PRELIMINARY INVESTIGATION ON EFFECTS OF BURANTASHI EXTRACT ON LIVER ENZYMES OF AIBINO MALE AND FEMALE WHISTAR RATS.

BY

OKONKWO IFEANYI LARRY

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CARITAS UNIVERSITY AMORJI-NIKE EMENE, ENUGU STATE.

SUPERVISOR: MR. EZE STEVEN PETER

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CERTIFICATION PAGE

This is to certify that this research project titled "The preliminary Investivation on Effects of Burantashi extract on liver Enzymes of albino male and female whistar rats." submitted by Okonkwo Ifeanyi Larry, with Registration Number BC/2010/306 for the award of Bachelor of science (B.sc) Degree In Biochemistry of caritas University, Amorji-Nike Emene Enugu state bears full responsibility for this work under my supervision.

....
MR. EZE STEVEN PETER DATE
SUPERVISOR

....
MR. MOSES EZENWALI DATE
HEAD OF DEPARTMENT

....
EXTERNAL SUPERVISOR DATE

DEDICATION

I dedicate this research project work to Almighty God, to Mary mother of Jesus the saviour and to my beloved parents Mr. And Mrs. Chuks Okonkwo (KSM) for their unending support, Love and care.

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My profound gratitude and thanks goes to my project supervisor Mr. Eze Steven Peter whom without his tolerance, kind hearted, commitment, skills and encouragement would have been impossible to engineer this work, Because holds the accelerator and also was the power house behind my aspiration today and tomorrow as a co-supervisor I call him "world changer because through his words framed my world.

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ABSTRACT

This work was carried out to investigate the effects of Burantashi extract on liver enzymes of albino male and female whistar rats. Burantashi is a popular seasoning agent to barbecued meat (suya) in Nigeria,mostly found in the northern part of the Nigeria. Liver Enzymes are those enzymes that plays important role in the liver both in function and regulation. Erectile dysfunction (ED) is defined as the consistent or recurrent inability of a man to attain or maintain penile erection, sufficient for sexual activity (2^{nd}) International consultation on sexual Dysfunction Paris, June 28^{th} July 1^{st}, 2003). Following the discovery and introduction of Burantashi research on the mechanism underlying penile erection, has had an enormous boost and many preclinical and clinical papers have been published in the last five years on the peripheral regulation of, and the mediators involved in human penile erection. The most widely accepted risk factors for ED are discussed. The research is focused on human data and the safety and effectiveness of Burantasni Stem as a phosphodiesterase -5- Inhibitors (PDE-5) used to treat Erectile Dysfunctions.

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CHAPTER ONE

INTRODUCTION

PHYSIOLOGY OF ERECTION

Penile Erection involves an integration of complex physiological processes involving the central nervous system, peripheral nervous system, hormonal and vascular systems. Any abnormality involving these systems whether from medications or disease has a significant impact on the ability to develop and sustain erection; ejaculate and experience orgasm. (Laumann et al., 1999).

The physiological process of erection begins in the brain and involves the nervous and vascular system. The chemicals that initiate erection are neurotransmitters present in the brain. Any kind of stimulation physical or psychological, causes nerves to send message to the vascular system which result in significant blood flow to the penis. Two arteries in the penis supply blood to erectile tissues and the corpora cavernous which become engorged and expand as a result of increased blood flow and pressures. Because blood must stay in the penis to maintain rigidity. An erectile tissue is enclosed by tunicae, which is fibrous elastic sheathes cinch which prevents blood leaving he penis during

electron. When muscle in the penis contract to stop the inflow of blood and open out flow channels and an electron is reserved.

HORMONAL INVOLVEMENT IN ERECTION

- **Oestrogen/Progesterone**: (These are female hormones that cause clitoral erection. If the body has two much oestrogen and or too little testost erone, she ca n get very wet but can not erect her clitoral and G-spot. (Haimen et al., 2002). Estrogen tends to increase the size of the bread, labia minors (inner lips) and clitoral hood, but shrinks the glans clitoris into the clitoral hood making it invisible. It also increases the thickness of the vaginal lining making the G-spot inaccessible. The mechanism of the clitoral and G-spot erection is the same as that of the penis. It is driven by the parasympathetic sexual nerve (The neurotransmitter acetylcholine) through the neurotransmitter. Nitric oxide and the erection dilator cGMP, which is continuously powered by the burning of testosterone without a testosterone burst and burning. She cannot pop the glans Clitoris and G-spot out. If she is on birth control pills there is a chance that her body is over flooded by estrogens and low progesterone. Over loaded liver cannot produce sufficient essential enzymes to synthesize sufficient NO, cGMP and testosterone to support the clitoral and G-spot erection infact excessive estrogen or progesterone in the body will shrink the penis, clitoral and G-spot, but likely increase the breast size (under the excessive estrogen action).

- **Testosterone:-** Testosterone is a hormone produced by the testicles and is responsible for the proper development of male sexual characters. The pump helps the penis to become erect while band maintains the erection.

Circulating levels of testosterone correlate with NO, production. Testosterone treatment can reduce central adiposity and insulin resistance, which may contribute to its beneficial effects on vascular NO, and ED. Raising low testosterone levels improves ED and can restore erectile function in response to PDE-5 inhibitors.

MECHANISM OF ACTION OF PDE-5 INHIBITION IN ERECTILE DYSFUNCTION.

A spinal reflex and the L-arginine nitric oxide guanglyl cyclase-cyclic guanosine monophonsphate (cGMP) pathway mediate smooth muscle relaxation that results in penile erection. Nerves and endothelial cells directly release nitric oxide in the penis, where it stimulates guanylyl cyclase to produce cGMP and lowers intracellular calcium level. This triggers relaxation of arterial and trabecular smooth muscle, leading to arterial dilation, venous constriction, and erection. Phosphodiesterases (PDEs) is the predominant phosphodiesterase in the corpus cavernosum. The catalytic site of PDE-5 normally degrades cGMP and PDE-5 inhibitors such as sildenafil potentiate endogenous increase in cGMP by inhibiting its breakdown at the catalytic site. Phosphorylation of PDE-5 increases its enzymatic activity as well as the affinity of its allosteric (noncatalytic/GAF domains) sites for cGMP. Binding of cGMP to the allosteric

site further stimulates enzymatic activity. Thus phosphorlation of PDE-5 and binding of cGMP to the non catalytic site mediate negative feed back regulation of the cGMP pathway.

In recent years a deeper understanding of the regulation of penile smooth muscle has led to greater insight into the physiology of normal erectile function and erectile dysfunction (ED), as well as the introduction of phosphodiesterase (PDE) inhibitor for the treatment of ED. The oral PDE-5 inhibitors sidenafil has proved to be a safe and effective treatment for this disorder and has fostered further research into the underlying mechanisms of such drugs. This article will review the biochemical pathways involved in erection. The role of PDE-5 in these pathway and the molecular mechanisms involved in PDE activity.

A penile erection result from the relaxation of smooth muscle in the penis .the process is mediated by a spinal reflex and incorporates sensory and mental stimuli. The Balance between factors that stimulate contraction and relaxation determines the tone of penile vasculature and the smooth muscle of the corpus cavernosum.

In primates, including humans the L-arginine nitric oxide guanylyl cyclase cyclic guanosine monophosphate (cGMP) pathway is the key mechanism of penile erection. Nitric oxide is produced from oxygen and L-arginine under the control of nitric oxide synthase (NOS). Sexual arousal stimulates neural pathways that result in the release of NO from nerves and endothelial cells directly into the penis. NO penetrates into the cytoplasm of smooth muscle cells

and binds to guanylyl cyclase. The interaction of NO with guanylyl cyclase causes a conformational change in the enzyme, which results in the catalytic production of 3,5 cyclic guanosine monophosphate from guanosine 5'triphosphate. Cyclic cGMP activities cGMP dependent protein kinase (PKG) which in turn phosphorylates several proteins. These protein kinase interactions results in reduced intraocular calcium levels and a consequent relaxation of arterial and trabecular smooth muscle leading to arterial dilation. Venous constriction and the rigidity of penile erection.

Since cGMP plays a key role in this process, potential interventions for inadequate smooth muscle relaxation include increasing the level of intracellular cGMP. PDE-5 normally inhibits penile erection by degrading cGMP. This degradation occurs at the catalytic site in the presence of bound zinc. PDE-5 inhibitors lower the activity of PDE-5 by competing with cGMP and consequently raise the level of cGMP. In the absence of stimulation of the NO pathway. PDE-5 inhibition is ineffective in isolated strips of corpus c avernosum, sildenafil relaxes the smooth muscle by amplifying the effects of the normal, endogenous cGMP- dependent relaxation mechanisms but produces little effect in the absence of a NO donor. Since sexual arousal stimulates this pathway specifically in the penis, PDE-5 inhibitor has a relatively small effect on smooth muscle in other tissues.

