HISTOMORPHOLOGICAL EFFECTS OF SILDENAFIL (VIAGRA) AS AN APHRODISIAC ON TESTICULAR AND CARDIAC TISSUES IN ADULT ALBINO RATS

BY

MOMOH, ABDULHAMID HABIB
BMS2001180

DEPARTMENT OF MEDICAL LABORATORY SCIENCE,
SCHOOL OF BASIC MEDICAL SCIENCES,
COLLEGE OF MEDICAL SCIENCES,
UNIVERSITY OF BENIN.
BENIN CITY

SEPTEMBER, 2025.

HISTOMORPHOLOGICAL EFFECTS OF SILDENAFIL (VIAGRA) AS AN APHRODISIAC ON TESTICULAR AND CARDIAC TISSUES IN ADULT ALBINO RATS

BY

MOMOH, ABDULHAMID HABIB
BMS2001180

A PROJECT WORK SUBMITTED TO THE DEPARTMENT OF MEDICAL LABORATORY SCIENCE, SCHOOL OF BASIC MEDICAL SCIENCES, UNIVERSITY OF BENIN, BENIN CITY, EDOSTATE IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF BACHELOR OF MEDICAL LABORATORY SCIENCE DEGREE (B.MLS) IN MEDICAL LABORATORY SCIENCE.

SUPERVISED BY
DR. N.T OMORODION

SEPTEMBER, 2025.

CERTIFICATION

This is to certify that the project was carried out by **MOMOH ABDULHAMID HABIB** with the matriculation number **BMS2001180** under the supervision of **Dr. N.T Omorodion** in the Department of Medical Laboratory Sciences, School of Basic Medical Sciences, University of Benin, Benin City in partial fulfillment of the requirement for the award of Bachelor of Medical Laboratory Science (BMLS) Degree.

DR. N.T OMORODION (SUPERVISOR)	**DATE**
DR. (MRS.) Z. OMORUYI (Ag. HEAD OF DEPARTMENT)	**DATE**
External Examiner	**DATE**

DEDICATION

I dedicate this project to my parents, teachers, and friends who have been my greatest source of encouragement, inspiration, and support. To my parents, my uncle, for their love, guidance, and sacrifices that made this journey possible. To my teachers, for their patience and commitment in shaping my knowledge and character. And to my friends I made in this school for their motivation and understanding. Without all of you, this achievement would not have been possible.

ACKNOWLEDGMENTS

First and foremost, I give thanks to Almighty God for giving me the strength, knowledge, and ability to complete this project successfully.

I would like to express my sincere gratitude to my teachers for their continuous support, valuable guidance, and encouragement throughout the course of this work. Their advice and constructive feedback helped me improve and complete this project with confidence.

I also wish to thank my parents for their endless love, encouragement, and prayers, which have been my driving force. Lastly, I appreciate my classmates and friends who offered their help, cooperation, and motivation whenever I needed it.

This project is the result of the collective effort, guidance, and support of many people, and I am truly grateful to each of them.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF PLATES

ABSTRACT

In the course of improving sexual performance, some men have chosen to use aphrodisiac substances as a source of intervention. The study aimed to determine the impact of aphrodisiac (sildenafil: Viagra) use on the testes and heart tissues of Adult Albino rats. Eighteen (18) male albino rats (weighing 200g-220g) were acquired from the animal house of Edo State University. The animals were randomly divided into 3 equal groups A, B and C (n=6/group). Group A served as control administered with feed and water only. Group B, included 6 rats that were orally given Viagra in a dose of 5 mg/kg body weight dissolved in saline daily for 4 successive weeks. Group C, included 6 rats that were orally given Viagra in a dose of 10 mg/kg body weight for 4 successive weeks and then were kept without treatment for 4 weeks. Body weight of experimental animals was checked at week 0 before Viagra administration and last day of drug administration before sacrifice. All experimental rats and control rats were anesthetized using formalin and sacrificed at the end of experimental period. Hematological analysis was done using auto-hematological analyzer while Serial slices were cut using a microtome and stained with hematoxylin and eosin at a thickness of 5 um. Selected tissue sections were photographed and presented as plates. Body weight analysis of the albino rats after four weeks indicated a slight weight difference between the control group and the Viagra administered albino rats. Sildenafil at doses 10mg/kg BW. Hematological parameters reveal there was high significant ($p<0.001$) decrease in HCT, Twbcs and Granulocytes in the experimental group (41.0 ± 1.66, 2.3 ± 0.55 and 32.8 ± 3.27) when compared with control group (45.6 ± 1.50, 7.4 ± 1.92 and 40.4 ± 1.82) respectively. While monocytes value was highly significant ($p<0.001$) increase in the experimental group (17.2 ± 2.38 vs 7.4 ± 1.14) when compared with control group. Histological examination showed a general decrease in response to sildenafil administration. While tissue sections of testes collected from rats administrated with 10mg/kg Sildenafil citrate had mild necrosis of both cardiac fibers, seminiferous tubules and the interstitial tissue, congested blood vessels, hypertrophy of the interstitial Leydig cells and degeneration of the spermatogonial cells. Understanding the molecular downstream events involved in long-term PDE5 inhibitor exposure through basic and clinical research can be useful in supervising the application of aphrodisiac substances so as to improve on corrective measures through a short-term administration of aphrodisiac substances at low doses.

CHAPTER ONE
INTRODUCTION

1.1 Background of the study

The increase in life expectancy of human beings has increased the demand for substances capable of improving quality of this longevity (Abdullahi and Tukur, 2023,). The need to increase sexual arousal, sexual pleasure and sexual potency can be said to be as old as life itself. Various cultures have different substances that serve as aphrodisiacs and knowledge of this is usually passed down across generations (Dabhadkar *et al.,* 2023; McNay, 2020). These aphrodisiacs are usually believed to be very important for sexual stimulation, relationship preservation, and satisfaction (Byers, 2019). The quest has been shown to increase rather than decline over the years. Sexual response in male and female reflects a dynamic balance between excitatory and inhibitory signals of the autonomic nervous system within the external genitalia and throughout the central nervous system (CNS) (Wamoyi *et al.,* 2019). The inhibitory signals pass via the sympathetic pathways while the excitatory is via parasympathetic pathways (Skopek *et al.,* 2022). The mere sight, thought or genital stimulation of an appealing partner can initiate excitatory signals in the brain that can lead to sexual arousal. Regardless of the source of these signals, proerectile neurotransmitters such as nitric oxide and acetylcholine are released by excitatory nerves in the penis; penile erection is thus, achieved when these neurotransmitters cause the smooth muscles of the penile arteries to relax and fill with blood (Walster *et al*., 2018). Many aphrodisiacs therefore modulate these pathways to either increase sexual arousal or increase sexual potency (effectiveness of erection). An aphrodisiac can be described as any substance that enhances sex drive and or sexual pleasure (Van *et al.,* 2020). The name comes from Aphrodite, the Greek goddess of sexuality and love; and substances used are derived from plants, animals or minerals. Aphrodisiacs

can be classified according to their mode of actions into three groups namely: substances that increase libido (i.e., sexual desire, arousal), substances that increase sexual potency (i.e., the effectiveness of erection) and substances that increase sexual pleasure (Goredema, 2020). Men and women have for centuries sought different ways of gaining sexual fulfillment including the use of aphrodisiacs (Bello, 2017). Among these are products that enhance sexual performance, treat impotence or erectile dysfunction. Sexual function is a fundamental part of human identity and how humans feel. Sexual function is linked to sexual satisfaction. Sexual satisfaction is a feeling that an individual obtains through mental and physical enjoyment of sexual intercourse. Sexual health ranges from physical, psychological to socio-cultural well-being about sexuality. A person's sexual health is a critical factor in determining the capacity for maintaining healthy relationships (Aidoo, 2018).

Sexual dissatisfaction could lead to sexual deprivation and vice versa among spouses which in turn can lead to extramarital affairs. Sexual dysfunction could be a disguised manifestation of other underlying conditions, such as hypertension, diabetics, heart failure and others (Al-Amin *et al.,* 2021*).* Couples suffering from sexual dysfunction are more likely to suffer from anxiety, depression and low self-esteem (Duyilemi *et al.,* 2018). This implies that a healthy intimate relation rests on the sexual relationship of the two partners, while low sexual function can split the intimate relation (Mbah *et al.,* 2015). It was reported in some studies that, about 15 to 41% of men suffer from sexual dysfunction or are not satisfied with sex life. It has, also, been reported that between 40–60% of men in Pakistan, Egypt, and Nigeria experience varying degrees of sexual dysfunction (Balasubramani *et al.,* 2021). While, sexual dysfunction is common among men, accurate data on sex-related matters seem not to exist globally and this has led to under treatment (Akanmode, 2015). It is not unlikely that men in

Nigeria may not discuss sexual dysfunction because of their belief about discussing sex (Akanmode, 2015). This belief may be a function of cultural orientation and background which emphasizes the hidden nature of heterosexual relationships. It is worthy of note that the significant disorder of sexual dysfunction in men is premature ejaculation, erectile dysfunction and Hypoactive Sexual Desire Disorder (HSDD). Of these three types of sexual dysfunction, premature ejaculation is likely the most prevalent sexual dysfunction according to the results of numerous epidemiological studies. Overall, the prevalence rate of premature ejaculation falls somewhere between 25 and 40% in the global population of men across all age groups Estimates vary, but, overall, 1 out of 3 men may be affected by premature ejaculation at some time in their life (Bancroft, 2020). In the course of improving sexual performance, some married men have chosen to use aphrodisiac substances as a source of intervention (Shamloul, 2016). The use could be due to the men's unwillingness to discuss sexual issues with doctors and their dislike for drug-mediated erections. Invariably, men believe in the efficacy of aphrodisiacs, and perhaps to keep their sexual dysfunction from being heard by the third party. Some of these aphrodisiac substances can possibly cause damages to the body or internal organs of the users such as the testis, heart, brain, kidneys and the liver (Shamloul, 2016).

One of such drugs that has been used as aphrodisiac agent in recent years to enhance sexual performance by men is sildenafil (Viagra) (Smith *et al.,* 2022). Sildenafil is a medication used in the management and treatment of erectile dysfunction and pulmonary arterial hypertension. It is in the phosphodiesterase-5 inhibitor (PDE5-I) class of medications (Smith *et al.,* 2022). Sildenafil was the first phosphodiesterase-5 (PDE5) inhibitor approved for use, receiving US Food and Drug Administration approval for use in erectile dysfunction. Sildenafil also has FDA approval for the

treatment of World Health Organization Group I pulmonary hypertension (also known as pulmonary arterial hypertension (PAH)) in adults to improve exercise tolerance and delay clinical worsening. Sildenafil-induced delay in clinical worsening is demonstrated when sildenafil was used concomitantly with epoprostenol therapy. Clinical trials have established effectiveness for short-term (12-16 weeks) and included patients, mainly patients with New York Heart Association (NYHA) Functional Class II-III symptoms and having idiopathic etiology or having connective tissue disease (CTD). However, the addition of sildenafil to bosentan therapy did not result in any improvement in exercise capacity. It is not indicated for children. Sildenafil is also occasionally used off-label for the treatment of secondary Raynaud phenomenon, female sexual arousal disorder, and as an adjunct in the treatment of altitude-induced hypoxemia. (Smith *et al.,* 2022).

1.2 Statement of the problem

The use of aphrodisiacs has substantially increased due to escalated prevalence and impact of sexual problems worldwide and estimates predicting the incidence to raise over 320 million by the year 2025 (Balasubramani *et al.,* 2021) Substances which are designed for other medical purposes has been utilized as aphrodisiac. The misuse and dependence on Viagra, especially among the youth, manual workers, commercial vehicle drivers and students in recent times has become a serious global issue in many countries, especially in Africa, Asia and Middle East. This increase in the use of substances perceived to be aphrodisiacs such as Viagra has proportionally increased the risk of internal organ complications such as anorexia, severe redness, drowsiness and loss of strength. This may also affect the weight of the user, cause testicular issues and heart tissue inflammation.

1.3 Justification of the study

The desire for intimacy and sexual gratification is a global phenomenon and has remained life-long expressions among couples. However, the prevalence of sexual dysfunction among men continues to increase, and they neither enjoy their sex life nor satisfy their partners. Sadly, many men do not present sexual dysfunction for medical treatment; they prefer to use substances perceived to be sexual boosters such as Viagra. Globally, the abuse of Viagra has become a primary concern only in the last few years. Concerns over Viagra has dominated the research, policy, and treatment agendas in the Middle East, Africa, parts of Asia, and even in developed countries. Clinical research on drug abuse and sexual function is an emerging field. To date, a small number of studies have been performed, and many of these have been flawed by sampling too few subjects. The histological effect and impact of Viagra on the testes and heart tissue have not been well researched.

1.4 Significance of the study

Aphrodisiacs have been shown to have a number of effects especially on male sexual patterns. The use of sex enhancing drugs globally varies from country to country. For instance, in Africa, studies have shown high prevalence of aphrodisiac use. In Nigeria, the use substances to enhance sexual performance are quite high in many communities. Considering the high usage of sexual enhancement aphrodisiac substances such as Viagra among the male folks, this study will help to explore the haematological and histological effects and impact of the drug (Viagra) on the testes and heart tissue.

1.5 Aim of the study

To Evaluate the impact of aphrodisiac (sildenafil: Viagra) use on the testes and heart tissues of adult albino rats

1.6 Objectives of the study

The Specific Objectives are;

1. to determine the effect of aphrodisiac (Sildenafil: Viagra) on weight

2. to determine the effect of aphrodisiac (Sildenafil: Viagra) on Hematocrit value

3. to evaluate the histological changes of aphrodisiac (Sildenafil: Viagra) in heart and testes

CHAPTER TWO
LITERATURE REVIEW

2.1 The testis

The testes are male sex glands that have both an endocrine and exocrine function. The testes are oval-shaped reproductive structures that are found in the scrotum and separated by the scrotal septum. The shape of the testes is bean-shaped and measures three cm by five cm in length and 2 cm to 3 cm in width (Krings, 2016). When palpated through the scrotum, the testes are smooth and soft. The spermatic cord suspends the superior aspect of the testes. At the inferior end, the testes are attached to the scrotum by the scrotal ligament which is a remnant of the gubernaculum. In general, the left testis is affixed slightly lower than the right testis. The double-layered tunica vaginalis envelop the testes except at the posterior and superior borders where the epididymis and spermatic cord are attached (Mason, 2022). The visceral or inner layer of the tunica vaginalis is close to the epididymis, testes and vas deferens. On the posterior lateral surface of the testes, there is a small space between the testes and body of the epididymis which is known as the sinus of the epididymis. Deep to the tunica vaginalis is located the tunica albuginea, which is a durable fibrous covering of the testes (Schwartz and Young, L, 2019). The epididymis is a small curved shaped elongated structure which is highly convoluted and tightly compressed. When open in a straight line, it is estimated that its length is about 20 feet. The epididymis is found on the posterior border of the testis and consists of three parts which include the head (caput), body (corpora), and tail (Cauda). The head of the epididymis lies at the upper pole of the testes and receive seminal fluid from the ducts of the testis. It then permits passage of sperm into the distal portion of the epididymis. Because of its length, the epididymal ducts have ample space for storage and maturation of sperm (Yoo *et al.,* 2019).

