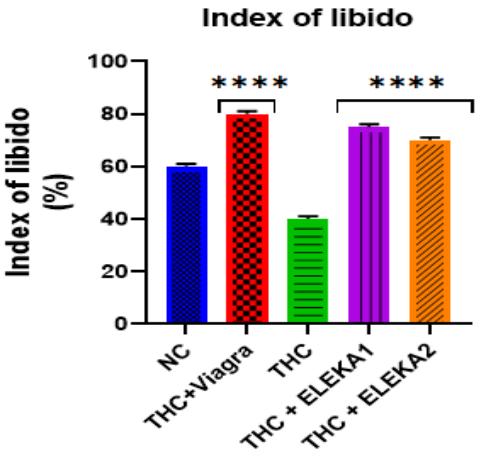

Fig. 27: The effect of *K. africana* extract on index of libido following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

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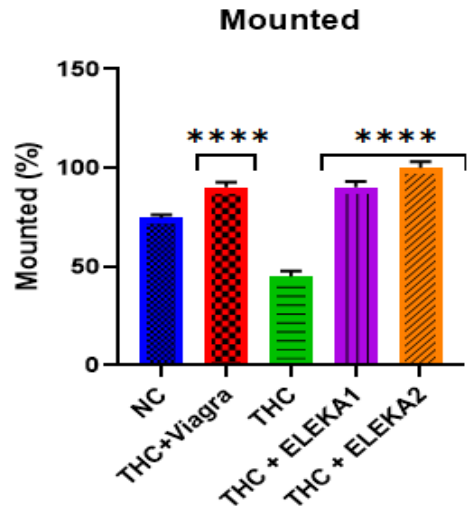

Fig. 28: The effect of *K. africana* extract on % mounted following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

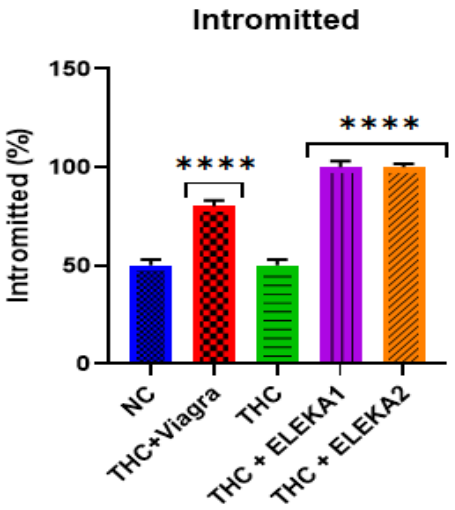

Fig. 29: The effect of *K. africana* extract on % intromitted following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

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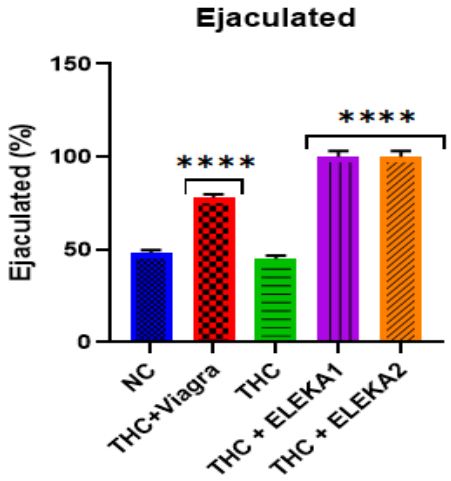

Fig. 30: The effect of *K. africana* extract on % ejaculated following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

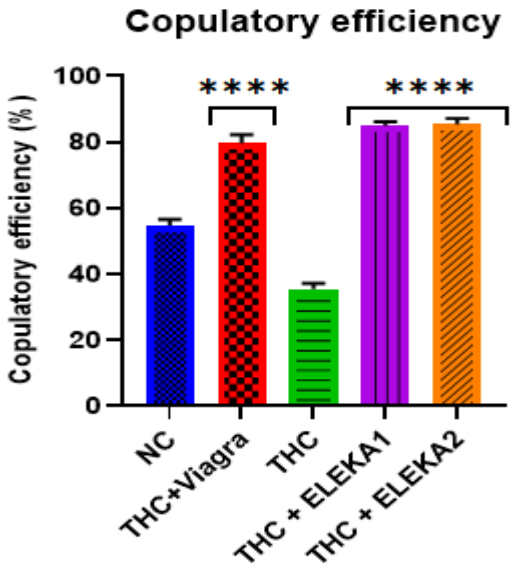

Fig. 31: The effect of *K. africana* extract on % copulatory efficiency following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