PDE-5 is the predominant phosphodiesterase in the corpus carvernosum, however, at least 11 families of PDE have been identified in mammals, some

PDE types are associated with more than one gene and some mRNA exhibit two or more splice variants. The result is more than 50 species of PDE. Some types of PDE are specific for either cyclic adenosine monophosphate (cGMP) or cGMP, and some degrade both PDE, for example degrades both cGMP and cGMP. Whereas PDE-4 is specific for Camp-5 and PDE-5 is specific for cGMP. The cross reactivity of PDE inhibitors can be attributed largely to similarities of their homologous catalytic domain. Messager RNA has been detected in human corpus cavernosum tissue for the human PDE isoforms-PDE-1A, PDE-1B, PDE-1C, PDE-2A, PDE-3A, PDE-4A, PDE-4B, PDE-4C, PDE-4D, PDE-5A, PDE-7A, PDE-8A, and PDE-9A. Most mammalian PDEs are dimers but the functional significance of this dimerization is unknown, some like PDE5, have two identical submits (homodimers) and some like PDE-6 have two different submits (heterodimers).

The PDE-5 also differs in the nature of the regulatory domain of the enzyme and in the role of phosphorylation. In all cases, the catalytic domain is located towards the carboxylterminus and the regulatory domain is located towards the amino terminus. A PDE-5 monomeric fragment retains the essential catalytic features of the domain full length enzyme.

NITRIC OXIDE REGULATION OF PENILE ERECTION

Biology And Therapeutic Implications

For approximately a decade now, substantial evidence has accrued supporting nitric oxide (NO) as the central component of major signal transduction system that ats in the penis to mediate the erectile response. This molecules subserve a Unique biochemical cascade invading production of the potent second messenger molecule, 3'5' cyclic guanosine monophosphate (cGMP) and its activation of protein kinase G (PKG) which induces physiologic penile erection by regulating the state of penile smooth muscle contractility (Burnett, 1997). In fact, current data support the notion that this NO based biochemical cascade represent a convergence of cellular biochemical and molecular inputs, which on the signal transduction regulatory level, is indispensable for the mechanism of penile erection (Hedland et al., 2000). Consistent with the importance of NO radiation of penile erection, its biology in the penis is quite complex, involving multiple regulatory interactions, the molecule itself may target several biochemical mechanisms that achieve erectile tissue relaxation but is also the target of a host of modulatory influences that determines its release and mode of action in erectile tissue. At the same time, premier signal transduction mechanism has been exploited for therapeutic purposes, specifically in the clinical management of erectile dysfunction. Discoveries pertaining to the field of NO biology in the penis have, in recent years been rapidly translated into the clinical management of the first orally effective pharmacotherapy for erectile dysfunction, sildenafil citrate (Viagra) (Goldstein et al., 1998).

NO BIOLOGY IN THE PENIS

Traditional understanding of the action of NO in the penis invokes the constitutive formation of this molecule under normal physiologic conditions with the expression and activities of the enzyme, sources localized to neural and endothelial components of the corporal tissue. The verification that NO derives from the autonomic innervations supplying the penis has directly supported the description of this molecule as a peripheral neurotransmitter of non adrenergic, no cholinergic-1992 mediated penile erection (Kim et al.,1991) the confirmation that the molecule also is produced within vascular and trabecular endothelium comprising the penile vascular supply, has offered additional support for the role of NO serving as an endothelial relaxation factor of penile erection (kimoto et al., 1990, knispel et al., 1991, azadzoic et al., 1992, Hedlund et al., 2000).

ATIEOLOGY OF ERECTILE DYSFUNCTION

Erectile dysfunction (ED) is a sexual dysfunction that affects the reproductive systems of both men and women.

According to the definition by national Institute of Health consensus Development (NIHCD) panel on importance (1993) in males. It is sexual dysfunction characterized with the inability to develop or maintain an erection of the penis sufficient for satisfactory sexual performance. It is also known as male impotence or Baby D syndrome. While in women according to American psychiatric Association (APA) (1994), it is characterized with the persistant or recurrent inability to attain, or maintain until completion of the sexual activity,

an adequate lubrication. Swelling response that otherwise is present during fem ale sexual arousal and sexual activity is thus prevented. Hence it is called woman impotence or female erectile dysfunction. (NIH, 2005).

The word importance may also be used to describe other problems that interfere with sexual intercourse and reproduction, such as lack of sexual desire and problems with ejaculation or orgasm. Using the term "erectile dysfunction however, makes it clear that those other problems are not involved (NIH, 2005)

An erection occurs as a hydraulic effect due to blood entering and being retained in sponge-like bodies within the penis and clitoris. The process is most often than not initiated as a result of sexual arousal, when signals are transmitted from the brain to nerves in the pelvis erectile dysfunction is therefore, indicated when an erection is consistently difficult or impossible to produce despite arousal (Laumann et al., 1999).

PREVALENCE OF ERECTILE DYSFUNCTION IN MEN.

Erectile dysfunction ED, varies in severity; some men have a total inability to achieve an erection others have inconsistent ability to achieve an erection, and still others can sustain only brief erection. The variation in severity of erectile dysfunction makes estimating its frequency difficult. Many men also are reluctant to discuss erectile dysfunction with their doctors, and thus, the condition is under diagnosed nevertheless experts have estimated that ED affects 30 million men in united sates, Again, according to the statistical research

carried out by Adegunloye and Eze in 2002 and 1994 respectively in Nigeria, results show that about 23-26.5% of men suffer from this condition while according to carey in 1990, discovered that about 4.9% of men suffer from the condition in the united states.

While erectile dysfunction can occur at any age, it is uncommon among young men and more common in the elderly. By the age of 45, most men have experienced erectile dysfunction at least some of the time. According to Massachusetts, male Aging study, complete impotence increase from 5% among men 40 years of age to 15% men 70 years and older. Population studies conducted in Netherlands found out that some degree of ED occurred in 20% men between 50-54 and in 50% of men between ages 70-78. In 1998, the National Ambulatory Medical care survey (NAMCS) counted 1,520,000 doctor offices visited for erectile dysfunction (ED).

PREVALENCE OF ERECTILE DYSFUNCTION IN WOMEN.

Erection dysfunction which is known as female erectile dysfunction in woman occurs about 43% of American women (NIH consensus conference, 1993). And this medical condition is a persistent or recurrent inability to attain or maintain clitoral erection until completion of the sexual activity, an adequate lubrication. Swelling response that is normally present during female sexual arousal and sexual activity is therefore absent. The individual having the condition is said to experience frigidity (American Psychiatric Association,

1994). Again according to Otuba et al in 1989, about 8.7% of women suffer from this very condition in the United States while between 35.3-40%, according t o Adegunloye in 2002 and Eze in 1994 of women in Nigeria suffer from this condition. Spector and carey in 1994 reported 5-10% in the united states.

In addition, female erectile dysfunction occurs at any age but majorly in old age. Hence, the most significant age related change is menopause (Karen, 2002) and (Rod et al., 2008).

However erectile dysfunction may be caused by diabetes, a atherosclerosis, hormonal imbalance, neurological problems e.t.c (Organic causes) or stress depression e.t.c (Psychological causes).

Besides treating the underlying causes (Organic or Psychological), the first line treatment of ED consist of a trail of phosphodiesterase 5'(PDE-5) inhibitor (The first of which was sildenafil or Viagra). In some cases, treatment can involve prostaglandin tablets in the urethra, intracarvenous injection with a fine needle into the penis or clitoris that causes swelling, a penis or Clitoris prosthesis, a penis or clitoris pump or vascular surgery, estrogens replacement therapy for the women e.t.c (Kendric et al., 2005)

AIM OF STUDY

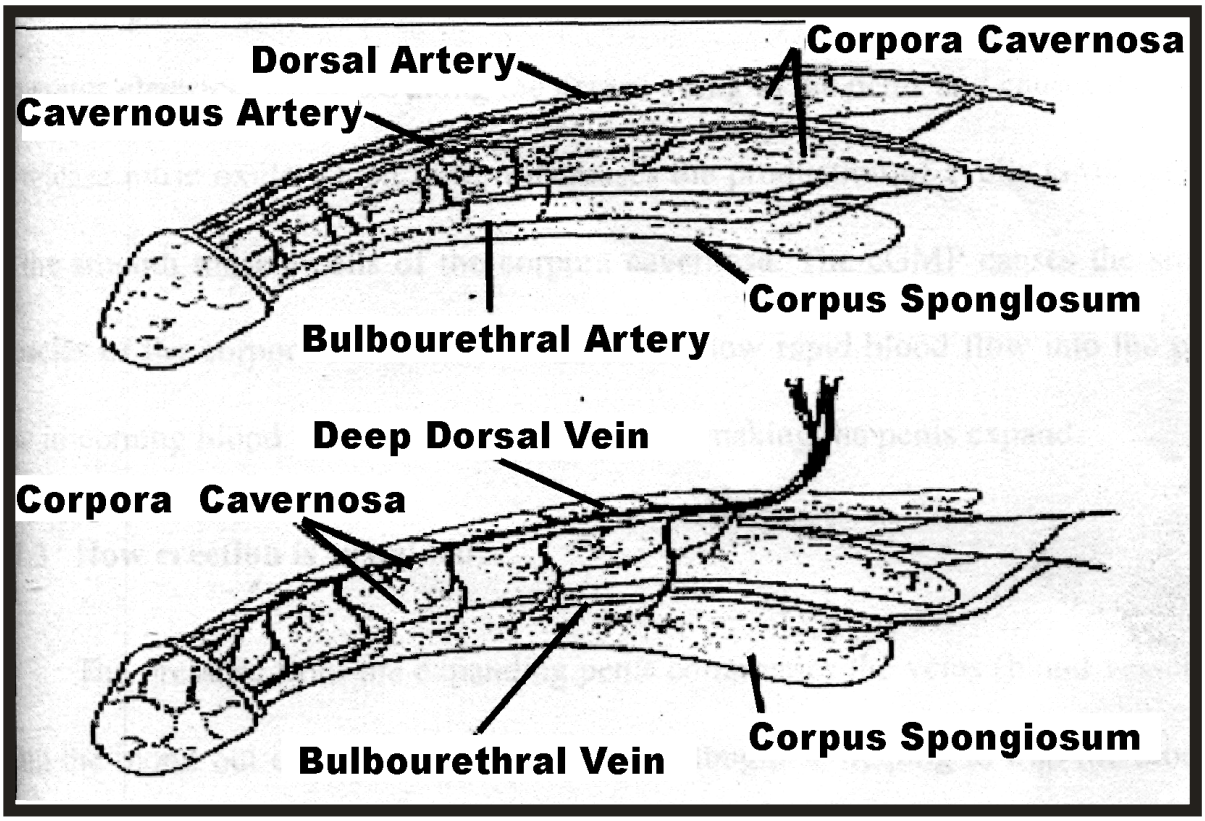
The aim of this research is to find out the effects of Barantashi. (pausinystalia yohimbe). Extract on the liver enzymes of albino male and female whistar rats.