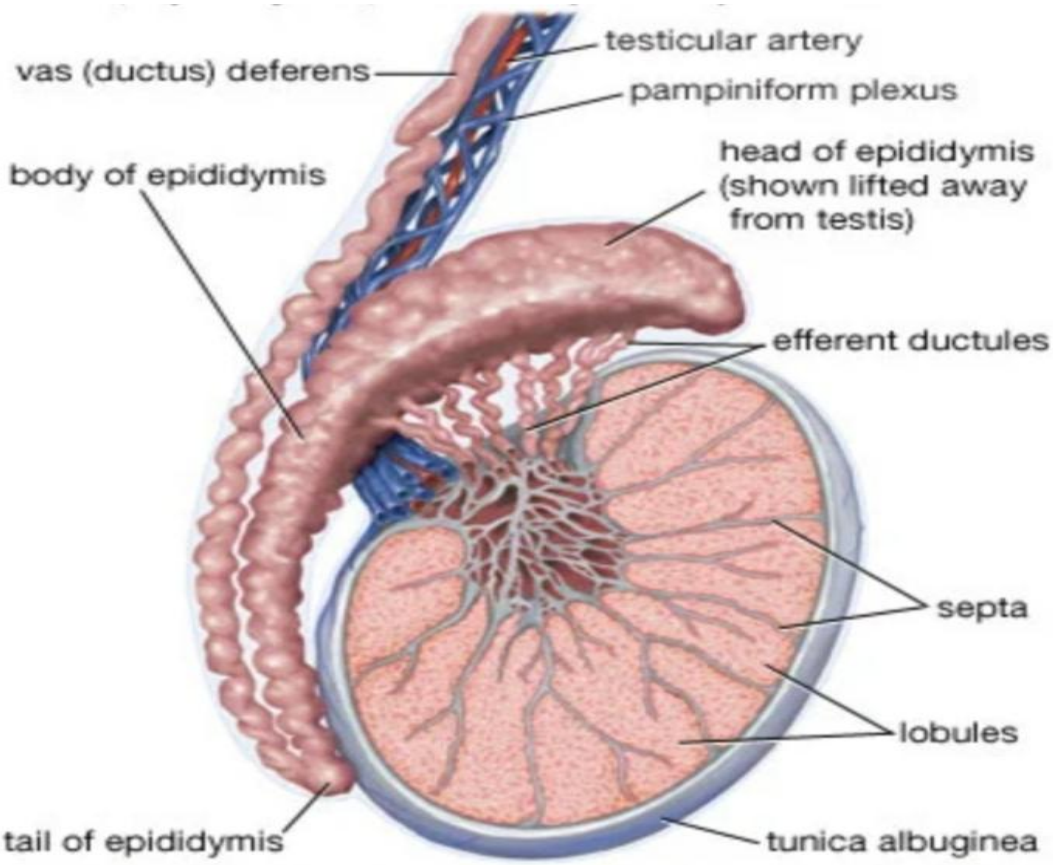

Figure 2.1: a cross sectional section of the the testis (Smith *et al*., 2022)

2.1.1Anatomy and Physiology of the testes

2.1.2 Structure and Function

The testis is the male reproductive gland that is responsible for producing sperm and making androgens, primarily. Testosterone levels are controlled by the release of Luteinizing Hormone (LH) from the anterior pituitary gland; whereas, Follicle-Stimulating Hormone (FSH) levels control sperm production (Idung *et al.,* 2019).

2.1.3 Embryology

The testes start as an undifferentiated gonad in the retroperitoneum area. The testis-determining factors (SRY gene) present on the Y chromosome causes the gonad to differentiate into the testes. In females, the SRY gene is absent, and hence the gonad turns into an ovary (Edelstein *et al.,* 2021). As the fetus starts to mature, the testes begin to produce the male sex hormone, testosterone. This sex hormone permits the development of the male genitalia. The tunica albuginea forms a connective tissue latery between the seminiferous tubules and the rest of the testis through invagination. The Sertoli cells start to make Mullerian-inhibiting Substance (MIS) which causes regression of the Mullerian ducts at 8 to 10 weeks (Govindasamy *et al.,* 2017). The only remaining remnants of the Mullerian ducts in an adult male are the appendix testis and the prostatic utricle. During the third trimester of pregnancy, the testes, which are located in the abdomen, starts their descent into the inguinal canal and then to its final destination in the scrotum. During this journey, they pass through the peritoneum, the abdominal wall, and the inguinal canal. During development the inguinal canal contains the processus vaginalis, which is a structure that develops from the peritoneum (Etuk *et al.,* 2017). It allows the testes to descend and then eventually undergoes apoptosis and becomes the tunica vaginalis which surrounds part of the testis. Failure of the closure of the processus vaginalis may lead to complications such as communicating hydrocele and inguinal hernia.

2.1.4 Blood Supply and Lymphatics

The testicular arteries supply blood to the testes. They arise from the anterolateral segment of the abdominal aorta just below the origin of the renal arteries. The vessels travel in the retroperitoneum and cross over the ureter, pass through the deep inguinal ring, and join the spermatic cord (Etuk *et al.,* 2017). Additional blood supply to the testes comes from the artery of the vas deferens and the cremasteric artery. Venous drainage from the testes is via the pampiniform plexus which lies anterior to the vas deferens. The veins converge superiorly to form the testicular vein. The right testicular vein joins the vena cava, and the left testicular vein drains into the left renal vein. Drainage of the lymphatics from the testes follows the same path as the testicular arteries and drain to the preaortic lymph nodes (Etuk *et al.,* 2017).

2.1.5 Nerves

The testes have innervations from both sympathetic and parasympathetic fibers.

2.1.6 Muscles

As the testes move from the abdomen into the scrotum, it is gradually enveloped by several layers of muscle tissue, the internal spermatic fascia, the cremasteric muscle and fascia, and the external spermatic fascia. The daily degree of testicular descent varies according primarily to temperature. This is controlled by the cremaster muscles (Del Mar Sánchez-Fuentes *et al.,* 2022).

2.1.7 Physiologic Variants

Two vestigial embryonic structures with no known physiologic function include the following: At the cranial end of the paramesonephric duct (Mullerian duct), sometimes one will find the appendix testis. This pear-shaped vestigial structure is found in about 2% of testes, and it is typically located at the superior pole in the groove between the head of the epididymis and testis (Del Mar Sánchez-Fuentes *et al.,* 2022). Also at the cranial end of the mesonephric duct one will sometimes find the

appendix of the epididymis which is found in about 25% of testes. Their location is variable but often project from the head of the epididymis. In about 7% of males, the epididymis may be located on the anterior surface of the testis.

2.1.8 Surgical Considerations

Cryptorchidism is an important disorder to recognize early in life not only to preserve sterility but also to reduce the risk of testicular cancer (Abubakar *et al.,* 2017). Unless the surgeon can surgically bring the testes back into the scrotum where it can be under surveillance, the undescended testes should be removed. It is also important to know that there is an increased risk of cancer in the contralateral testes and hence regular self-examinations are highly recommended. Sometimes serous fluid can accumulate in between the layers of the tunica vaginalis leading to a hydrocele. This could be triggered by inflammation, trauma or a congenital cause due to persistent communication with the abdominal cavity. In young men, testicular torsion is a surgical emergency. The blood supply must be restored within 6 hours of the start of symptoms; the testes need to be fixed in the scrotum to prevent recurrence. Most urologists will also fix the contralateral testes at the same time. The descent of the testes may be delayed or arrested along the course in the inguinal canal and may be complicated by an inguinal hernia. All true undescended testes will have associated inguinal hernias. This is not true for retractile testicles (Del Mar Sánchez-Fuentes *et al.,* 2022).

2.1.9 Clinical Significance

Cryptorchidism (non-descent of the testis) not only leads to infertility but carries a risk of testicular cancer. If the abnormal testis is not removed, close surveillance is necessary. The primary treatment for cryptorchidism is repositioning of the cryptorchid testes which is called orchidopexy. It should be performed before 1 year of birth in those with congenital cryptorchidism in order to best prevent cancer (Abubakar *et al.,* 2017). Sometimes a hydrocele (serous fluid) can result when fluid collects between the layers of the tunica vaginalis. A hydrocele may be due to an infection, trauma, or congenital factors. One common congenital factor is through incomplete closure of the processus vaginalis.

2.2 Testosterone

Testosterone is the primary male hormone responsible for regulating sex differentiation, producing male sex characteristics, spermatogenesis, and fertility. Testosterone's effects are first seen in the fetus. During the first 6 weeks of development, the reproductive tissues of males and females are identical. At around week 7 in utero, the SRY (sex-related gene on the Y chromosome) initiates the development of the testicles. Sertoli cells from the testis cords (fetal testicles) eventually develop into seminiferous tubules. Sertoli cells produce a Mullerian-inhibiting substance (MIS), which leads to the regression of the Fallopian tubes, uterus, and upper segment of the vagina (Mullerian structures normally present in females). Fetal Leydig cells and endothelial cells migrate into the gonad and produce testosterone, which supports the differentiation of the Wolffian duct (mesonephric duct) structures that go on to become the male urogenital tract. Testosterone also gets converted to dihydrotestosterone (DHT) in the periphery (discussed below) and induces the formation of the prostate and male external genitalia. Testosterone is also

responsible for testicular descent through the inguinal canal, which occurs in the last 2 months of fetal development. When an embryo lacks a Y chromosome and thus the SRY gene, ovaries develop. Fetal ovaries do not produce adequate amounts of testosterone, thus the Wolffian ducts do not develop. There is also an absence of MIS in these individuals, leading to the development of the Mullerian ducts and female reproductive structures.

2.2.1 Function

Testosterone is responsible for the development of primary sexual development, which includes testicular descent, spermatogenesis, enlargement of the penis and testes, and increasing libido. The testes usually begin the descent into the scrotum around 7 months of gestation, when the testes begin secreting reasonable quantities of testosterone. If a male child is born with undescended but normal testes that do not descend by 4 to 6 months of age, administration of testosterone can help the testes descend through the inguinal canals.

Testosterone is also involved in regulating secondary male characteristics, which are those responsible for masculinity. These secondary sex characteristics include male hair patterns, vocal changes, and voice deepening, anabolic effects, which include growth spurts in puberty (testosterone increases tissue growth at the epiphyseal plate early on and eventual closure of plate later in puberty) and skeletal muscle growth (testosterone stimulates protein synthesis). Testosterone also stimulates erythropoiesis, which results in a higher hematocrit in males versus females. Testosterone levels tend to drop with increasing age; because of this, men tend to experience a decrease in testicular size, a drop in libido, lower bone density, muscle mass decline, increased fat production, and decreased erythropoiesis, which leads to possible anemia.

2.2.2 Mechanism

In puberty, the hypothalamic-pituitary-gonadal axis plays a major role in regulating testosterone levels and gonadal function. The hypothalamus secretes GnRH, which travels down the hypothalamohypophyseal portal system to the anterior pituitary, which secretes luteinizing hormone (LH) and follicle-stimulating hormone (FSH). LH and FSH are two gonadotropic hormones that travel through the blood and act on receptors in the gonads. LH, in particular, acts on the Leydig cells to increase testosterone production. Testosterone limits its own secretion via negative feedback. High levels of testosterone in the blood feedback to the hypothalamus to suppress the secretion of GnRH and also feedback to the anterior pituitary, making it less responsive to GnRH stimuli.

Throughout the reproductive life of males, the hypothalamus releases GnRH in pulses every 1 to 3 hours. Despite this pulsatile release, however, average plasma levels of FSH and LH remain fairly constant from the start of puberty, where levels spike, to the third decade of life, where levels peak and slowly begin to decline. Prior to puberty, testosterone levels are low, reflecting the low secretion of GnRH and gonadotropins. Changes in neuronal input to the hypothalamus and brain activity during puberty cause a dramatic rise in GnRH secretion.

Leydig cells in the testes function to turn cholesterol into testosterone. LH regulates the initial step in this process. Two important intermediates in this process are dehydroepiandrosterone (DHEA) and androstenedione. Androstenedione is converted to testosterone by the enzyme 17-beta-hydroxysteroid dehydrogenase. The majority of testosterone is bound to plasma proteins such as sex-hormone-binding-globulin and albumin. This majority supply of protein-bound testosterone acts as a surplus of testosterone hormone for the body. The small amounts of free testosterone in the

blood act at the level of the tissues, primarily the seminal vesicles, bone, muscle, and prostate gland. At the cellular level, testosterone gets converted to dihydrotestosterone by the enzyme 5-alpha-reductase. Testosterone and dihydrotestosterone can bind to cell receptors and regulate protein expression. Both men and women also produce weak acting androgens in the zona reticularis of the adrenal glands. These weak-acting androgens are known as dehydroepiandrosterone and androstenedione. They bind to testosterone receptors with weaker affinity but can also be converted to testosterone in the peripheral tissues if produced at high amounts.

2.3 The Heart

The heart is a muscular organ situated in the center of the chest behind the sternum. It consists of four chambers: the two upper chambers are called the right and left atria, and the two lower chambers are called the right and left ventricles (Abubakar, 2019). The right atrium and ventricle together are often called the right heart, and the left atrium and left ventricle together functionally form the left heart.

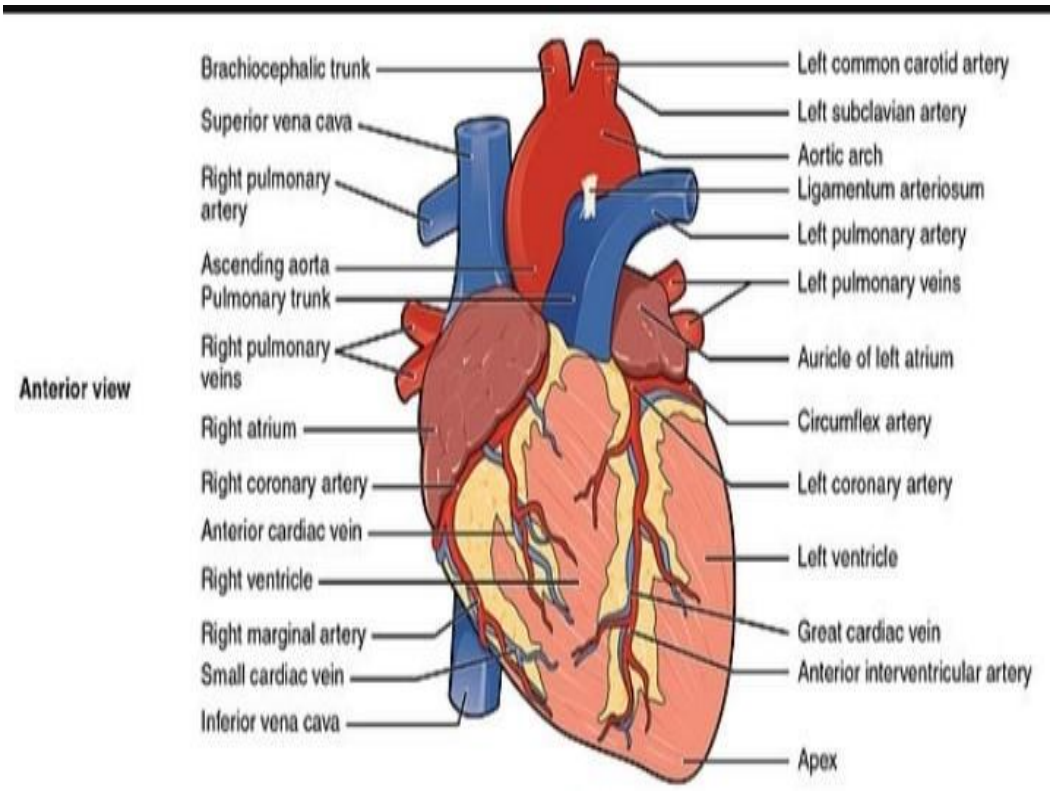

Figure 2.2: The anterior section of the heart (Aderinto, 2022)

2.3.1 Anatomy and Physiology of the Heart

2.3.2 Structure and Function

The heart consists of four chambers organized into two pumps (right and left) to provide blood flow to the systemic and pulmonary circulations (Abubakar, 2019). The right atrium receives deoxygenated blood from the entire body except for the lungs (the systemic circulation) via the superior and inferior vena cava. Also, deoxygenated blood from the heart muscle itself drains into the right atrium via the coronary sinus. The right atrium, therefore, acts as a reservoir to collect deoxygenated blood. From here, blood flows through the tricuspid valve to fill the right ventricle, which is the main pumping chamber of the right heart (Aderinto, 2022).