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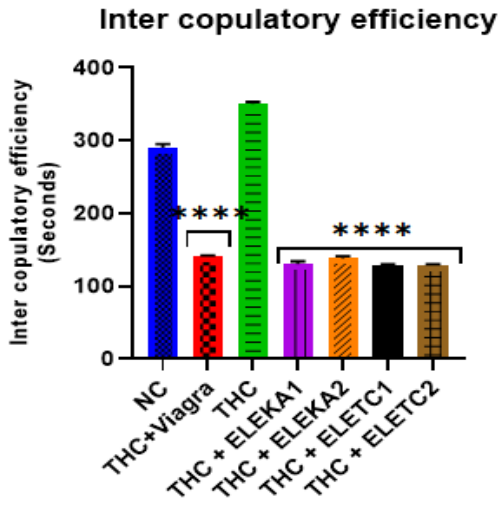

Fig. 32: The effect of *K. africana* extract on % intercopulatory efficiency following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

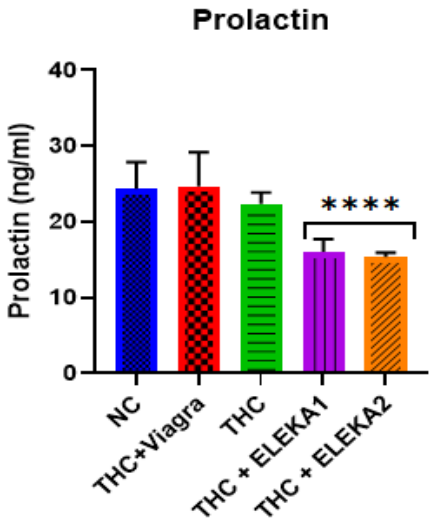

Fig. 33: The effect of *K. africana* extract on serum prolactin following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

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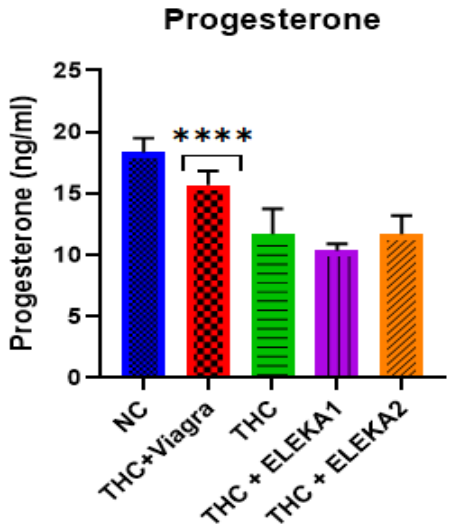

Fig. 34: The effect of *K. africana* extract on serum progesterone following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

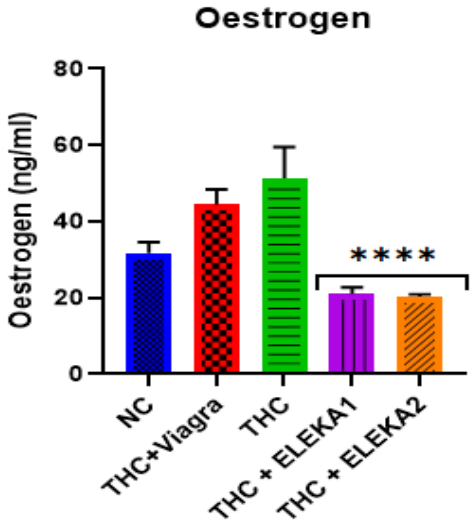

Fig. 35: The effect of *K. africana* extract on serum oestrogen following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

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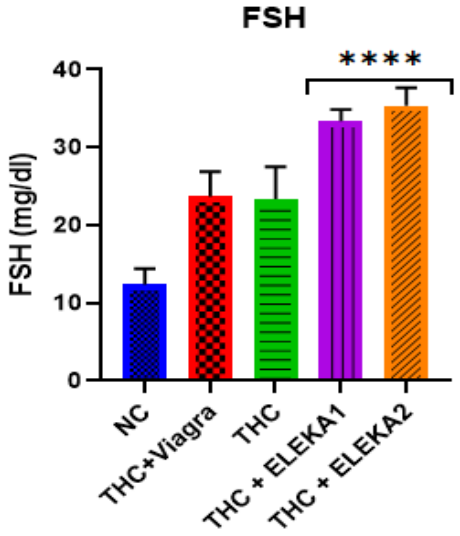

Fig. 36: The effect of *K. africana* extract on serum FSH following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