CHAPTER TWO.

LITERATURE REVIEW ON MALE ERECTILE DYSFUNCTION .

ANATOMY OF THE PENIS.

Figure 1: Penis Anatomy.



The penis contains two chambers called the corpora cavernosa, which run the length of the upper side of the penis and another chamber called the corpus spongiosum, forms the ventral portion of the penis over the distal end of the penis. The spongy urethra passes through the corpus spongisum penetrates the

glans penis and open as the external for urethra orifice. The urethra is the channel for urine and ejaculate filling the corpora cavernosa is a spongy tissue; spaces, veins and arteries. A membrane called the tunica albuginea surrounds the corpora cavernosa. Veins located in the tunica albuginea drain blood out of the penis.

HOW ERECTION OCCUR IN MEN

Erection begins with sexual stimulation; sexual stimulation can be tactile (e.g. by touching the penis) or mental (e.g. by having sexual fantasies). Sexual stimulation generates electrical impulses along the nerves going to the penis and causes the nerves to release nitric oxide which in turn increase the production of cyclic cGMP (cGMP) in the smooth muscle cells of the corpora cavernosa. The cGMP causes the smooth muscles of the corpora cavernosa to relax and allow rapid blood flow into the penis. The in-coming blood fills the corpora cavernosa, making the penis expand.

HOW ERECTION IS SUSTAINED:

The pressure from the expanding penis compresses the veins. (blood vessel that drain the blood out of the penis) in the tunica albuginea, helping to trap the blood in the corpora cavernosa, thereby sustaining erection. Erection is reversed when cGMP levels in the corpora cavernosa fall, causing the smooth muscles of the corpora cavernosa that drain blood away from the penis. The levels of the cGMP in the corpora cavernosa fall because it is destroyed by an enzyme called phosphodiesterase type 5'(PDE-5) (Nkudic, 2003).

CAUSES OF ERECTILE DYSFUNCTION IN MALES

The ability to achieve and sustain erection generally requires:

1. A healthy nervous system that conducts nerve impulses in the brain, spinal column, penis and the clitoris.
2. Healthy arteries in and near the corpora cavernosa.
3. Healthy smooth muscles and fibrous tissues within the corpora cavernosa,
4. Adequate levels of nitric oxide in the penis and clitoris (American psychiatric Association, 1994) and (Nkudic, 2003)

The causes of Erectile Dysfunction in males could be:

a. Physical
b. Psychogenic.

Physical causes of Erectile Dysfunction in males.

1. Diabetes mellitus:

According to the Canadian Diabetes Association (CDA), erectile dysfunction, ED. Is common for men who have diabetes often, it is the first symptom that men may notice and the one that may lead them to the doctor in the first place. Only after they have sought medical help to ED, do they also receive a diagnosis of diabetes.

Erectile dysfunction tends to develop. 10-15years earlier in diabetic men than among non-diabetic men. In a population study of men with type I diabetes for more than 10years. ED was reported by 55% of men between the ages of 50 to 60 years. The increased risk of ED among men with diabetes mellitus may be due to the earlier onset and greater severity of atherosclerosis that narrows the arteries and thereby reduces the delivery of blood to the penis when insufficient blood is delivered to the penis. It is not possible to achieve an erection.

Diabetes mellitus also causes erectile dysfunction by damaging both sensory or and automic nerves, a condition called diabetic neuropathy. Smoking cigarette, obesity, poor control of blood glucose levels and having diabetes mellitus for a long time further increases the risk of ED in diabetes. In addition to a atherosclerosis and/or neuropathy causing ED in which the compliance of the muscle in the corpora cavernosa is decreased and clinical, this presents as inability to maintain the erection (Canadian Diabetes Association, 2006).

2. <u>Hormonal Imbalances:</u>

Imbalance of hormones, such as thyroid hormones, prolaction and testosterone can affect a man's response to sexual stimulation. These imbalances can be the result of a tumour of the pituitary gland, kidney disease, liver disease, or hormonal treatment of prostate cancer (John, M.B. CED, 2007).

The most common cause of cardiovascular disease in the united state is atherosclerosis. The narrowing and hardening of arteries that reduces blood flow.

Atherosclerosis typically affects arteries throughout the body and is aggravated by hypertension, high blood cholesterol levels. Cigarette smoking and diabetes mellitus when coronary arteries (arteries that supply blood to the heart muscles) are narrowed by atherosclerosis. Heart attacks and angina occur when cerebral arteries (arteries that supply blood to the heart) are n arrowed by atherosclerosis, stroke occurs (Nkudic, 2003).

In this vein, when arteries that supply blood to the penis and pelvic organs are narrowed by atherosclerosis, insufficient blood is delivered to the penis to achieve an erection. There is a close correction between the severity of atherosclerosis in the coronary artery and erectile dysfunction for instance, men with more severe coronary atherosclerosis also end to have more erectile dysfunction than men with mild or no coronary artery atherosclerosis, some doctors suggest that men with new onset erectile dysfunction should be evaluated forsilent coronary artery disease (advanced coronary artery atherosclerosis that has not yet caused angina or heart attacks) (Nkudic, 2003).

3. <u>Tobacco Alcohol or Drug use:</u>

All three of these substances can damage a person's blood vessels and/or restrict blood flow to the penis, causing ED. Smoking in particular flags a large role in causing ED in people with arteriosclerosis.

Marijuana, heroin, cocaine and alcohol abuse contribute to erectile dysfunction. Alcoholism, in addition to causing nerve damage can lead to atrophy of the testicles and lower testosterone levels (John, M.B; (ED), 2007).

4. Nerve or Spinal Cord Damage:

Damage of the spinal cord and nerves in the pelvis can cause erectile dysfunction. Nerves damage can be due to disease, trauma, or surgical procedures. E.g injury to the spinal cord from automobile accidents, injury to the pelvic nerves from prostate surgery, multiple sclerosis, Alzheimer's disease, parkinson's disease, peyronies disease and long term diabetes mellitus (healthwise, 2006)

5. Hypertension (High Blood Pressure)

Patients with essential hypertension or arteriosclerosis have increased risk of developing erectile dysfunction. Essential hypertension is the most form of hypertension. It is called essential hypertension because it is caused by other diseases for instance, by kidney disease (Kendric et al., 2005)

It is the clearly known how essential hypertension causes ED. However, patients with essential hypertension have been found to have low production of nitric oxide by the arteries of the body, including the arteries in the penis. Scientists now suspect that the decreased levels of nitric oxide in patients with essential hypertension may contribute to erectile dysfunction (Kendric et al., 2005).

6. Medications.

Many common medicines produce ED as a side effect medicine that can Cause erectile dysfunction include many used to treat high blood pressure, anti-histamines, antidepressants, tranquilizer and appetite suppressants. Examples of

common medicine that can cause ED include beta blockers such as propanol, hydrochlorothiazide, digoxin indomethacin etc (Nkudic, 2003)

7. Venus leak:

If the veins in the penis cannot prevent blood from leaving the penis during an erection, an erection cannot be maintained, this is known as venous leak and can be a result of injury or disease (Kendric et al; 2005).

8. Surgery:

Surgery performed to treat disease such as prostate cancer and bladder cancer often require the removal of nerves and tissues around the affected area which can lead to ED, some of these surgeries result in only temporary problems (lasting 6-18 months) which in others results is a permanent damage to the nerves and tissues around the penis and require treatment in order for an erection to be achieved (James., 2010).

9. Prostate cancer:

Prostate cancer doesn't cause ED on its own but treatment (radiation, Hormonal manipulation or surgery to remove the cancer) can lead to erectile problem s (John , MB; (ED), 2007).