The right ventricle pumps blood through the right ventricular outflow tract, across the pulmonic valve, and into the pulmonary artery that distributes it to the lungs for oxygenation. In the lungs, the blood oxygenates as it passes through the capillaries, where it is close enough to the oxygen in the alveoli of the lungs (Aderinto, 2022). This oxygenated blood is collected by the four pulmonary veins, two from each lung. All four of these veins open into the left atrium that acts as a collection chamber for oxygenated blood. As with the right atrium, the left atrium passes the blood onto its ventricle both by passive flow and active pumping (Bloch *et al.,* 2017). Oxygenated blood thus fills the left ventricle, passing through the mitral valve. The left ventricle is the main pumping chamber of the left heart, then pumps, sending freshly oxygenated blood to the systemic circulation through the aortic valve. The cycle is then repeated all over again in the next heartbeat. All four valves of the heart mentioned above have a singular purpose: allowing forward flow of blood but preventing backward flow (Bloch *et al.,* 2017).

2.3.3 Conduction System

An electrical conduction system regulates the pumping of the heart and the timing of contraction of various chambers. Heart muscle contracts in response to the electrical stimulus received. The sinus node, which is the main pacemaker of the heart, is situated at the junction of the superior vena cava and the right atrium (Bloch *et al.,* 2017). It rhythmically generates an electrical discharge about 70 times a minute. This electrical signal is carried to the left atrium via the Bachmann's bundle. Conduction occurs through the right atrial muscle to the atrioventricular node (AV node), located in the triangle of Koch, a small triangular area formed by the tricuspid valve, tendon of Todaro, and lip of the coronary sinus ostium. The AV node receives the electrical signal and conducts it to the bundle of His with some delay. This delay allows the emptying of the atria into the ventricles before the ventricles contract in response to the electrical signal. The bundle of His divides into the right and left bundles that successively branch into thousands of small branches called Purkinje fibers (Brotto and Smith, 2019). The His-Purkinje tree serves to rapidly conduct the electrical signal to all parts of both ventricles to produce a near-simultaneous contraction of all parts of both ventricles, producing a uniform and coordinated squeeze (Aderinto, 2022).

2.3.4 Embryology

The heart develops from two endocardial tubes that merge, loop, and septate to form the heart. During the intrauterine stage, the septum between the two atrial is open, and a ductus connects the pulmonary artery to the aorta, effectively bypassing the pulmonary circulation because the lungs are not functional (Brotto and Smith, 2019). Rapidly after birth, these two connections close, establishing separate pulmonary and system circulations.

2.3.5 Blood Supply and Lymphatics

The heart is supplied by two coronary arteries: the left main coronary artery and the right coronary artery. The left main coronary artery carries 80% of the flow to the heart muscle. It is a short artery that divides into two branches, the left anterior descending artery that supplies anterior two-thirds of the inter-ventricular septum and adjoining part of the left ventricular anterior wall, and the circumflex coronary artery that supplies blood to the lateral and posterior portions of the left ventricle (Ezumah, 2023). The right coronary artery and its branches supply the right ventricle, right atrium, and left ventricle's inferior wall. Coronary arteries and veins course over the surface of the heart. Most coronary veins coalesce into the coronary sinus that runs in the left posterior atrioventricular groove and opens into the right atrium. Other small veins, called thebesian veins, open directly into all four chambers of the heart (Ezumah, 2023).

Small lymphatic vessels form a dense network beneath the epicardium and endocardium of the ventricles and open into a lymphatic duct in the atrioventricular groove. However, the detailed lymphatic anatomy of the human heart has not been worked out.

2.3.6 Nerves

The sinus node and the AV node are both supplied by sympathetic nerve fibers from the sympathetic ganglia and parasympathetic fibers through the vagus nerve and parasympathetic ganglia behind the heart (Giorgi, 2019).

2.3.7 Muscles

The heart is a muscular organ. It has no bones. Sheets of muscle fibers are arranged over a fibrous skeleton to give the heart chambers their shapes. However, the atrial muscle is completely separated from the ventricular muscle by a fibrous

atrioventricular scaffolding such that no electrical conduction can occur between the two, except through the AV node (Giorgi, 2019).

2.3.8 Physiologic Variants

The general structure of the heart is quite uniform in healthy individuals. However, some variations do occur. The heart is arranged more horizontally in the chest in short and obese individuals, while it is more vertical in tall and thin people. An athlete's heart may be physically larger. Coronary arteries show variations in branching patterns and relative sizes (Kisler and Scott Christopher, 2019).

2.3.9 Surgical Considerations

Cardiac valves can become fibrosed and calcific with age or disease, producing clinically significant stenosis requiring surgical or trans-catheter replacement. Similarly, valves may become incompetent, allowing backward flow called regurgitation, also necessitating replacement or repair (Kisler and Scott Christopher, 2019). Coronary arteries can become clogged with thrombus or atherosclerotic plaque, causing reduced blood supplies to cardiac muscle. This may result in angina or myocardial infarction and often requires revascularization.

2.4 Clinical Significance

The heart is a vital organ. If the heart stops, cessation of blood flow and oxygen supply will occur, leading to irreversible brain damage within 4 to 5 minutes (Schmitt, 2021). Cessation or impairment of cardiac function may occur due to a lack of blood supply to the cardiac muscle (coronary artery disease), stenosis or regurgitation in cardiac valves (valvular heart disease), intrinsic weakness of heart muscle (cardiomyopathy), or ineffective cardiac rhythms (Schmitt, 2021).

2.5 The global origin of pre-modern aphrodisiacs

An aphrodisiac is defined as any food or drug that arouses the sexual instinct, induces venereal desire and increases pleasure and performance. This word is derived from ëAphroditaeí the Greek Goddess of love and these substances are derived from plants, animals or minerals and since time immemorial they have been the passion of man (Patrick *et al.,* 2017). A lot of natural substances have historically been known as aphrodisiacs in Africa and Europe, like yohimbine and the mandrake plant, as well as ground rhinoceros horn in the Chinese culture and "Spanish fly" which is actually toxic. Even in today's culture, there are certain foods that are used as aphrodisiacs, including strawberries and raw oysters (Scorgie *et al.,* 2021). Chocolate, coffee, and honey are also believed to have aphrodisiac potential. Although these natural items are claimed as aphrodisiacs, there is no or little scientific confirmation supporting those assertions.

In a recent study conducted in the Boston area, 52% of men between the ages of 40 and 70 reported some degree of erectile dysfunction (ED). Enhanced sexual behavior may provide increased relationship satisfaction and self-esteem in humans. The hunt for an effective aphrodisiac has been a constant pursuit throughout history (Kontula, 2018). The role of various dopaminergic, adrenergic, and serotonergic agents has been intensively examined in both human and animal studies. Some of these drugs have been considered for their potential role for the treatment of sexual dysfunction, while some others have contributed to the basic neurophysiological processes in sexual arousal (Scorgie *et al.,* 2021).

Aphrodisiacs can be classified by their mode of action into three types: Those that increase libido, potency, or sexual pleasure. Various substances of animal and plant origin have been used in folk medicines of different cultures to energize, vitalize and

improve sexual function, and physical performance in men, out of these very few have been identified pharmacologically (Scorgie *et al.,* 2021). For increasing libido, ambrein, a major constituent of Ambra grisea, is used in Arab countries. It contains a tricyclic triterpene alcohol which increases the concentration of several anterior pituitary hormones and serum testosterone. Bufo toad skin and glands contain bufotenine (and other bufadienolides), a hallucinogenic congener of serotonin. It is the active ingredient in West Indian "love stone" and the Chinese medication Chan Su. In traditional Chinese medicine, Panax ginseng is used as a sex stimulant. It works as an antioxidant by enhancing nitric oxide (NO) synthesis in the endothelium of corpora cavernosa (CC); ginsenosides also cause transmural nerve stimulation-activated relaxation associated with increased tissue cyclic guanosine monophosphate. For increasing sexual pleasure, cantharidin ("Spanish fly") from blister beetles, which have been used for millennia as a sexual stimulant (Ojewole, 2017).

Most existing scholarship has assumed that ancient Greece was the source of early modern English, French, Latin, and Dutch uses of aphrodisiacs. Early modern Christianate scholars, like medieval Islamicate ones, referred frequently to ancient medical traditions of Galenic and Hippocratic medicine (Ojewole, 2017). Yet later scholars elaborated significantly on the ancient Greek knowledge they cited, and little existing scholarship has considered the importance of medieval Islamicate pharmacology as a source of much European knowledge about ancient Greek aphrodisiac usage (Ojo, 2017).

2.6 Causes of impotence

Sexual dysfunction is a serious medical and social symptom that occurs in 10-52% of men and 25-63% of women. ED, the main reason of male impotence, is considered as one of the most important public health problems, since it affects a great percentage

of men. ED is defined as the consistent inability to obtain or maintain an erection for satisfactory sexual relations (Meana, 2020). An estimated 20-30 million men suffer from some degree of sexual dysfunction. It occurs commonly in middle-aged and older men. Impotence occurs in 50% of men with diabetes mellitus. Atherosclerosis is the cause of approximately 40% of ED in men older than 50 years. Among the most commonly recognized conditions associated are high blood pressure, lipid problems (cholesterol, triglycerides), diabetes, and cigarette smoking. Endocrine disorders like low testosterone and thyroid problems also contributes to ED. Pelvic trauma, pelvic surgery (major prostate, bladder, and bowel operations) and pelvic radiation therapies are also connected with ED (Ojo, 2017). Direct trauma to the perineum can cause vascular problems in the penis and lead to ED that may be treatable by penile artery bypass surgery. Sexual dysfunction is also caused by various factors such as psychological disorders like anxiety, depression, stress, fear of sex, neurological disorders, stroke, cerebral trauma and Parkinson's disease, penile diseases like phinosis, peyroniesetc. Other organic causes include chronic renal failure, hepatic failure, multiple sclerosis, Alzheimer's disease, sleep apnea and chronic obstructive pulmonary disease. Chronic alcohol abuse and cigarette smoking also adversely affect sexual potency (Meana, 2020). Decrease in hormone level with age, systemic diseases like cancer also influences sexual ability. ED is also associated with some therapeutic agents like antihypertensives, antipsychotics, antidepressants, and drugs for diabetes mellitus increased significantly in both the CB groups, 125 mg/kg and 250 mg/kg, in a dose dependent manner. They concluded that the roots of CB can be useful for the treatment of certain forms of sexual inadequacies, such as premature ejaculation and oligospermia (Sell, 2017).

2.7 Synthetic aphrodisiacs substances

2.7.1 Phosphodiesterase V inhibitors

Recently synthetic substances, such as sildenafil or other phosphodiesterase 5 (PDE-5) inhibitors are taken to treat ED. These are supposed to only work when the patient is sexually stimulated; however, the substances themselves do not increase libido (Zare, 2021). Therefore, they only work in male users. In Germany, products containing sildenafil (Viagra® 25mg/50mg/100mg), tadalafil (Cialis® 5mg/10mg/20mg), vardenafil (Levitra® tablets 5mg/10mg/20mg) are officially available. Furthermore, to date more than 50 analogues of PDE-5 inhibitors have been reported. Barta *et al*., (2018) analyzed 150 herbal dietary supplements marketed for improving sexual performance (Zare, 2021). Although all of these formulations were claimed to contain only natural compounds, plant extracts and/or vitamins, 61% of the products were adulterated with phosphodiesterase-5 inhibitors (27% with sildenafil, tadalafil and vardenafil, and 34% with structurally modified analogues). Among them, 64% contained only 1 PDE-5 inhibitors and 36% mixtures of 2, 3 and even4.

medicines were higher than the maximum recommended dose in 25% of dietary supplement tainted with these drugs (Adams, 2015).

2.7.2 Yohimbine

Yohimbine is an indole alkaloid from the leaves and the bark of the yohimbe tree, Pausinystalia johimbe, that has important forensic implications due to its varied applications. A study by Alkali *et al.,* (2019) on dietary supplements contain ing yohimbe extracts has shown that the yohimbine content may range from <0.1 to 489ppm compared with 7089 ppm in the authentic plant material, which has been attributed to the intense dilution of final products. Modern yohimbine manufacturing and purification for pill formation is achieved through ethanol or chloroform

extraction. The yohimbe bark is ground and submerged in the solvent, followed by filtration and evaporation of the solvent.

It is a highly potent antagonist on presynaptic and post synaptic alpha2adrenoreceptorswithin the smooth muscles and blood vessels (Alkhali *et al.,* 2015). The enhancement of sexual impulse is generally believed by blocking the α2-adrenoceptors in the locus coeruleus in the brain, which media teserection-inhibiting impulses in the central nervous system. Yohimbine has also been abused on the streets as an aphrodisiac and hallucinogen, while more recently it has gained popularity in the body building community for its lipolytic and sympathomimetic effects for fast weight loss and body building supplement. Because of the resulting dilatation of the vessels, it has been approved for use in the USA and in Germany (Yocon Glenwood tablets® 5mg) to treat ED (Beres, 2019). An average oral dose of 5–15mg (1–3 tablets) is taken for the treatment of ED. Due to its central and libido-enhancing effects, however, if given in drug-facilitated sexual assaults, not also men but also women could be the victims of yohimbine administration. The side effects of yohimbine include high blood pressure, increased heart rate, manic reactions, bronchospasm, palpitations, insomnia, anxiety, irritability, shivering, sweating, nausea, flushing, and headaches, which can all be attributed to its central adrenergic activities (Bradbury-Jones *et al.,* 2020). According to the California poison control system, 238casesofadversereactions after yohimbine consumption have been identified within a 7-year period (2000–2006), where the most commonly reported adverse events were gastrointestinal distress, tachycardia, anxiety, agitation, and hypertension. Overdoses leading to neurotoxic effects were seen from doses of 200–500m. Symptoms reported with yohimbine overdose include anxiety, drowsiness, disorientation, tremors and seizures with higher doses. Furthermore, yohimbine intake in a fasting state can lead

to panic attacks (Bradbury-Jones *et al.,* 2020). Some case reports after yohimbine intoxication are described reporting of side effects, such as anxiety, tremors, hypertension, nausea, headache, rash and dissociative reactions drowsiness, confusion, atrial fibrillation, seizures and unconsciousness. Interestingly, Butzer and Campbell (2018) additionally reported retrograde amnesia after the intake of 350mg in a 38-year-old man. Sandler and Aronson described the development of progressive renal failure, cutaneous eruption, and a lupus-like syndrome in a 42-year-old Afro-American man following yohimbine use. Myers and Barrueto reported a case of refractory priapism in a 42-year-old man who self-administered a product containing yohimbine to treat ED and was subsequently admitted to emergency department with a 20-h lasting erection. Chatterji *et al*., (2015) reported a case of a 16-year-old girl who experienced an acute dissociative reaction accompanied by weakness, paresthesia, incoordination, anxiety, headache, and chest pain after the ingestion of the drug.