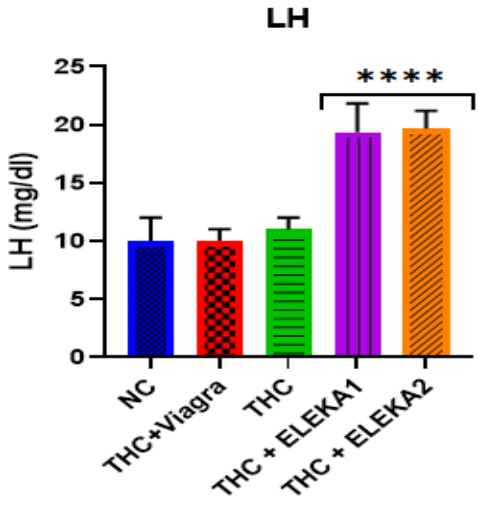

Fig. 37: The effect of *K. africana* extract on serum LH following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

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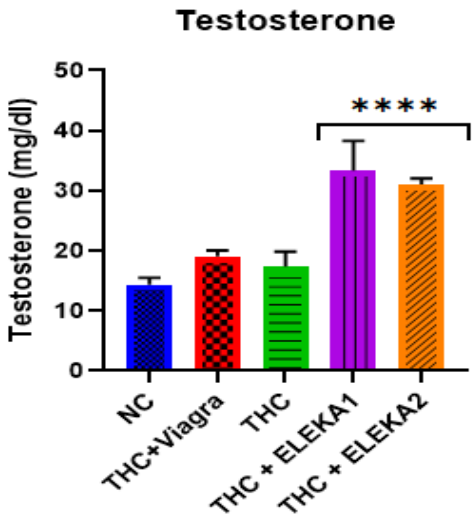

Fig. 38: The effect of *K. africana* extract on serum testosterone following THC induced erectile dysfunction in male Wistar rats

Key: NC: Normal Control, THC + Viagra: Δ^9 tetrahydrocannabinol + Viagra, THC: Δ^9 tetrahydrocannabinol, THC + ELEKA1: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (200 mg/Kgbwt), THC + ELEKA2: Δ^9 tetrahydrocannabinol + Ethanol leaf extract of *Kigelia africana* (400 mg/Kgbwt).

Table 1: The phytochemical composition of ethanol extracts of *K. africana* leaf

Phytochemicals	Ethanol extract
Flavonoids	+++
Tannins	++
Steroids	+++
Phlobatannins	++
Saponins	++
Triterpenoids	+++
Glycosides	++
Alkaloids	+++

where: + = sparingly present; ++ = moderately present; +++ = highly present; and ++++ = very highly present.

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DISCUSSION

The quest for plants with sex enhancing ability or aphrodisiacs with little or no side effect is of great concern. Various substances of animal and plant origin have been used in folk medicine of different cultures as aphrodisiac, some of which have been identified pharmacologically to exert their effects on the hypothalamic – pituitary – testicular axis (Yakubu *et al.,* 2011). Plant preparations, including *K. africana* as sex enhancer, have become prominent in folk medicine. To understand the scientific reasons behind these folk claims instigated the need for investigation of the effects of ethanol extract of *K. africana* in THC induced erectile dysfunction in this study. The parameters of the sexual behaviour of the male albino rats such as MF, IF, EF, ML, EL, PEI, sperm parameters and reproductive hormones levels were assessed in this present research work.

Mount frequency and intromission frequency are useful indices of vigour, libido and potency (Dasofunjo *et al*., 2015). While the number of mount (MF) reflects sexual motivation, increase in the number of intromission (IF) shows the efficiency of the erection, penile orientation and the ease by which ejaculatory reflexes are activated (Mobley *et al.,* 2017; Goel & Kumar, Maurya, 2020). Therefore, the significant increase in MF and IF following the administration of *K. africana* on Days 7 and 14 of the observation days suggests that the enhanced libido following THC induced erectile dysfunction; the enhancement of libido might have arisen from an increase in the concentration of several anterior pituitary hormones and serum testosterone which might suggest that the extract stimulated dopamine receptor synthesis and sexual behaviour, which is in line with the report of Santos *et al.* (2019). It may therefore be logical to suggest that the sex-enhancing behaviour of the Wistar rats may be due to flavonoid/saponin constituents of the plant since they have been reported to alter androgen levels (Dasofunjo *et al*., 2013; Dasofunjo *et al*., 2018).

The discrepancies in the values of MF and IF in this study suggests that it was not every mount by the male rats that resulted in intromission. Similarly, the increase in EF by the leaf extract of *K. africana* at 200 mg/kg body weight on Day 7 and Day 14 is an indication of enhanced aphrodisiac potential of the plant extract.