10. Aging :

There are two reasons why older men are more likely to experience

Erectile dysfunction than younger men first, older men are more likely to develop disease such heart attacks, angina, strokes, diabetes mellitus and high blood pressure that are associated with ED, secondly the aging process alone can cause erectile dysfunction in some men; primarily by decreasing the compliance of the tissue in the corpora cavernosa, although it has been suggested but not proven that there is also decreased production of nitric oxide in the nerves that innervate the corpora smooth muscle within the penis (Nkudic, 2003).

11. Sexually transmitted Disease: (STD):

Sexually transmitted disease which is also known as veneral disease play a role in erectile dysfunction STD's such as gonorrhoea, syphilis staphylococcus Aurens, genital herpes etc. (Hashmi, 1998).

PSYCHOLOGICAL CAUSES OF ED IN MALES:

Psychological factors are responsible for about 10%-20% of all cases of ED. I t is often a secondary reaction to an underlying physical cause. In some cases, abuse or sexual trauma. However the most common psychological causes of ED include.

1. **Stress:**

This can be Job related, money related or result of marital problems, among other factors.

2. Anxiety :

Once a man experiences erectile dysfunction, he may become over worried that the problem will happen again . This can lead to "Performance anxiety or a fear of sexual failure, and consistently causes erectile dysfunction.

Guilt: a man may feel guilty that he is not satisfying his partner.

3. **Depression:**

A common cause of erectile dysfunction, depression affects a person physically and psychologically. Depression can cause erectile dysfunction even when a man is completely comfortable in sexual situation. Drugs used to treat depression may also cause erectile dysfunction.

4. **Low self-esteem:** This can be due to prior episodes of erectile dysfunction (thus a feeling of inadequacy) or can be the result of other issues unrelated to sexual performance.

5. **Indifference:**

This may come as a result of age and a subsequent loss of interest in Sexual the result of medications or stem from problems in a couple's relationship.

All men at one time or another will experience ED only if the problems becomes persistent, occurs more than 50% of the time, or becomes a sources of distress for you or your partner should you be concerned and consider seeking

medical advice and treatment for men whose erectile dysfunction is caused by psychological problems, therapy may be needed (Traish et al., 1999).

Diagnosis of Erectile Dysfunction.

Patient History:

A diagnosis of erectile is made in men who have repeated inability to achieve and / or maintain an erection for satisfactory sexual performance for at least 3 months. Candid communication between the patient and the doctor is important in establishing the diagnosis of ED, assessing its severity and determining the cause. During patient interviews, doctors try to answer the following questions.

- Is the patient suffering from erectile dysfunction or from loss of libido or disorder of ejaculation?
- Is erectile dysfunction due to psychological or physical factors? Healthy men have involuntary erections in the early morning and during REM stage (a stage in the sleer cycle with rapid eye movements). Men with psychogenic ED (ED due to psychological factors such as stress and anxiety rather than physical factors) usually maintain these involuntary erections. Men with physical causes the erectile Dysfunction (for example atherosclerosis, smoking and diabetes) usually do not have these involuntary erections.
- Are there physical causes of erectile dysfunction? A prior history of cigarette smoking, heart attacks, strokes and poor circulation in the extremities suggest atherosclerosis as the cause of the erectile dysfunction

diminished sensation of the penis and the testicles, bladder dysfunction and decreased nerve damage loss of sexual desire and drive, lack of sexual fantasies, gynecomastia (enlargement of breasts) and diminished facial hair suggest low testosterone levels.

- Is the patient taking medications that can contribute to erectile dysfunction?

Physical Examination.

The physical examination can reveal clues for physical causes of erectile dysfunction. For example, if the penis does respond as expected to touching, a problem in the nervous system may be the cause. Small testicles, lack of facial hair and enlarged breasts can point to hormonal problems such as hypogonadism with low testosterone levels. A reduced flow of blood as a result of atherosclerosis can sometimes be diagnosed by finding diminished arterial pulses in the legs or listening with a stethoscope for bruits (the sound of blood flowing through narrowed arteries). Unusual characteristics of the penis itself could suggest the root of the ED, for example, bending of the penis during erection could be the result of peyronnie's disease.

Laboratory Tests:

Common laboratory Tests to evaluate ED include:

- Complete Blood Count (CBC): This is to check if the individual has low blood count against any form of anaemia.

- Urinalysis: an abnormal urinalysis may be a sign of diabetes mellitus and kidney damage.
- Lipid profile: high of LDL cholesterol (bad cholesterol) in the blood promote atherosclerosis.
- Blood Glucose Levels: abnormally high blood glucose levels may be a sign of diabetes mellitus.
- Serum Creatinine: an abnormal serum Creatinine may be the result of kidney damage due to diabetes.
- Total Testosterone levels: blood samples for total testosterone levels should be obtained in the early morning (before 8a.m) because of wide fluctuations in the testosterone levels throughout the day. A lo w testosterone level suggest hypogonadism measurement of bio-available measurement testosterone may be a better measurement of bio-available measurement testosterone may be a better measurement that total testosterone especially in obese men and women with liver disease, but measurement of bio-available testosterone is not widely available.
- PSA levels: PSA (prostate specific Antigen) blood levels and prostate examination to exclude prostate cancer is important before starting testosterone treatment since testosterone can aggravate prostate cancer.

Psychosocial Examination:

A psychosocial examination using in interview and questionnaires may reveal psychological factors contributing to erectile dysfunction. The sexual

partner also may be interviewed to determine sexual intercourse (Canadian Diabetes Association, 2006).

Treatment of male impotence

Treatment of ED in 2005 include

- Working with doctors to select medications that do not impair ED
- Making lifestyle improvement (e.g quitting smoking and exercising more)
- Drugs such as sildenafil (Viagra), vardenafil (levitra) or tadalafil (cialis)
- Inserting medications into the urethra (intraurethral suppositories)
- Injecting medications into the corpora cavernosa (intracavernosal injections).
- Penile prostheses and
- psychotherapy

1. **Adjusting medications:**

Many common medications for treating hypertension, depression and high blood lipids can contribute to ED treatment of hypertension is an example. There are many different types (classes) of anti- hypertension medications (medications that lower blood pressure). These include beta blockers, calcium channel blockers, diuretics (medication that increase urine volume) angiotensin converting enzymes inhibitors (ACE Inhibitors), and angiotension receptor blockers (ARBs). Anti-hpyertensives have different effects on erectile dysfunction. Inderal (a beta blocker) and hydrochlorothiazide (a diuretic) are known to cause ED while calcium channel blockers and ACE inhibitors do not

seem to affect ED functions. On the other hand angiotensin receptor blockers (ARBs) such as ivesartan (cozaar) and valsarta (Diovan), may actually increase sexual appetite, improve sexual performance, decrease erectile dysfunction therefore, choosing an optional anti hypertension combination is an important part of treating ED.

2. LIFESTYLE IMPROVEMENTS.

Quitting smoking, exercising regularly, loosing excess weight, curtailing excessive alcohol consumption, controlling hypertension, and optimizing blood glucose levels in patients with diabetes are not only important for maintaining good health but also may improve ED. Some studies suggest that men women who have made lifestyle improvement experience increased rates of success with oral medication (John, M.B.,) 2007).

3. Medication for ED include.

a. Testosterone and Estrogen therapy
b. Oral phosiesteraase type 5'(PDE-5) inhibitors (sildenafil, levitra and tadalafil).
c. Intracavernosal injections
d. Intraurethral suppositories.

The use of testosterone and estrogen in treating ED in patients with hypogonadism, testosterone, can improve libido and ED, but the response of

ED in men with hypogonadism to testosterone is not complete; many men still may need additional oral medications such as sidenafil, vardenafil and tadalafil.

In men 40 years of age or older, a breast examination, digital examination of prostate and a PSA level should be done to exclude breast and prostate cancer before starting testosterone treatment since testosterone can aggravate breast and prostate cancers or are suspected of having them should not use testosterone. Notice that testosterone is also used in treating sexual dysfunction, erectile dysfunction, and erectile dysfunction in women (Johnson, 1997).

However, in estrogen replacement therapy, estrogen is used in the treatment of ED in women that experience hypoestrogenism. The mechanism of estrogen's effect on desire is indirect and occurs through improvement in urogential atrophy, vasomotor symptoms and menopausal mood disorders (i.e depression) and also correlates positively with sexual activity and fantasies – the later thought to represent desire (Nathorst-Boos et al., 1993).

4. <u>Oral phosphodiesterase type 5'(PDE-5) inhibitors:</u>

Sildenafil sold as Viagra, Revatio and under various other trade names is a drug used to treat ED for men which is now approved for women too with ED by FDA. sildenefil works by inhibiting cGMP specific phosphodiesterase type 5, an enzyme that regulate blood flow in the penis and clitoris (John (ED), 20 07 and Pfizer, inc, (2007). Since becoming available in 1998, sildenafil has been the primary treatment for ED; its primary competitors are tadalafil and vardenafil.

Note that it is also used in the treatment of pulmonary artery hyper tension (PAH) (Pfizer, Inc. 2005) .

The effectiveness of sildenafil (Viagra) Sildenafil is used for the treatment of ED of either physical or psychological pause. It has been found to he effective in treating UD in both men and women with coronary artery disease, diabetes mellitus, hypertension, depression, coronary artery bypass surgery, and men who arc taking anti depressants and several classes of anti-hypertensives.