2.7.3 Flibanserin

Flibanserin is a drug which was approved by the Food and Drug Association (FDA) (Addyi®) for the treatment of hypoactive sexual desire disorder (HSDD) in women. Flibanserin was identified in 2 of 150 supplements from the internet marketed for improving female libido and low levels were identified (11mg per capsule) in a pharmacy-sold herbal dietary supplement for female HSDD treatment. A clinical trial for the substance demonstrated its efficacy against HSDD for women treated with a 100mg daily dose for 24 weeks (Eatough and Smith, 2018). Flibanserin is an agonist of 5-HT1A and an antagonist of 5-HT2A receptors, furthermore a partial agonist on D4 receptors. The most frequently reported adverse events in the flibanserin group during a clinical tyric acid (GABA) and usually given as a knockout drug during drug-facilitated crimes due to its narcotic effects; however, GHB is also an

aphrodisiac in man. It has four sexually enhancing effects: disinhibition (e.g. relaxation), heightened sense of touch, enhancement of male erectile capacity and increased power of orgasm. Adverse effects are dose-dependent and are part of several reviews (Glass, 2017). Briefly, GHB doses of up to 1.5g lead to a euphoric status, relaxation and disinhibition. It acts as an anxiolytic and has socially opening effects comparable to a mild alcohol intoxication. In doses up to 2.5g mood and impulse are increased and GHB acts as an aphrodisiac. The narcotic effects are primarily seen with higher doses >3–4g and GHB shows a stimulating sedative profile: within the first hours the psycho stimulating effects dominate. Sideeffectsaredescribed15minafterthe intake and include headache, somnolence, psychomotor difficulties, nausea and vomiting, dizziness, hypertension, disturbances of speech, seizures, disorientation, and can lead up to drowsiness, deep sleep, unconsciousness and death due to breathing arrest. Duration of action of GHB can be 1–7h depending on the dose. Precursors of GHB which can be converted into GHB within the body and are easier available (gamma-butyrolactone and 1,4-butandiol) can also be taken as aphrodisiacs (Humphreys and Herold, 2017).

2.8 Products with herbal or animal origin

2.8.1 Tribulus terrestris and other protodioscin-containing species (fenugreek and Dioscorea)

Tribulusterrestris (TT) is an annual herb found in temperate climates all over the world. The plant, its fruits and its extracts have traditionally been used as asexualstimulant (Gonzales, 2022). According to The Canon of Medicine and Aghili Khorasani's Makhzan al-Advia (The treasury of spices, eighteenth century), Bindii or TT influences libido andisableto boost sex drive in human beings; however,it is also supposed to have a positive effect on penile erection. It is most often used for infertility and loss of libido; therefore, it is also imaginable to drug women and men.

It is also present in over-the-counter herbal supplements purportedly able to treat various ailments such as urolithiasis, cardiovascular disease, and for the use of enhancing physical performance of body builders (Ekeh, 2020).

The aphrodisiac properties of TT are due to the steroid al saponin protodioscin (PTN, chemical structure in which is also ingredient of the fenugreek (Trigonella foenum graecum) and Dioscorea (yam) species. Both have been mentioned to be used as aphrodisiacs in the literature. Regarding potential side effects, on internet pages selling these products mostly gastrointestinal problems and icterus are listed. In a randomized double-blind placebo-controlled study using TT for treatment of sexual dysfunction, women took 7.5mL of a 60% solution of the drug over the course of 4 weeks twice daily. Women described side effects including abdominal pain, cramp, nausea, vomiting, diarrhea and constipation. Toxicity in animals is also well documented (Gonzales, 2022). A TT extract showed central nervous system (CNS) stimulant activity at a dosage of 20mg/kg in rats. The TT toxin causes progressive astrocyte degeneration, glutamatergic neuronal excitation reduction and decreases subthalamic nucleus normal excitatory function. Motor neuron disease, neuromuscular ataxia, hepatotoxicity, and photosensitization termed geeldikkop have been described in animals in the natural and in experimental settings. In humans, mainly nephrotoxicity was described. Knowles *et al.,* (2019) described a case of TT intoxication in a young healthy male who consumed the drug (one table today for a few months) for body building reasons, presenting with severe hyperbilirubinemia followed by acute renal failure and bile containing casts in the tubules. A similar case was described by Indongo and Pazvakawambwa, (2015) with neurotoxicity, hepatotoxicity, and renal toxicity in a young healthy male who consumed large quantities of TT extract, for its antiurolithic properties. Serum creatinine rose up to

17mg/dL, requiring dialysis, and urinalysis findings were suggestive of acute tubular necrosis (ATN). Additionally, the patient developed hypertension, seizures, and markedly elevated serum aminotransferases. Necropsy findings included distortion of bile ducts with yellow-green birefringent crystals, inflammation, apoptotic hepatocytes, and cholestasis. The hepatotoxin is believed to be a further steroidal saponin called diosgenin These toxic side effects have, however, only been described with frequent applications (Indongo and Pazvakawambwa, 2015).

2.8.2 Ambrein

Ambergris is a physiological product found either in the intestines of the sperm whale, Physeter macrocephalus L. (Physeteridae) and is mostly discarded into the sea as a waste product (emesis or feces). It occurs in gray or brown waxy masses and consists primarily of undigested squid and cuttlefish beaks, the sperm whale's main food, mixed with fatty digestive fluids (Ajuwon, 2015). The triterpen alcohol ambrein was isolated as the major constituent of ambergris. Ambrein capsules are sold over the internet. Historically, its use ranged from perfume preparations to the treatment of health conditions. It has been used to enhance sexual performance, with studies supporting its validity as a natural aphrodisiac in male rats. The intake led to a general depressed activity and somnolence in mice with a LD50 described to be 7500mg/kg body weight after intraperitoneal intake. A subcutaneous dose of 250mg/kg of ambrein markedly decreased both ambulatory activity and cerebral contents of norepinephrine, dopamine and their metabolites in mice. Side effects in humans have not been described in the literature or on the internet (Ajuwon, 2015).

2.8.3 Bufo Toad (love stone)

The skin and gland secretions of several Bufo species have traditionally been used for medicinal and aphrodisiac purposes. The ancient Chinese medication Chan su and

Indian aphrodisiac love stone are produced from these secretions. If used as an aphrodisiac, Bufo toad is administered topically (Ekeh, 2020). Its aphrodisiac properties is explained by the presence of the psychoactive substances bufotenine and its O-methylated derivative 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT) (chemical structure see which are hallucinogenics that provide stimulatory effects. Ayahuasca preparations can also contain 5-MeO-DMT. Both substances are structurally related with serotonin and psilocin and have a high affinity to the 5-HT1A receptor (Ekane, 2021). These hallucinogenic properties are the reason why Bufo Toad is only seldomly used as aphrodisiac. 5-MeODMT is a potent, fast-acting hallucinogen with short duration of action in humans. Human self-experiments have revealed that 5-MeO-DMT causes visionary and auditory changes and distorts the perception of time. The effects start at 3–4min, peak after about 35–40min, and end around 60–70min after insufflation. Studies with mouse, rat, sheep, and monkey models revealed remarkable ataxia, mydriasis, head nodding, tremor, convulsion and shiveringafteradministrationof5-MeODMT. Sheep were found to be the most susceptible to 5-MeO-DMT and exhibited stringy salivation, tachycardia, and respiratory failure when exposed to 1mg/kg of 5-MeO-DMT. The LD50 values of 5-MeO-DMT in mice ranged from 48mg/kg to 278mg/kg for different administration routes. In humans, optical hallucinations, such as flashes, dizziness, nausea, hypertension and disorientation have been described. During 1993–1995 the New York City Poison Control Center (NYCPCC) was informed about onset of illness in five previously healthy men after they ingested a substance marketed as a topical aphrodisiac; four of the men died. They all took Chan Su—used as a topical anesthetic and cardiac medication—which contained bufotenin.

2.8.4 Spanishfly (Cantharides)

The Spanish fly is the most well-known of a collection (more than 2000 species) of beetles traditionally used as aphrodisiacs. All of the beetles contain a vesicant liquid and are known as blister beetles. The beetles are most commonly found in southern Europe, Africa, and Asia (Ekane, 2021). The Mediterranean beetle Cantharisvesicatoria is the most well known as the Spanish fly, while Epicauta vittata is the most common of over 200 blister beetles identified in the USA. Most commonly available preparations of Spanish fly contain cantharidin in negligible amounts; however, the chemical is available illicitly in concentrations capable of causing severe toxicity. At high doses cantharidin is toxic to humans but despite the risk it has historically been used to enhance sexual function. Its use dates back 2000 years in Chinese and African herbal remedies by grinding the beetle to a powder before dissolution in a solvent for ingestion (Ekane, 2021). When ingested, urethral irritation occurs, this may cause priapism in both male and female. This occurs by inhibition of phosphodiesterase and protein phosphatase activity by cantharidin, which stimulates beta-receptors, inducing vascular inflammation of the genitourinary tract. This can lead to renal dysfunction which is common and related to acute tubular necrosis and glomerular destruction.

2.8.5 Muira puama (potency wood)

Ptychopetalum olacoides Bentham (Olanaceae), indigenous to the Amazon in Brazil and known as Mara puma/ Muira puama or potency wood has a long history of use by Amazonian people (Maxwell, 2022). It is commercially used as a sexual enhancer due to the popular belief that preparations from the roots can increase libido and the strength of the erection and also for the intensification of sexual performance, as a body stimulant, nerve tonic and for the treatment of chronic degenerative conditions.

Phytochemical analysis revealed the presence of alkaloids, tannins, saponins, flavonoids and 7 compounds. Muira puama was shown to increase the level of the cyclic adenosine monophosphate (cAMP). This could explain the demonstrated smooth muscle relaxant effects of the corpus cavernosum of rabbits and furthermore the prosexual effects for men. The observed relaxation had a rapid onset but only a short duration of action. Mauss, (2018) examined the psychopharmacological effects of Muira puama, reasonable by interacting with neurotransmitter systems and showed an excitatory action on the central nervous system which could support the proposed hypothesis of the interaction with dopaminergic and/ornoradrenergic systems. Data on safety and toxicity are very rare. There is just some information available from research on mixed formulation, containing other ingredients beside Muirapuama. One of these herbal formulations is Herbal vX, which was assessed in 2702 healthy women in a study conducted by Waynberg and Brewer in 2000 (Lammers *et al.,* 2021). Only eight of these women reported adverse effects, which included sweats/headache/irritability, headache/ thrush and stomach cramps. None of the mentioned adverse events were reported twice. Several women reported positive side effects as for example increasing energy Catuama® capsules contain a herbal extract of Paullinia cupana (Guarana), Trichilia catigua (Catuaba), Ptychopetalum olacoides (Muira puama), and Zingiberofficinale (Ginger)andarecommercially available in Brazil and over the internet in other countries (Mark *et al*., 2021).

2.8.6 Maca root

Maca (Lepidium meyenii) belongs to the Brassicaceae family and grows almost exclusively at high altitude in the Peruvian Central Andes. Its root has been used as food and in traditional medicine by the inhabitants of the Peruvian Central Andes for approximately 2000 years. They attribute the improvement of sexual function,

increasing of sexual desire and enhancement of fertility to the dried hypocotyls (Marshall and Rossman, 2019). On the Internet, maca is one of the most cited plant extracts for the improvement of sexual desire (especially for women). The root contains different secondary plant compounds, mainly glucosinolate and imidazole alkaloids, fatty acids and macamide were proven. There are only few publications which could be used for an evaluation of acute side effects related to Maca products with only small study collectives and some systematic flaws. Shin *et a*l. made a systematic review about maca for improving sexual function. During their research they found four randomized controlled trials. All of these trials did not attempt to assess adverse effects of maca. Kolawole, (2019) showed that black maca and, in smaller proportions, red maca reduced hemoglobin levels in highlanders with abnormally high hemoglobin levels; neither ariety of macareduced hemoglobin levels in lowlanders. Black maca reduced blood glucose levels. Maca extracts did not show serious adverse effects. Idoko *et al.,* (2018) showed the existence of 1R,3S-1-methyl-1,2,3,4-tetrahydroβ-carboline-3-carboxylic acid (MTCA) in the extracts of maca. This has been suggested to be an inhibitor of the monoamine oxidase (MAO) enzyme and is a comutagenic or a precursor to mutagenic compounds (Idoko *et al.,* 2018).

2.9 Viagra

Viagra is the trade name for the drug sildenafil citrate, which is used to treat erectile dysfunction in adult males (Ekeh, 2019). According to the Viagra Website, the drug works by increasing blood flow to the penis, which increases hardness and sexual satisfaction (Okodudu, 2022). It can be taken an hour before sexual activity and only works when the user is aroused (Oloruntoba-Oju, 2017).

Figure 2.3: Viagra Tablets (Ing, 2020)

2.9.1 Mechanism of Action

The molecular structure of sildenafil mimics that of cyclic guanosine monophosphate (cGMP). This similarity protects cGMP from degradation because sildenafil can bind to the catalytic site to act as a competitive inhibitor of cGMP-specific PDE-5, the enzyme that normally catalyzes the breakdown of vasodilatory cGMP (Giorgi, 2018). When PDE5 is active, cGMP is degraded, causing the vascular smooth muscle contraction, thereby limiting blood flow (Brown, 2023). When PDE5 becomes inhibited, the accumulation of cGMP leads to increased cGMP-dependent protein kinase activity, which phosphorylates multiple targets in the smooth muscle cell (Sekaran and Bougie, 2023). The result of smooth muscle cell target protein phosphorylation is a decrease in intracellular calcium, increased efflux of potassium, and deactivation of myosin light chain kinase, ultimately causing smooth muscle relaxation (Aidoo, 2019).

Relaxation of vascular smooth muscle in the corpus cavernosum leads to penile erection when the cavernosal sinusoids engorge with blood to compress the subtunical veins against the tunica albuginea. In patients with vasoactive pulmonary arterial hypertension, vasodilation of the pulmonary artery leads to reduced resistance to blood flow, with subsequent reductions in mean pulmonary arterial pressure (Sekaran and Bougie, 2023).

2.9.2Administration

2.9.2.1 Erectile Dysfunction

Sildenafil is available as oral tablets of 25 mg, 50 mg, and 100 mg strength for erectile dysfunction (ED). Most patients receive a prescription for 50 mg of oral sildenafil, taken as needed approximately 1 hour before sexual activity (Cate *et al*.,2019). The dose can be titrated upward to a maximum of 100 mg or down to 25 mg based on individual effectiveness and tolerance (Lawrance and Byers, 2022; Glass and Staeheli,

2022). Patients are advised not to exceed a maximum dosing frequency of once daily. It can be taken 30 min to 4 hours before desired intercourse. The onset of action can occur within 30 minutes, while the duration of the effect can last up to 18 hours (Cate *et al*.,2019).