However, since intromission is not possible without adequate erection and coordinated activity of penile muscles (Chibuike & Prince, 2020), the increase in IF by the extract in this study suggests that the ethanol extract of *K. africana* leaf may increase potency possibly either by initiating or sustaining erection.

Moreso, hormones play a vital role in semen production and men's fertility (Dasofunjo *et al.,* 2020). Due to chemical agents contained in plant extracts. Phytochemical screening has revealed many bioactive agents of plant extracts that can affect reproduction. Alkaloids and flavonoids have been shown to alter the concentrations of some fertility hormones (Dasofunjo *et al.,* 2018; Dasofunjo, 2024). Therefore, the presence of these phytochemicals may account for the alterations in the levels of the circulating hormones observed in this study.

Testosterone is a male hormone that has a significant impact on spermatogenesis. It is secreted by the leydig cells of the testicles, the adrenals and the ovaries, and is the most important androgen secreted into the blood. A low sperm count may indicate a problem with testosterone levels (Mansoureh *et al.,* 2016).

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In this study, the significant increase in serum testosterone could be as a result of some potent phytoandrogen in the ethanol extract of *K. africana* that stimulates the synthesis and subsequent release of these hormones in the anterior pituitary glands or by increasing androgen hormones which may regulate and/or controls testosterone secretion via feedback effect or alters the hypothalamus and controls lutein releasing hormone and partly follicle stimulating hormone via negative feedback mechanism.

More so, follicle stimulating hormone regulates the growth of seminiferous tubules and maintenance of spermatogenesis in males. It is also critical for sperm production and may support the function of sertoli cells, which in turn enhances sperm cell maturation. Therefore, the significance increases in FSH following the administration of the extract of *K. africana* in THC induced erectile dysfunction may indicate that the extract may stimulate or increase cAMP that might lead to the secretion of ABP (androgen binding protein) which might bind to the sertoli cell to enhance spermatogenesis.

It has been scientifically proven that diminished secretion of LH or FSH can result in failure of gonadal function (hypogonadism) (Dasofunjo, 2024). This condition is typically manifested in males as failure in production of normal numbers of sperm which was typical of the THC treated groups. In males, LH acts upon the Leydig cells of the testis and is responsible for the production of testosterone, an androgen that exerts both endocrine activity and intra-testicular activity on spermatogenesis (Nguyen *et al.,* 2016). We observed from this present work that the ethanol extract of *K. africana* boosted the reproductive hormones levels in the treated groups in a dosage dependent manner which suggests that ethanol leaf extract of *K. africana* improves sexual drive and/or health. Likewise, upon examination of sexual behaviour following chronic THC administration, the rats treated with the extract were found to exhibit significant improvement and recovery from loss of libido imposed by chronic THC administration. This results in significant values for mounting frequency, sperm positive females and pregnant females for ethanol extract of. *thonningii* treated group compared with the control. These results are clear indications that ethanol extract of *K. africana* could be used to positively enhance sexual behaviour in male rats.

More so, the observed significant increase in sperm count and sperm motility observed in the groups treated with higher doses of the extract could be as a result of aphrodisiac activities of *K. africana* on the reproductive cells. Thus, this study supports the acclaimed aphrodisiac or libido activities of the plant in folk medicine.

Phytochemical screening revealed the presence of tannins, flavonoids, alkaloids, glycosides, sterols and triterpenes in ethanolic *K. africana* extract. The presence of these phytochemicals may be responsible for the observed spermatogenic, libido enhancing effect and other physiological activities. It has been reported that steroids can enhance androgen production; flavonoids trigger testosterone synthesis, alkaloids drive blood vessels to the penile tissues; and tannins activate both the gonadal tissues and CNS (Dasofunjo *et al*., 2015; Roozbeh, 2021). Therefore, the improvement in sexual function demonstrated in the current study following THC induced erectile dysfunction might be due to the presence of such compounds in the extract *K. africana.*

We hereby propose that sexual desire following the administration of *K. africana* may be controlled and regulated either centrally or peripherally which may integrate both tactile, olfactory and mental stimuli or simply provide a burst of nutritional value which may improve

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the immediate health or well-being of the consumer and consequently improve sexual health, performance and libido. It also appears that the extract may trigger a reflex action that may either involve both autonomic and somatic afferents which may be modulated by supraspinal influences peripherally, thereby leading to sustained erection. We also suggest that *K. africana* may contain some bioactive compounds which may trigger specific physiological effects to increase blood flow and duration of sexual activity.

It will be logical to conclude that extracts of *K. africana* may elicit spermatogenic, androgenic and libido enhancing activities in THC induced erectile dysfunction in a dosage dependent manner.

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