In randomized controlled trials, an estimated 60% of men and women with diabetes, and 80% of men and women without diabetes experienced improved erections with sildenafil (John, (l:d.), 2007) and (Kaplan *el al,* 1999).

How to administer sildenafil (Viagra)

Sildenafil is available as oral tablets at doses of 25, 50,. lOOmg. It should be taken approximately one hour before sexual activity. In some men, the onset of ac ion the drug may be as early as 11- 20 minutes.

Sildenafil should be taken on an empty stomach for best possible results since sorplion and effectiveness of sildenafil can be diminished if it is taken shortly after a meal, particularly a meal that is high in fat (Shcn *el al,* 1999).

The dose of Sildenafil (Viagra)

In prescribing sildenafil, a doctor considers the age, general health status, and other medications the patient is taking. The usual starting dose for most men is 50mg; ever, the doctor may increase or decrease the dose depending on side effects and effectiveness. The maximum recommended dose is lOOmg every

24hrs, however, many men will need lOOmg of sildenafil for optimal effectiveness and some doctors arc recommending 1OOmg as the starting dose.

The metabolism (breakdown) of sildenafil is slowed by factors such as aging, liver and kidney dysfunction and concurrent use of certain medications (such as erythrornycin - an antibiotics, and protease inhibitors, for HIV). Slowed breakdown of sildenafil to accumulate in the body and potentially may increase the risk of side effects. Therefore, in men over 65ycars and postmenopausal women, in men LHH! women with substantial kidney and liver disease, and in men and women who also are taking protease inhibitors, the doctors will initiate sildenafil at a lower dose (25mg to avoid accumulation of sildenafil in the body. A protease inhibitor rilonavir (Norvir) is especially potent in increasing the accumulation of sildenafil, thus men and women who arc taking Norvir should not take sildenafil doses higher than 25mg and at a frequency of no greater than once in 48 hours (John, (Hd.), 2007).

Side effects of Viagra:

In clinical trials, the most common adverse effects of sildenafil use included headache, flushing, dyspepsia, nasal congestion and impaired vision, including photophobia and blurred vision (Pfizer, Inc., 2007). Some sildenafil users have complained of seeing everything tinted blue (cyanophobia) (Visionweb, 2001). Some complained of blurriness and loss of peripheral vision. In July 2005, the U.S Food and drug Administration found out that sildenafil could

lead to vision impairment in rare cases(FDA, Inc., 2005) and a number of studies have linked sildenafil use with non arteritic anterior ischaemic optic-neuropathy (Pomeranz *et* al., 2005), (Egan *et al.*2000).

(Pomeranz *et al,* 2002), (Cunnighan *et al,* 2001), (Boshier *at al.,* 2002) and (Akashi *cl ai,* 2005).

Rare but serious adverse effects found through post marketing surveillance include priapism, severe hypotension, myocardial infarction, ventricular arrhylhmias, stroke, increased intraocular pressure, and sudden hearing loss (Pomeranz et al., 2005). As a result of these posts - marketing reports, in October 2007, The FDA announced that the labeling of PDE5 inhibitors, including sildenafil, required a more prominent warning of the potential risk of sudden hearing loss (Pfizer, Inc., 2007).

Mechanism of action of Sildenafil:

The mechanism of action of Sildenafil citrate involves the release of nitric oxide (NO) in the corpus cavernosum of the penis and clitoris. NO binds to the receptors of the enzyme guanylate cyclase, which results in increased levels of cyclic guanosine monophosphate (cGMP), leading to smooth muscle relaxation (vasodilation) of the intimal cushions of the helicine arteries, resulting in increased in flow of blood and an erection (Webb *et al.,* 1999). Robert F. Furchgott won the Nobel Prize in physiology or medicine in 1998 for his discovery and analysis of endothelium-derivcd relaxing factor, a key part of the NO mechanism of action.

Sildenafil is a potent and a selective inhibitor of cGMP spec'lic phosphodiesterase type 5 (PDIt5), which is responsible for degradation of cGMP in the corpus cavernosum. The molecular structure of Sildenafil is similar to that of cGMP and acts as a competitive binding agent of PDE5 in the corpus cavernosum,

resulting in more cGMP and better erections- (Revill, 2003). Without sexual Stimulation, and therefore lack of activation of the NO/ cGMP system, sildcnafil should not cause an erection. Other drugs that operate by the same mechanism include tadalafil citrate (cialis) and vardenafil hypochlorite (levitra).

Although sildcnafil (Viagra), vardenafil (levilra), and tadalafil (cialis) all *work* by inhibiting PDH5, tadalafils pharmacologic distinction is its longer half-life (17.5 hours) compared to Viagra (4.0 - 5.0 hours) and levitra (4.0 5.0 hours) resulting in longer duration of action , and so partly responsible for 'the weekend pill" sobriquet (Revill, 2003).

5. a. **Intracavernosal injections;**

Medications can be injected directly into the corpora cavernosa to attain and Maintain erections. Medications such as papaverine hydrochloride, phentolamine, and prostaglandin E1 can be used alone or in combinations to attain erections. Combining small amounts of each drug is preferred over using a single drug because of increased efficacy and fewer side effects. Even

though such injection can be effective, they are not widely used because the injections are painful, there may be scanning of the penis and clitoris and there is a risk of developing priapism (John, M.B., (Kd.), 2007) and (Alvaro, 2005)

b**. Intraurethral suppositories:**

Prostaglandin E1 can be inserted in a pellet (suppository) form into the urethra to attain erections. This technique also is not popular because of occasional side effect of pain in the penis and sometimes in the testicles, mild urethra bleeding, dizziness, and vaginal itching in the sex partner. Men also need to remain standing after inserting the pellet in order to increase blood flow to the penis. It may take 15-30 minutes to attain an erection. Prostaglandin can cause uterine contractions and should not be used by men having intercourse with pregnant women unless condom or other barrier devices are used.

6. VACUUM DEVICES.

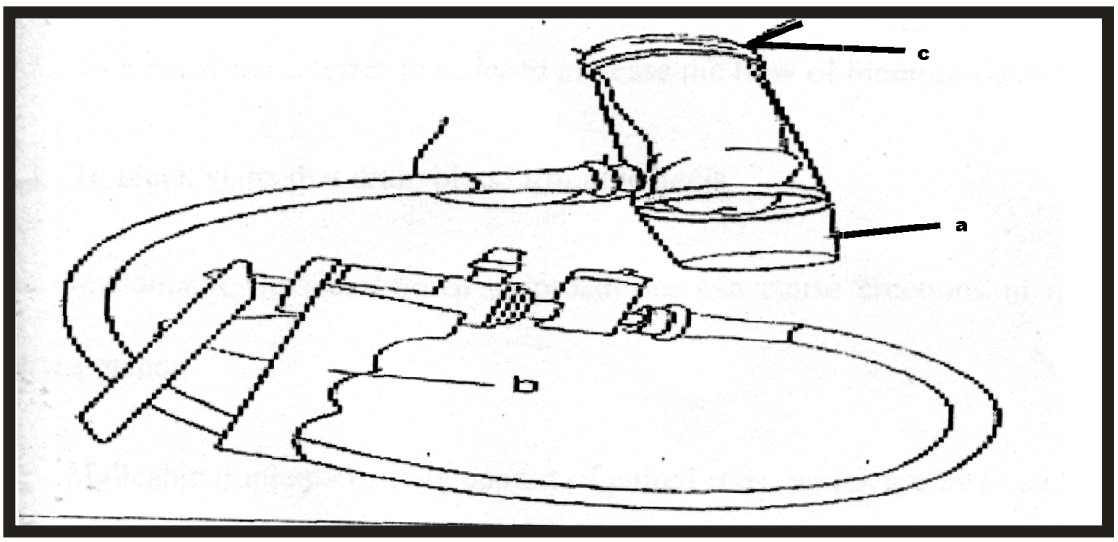


FIGURE 2: The penis vacuum Device.

Mechanical vacuum devices cause erections by creating a vacuum around the penis that draws blood into the penis, engorging it and expanding it.

The devices have three components:

A plastic cylinder, in which the penis is placed

A pump, which draws air out of the cylinder, and an elastic b and, which is placed around the base of the penis, to maintain the erection after the cylinder is removed and during intercourse by pre venting blood from flowing back into the body. One variation of the vacuum device involves a semi-rigid Sheath that is placed on the penis and remains there after attaining erection and during intercourse.

Surgery for ED.

Surgery for ED may have as its goal;

To implant a device that causes the penis to become erect

To reconstruct arteries in order to increase the flow of blood to the penis or To block veins that drain blood from the penis

Implantable devices known as prostates can cause erection in many men with impotence.

Malleable implants usually consist of paired rods, which are inserted surgically into the corpora cavernosa, the twin chambers running the position of the penis and therefore, the rods. Adjustment does affect the width or length of the penis.