Consider starting at a dose of 25 mg in patients with hepatic dysfunction (e.g., cirrhosis), patients with CLcr less than 30 mL/minute (severe renal impairment), and patients age 65 years and above, as the administration of sildenafil in these group patients have resulted in higher plasma levels of sildenafil. Patients taking concomitant inhibitors of CYP3A4 may benefit from initiation at the lower dosage (Ekeh, 2020).

2.9.3 Adverse Effects

Sildenafil has systemic vasodilatory effects and, as such, should be prescribed with caution to patients who may be sensitive to such blood pressure changes, such as patients with left ventricular outflow obstruction and impaired autonomic control of blood pressure. Caution is needed when combining sildenafil with alpha-adrenergic blocking drugs and other antihypertensive agents.

The use of sildenafil can infrequently result in a prolonged erection lasting more than 4 hours, also known as priapism, which, if left untreated, may result in damage to the penile tissue. Furthermore, sildenafil use requires caution in patients with anatomical deformation of the penis and patients with conditions potentially predisposing them to priapism, such as sickle cell anemia or multiple myeloma. The use of PDE5 inhibitors, such as sildenafil, may increase the incidence of non-arteritic anterior ischemic optic neuropathy (NAION) in males over age 50. Therefore, patients with a previous history of NAION or with a “crowded” optic disk should be prescribed sildenafil with caution.

Sildenafil metabolism is catalyzed primarily by CYP3A4 and, to a lesser extent, by CYP2C9; thus, strong inhibitors of these isoenzymes may lead to the accumulation of sildenafil with subsequent toxicity. The coadministration of sildenafil and ritonavir increased plasma sildenafil concentration (11-fold increase in the AUC) due to CYP 3A4/2C9 inhibition. Accordingly, caution is necessary for patients already on ritonavir when prescribing sildenafil. The recommendation is not to exceed a dose of 25 mg of sildenafil in 48 hours if taking ritonavir. The combination of sildenafil with the endothelin antagonist bosentan to manage pulmonary arterial hypertension has correlated with increased serum concentrations of bosentan and reduced levels of sildenafil. Combining sildenafil with other CYP3A4 inducers can similarly lead to reduced sildenafil levels; thus, such combinations are not recommended with chronic sildenafil dosing as performed in the management of PAH.

Sildenafil, at its lowest dose, is recommended when initiating therapy in patients who are on alpha-blockers due to potential systemic hypotension. Caution is also a requirement in patients taking mixed alpha/beta-blockers unless there is specific information regarding coadministration. Doses greater than 100 mg of sildenafil have resulted in no increase in efficacy but an increase in side effects. Patients on sildenafil most commonly (2%) reported headaches, flushing, dyspepsia, nasal congestion, back pain, myalgia, nausea, dizziness, and rash. Sildenafil has shown associations with changes in color vision, alterations in light perception, and hazy vision. Rarely, sildenafil has shown correlations with ototoxicity resulting in hearing loss that may be reversible in some cases. Epistaxis was reported in 13% of patients taking sildenafil with PAH secondary to connective tissue disorder. Epistaxis was not observed in patients with idiopathic PAH. Epistaxis was reported higher in sildenafil-treated

patients with a concomitant oral vitamin K antagonist. The safety of sildenafil is not established in patients with active peptic ulceration or bleeding disorders.

Cases of a sudden loss of hearing or decrease in hearing, sometimes accompanied by tinnitus and dizziness, with the use of PDE-5 inhibitors, including sildenafil. It is not possible to decide if reported cases are related directly to the patient's underlying risk factors attributing to hearing loss, the use of sildenafil, or both or to other factors. Advise patients to seek prompt medical care in the event of a sudden loss of hearing or decrease while taking sildenafil.

2.9.4 Contraindications

Nitrates increase cGMP formation, while sildenafil inhibits cGMP degradation causing the combination to produce severe life-threatening hypotension synergistically; coadministration of sildenafil with nitrates is contraindicated. Nitrate administration is safe after five or more sildenafil elimination half-lives (24 or more hours) have elapsed since the last sildenafil dose administration. Similarly, severe hypotension from other causes (e.g., volume depletion) contraindicates using sildenafil. Other contraindications include hypersensitivity to any component of the formulation, pulmonary veno-occlusion, left ventricular outflow obstruction, PAH associated with sickle cell anemia, and multiple system atrophy. Ischemic optic neuropathy and inherited degenerative retinal disorders contraindicate sildenafil use; discontinuation of sildenafil is recommended if sudden vision loss occur.

2.9.5 Monitoring

Typically, no regular monitoring is necessary for this medication. Occasionally patients may be asked to monitor their blood pressure and pulse after being newly prescribed sildenafil, after an increase in dosage, or after the addition of CYP3A4 inhibitors. During the review of systems, assessment for visual changes is

recommended. In the treatment of pulmonary arterial hypertension, patients should also receive monitoring for signs and symptoms of pulmonary edema.

2.9.6 Toxicity

In healthy subjects, research demonstrated that single doses up to 800 mg resulted in adverse effects similar to those seen in lower doses but with increased frequency and severity. There are no antidotes available for sildenafil. In case of overdose, patients should receive supportive care. Dose-related visual disturbances occurred more frequently at toxic levels, while blood pressure changes showed a low correlation. As sildenafil is highly bound to plasma proteins and not excreted renally, dialysis does not help expedite the clearance of sildenafil. When considering the duration of toxicity, the activity of N-desmethyl-sildenafil must be considered; this metabolite retains PDE5 specificity at lower potency, with plasma concentrations that approach 40% of the parent compound.

2.9.7 Advantages of Viagra

There are many purported benefits of taking Viagra. Some of these include:

You can take it 30 minutes to 4 hours before engaging in sexual activity. It increases the hardness of the penis in order to make penetration easier and sex more satisfying (Ahikire, 2021). Viagra only works when one is already sexually stimulated, so there isn't an unwanted or embarrassing erection. The effects of Viagra wear off after sexual activity, so the penis does not remain hard long after intercourse (Glass and Staeheli, 2022).

2.9.8 Disadvantages of Viagra

According to the drug company's own website, "Viagra can cause serious side effects". Side effects, though apparently rare, include the following: Priapism – an erection that does not go away (Glaser and Strauss, 2017). This is an erection lasting

more than four hours, which requires immediate medical attention before long term damage occurs to the penis. Abrupt loss of vision in one or both eyes, which could be a sign of non-arteritic anterior ischemic optic neuropathy (NAION). Abrupt hearing loss or decreased ability to hear (Glass and Staeheli, 20022).

CHAPTER THREE
MATERIALS AND METHOD

3.1 Laboratory equipment

Lancets, Alcohol prep pads, Gauze pads, Microhematocrit tubes (heparinized), Sealant (”Seal-Ease,” “Crit-Seal,” etc.), Microhematocrit centrifuge, Microhematocrit reader, tourniquet, 2ml syringe, tube containing anticoagulant (EDTA, citrate) Dissecting materials, capillary tubes, hot plate, cotton wool, knives, measuring cylinder, digital weighing balance, scissors, lithium heparin bottles, cover slips, stainless steel, blender, tissue gauze, 5mil syringe, forceps, microscope, cutup board, universal container, tissue cassette, rotary microtones, lead pencil automatic tissue processor, frosted-end slides.

3.2 Drugs and chemicals

Viagra was made available in the form of sildenafil citrate tablets (100 mg per tablet) from Airen Pharmaceutical Co. in Benin City (Catalog Number: T712515). Each tablet was suspended in a distilled water solution of 20 mL. The daily dose of Viagra was 20 mg/kg.bw, which was equivalent to human effective therapeutic dose according to (Paget and Barnes, 2018).

3.3 Preparation and experimental design

18 (Eighteen adult) male albino rats (weighing 200g-220g) were acquired from the animal house of Edo State University. Rats were kept in steel mesh cages (6 rats per cage) and fed on commercial standard chow and free tap water for one-week acclimation periods. The animals were randomly divided into 3 equal groups A B C (n=6/group). The first group (group A) served as control were administered feed and water only. The second group (group B), included Six (6) rats that were orally given Viagra in a dose of 5 mg/kg body weight dissolved in saline daily for 4 successive weeks. The third group (group C), included Six (6) rats that were orally given Viagra

in a dose of 10 mg/kg body weight for 4 successive weeks and then were kept without treatment for 4 weeks. The calculated sildenafil citrate doses were given orally to each animal using a curved needle-like oral tube that was administered orally for a period of four(4) weeks. Rats were sedated with 4 percent isoflurane in 100 percent oxygen after six weeks. Immediately after four (4) weeks, the blood sample was collected from the heart into an EDTA container for hematological analysis. The organs were harvested and placed in 10% Neutral buffered formalin for onward tissue processing.

3.4 Determination of body weight

Body weight of experimental animals was checked at week 0 before Viagra administration and last day of drug administration before sacrifice. Percentage weight change was calculated.

3.5 Determination Haematocrit Total WBC and Differential Cell Count Analysis.

The SFRI auto-haematological analyzer was used to do a full blood count immediately upon collection. This auto-analyzer is used to perform a comprehensive blood count to determine the quantity of blood cells. Calibration and standardization of the equipment, processing, and analysis were performed exactly in accordance with the manufacturer's instructions.

Principle

It works on the premise of counting and quantifying cell types utilizing radio frequency and direct current (Gopal *et al.* 2005). It analyses blood using three detector blocks, a cell pack, and stromatolyser reagents. The WBC detector block measures the number of white blood cells (WBC), whereas haemoglobin detectors use the direct current (DC) detection method to measure the number of red blood cells and platelets.

Procedure

The procedure is such that the sample for analysis is mixed using a vortex mixer and the lid of the sample container is opened and the sample fed into the Auto-analyzer via the probe, the analysis was done by the machine and the results of the analysis displayed at the read-out screen which can also be printed.

3.6 Tissue Processing

The tissues were cut open and placed in a tissue cassette and were processed using 22hours automatic tissues processor schedule, where the tissues were dehydrated, cleared and infiltrated. Tissues were embedded, sectioned, floated, dewaxed and stained.

3.7 Hematoxylin and Eosin (H and E) Staining

Each rat's left testis was delivered and preserved in a 10% formalin solution before being dehydrated in increasing degrees of alcohol. The specimens were embedded in paraffin blocks after being treated with xylene. Serial slices were cut using a microtome and stained with hematoxylin and eosin at a thickness of 5 um.

3.8 Testicular Histopathology

The preparation of tissues for histopathological study was done using the standard technique outlined by Drury *et al*. (2017). And testes of experimental rats were dissected out, cut into small slices, and fixed in 10% formaldehyde buffer for 24 hours. The tissues were washed free of 10% formaldehyde and stored in 70% alcohol until being embedded. The tissues were dehydrated in alcohol series and embedded in paraffin. Tissue sections of 5 μm thickness was prepared and placed on glass slides. The sections were stained with hematoxylin and eosin and mounted in mounting medium. The slides were examined under the light microscope. For each testis several

cross sections composing of 20-50 tubule sections will be examined for signs of interstitial edema, somniferous tubule degeneration, and congestion.

3.9 Slide Preparation and Slide Reading

For histological analysis, the hearts were fixed with 10% formalin and then embedded in paraffin and sectioned into 5-µm thick sections and stained with hematoxylin and eosin (H&E). The sections were examined under a light microscope by Supervisor

3.10 Photomicrograph

Selected tissue sections were photographed and presented as plates

CHAPTER FOUR

4.0 RESULTS

Sidenafil administration for 4 weeks reveals changes in weight, haematological parameters with no histopathological damages. The results are explained separately in different sections as follows.The collated values were expressed in mean ± SD. ($P<0.05$) was considered significant. The average weight of animal after the 4 weeks administration of Sildenafil shows significant reduction ($P<0.05$) when compared with the control as presented in table 4.1. The hematocrit and white blood cell count value were significantly reduced ($P<0.05$) in the test group when compared to the control. They were no significant changes in lymphocytes of the experimental group when compared with control. There was significant increase in monocytes count ($P<0.05$) in the test group in comparison with the control group

The histological sections of the heart and testes did not present any degenerative changes as presented in the plates below.

Table 4.1: Showing the Effect of Sildenafil on the body weight across group (Experimental and Control)

Weight (control group)	Weight (Exp. group)	t-value	p-value
210.0 ± 5.30	202.7 ± 3.11*	5.987	0.0001

Table 4.2: The effect of Sildenafil on hematological parameters across group (Experimental and Control)

	Control	Experimental group	t-value	p-value
HCT	45.6 ± 1.50	41.0 ± 1.66*	20.917	0.0001
WBC	7.4 ± 1.92	2.3 ± 0.55*	9.039	0.004
LYM	52.2 ± 2.49	46.7 ± 12.98	0.925	0.369
MON	7.4 ± 1.14	17.2 ± 2.38*	-8.684	0.0001
GRAN	40.4 ± 1.82	32.8 ± 3.27*	4.876	0.0001

Key

HCT = Hematocrit
WBC= White blood count
LYM = Lymphocytes
MON = Monocytes
GRAN= Granulocytes

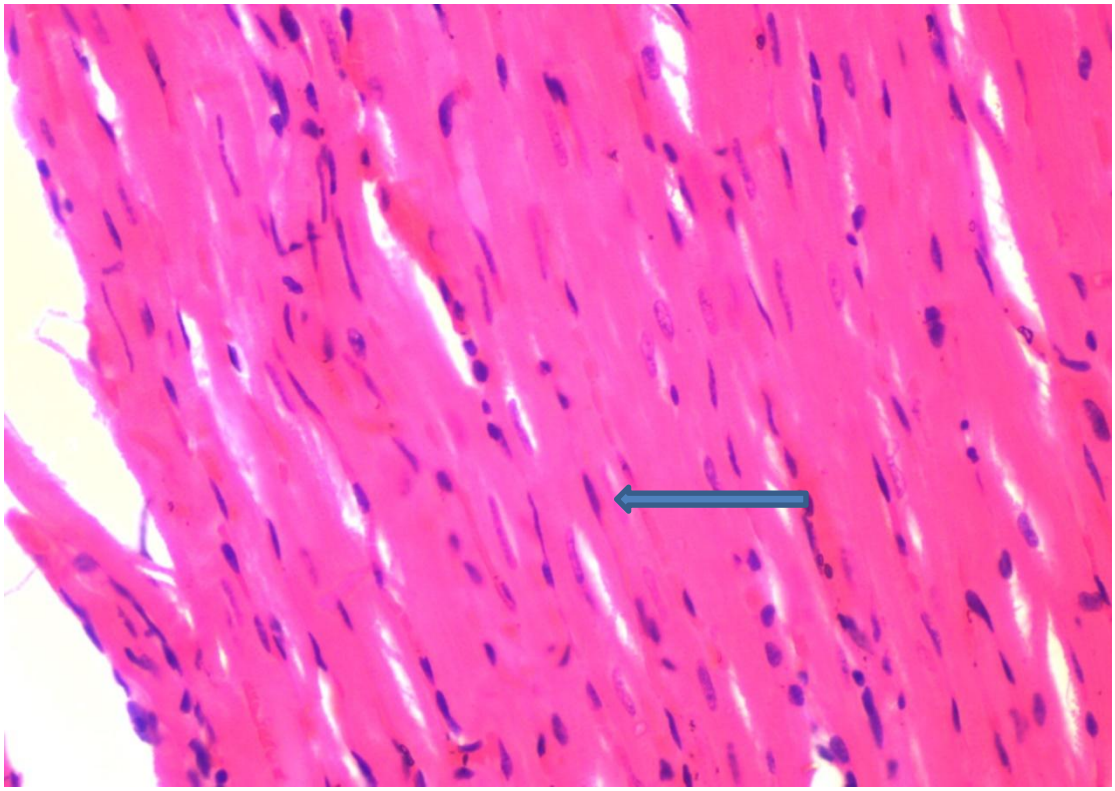

Plate 4.1: Control Section of cardiac muscle shows myocytes with peripherally placed nuclei surrounded by eosinophilic cytoplasm. NORMAL HEART MUSCLE Haematoxylin and Eosin X 400

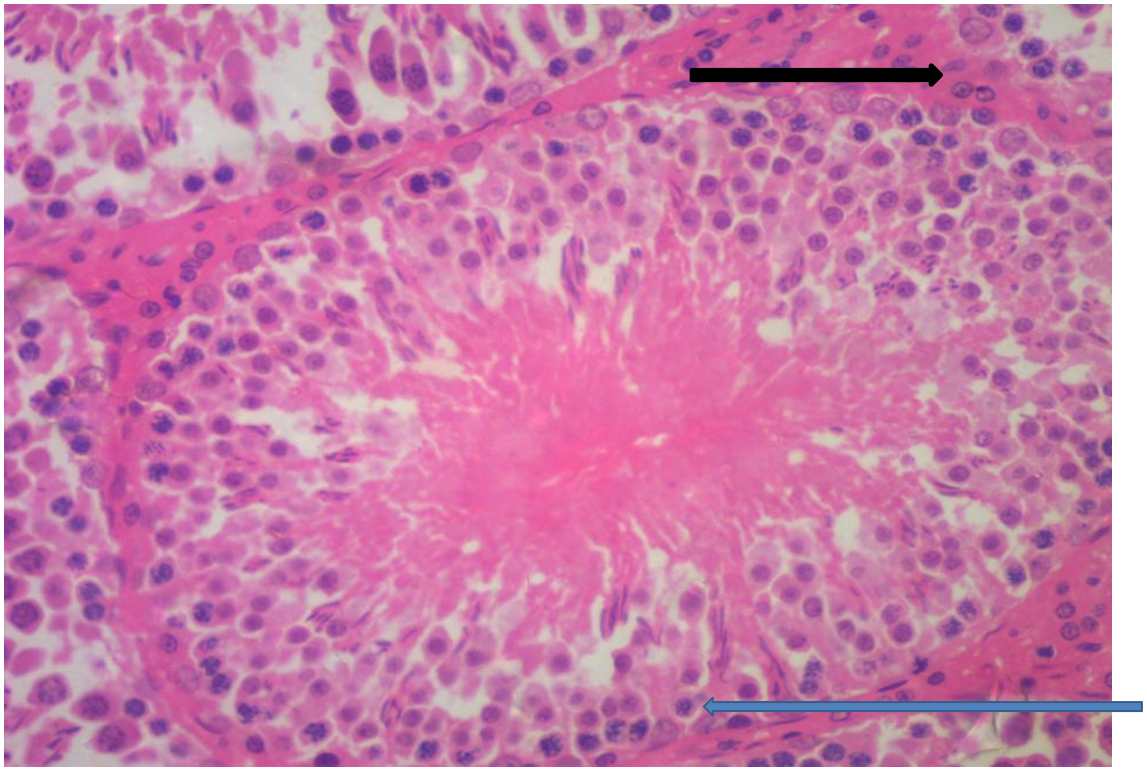

Plate 4.2: Control section of the testis shows normal seminiferous tubules (blue arrow) containing sertoli cells and spermatozoa. The interstitium contains Leydig cells (black arrow). Features of NORMAL TESTIS. H AND E X400

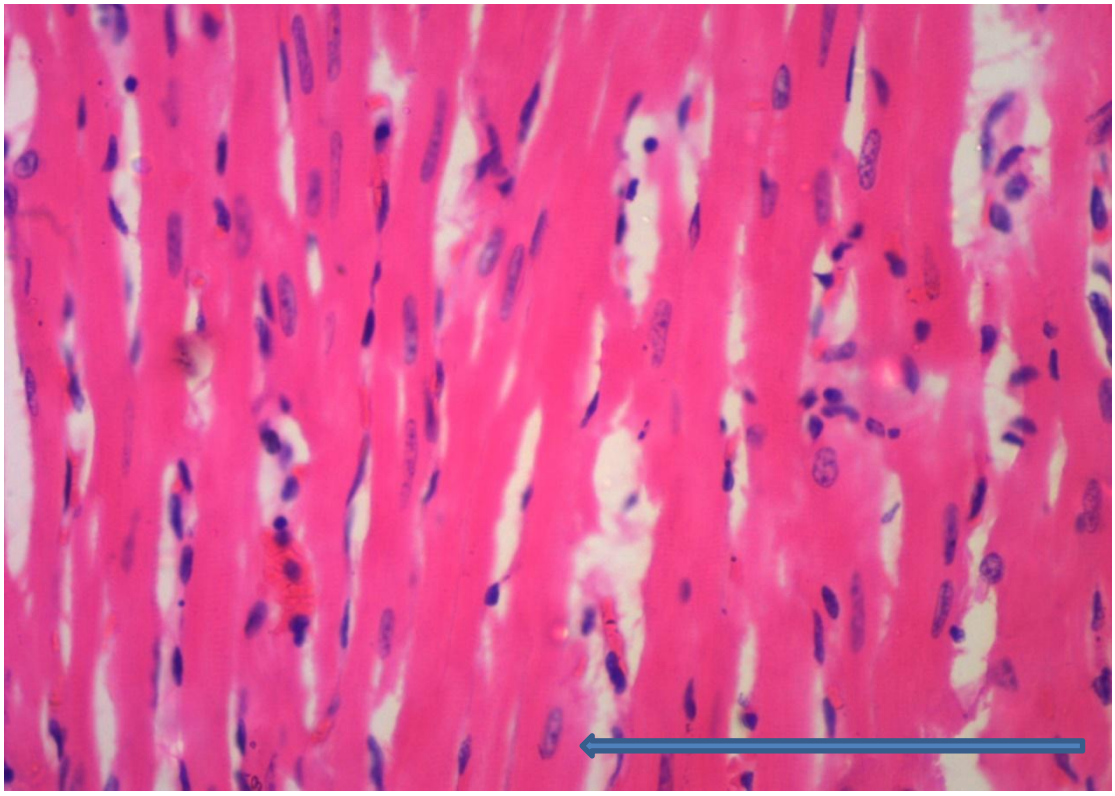

Plate 4.3: Section of rat cardiac tissue from the experimental Group B, Treated with 5mg shows myocytes with peripherally placed nuclei surrounded by eosinophilic cytoplasm. NORMAL HEART MUSCLE
Haematoxylin and Eosin X 400

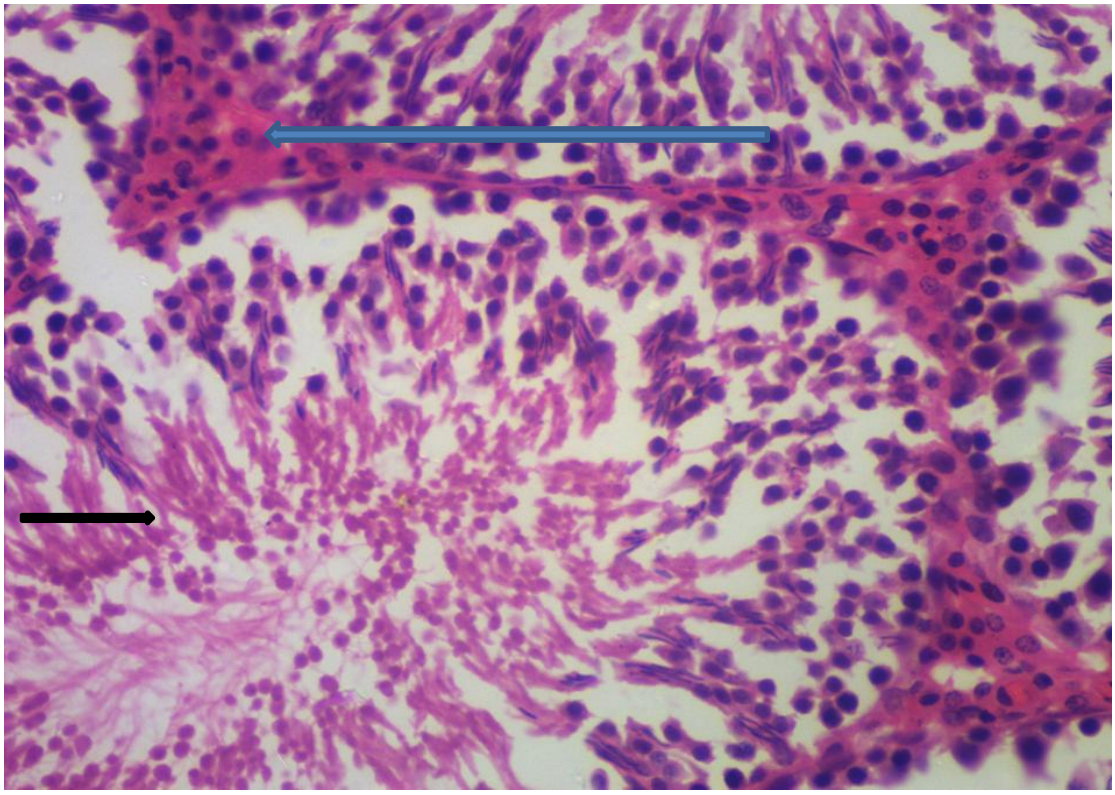

Plate 4.4: Section of the testis administered with 5mg/kg body weight from the experimental group B. see normal seminiferous tubules (black arrow) containing Sertoli cells and spermatozoa. The interstitium contains Leydig cells (blue arrow). Features of NORMAL TESTIS. H AND E X400

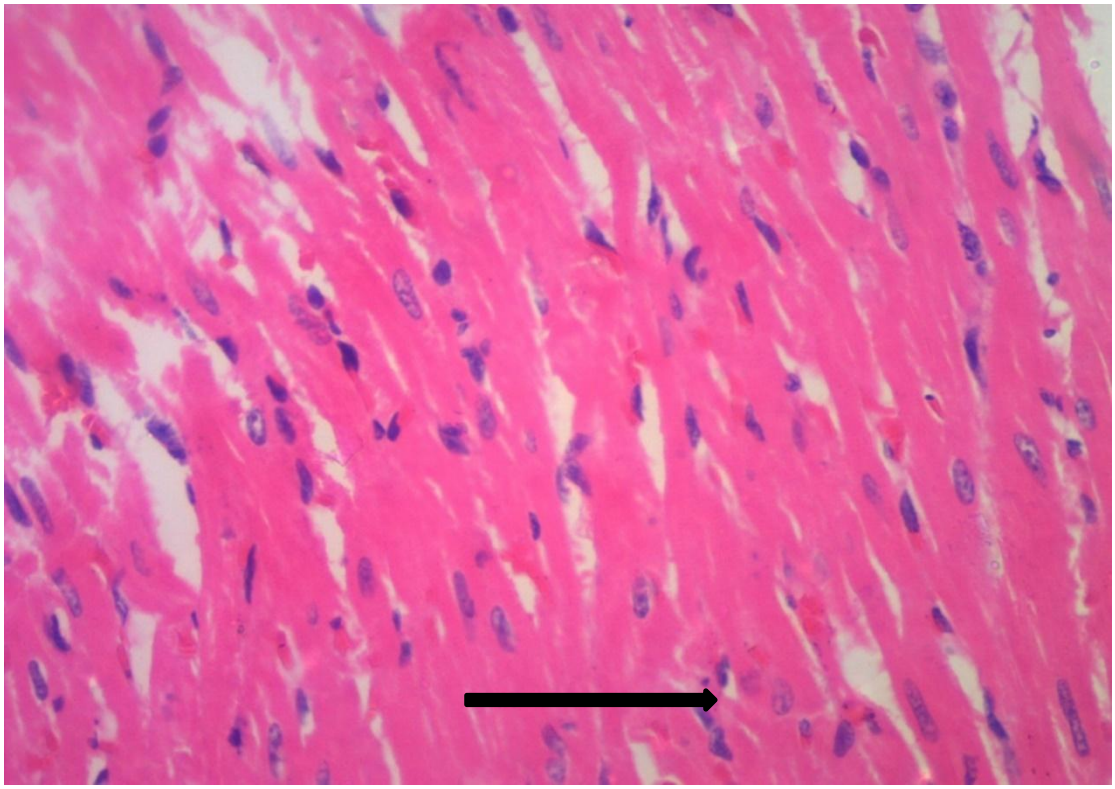

Plate 4.5: Section of rat cardiac tissue from the experimental Group C; Treated with 10mg/kg shows myocytes with peripherally placed nuclei surrounded by eosinophilic cytoplasm. NORMAL HEART MUSCLE
shows slight degeneration of both the cardiac fibers (CF), and the nucleus (N). Haematoxylin and Eosin X 400

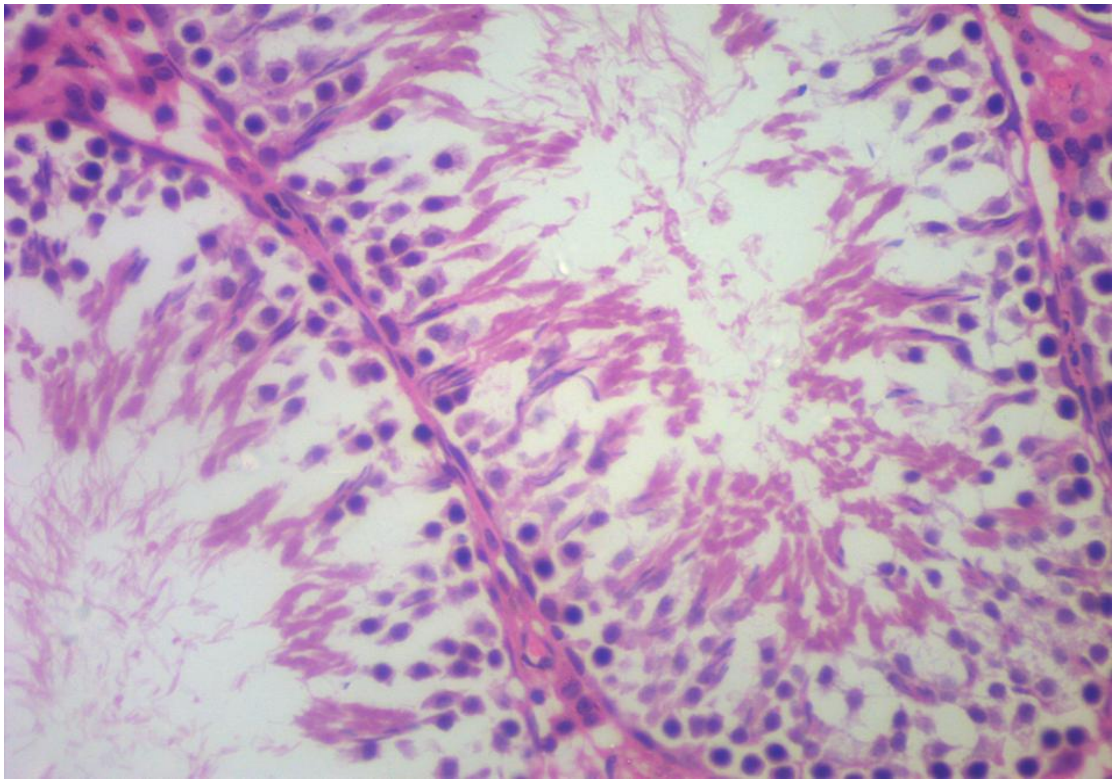

Plate 4.6: Section of the testis administered with 10mg/kg from the Experimental group C; see normal seminiferous tubules containing Sertoli cells and spermatozoa. The interstitium contains Leydig cells . Features of NORMAL TESTIS. H AND E X400

CHAPTER FIVE
DISCUSSION, CONCLUSION AND RECOMMENDATION

5.1 Discussion

Application of sildenafil (Viagra) has been one of the most practices of recent especially in young adult males with a history of quick ejaculation (Alkali *et al.,* 2019; Beres, 2017).