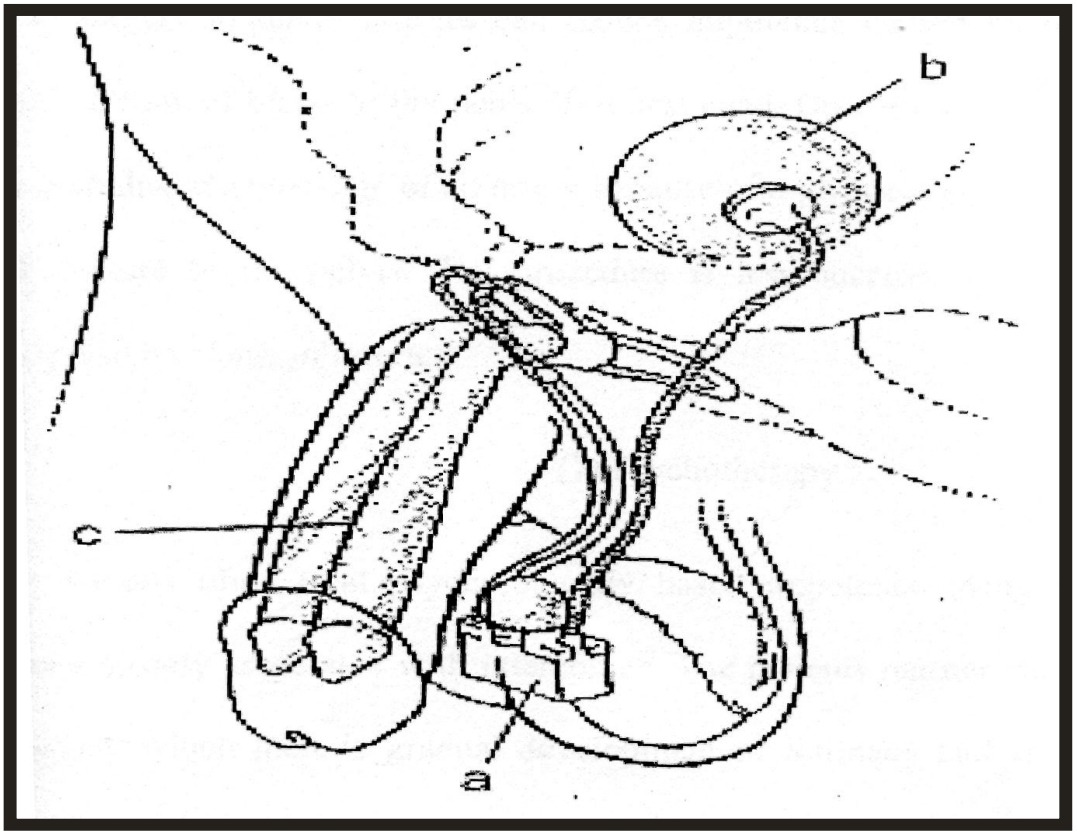


Figure 3: The penis prosthesis.

- Implanted in a scrotum. The pump causes fluid to flow from a reservoir.
- Residing in the lower pelvis to two cylinders.
- Residing in the penis. The cylinders expand to create the erection.

Inflatable implants consist of paired cylinders, which are surgically inserted inside the penis and can be expanded using pressurized fluid. Tubes connect the cylinders to a fluid reservoir and pump, which also are surgically implanted. The patients inflates the cylinders by pressing on the small pump, located under the skin in the scrotum. Inflatable implants can expand the length and width the penis some what. They also leave the penis in a more natural state when inflated.

LITERATURE REVIEW ON FEMALE ERECTILE DYSFUNCTION

Female erectile dysfunction which is a sexual impotence occurs when a woman is unable to attain and maintain a complete erection of her clitoris through orgasm (Mc vary, 2008)

ANATOMY OF THE FEMALE EXTERNAL GENITALIA

The external female genital also referred to as the vulva or the pudendum consist of the vestibule and Its surrounding structure. The vestibule is the space into which the vagina opens posteriorly and urethra opens anteriorly. A pair of thin, longitudinal skin folds called the labia minora form a border on each side of the vestibule.

A small erectile structure called the clitons is located in the anterior

margin of the vestibules, Anteriorly. The labia minora unit over the clitoris to form a fold of skin called the prepuce (Rod et al., 2008).

The clitoris is usually less than 2cm in length and consist of a shafts and a distal glans well supplied with sensory receptors. It initiates and intensifies levels of Sexual tension. The clitoris contains two erectile structures, the corpora cavernosa, each of which expands at the base end of the clitoris to form the crus of the clitoris and attaches the clitoris to the coxal bones. The corpora cavernosa of the clitoris are comparable to that of the penis and they become engorged with blood as a result of sexual excitement. In most women, this engorgement results in an increase in the diameter, but not the length of the clitoris. With increased diameter, the clitoris makes better contacts with the prepuce and the surrounding tissues and is more easily stimulated.

Erectile tissue that corresponds to the corpus spongiosum of the male lies deep into and on the lateral margins of the vestibular floor on each side of the vaginal orifice. Each erectile body is called bulb of the vestibule like other erectile tissues. It becomes engorged with blood and more sensitive during sexual arousal. Expansion of the bulbs causes narrowing of the vaginal orifice and produce better contacts of the vagina with the penis during intercourse (Rod et al, 2008).

On each side of the vestibule, between the vaginal opening and the labia minora, is an opening of the duct of the greater vestibula glands. Additional small mucous gland. The lesser vestibular glands. Paraurethral glands, are located rear

the clitoris. They produce a lubricating fluid that helps to maintain the moistness of the vestibule.

Laternal to the labia minora are two prominent rounded folds of skin called the labia majora. Subcuta neons fat is primarily responsible for the prominence of the labia majora. The two labia majora unite anteriorly in an elevation over the symphysis pubis caved the mons pubis are covered coarse hair. The media surface are covered numerous sebaceous and sweat gland. The space between the labia majora is called the pudenda cleft. Most of the time, the labia majora are in contact with each other across the midline closing the pudendal cleft and concealing the deeper structures within the vestibule (Philip et al., 2008).

How Women attain Clitoral Erection

The mechanism of clitoral erection is likened to the mechanism of penis erection (ignorro et al., 1990).

Causes of E D in females.

Note that just like in males the case of ED in female could also be;

a. Physical or
b. Psychogenic.

Physical causes of E D in females

- ✓ **Estrogen Low Concentration**

Estrogen plays a significant role in regulating female sexual performance. Estrodial levels affect cell throughout. The peripheral and central nervous system and influence nerve transmission. A decline in serum estrogen levels result in the

thinning of the vaginal mucosal epithelium and a trophy of vaginal wall smooth muscle. Decreased estrogen level also result in a less acidic environment in the vaginal canal. This can ultimately lead to vaginal infection. Urinary tract infections and incontinence as well as complaints of sexual dysfunction (Shen et al., 1999).

Estrogen also have vasoprotective and vasodilatory affects which result in increased vaginal, clitoral and urethra arterial flow resulting in maintenance of the female sexual response by preventing atherosclerotic compromise to pelvic arteries and arterioles (Sherwin et al., 1995).

With estrogen in menopause and decline in circulating estrogen levels, a majority of women experience some degree of change in sexual function. Common sexual complaints include loss of desire, decreased frequency of sexual activity, painful intercourse, diminished sexual responsiveness, difficult achieving orgasm and decreased genital sensation.

Masters and Johnson first published the findings of the physiologic changes occurring in menopausal women that related to sexual function in 1966. We have since learned that symptoms related to alterations in genital sensation and blood flow are in part, secondary to declining estrogen levels and that there is direct correlation between presence of sexual complaints and levels of estradiol below 50pg $1cm^3$ (Shen et al., 1999).

- ✓ **Low Testosterone:**

Low testosterone levels are also associated with a decline in sexual arousal, genital sensation, libido and orgasm. This can be accompanied by loss of hair, vaginal mucosal thinning and overall diminished sense of well-being (Sarrel, 1998) and (Davis, 2000).

Therapeutic success with testosterone for inhibited desire in naturally menopausal women has been reported using a testosterone pellet (Tarcan et al., 1990).

- ✓ **Vasuclar Insufficiency Syndrome:**

The recently named clitoral and vaginal vascular insufficiency syndromes are directly related to direct diminished genital blood flow secondary to atherosclerosis of the ill hypogastric (Pudendal arterial bed (Goldstein et al., 1998). Although other underlying conditions psychological or physiological / organic may also manifest as decreased vaginal and clitoral engorgement, arterial insufficiency is one etiology that should be considered. Diminished pelvic blood flow secondary to aorttoiliac or atherosclerotic disease leads to vaginal wall and clitoral smooth muscle fibrosis. This can ultimately result in symptons of vaginal dryness and dyspareunia. It is tomorphometric evaluation of clitoral erectile tissue from atheroscirotic animal demonstrates clitoral cavernosal artery wall thickening, loss of corporal smooth muscle with smooth muscle with replacement by fibro connective tissue in association with atherosclerosis of clitoral cavernosal arteries (Park et al., 1998). While the precise mechanism is unknown, it is possible that the atherosclerotic changes that occur in clitoral

vascular and trabecular smooth muscle interfere with normal relaxation and dilation responses to sexual responses. Aside form atherosclerosis disease, alteration in circulatory estrogen levels associated with menopause contributes to age-associated changes in vaginal and clitoral smooth muscles. In addition, any traumatic injury to the iliohypogastric / pudendal arterial bed from pelvic fracture, blunt trauma, surgical disruption, or chronic perineal pressure from bicycle riding, for instance can result in diminished vaginal and clitoral blood flow and complaints of sexual dysfunction (Goldstein et al., 1998).