The Result of present expressed that the Hematocrit test showed that red blood cells (RBCs) count showed a general decrease in response to sildenafil administration. This finding may be explained on the basis of inhibitory effect of sildenafil on erythropoiesis. The decreased in RBC count and hemoglobin (Hb) lowered the oxygen supply to different tissues thus resulting in low energy production. This study is in agreement with the study by Bella and Shamloul, (2020) and Cheng *et al.,* (2021). In the research by Bella and Shamloul, (2020) where natural aphrodisiacs and sildenafil were used, increase in WBC and decrease in RBC count after treatment using 50mg/kg to 100mg/kg were reported.

Weight analysis of the albino rats after four weeks indicated a slight weight difference between the control group (210.0 ± 5.30) and the Viagra administered albino rats (202.7 ± 3.11) Different doses and durations of administration, sex differences, eating habits or environmental factors may account for the observed disparity. This is in agreement with the findings of Agunbiade and Ayotunde, (2022), where after at day 14 there was a significant decrease in the percentage difference in group G (sildenafil only) when compared to group C. The significantly lower percentage difference observed in groups A, E and G (all treated with sildenafil) is an indication that sildenafil citrate has effect in reducing the rate of body weight loss in diabetic and non-diabetic rats.

Also, in research conducted by Scorgie *et a*l., (2019) on a high-fat diet albino rats, fed with Viagra, were able to metabolize the excess fat so fast that they maintained their weight. And the mice didn't put on weight because of increased sexual activity. "they further found that the white fat of the mice which get sildenafil, was becoming more brownish. Brown fat is the type of fat that burns fat.

Other similar findings by Mc carberg, (2020) recorded substantial increase in the body weight of aphrodisiac-administered male Wistar rats. Organ weight loss was also observed in all groups that received Viagra citrate (30 mg/kg).

This is contrary to the results of Bowling, (2018), where no significant difference was observed in body weight, paired testicular weight and relative tissue weight index of male adult albino rats amongst the three groups under study, i.e control, experimental B and C groups. He Concluded that sildenafil citrate had no effect on body weight, paired testicular weight and relative tissue weight on the Albino rats tested.

Sperm structural and functional integrity is critical for fertilization and progeny quality. Male infertility is heavily influenced by sperm quality and quantity. A sperm reproductive capacity is an important factor in determining the success of in vitro fertilization and insemination procedures. Previous human studies have shown that using Sildenafil citrate for a short period of time can improve spermatic functions and activate the acrosomal reaction (Vilakati, 2019). The results of the present study indicated that the administration of 10mg/kg of Viagra for male rats caused slight histopathological changes in testis and the cardiac tissue of male rats. Three (3) sections of testes collected from rats administrated with 10mg/kg Sildenafil citrate had mild necrosis of both cardiac fibers, seminiferous tubules and the interstitial tissue, congested blood vessels, hypertrophy of the interstitial Leydig cells and degeneration of the spermatogonial cells (Plates 4, 5 and 6). However, the control rats

did not record these histological abnormalities, but possessed normalcy of testicular cyto-architecture (Plate 1). These results obtained are consistent with the results obtained by Balasubramani *et al,* (2021) where the histopathological examinations of the heart of Wistar albino rats showed no serious histopathological changes between the control and treatment groups. The stained micrograph of the heart of these animals showed normal cardiac myocytes arranged in interlacing and parallel arrays. But is inconsistent with the study of Zhang, (2021). Where Viagra was found to have very high necrotic and inflammatory effect on the wester rat used as animal model.

In a similar research set up, Bello and Isah, (2018), selected twenty (20) albino male Wistar rats into four groups (n=5) randomly. The control group was administered 1 mL/kg of distilled water while 50 mg/kg, 100 mg/kg, and 200 mg/kg body weight of Sildenafil citrate were administered once in a day for 28 days to three treatment groups of rats. Oral administration was done using oropharyngeal cannula once daily for 28 days. At the end of the trial period animals were sacrificed on the 29th day, and epididymal sperm and testes were collected subject to various analytical assays. Findings showed significant reduction in sperm count and sperm normality, with a significant incremental in sperm malformations/abnormality in 28 days Viagra exposed animal when compared to the control. The testicular assay depicted histopathological alterations in testes of male rats treated with Sildenafil citrate at all dose levels. My study clearly demonstrated that long-term use of Viagra can cause changes in perm quality and quantity, this can result in a decrease in fertility rate

Also, Del Mar Sánchez-Fuentes *et al., (*2022) setup an experiment of male Albino rats divided into 8 groups, each being treated for a maximum of 45 days as follows. In the 4 short-term treatment groups, control rats were administered normal saline orally, whereas experimental animals were fed sildenafil citrate (Viagra) 1 mg/g with 18%

ethanol (5 g/kg body weight), which was given orally as a single dose. After 1, 2.5, 4 and 24 h the rats were killed. In the 4 long-term treatment groups, daily continuous doses of drug and ethanol with a single dosage were given for 15, 30 and 45 days and the animals killed 4 h after the last dosage. Changes in the testis were compared with the normal healthy rat testis. There were observable morphological changes of the surface of the tissue structure.

The results of the present study also explained that sildenafil at doses 10mg/kg BW showed a significantly increase in Monocytes (MON) and Granulocytes (GRAN) levels in male rats after days of injection. The presents study also revealed that the total white blood cell (WBC) counts, and lymphocyte, were significantly elevated at 10mg/kg. This significant increase in WBCs count indicated the activation of defense mechanism and immune system of rats. According to Brena and Sander, (2021), this induction of white blood cells is a positive response for survival due to cell mediated immune response of animals.

In a similar study by Ezumah, (2023), it was found that, White blood cell (WBC) count of diabetic and non-diabetic rats showed a significant increase of the WBC count in the diabetic groups compared to their prediabetic values indicating that diabetes increases the WBC counts of the rats. Furthermore, in the sildenafil a treated diabetic group A and B, there was a significant increase in the WBC count throughout the days of the experiment unlike in groups C and D that showed a non-significant increase at day 14 compared to values at day zero. Similarly, in the non-diabetic groups (E, F and G), there was a significant increase in the sildenafil treated non diabetic groups E and G while a non-significant increase in group F which was not treated with sildenafil citrate. This result can be interpreted that sildenafil citrate increases the WBC count of both diabetic and non-diabetic rats which confers

favorably with my findings that also reported a significant increase of WBCs in sildenafil treated albino rats.

5.2 Conclusion

1). The application of Sildenafil at doses 10mg/kg BW showed an increase in Monocytes (MON) and decrease in Granulocytes (GRAN) levels in male rats after days of injection

2). The presents study also revealed that the total white blood cell (WBC) counts, and lymphocyte, were significantly decreased in 10mg/kg administration of Viagra

3). The Hematocrit test showed that red blood cells (RBCs) count showed a general decrease in response to sildenafil administration.

4) Administration of Sildenafil citrate in a dose can be implicated to have effect on cardiac tissues, spermatogenesis as well as the caudal epididymis and vas deferens functions.

5.3 Recommendations

Understanding the molecular downstream events involved in long-term PDE5 inhibitor exposure through basic and clinical research can be useful in supervising the application of aphrodisiac substances so as to improve on corrective measures through a short term administration of aphrodisiac substances at low doses.

The use of scanning electron microscopy can potentially make a histopathological study to be more apparent. The use of scanning electron microscope for evaluation of the changes in the testis is recommended for more suitable observation of the surface and morphological shapes of the tissue structures. Further study using graded dose of sildenafil may reveal a better relationship between the effect of sildenafil and the measured parameters in this study.

5.4 Contribution to knowledge

1. **Internal Organs and Cells Effects:** This study has affirmed that the use of substances perceived to be aphrodisiacs such as Viagra (sildenafil) has proportionally increased the risk of internal organ complications such as necrosis of cardiac fibers, seminiferous tubules and the interstitial tissue, congested blood vessels, hypertrophy of the interstitial Leydig cells and degeneration of the spermatogonial cells.
2. **Potential Weight Fluctuation and Complication Effects:** It has also affirmed the possibility of the drugs to contribute to weight gain and weight loss. This implies that users of Viagra are likely to develop one or more complications from the usage such as the weight issue.
3. **Histopathological Insight:** The histopathological findings provided by this study offers confirmation that consistent use of Viagra can potentially contribute to this growing testicular problem and testicular issues. In southern part of Nigeria alone, there are 26 cases of testicular and para-testicular issues with an average incidence of 1.5 cases per year. The incidence of testicular cancer in some studies was 0.55 per 100,000 population (95% CI, 0.52–0.57) and accounted for 1.1% of all male cancers. Rhabdomyosarcomas were the most common variety (70% of the paratesticular tumors and 26.8% of all tumors of the testis). Seminomas comprised 50% of the germ cell tumors and 15.4% of all testicular tumors in this series.

Overall, the study shows that consistent use of Viagra and further study may potentially contribute to further histopathological findings and changes

REFERENCES

Abdullahi, H. and Tukur, J. (2023). Sexual stimulants and their effects on women of reproductive age group in Kano, Northern Nigeria. *Nigerian Journal of Basic and Clinical Sciences, 10(1)*, p.13.

Abubakar, A. (2019). Aphrodisiac fueled sex on the rise in Northern Nigeria. Mail and Guardian 14 June 2019. Accessed on: https://mg.co.za/article/2009-06-14-aphrodisiacfuelled-sex-on-the-rise-in-northern-nigeria

Abubakar, M. S., Musa, A.M., Ahmed, A. and Hussaini, I. M. (2017). The perception and practice of traditional medicine in the treatment of cancers and inflammations by the Hausa and Fulani tribes of Northern Nigeria. *Journal of Ethnopharmacology, 111(3),* pp.625-629.

Adegoke, T. G. (2020). Socio-cultural factors as determinants of divorce rates among women of reproductive age in Ibadan metropolis, Nigeria. Studies of Tribes and Tribals, 8(2), pp.107-114.

Aderinto, S. (2022). Dangerous aphrodisiac, restless sexuality: venereal disease, biomedicine, and protectionism in colonial Lagos, Nigeria. *Journal of Colonialism and Colonial History, 13(3)*. .

Agunbiade, O. M. and Ayotunde, T. (2022). Ageing, sexuality and enhancement among Yoruba people in south western Nigeria. Culture, health and sexuality, 14(6), pp.705-717.

Ahikire, J. (2021) African feminism in context: Reflections on the legitimation battles, victories and reversals. Feminist Africa, 19, pp.7-23.

Aidoo, A.A. (2019). Unwelcome Pals and Decorative Slaves: The Woman as Writer in Modem Africa. Afa: *Journal of Creative Writing,* p.40.

Aidoo, A. A. (2018). The African Woman Today. Sisterhood Feminisms and Power: From Africa to the Diaspora. O. Nnaemeka, ed

Ajomale, O. (2017). Country report: Ageing in Nigeria—Current state, social and economic implications. Summer Newsletter, pp.15-20.

Ajuwon, A. (2015). Attitudes, norms and experiences of sexual coercion among young people in Ibadan, Nigeria. Sex without Consent: Young people in Developing Countries. London and New York, Zed Books, pp.96-104.

Akanmode, O.A. (2015). Snail-sense strategies for women emancipation in promise Okekwe's trilogy. *African Journal of Gender and Development, Ile-Ife*: *Journal of the Centre for Gender and Social Policy Studies, Obafemi Awolowo University, 2(2),* pp.17-28. .

Al-Amin, U., Shehu, H.B., Tor, A.B. and Babagana, A.Y, (2021). Nalle Arts: Notes on some aspects of henna application among the Kanuri people of Borno, Nigeria. *Journal of science, humanities and arts, 5 (6),* pp.1-24

Alkali, B., Ismaila, A.B. and Muhindo, J. (2019). Validation of antibacterial and aphrodisiac activities of Fodogia agrestis in Kano state, Nigeria. *Special Bacterial Pathogens Journal (SBPJ), 1(1),* pp.00023-0026.

Alkhali, H.A. and Sum, C.W., (2015). The Kati Formation: A Review. In ICIPEG 2014 pp. 303-31.

Balasubramani, S.P., Seethapathy, G.S. and Venkatasubramanian, P. (2021). Nuclear ribosomal DNA-ITS region based molecular markers to distinguish botanical entities traded as 'Vidari'. *Journal of Herbal Medicine, 1(3-4)*, pp.83-89.

Bancroft, J., (2020). Sexual desire and the brain revisited. Sexual and Relationship Therapy, 25(2), pp.166-171. .

Bancroft, J. and Graham, C.A. (2021). The varied nature of women's sexuality: Unresolved issues and a theoretical approach. Hormones and Behavior, 59(5), pp.717-729.

Banda, D., Nyirenda, J. and Sijumbila, G., (2017). Aphrodisiac Properties of Mutimba Vula and Mwana Apeluke Herbs sold in Lusaka, Zambia. *Medical Journal of Zambia, 44(3),* pp.133-139. .

Barta, W.D. and Kiene, S.M. (2018). Motivations for infidelity in heterosexual dating couples: The roles of gender, personality differences, and sociosexual orientation. *Journal of Social and Personal Relationships, 22(3),* pp.339-360.

Bella, A.J. and Shamloul, R. (2020). Traditional plant aphrodisiacs and male sexual dysfunction. Phytotherapy research, 28(6), pp.831-835.

Bello G. (2017). Condition of Women in Nigeria: Issues and Challenges. *Arts Social Science Journal, (8)293*. doi: 10.4172/2151-6200.1000293

Bello, U.L. and Isah, J.N. (2018). Use of herbal medicines and aphrodisiac substances among women in Kano state, Nigeria*. IOSR J Nursing Health Sci, 4(3),* pp.41-50. .

Beres, M.A. (2019). Rethinking the concept of consent for anti-sexual violence activism and education. Feminism and Psychology, 24(3), pp.373-389.