- ✓ **Neurogenic Helalth Conditions:**

The same neurogenic etiologies that cause erectile dysfunction in men can also cause sexual dysfunction in women. These include;

1. Spinal cord injury or disease of the central or peripheral nervous system including diabetes and
2. Complete upper motor neuron injuries affecting sacral spinal segments.\

Women with incomplete injuries retain that capacity for physchogen arousal and vaginal lubrication (Traish et al., 1999). With regard to organism, women with spinal cord injury have significantly more difficult achieving orgasm than normal controls. The effects of srecific spinal cord injuries on female sexual response as well as the role of vaso active pharmaco therapy in this population are being investigated. One recent report suggested a potential role for sildenatol in women with spinal cord injury.

- ✓ **Sexually Transmitted Disease (STD)**

Sexually transmitted diseases caused by micro organism such as Neisseria gonorrhea, Chlamydia trichomonas, staphylococcus aureus etc. can also cause erectile dysfunction (John (ED), 2007).

Psychological causes of ED in females.

In women, despite the presence or absence of organic disease, emotional and relational issues significantly affect sexual around. Issues such as self-esteem, body image and the quality of the relationship with her partner can all affect her ability to respond sexually. In addition, depression and other psychological and mood disorders are associated with female sexual dysfunction. Further more, the medications commonly used to treat depressions can significantly affect the female sexual response. The most frequently used medications for uncomplicated depression are serotonin re-uptake inhibitions (SSRI). Women receiving these medications often complain of decreased desire, decreased arousal, decreased genital sensation and difficulty achieving orgasm. Severel studies have recently been published documentary improvement of SSRI – induced, sexual dysfunction in women with sildenafil (John EO, 2009).

The Diagnosis of female Erectile Dysfunction

Note: That the same patterns of diagnosis carried out in males are also experienced in female. However, PSA test cannot be carried out since women do not have prostate gland.

Treatment of Female Erectile Dysfunction

1. Working with doctors to select medications that do not impair ED.

2. Making lifestyle improvement (e.g quitting smoking and exercising more)
3. Drugs such as sildenafil (viagra), vardenafil (levita) or tadalafal (cialis)
4. Inserting medications into the urethra (intrauretural suppositories)
5. Inserting medications into the corpora cavernosa (intra cavernosal injections).
6. Vacuum constructive devices for the clitoris
7. Clitoral prostheses and
8. psychotherapy.

2.3 Literature Review on Burantashi (pausinystalia Yohimbe)

2.3.1 Species Identity

2.3. Taxonomy

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order: Rubiales

Family: Rubiaceae

Genus: Pausinystalia

Species: Yohimbe

Botanical Name: Pausinystalia Johimbe

(Oliver – Beyer, 1986)

Common Names:

Englis: Yohimbe

Yoruba: Idagbon

Hausa: Burantashi

Trade Name: Yohimbe

(Sunderland et al., 1997)

HISTORY:

Yohimbe was first discovered and used by the pygmies and Bushmen in West Africa, where it grows wild. The Bantu speaking tribe of West Africa still use and praise Yohimbe for its powerful and aphrodisiac effects. But these West Africans tribes considered it a treatment of fevers, leprosy and coughs. It has also been used to dilate pupil, for heart disease, and as a local anesthetic. It has a more recent history of use as aphrodisiac and as a hallucinogen (Sahelian, 2010). In the 19th century, some German missionaries discovered Yohimbe while in West Africa and brought it back to Europe where it quickly became very popular. The Yohimbe tree was nick-named "love tree" and the bark extract was inserted into delicious little candies. These "love candies" as they were appropriately named, were a popular gift among European lovers.

In the 1960's, the American government the US food and drug administration to run scientific tests on Yohimbe to see if it actually worked as an aphrodisiac. These scientists discovered that Yohimbe was in fact a powerful effective aphrodisiac especially for men. But it unfortunately, is not able to help those who suffer from organic impotency. These studies also reported that

yohimbe helps to heighten the sense of touch and send tickling sensation up and down the spine (Sahelian, 2010).

Mechanism of Action

Yohimbe works by blocking alpha –2-adrenoreceptors to increase blood flow. There are a number of feedback mechanism that prevents the release of norepinephire (NE), one of the body's lipolytic hormones (Kucio et al., 1991) when NE is released such as in the period of stress or after taking a sympathomimetic (such as epinephrine). It stimulates both the alpha and beta adrenoreceptors stimulation of the beta adrenoreceptors cause the breakdown of fat while stimulating the alpha-2-adrenoreceptors has the opposite effects, preventing the release of NE and lipolysis. Yohimbe prevents this negative feed back mechanism. Thus increasing NE release and lipolysis (Galitzky et al., 1988).

Botanic Description

Pausinystalia Yohimbe is a tree of 9 -30cm tall with ternate vegetative and regenerative ramification rarely decussate (Adeniyi et al., 2007). Bark usually occurs in channeled pieces, 4 – 10mm, and thick with a varying tinge of red in the grey brown outer and inner surface (Anderson et al., 2001). The outer surface is longitudinally furrowed and bears numerous narrow transverse cracks at fairly regular intervals of 1 – 2 cm. leaves with petiole up to 5mm long; bladely 24 – 47 x 10 – 17.5cm glabious obovate, cuneate or rounded. Some times angustate or cordate at the base, acumen less than 5mm long; (8) – 13 – 18 pairs of prominent

secondary nerves and reticulate interse condary nerves, domatia, if present, glabrous intermediate between cryupt and pit type (Guay et al., 2002). Influorescence terminal or auxillary, 10- 21 (110) cm long and 9 – 15cm wide; stipules at the base persistant (sunderland et al., 1997). Flowers (4-) 5 – merous. Calyx outside densely hairy inside with many long hairs. Capsule almost 100% septicidal and some what loculicidal 1- 1.5 x 0.6cm seeds 8 – 12 x 18.2 – 5mm (Oliver-Beyer, 1986). P. Yohimbe is closely related to P. mocroceras and historically they have been exploited for some purpose. The species are easily distinguished through slash characters. The difference being that P. Yohimbe oxidizes very rapidly (Anderson, 2001).

Ecology and Distribution

- **Natural Habitat**

  Occurs mostly in the Atlantic evergreen forest with caesalpiniaceae, on extensive forest formation extending from south-east Nigeria to Congo (Guay et al., 2001). The species occurs mainly in closed canopy forest. Most common in coastal forest, although not widespread throughout its range. Endermis to its region (Sunderland et al., 1997).

- **Geographical Distribution**

  Native: Cameroun, Congo, Democratic Republic of Congo, Equatorial Guinea Gabon, Nigeria (Oliver Beyer, 1989).

- **Reproductive Biology**

  The seeds are wind dispersed and their lightness and winged structure

means that they can travel long distances in the mildest of breezes. The reproductive system is entomophilous (Anderson, 2001).

Propagation and Management

Propagation Methods

Although the seed and the seedlings need light for their development. They cannot survive in full sun and thus, desiccate and die rapidly (Sunderland et al., 1997). The older stems (3m high or 5cm). However, one able to grow and reproduce in high light situations leading themselves to inclusion ion both agro forestry and monoculture systems (Adeniyi et al., 2007). Natural regeneration is good for seed collection: the optimum period for field work in both Cameroun and Equatorial Guinea would be between November – January (Guay et al., 2002).

Tree Management

A fast growing tree but never reaching great diameter with the maximum being around 50cm (Anderson, 2001).

Germplasm Management

Produces prolific quantities of seed, the characteristics of which indicate that it might lend itself to long-term storage (Sunderland et al, 1997).

FUNCTIONAL USES

- **Economic Uses**

1. It is used as fuel for cooking and other purposes

2. The fibre obtained from the inner back is utilized as straps for hunting panniers
3. The young poles are used for construction purposes (timber)
4. The species is widely used as a snare-strap due to its flexibility
5. The back contains tannin which is an important chemical in wine producing industries
6. Poisonous doses of Yohimbe are reported to paralyze respiration and the drug can cause severe hypertension, abdominal distress and weakness. It can also be used as ichthy toxicant (fish poison) (Oliver – Beyer, 1988).

- **Medicinal uses**

  The back contains up to 6% of a mixture of alkaloids, the principle are being Yohimbe, which is also known as aphrodine, quebrachine or cognine. The presence and the amount of alkaloid activity in P. Yohimbe back is highly variable (Adeniyi et al., 2007). P. Yohimbe is the source of the only clinical proven cure for impotence and has long been used as a traditional stimulant in Africa. Both the crude drug and yohimbe have a long history of use as aphrodisiacs in western medicine in both prescriptions and herbal markets (Sunderland et al., 1997). Yohimbe is symetolytic and hypertensive and has a local anaesthetic action similar to that of cocaine but it is not mydriatic (Anderson, 2001). The vasolidating action of Yohimbe is particularly strong on the sex organ hence, its amordisiac action (Adeniyi et al., 2007). P. Yohimbe is also used as a

local anaesthetic, a mild stimulant to prevent drowsiness, a hallucinogen, a treatment for angina, hypertension, a general tonic, a remedy to increase the clarity of the voices of singers during long festicals and as a treatment to increase the nesilience of hunting dogs (Ostoic, 2006)

Pests and Disease

Although P. Yohimbe trees call us well after a small amount of back removal, removal of large quantities of back can lead to an attack by a small stem borer which penetrates the unprotected stem, killing the tree (sunderland et al., 1997).