Beres, M.A. and MacDonald, J.E. (2017). Talking about sexual consent: Heterosexual women and BDSM. Australian Feminist Studies, 30(86), pp.418-432.

Bloch, L., Haase, C.M. and Levenson, R.W. (2017). Emotion regulation predicts marital satisfaction: More than a wives' tale. Emotion, 14(1), p.130.

Blow, A.J. and Hartnett, K. (2017). Infidelity in committed relati0nships ii: A substantive review. *Journal of marital and family therapy, 31(2)*, pp.217-233.

Bowling, A. (2018). Research methods in health: investigating health and health services. McGraw-Hill Education, United Kingdom.

Bradbury-Jones, C., Irvine, F. and Sambrook, S. (2020). Phenomenology and participant feedback: convention or contention? Nurse Researcher, 17(2), p.25.

Braun, V. and Clarke, V. (2018). Using thematic analysis in psychology. Qualitative research in psycholo2y, 3(2), pp.77-101.

Brotto, L.A., (2020). The DSM diagnostic criteria for hypoactive sexual desire disorder in women. Archives of sexual behavior, 39(2), pp.221-239.

Brotto, L.A. and Smith, K.B. (2019). Sexual desire and pleasure. APA handbook of sexuality and psychology, 1, pp.205-244.

Brown, E.M. (2023). Patterns of infidelity and their treatment. Philadelphia: Routledge.

Bryant, J., and T. Schofield. (2017). "Feminine Sexual Subjectivities: Bodies, Agency and Life History." Sexualities 10 (3): 321–340.

Butzer, B. and Campbell, L. (2018). Adult attachment, sexual satisfaction, and relationship satisfaction: A study of married couples. Personal relationships, 15(1), pp.141-154.

Byers, E.S. (2019). The Interpersonal Exchange Model of Sexual Satisfaction: Implications for Sex Therapy with Couples. *Canadian Journal of Counselling, 33(2),* pp.95-111.

Byers, E.S. (2019). Relationship satisfaction and sexual satisfaction: A longitudinal study of individuals in longterm relationships. *Journal of sex research, 42(2),* pp.113-118.

Brena, S. and Sander, S.H. (2021). Opiods in non-malignant pain. Questions in search of answers;clin J. pain 7: 342-345

Catacutan, D., McGaw, E. and Llanza, M.A., (2018). In equal measure: a user guide to gender analysis in agroforestry. Los Banos, the Philippines.

Cate, R.M., Lloyd, S.A., Henton, J.M. and Larson, J.H., (2019). Fairness and reward level as predictors of relationship satisfaction. Social Psychology Quarterly, pp.177-181.

Cense, M., (2019). Rethinking sexual agency: proposing a multicomponent model based on young people's life stories. Sex Education, 19(3), pp.247-262.

Chan, Z.C., Fung, Y.L. and Chien, W.T., (2023) Bracketing in phenomenology: Only undertaken in the data collection and analysis process. The Qualitative Report, 18(30), pp.1-9.

Chatterji, M., Murray, N., London, D. and Anglewicz, P., (2015). The factors influencing transactional sex among young men and women in 12 sub-Saharan African countries. Social biology, 52(1-2), pp.56-72.

Cheng, J. T., Min, L, TzongCherng, C., Thing-Fong, T., Feng-Hwa, L. and Chih Jen C. (2022) Plasma Glucose–Lowering Effect of Sildenafil in Streptozotocin-Induced DiabeticRats. DIABETES, 50:

Dabhadkar, D. and Zade, V., (2023). Evaluation of the potential aphrodisiac activity of Psoralea corylifolia in male albino rats. *Asian Journal of Biomedical and Pharmaceutical Sciences, 3(22),* p.18.

Davis, C.M., Yarber, W.L., Bauserman, R., Schreer, G. and Davis, S.L., 1998. Handbook of sexuality-related measures. Sage. .

Del Mar Sánchez-Fuentes, M., Santos-Iglesias, P. and Sierra, J.C., (2022). A systematic review of sexual satisfaction. *International Journal of Clinical and Health Psychology, 14(1),* pp.67-75.

Duyilemi, A.N., Tunde-Awe, B.M. and Lois, L.O.A., (2018). Cohabitation in Nigeria Tertiary Institutions: A Case Study of Adekunle Ajasin University, Akungba-Akoko, Ondo State Nigeria. *International Journal of Social Sciences and Humanities, 3(1),* pp.27-37.

Eatough, V. and Smith, J.A., (2018). Interpretative phenomenological analysis. The Sage handbook of qualitative research in psychology, 179, p.194.

Edelstein, R.S., Chopik, W.J. and Kean, E.L., (2021). Sociosexuality moderates the association between testosterone and relationship status in men and women. Hormones and Behavior, 60(3), pp.248-255.

Ekane, D., (2020). Contemporary Family patterns in Sub Saharan Africa. Stockholm: Department of Human Geography, Stockhom University, Faculty of Social Sciences. .

Ekeh, P. (2022). Social exchange theory: The two traditions. Cambridge, MA: Harvard University Press.

LEtuk, E.U., Muhammad, A.A., Igbokwe, V. and Okolo, R.U., (2017). Sexual stimulatory effects of aqueous stem bark extract of Lophira laceolata in male Sprague Dawley rats. *Journal of Clinical Medicine and Research, 1(2),* pp.018-021.

Ezenwa-Ohaeto, N., 2015. Fighting Patriarchy in Nigerian Cultures Through Children's Literature. Studies in Literature and Language, 10(6), pp.59-66.

Ezumah, N.N., (2023). Gender issues in the prevention and control of STIs and HIV/AIDS: lessons from Awka and Agulu, Anambra State, Nigeria. *African journal of reproductive health*, pp.89-99.

Giorgi, A., (2018). Concerning a serious misunderstanding of the essence of the phenomenological method in psychology. *Journal of Phenomenological Psychology, 39(1),* pp.33-58.

Giorgi, A., (2019). The descriptive phenomenological method in psychology: A modified Husserlian approach. Duquesne University Press. .

Giorgi, A., (2022). The descriptive phenomenological psychological method. *Journal of Phenomenological psychology,* 43(1), pp.3-12.

Glass, S., (2017). Not" just friends": rebuilding trust and recovering your sanity after infidelity. New York: Simon and Schuster.

Glass, S.P. and Staeheli, J.C., (2022). Not" just friends": Protect your relationship from infidelity and heal the trauma of betrayal. New York: Free Press.

Gonzales, G.F., (2022). Ethnobiology and ethnopharmacology of Lepidium meyenii (Maca), a plant from the Peruvian highlands. Evidence-Based Complementary and Alternative Medicine, 2012.

Goredema, R., (2020). African feminism: the African woman's struggle for identity. African Yearbook of Rhetoric, 1(1), pp.33-41.

Govindasamy, R., Simon, J., Puduri, V.S., Juliani, H.R., Asante-Dartey, J., Arthur, H., Diawuo, B., Acquaye, D. and Hitimana, N., (2017). Retailers and wholesalers

of African herbal and natural products: case studies from Ghana and Rwanda. Issues in New Crops and New Uses. Virginia: ASHP, pp.332-337

Humphreys, T. and Herold, E., (2017). Sexual consent in heterosexual relationships: Development of a new measure. Sex Roles, 57(3-4), pp.305-315.

Idoko, L.C., (2018). Public Perception On The Prevalence And Causes Of Marital Infidelity Among Married Women In Enugu North Lga, Enugu State Nigeria (Doctoral Dissertation, Godfrey Okoye University).

Idung, A.U., Abasiubong, F., Ukott, I.A., Udoh, S.B. and Unadike, B.C., (2019). Prevalence and risk factors of erectile dysfunction in Niger delta region, Nigeria. African health sciences, 12(2), pp.160-165.

Indongo, N. and Pazvakawambwa, L., (2015). Perceptions of women on marriage in Namibia. Psychology, 6(11), p.1413.

Kisler, T.S. and Scott Christopher, F. (2019). Sexual exchanges and relationship satisfaction: Testing the role of sexual satisfaction as a mediator and gender as a moderator. *Journal of Social and Personal Relationships, 25(4),* pp.587-602.

Knowles, M., Nieuwenhuis, J. and Smit, B., (2019). A narrative analysis of educators' lived experiences of motherhood and teaching. *South African Journal of Education, 29(3).*

Kolawole, M.E.M., (2019). Self-Representation and the Dynamics of Culture and Power in African Women's Writing. *Journal of Cultural Studies, 1(1),* p.1.

Kontula, O., 2018. The Mysteries of Sexual Desire. *SexuS Journal 3 (8),* pp.511-532. Korieh, C.J., 2005. Islam and Politics in Nigeria: Historical Perspectives. Religion, History, and Politics in Nigeria, pp.109-24.

Krings, M., (2016). Muslim martyrs and pagan vampires: Popular video films and the propagation of religion in Northern Nigeria. Postscripts, 1(1.3), pp.183-205.

Lammers, J., Stoker, J.I., Jordan, J., Pollmann, M. and Stapel, D.A., (2021). Power increases infidelity among men and women. Psychological science, 22(9), pp.1191-1197.

Lawrance, K.A. and Byers, E.S., (2022) Development of the interpersonal exchange model of sexual satisfaction in long term relationships. *Canadian Journal of Human Sexuality 1(3),* 123–128.

Mark, K.P., Janssen, E. and Milhausen, R.R., (2021). Infidelity in heterosexual couples: Demographic, interpersonal, and personality-related predictors of extradyadic sex. Archives of sexual behavior, 40(5), pp.971-982. .

Marshall, C. and Rossman, G.B., (2019). Designing qualitative research. Sage Publications.

Mason, M., (2020), August. Sample size and saturation in PhD studies using qualitative interviews. In Forum qualitative Sozialforschung/Forum: qualitative social research (Vol. 11, No. 3).

Mauss, M., (2018). The gift: The form and functions of exchange in archaic societies. New York: Free Press.

Maxwell, J.A., (2022). Qualitative research design: An interactive approach (Vol. 41). Sage Publications.

Mbah, P.E. and Azubike, O., (2015). Socio-cultural issues facing contemporary families in Nigeria: An appraisal of women holding administrative positions. *Merit Research Journal of Education and Review, 3(1),* pp.1-5.

Mc carberg, B.H and Barkin, R.L. (2020). Long acting opiods for chronic pain: pharmacotherapeuticopportunities to enhancecompliance, quality of life andanalgesia; Am. J. Ther. 8:181-186

McNay, L (2020). Gender and Agency: Reconfiguring the Subject in Feminist and Social Theory. Cambridge: Polity Press. .

Meana, M., (2020) Elucidating women's (hetero) sexual desire: Definitional challenges and content expansion. *Journal of sex research, 47(2-3),* pp.104-122.

Ojedokun, I.M., (2015). Extramarital affair as correlate of reproductive health and home instability among couples in Ibadan, Nigeria. *African Journal of Social Work, 5(2),* pp.1-40.

Ojewole, J.A., (2017). African traditional medicines for erectile dysfunction: elusive dream or imminent reality? *Cardiovascular journal of Africa, 18(4)*, p.213.

Ojo, M.A., (2017). Pentecostal movements, Islam and the contest for public space in Northern Nigeria. Islam–Christian Muslim Relations, 18(2), pp.175-188.

Okodudu S.A., (2020). Fundamentals of Sociology: Second Edition. Port Harcourt. Thompson and Thompson Nigeria Ltd.

LOloruntoba-Oju, T., (2017). Body images, beauty culture and language in the Nigeria, African context. Understanding Human Sexuality, 2007 Series

Patrick, S., Sells, J.N., Giordano, F.G. and Tollerud, T.R., (2017) Intimacy, differentiation, and personality variables as predictors of marital satisfaction. *The family journal, 15(4),* pp.359-367.

Schmitt, D.P., (2021). Universal sex differences in the desire for sexual variety: Tests from 52 nations, 6 continents, and 13 islands. *Journal of personality and social psychology, 85(1),* p.85.

Schwartz, P. and Young, L., (2019). Sexual satisfaction in committed relationships. Sexuality Research and Social Policy, 6(1), pp.1-17.

Scorgie, F., Kunene, B., Smit, J.A., Manzini, N., Chersich, M.F. and Preston-Whyte, E.M., (2019). In search of sexual pleasure and fidelity: vaginal practices in KwaZulu-Natal, South Africa. Culture, health and sexuality, 11(3), pp.267-283.

Scorgie, F., Smit, J.A., Kunene, B., Martin-Hilber, A., Beksinska, M. and Chersich, M.F., (2021) Predictors of vaginal practices for sex and hygiene in KwaZulu-Natal, South Africa: findings of a household survey and qualitative inquiry. Culture, health and sexuality, 13(04), pp.381-398.

Seabrooke, L. and Tsingou, E., (2016). Bodies of knowledge in reproduction: Epistemic boundaries in the political economy of fertility. New Political Economy, 21(1), pp.6989.

Sekaran, U. and Bougie, R., (2023). Research Methods For Business, A Skill Building Approach, John Willey and Sons. Inc. New York.

Sell, R.L., (2017). Defining and measuring sexual orientation for research. In The health of sexual minorities (pp. 355-374). Springer, Boston, MA.

Shamloul, R., (2016). Natural aphrodisiacs. *The journal of sexual medicine, 7(1pt1),* pp.39-49.

Skopek, J., Schulz, F. and Blossfeld, H.P. (2022). Who contacts whom? Educational homophily in online mate selection. European Sociological Review, 27(2), pp.180-195.

Smith, A.M.A., Patrick, K., Heywood, W., Pitts, M.K., Richters, J., Shelley, J.M., Simpson, J.M. and Ryall, R., (2022). Body mass index, sexual difficulties and sexual satisfaction among people in regular heterosexual relationships: a population-based study. *Internal medicine journal, 42(6)*, pp.641-651.

Van de Rijt, A. and Macy, M.W., (2020). Power and dependence in intimate exchange. Social Forces, 84(3), pp.1455-1470.

Van Manen, M., (2020). Phenomenology of practice: Meaning-giving methods in phenomenological research and writing. New York: Routledge.

Vilakati, C.Z., (2019). Mozambican women's experience of labour pain (Doctoral dissertation).

Walster, E., Walster, G.W. and Berscheid, E., (2018). Equity: Theory and research.

Wamoyi, J., Fenwick, A., Urassa, M., Zaba, B. and Stones, W. (2022). "Women's bodies are Shops": Beliefs about transactional sex and implications for understanding gender power and HIV prevention in Tanzania. Archives of sexual behavior, 40(1), pp.5-15.

Wamoyi, J., Ranganathan, M., Kyegombe, N. and Stoebenau, K. (2019). Improving the measurement of transactional sex in sub-Saharan Africa: A critical review. Journal of acquired immune deficiency syndromes (1999), 80(4), p.367.

Yoo, H., Bartle-Haring, S., Day, R.D. and Gangamma, R. (2019). Couple communication, emotional and sexual intimacy, and relationship satisfaction. *Journal of sex and marital therapy, 40(4),* pp.275-293.

Zare, B., (2021). Review of studies on infidelity. International Proceedings of Economics Development and Research, 19(2), pp.182-186.

Zhang, E.Y., (2021) Switching between traditional Chinese medicine and Viagra: cosmopolitanism and medical pluralism today. Medical Anthropology, 26(1), pp.53-96.