The Liver

Anatomy of the Liver

The live is a large meaty organ that sits on the right side of the belly weighing about 3 pounds. The liver is the largest glandular organ of the body. It is reddish –brown in colour and is divided into four lobes of unequal size and shape. It is rubbery to touch; normally you can't feel the liver because it is protected by the lobes. The gall bladder sits under the liver along with parts of the pancreas and intestines.

The liver and these organs work together to digest absorb and process food (Athar et al., 2007).

The liver's main function is to filler the blood coming from the digestive tract, before passing it to the rest of the body. The liver also detoxifies chemicals and metabolizes drugs, as it does so. The liver secretes bile that ends up back in

the intestines; the liver also makes protein important from blood clothing (Song et al., 2004).

Blood is carried to the liver via two large vessels called the hepatic artery and the portal vein. The hepatic artery carries oxygen-rich blood from the aorta (a major vessel in the heart). The portal vein carries blood containing digested food from the small intestine. These blood vessels subdivide in the liver repeatedly, terminating in very small capillaries. Each capillaries leads to a lobule liver tissue is composed to thousand of lobules and each lobule is made up of hepatic cells, the basic metabolic cells of the liver (Athar et al., 2007).

The liver is located in the upper hand portion of the abdominal cavity beneath the diaphragm and on top of the stomach. Right kidney and intestine shaped like a cone. The liver is a dark reddish brown organ that weighs about 3 pounds.

The liver is located in the upper hand portion of the abdominal cavity beneath the diaphragm and on top of the stomach, right kidney and intestine shaped like a cone. The liver is a dark reddish brown organ that weighs about 3 pounds.

The liver is the largest internal organ of the human body (liver Microsoft Encarta ® 2009 (O Redmond, WA; Microsoft cooperation 2008).

Histology of the liver

A connective tissue capsule and visceral peritoneum cover the liver, except for the bare area which is a small area on the diaphragmatic surface

surrounded by the coronary ligament. At the porta, the connective tissue capsule sends a branching network of septa (walis) into the substance of the liver to provide its main support vessels, nerves and ducts follow the connective tissue branches throughout the liver (Rod et al., 2003).

The connective tissue septa divide liver into hexagonal shaped lobules with a portal tried at each corner. The treads are so named because of three vessels. The hepatic portal vein, hepatic artery and hepatic duct are commonly located in them. Hepatic nerves and lymphatic vessels often too small to be easily seen in light micrographs are also located in these areas. A central vein is in the center of each lobule. Central veins united to form hepatic veins, which exist on its posterior and superior surfaces and empty into the inferior venacava (Murray et al., 2003).

Hepatic cords radiate out from the central vein of each lobule like the spokes of a wheel. The hepatic cords are composed of hepatocytes. The functional cells of the liver. The space between the hepatic cord and blood channels called hepatic sinusoids. The sinusoids are lined with a very thin, irregular squamous endothelium consisting of two cell population.

Extremely thin, sparse endothelium cells and hepatic phagocytic cells (Kupffer cells).

A cleft like lumen, the bile canaliculus lies between the cells within each cord.

Hepatocytes have six major functions:-

1. Bile production
2. Storage
3. Inter-conversion of nutrients
4. Detoxification
5. Phagocytosis
6. Synthesis of blood components.

Nutrient rich oxygen poor blood from the …… and enters the hepatic sinusoids from branches of the hepatic portal vein and mixes with oxygen rich depleted blood from the hepatic arteries. From the blood the hepatocytes can take up the oxygen and nutrients which are stored, detoxified, used for energy, or used to synthesize new molecules. Molecules produced by or modified in the hepatocyte are released into the hepatic sinusoids or into the bile canaliculi (Athar et al., 2004).

Mixed blood in the hepatic sinusoids flows to the central vein where it exits the lobule and then exits the liver through the hepatic vein. Bile produced by the hepatocytes and consisting primarily of metabolic by products. Flows through the bile canaliculi towards the hepatic ducts. Blood therefore flows from the triad towards the center of each lobule, whereas bile flows away from the center of the lobule towards the triads.

In the fetus, special blood vessel by pass the liver sinusoids, the remnants of fetal Blood vessels can be seen in the adult as the round ligament. (ligamentum teres) and ligamentum venosum (Garrett et al., 1999).

Structure of the Liver

The human liver is a darkened brown organ with a soft, spongy texture. It is located at top of the abdomen, on the right side of the body just below the diaphragm – a sheet of muscle tissue that separates the lungs from the abdominal organs. The lower part of the rib cage covers the liver, protecting it from injury. In a healthy adult, the liver weighs about 1.5 kg (31b) and is about 15cm (6 in) thick (Rod et al., 2003).

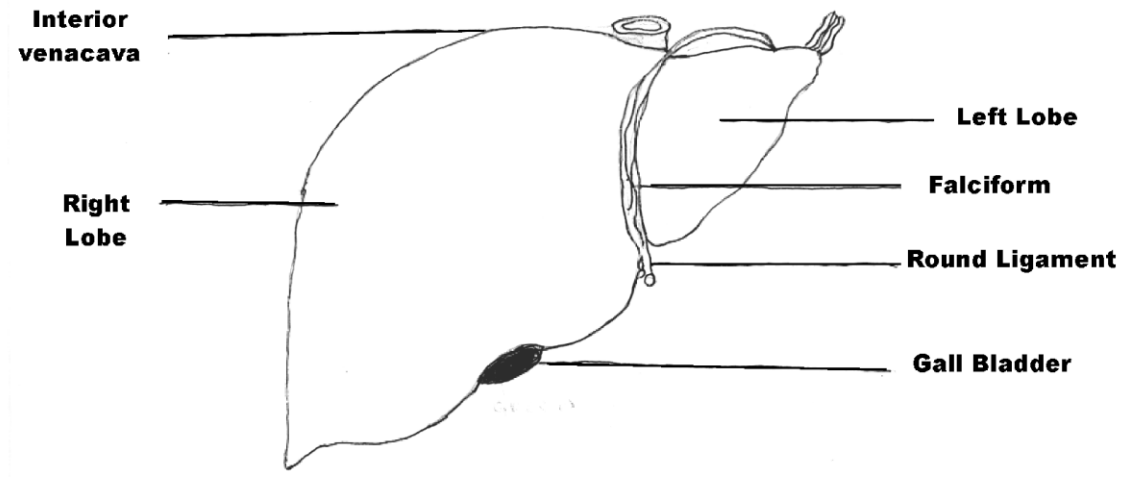


FIG 2.4 ANTERIOR VIEW OF THE HUMAN LIVER

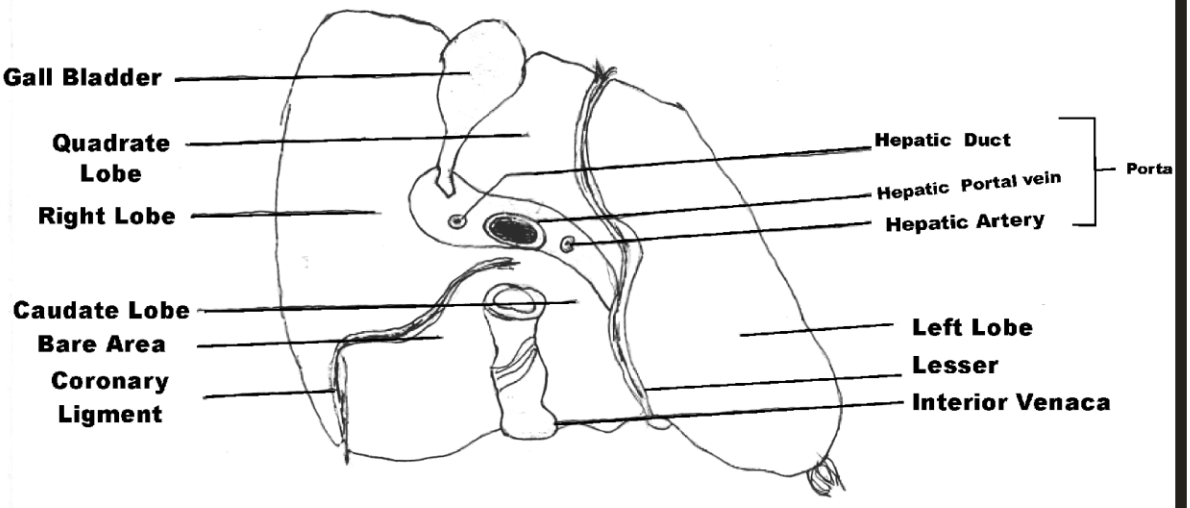


FIG 2.5 INTERIOR VIEW OF THE HUMAN LIVER

FIG 2.6 SUPERIOR VIEW OF THE HUMAN LIVER

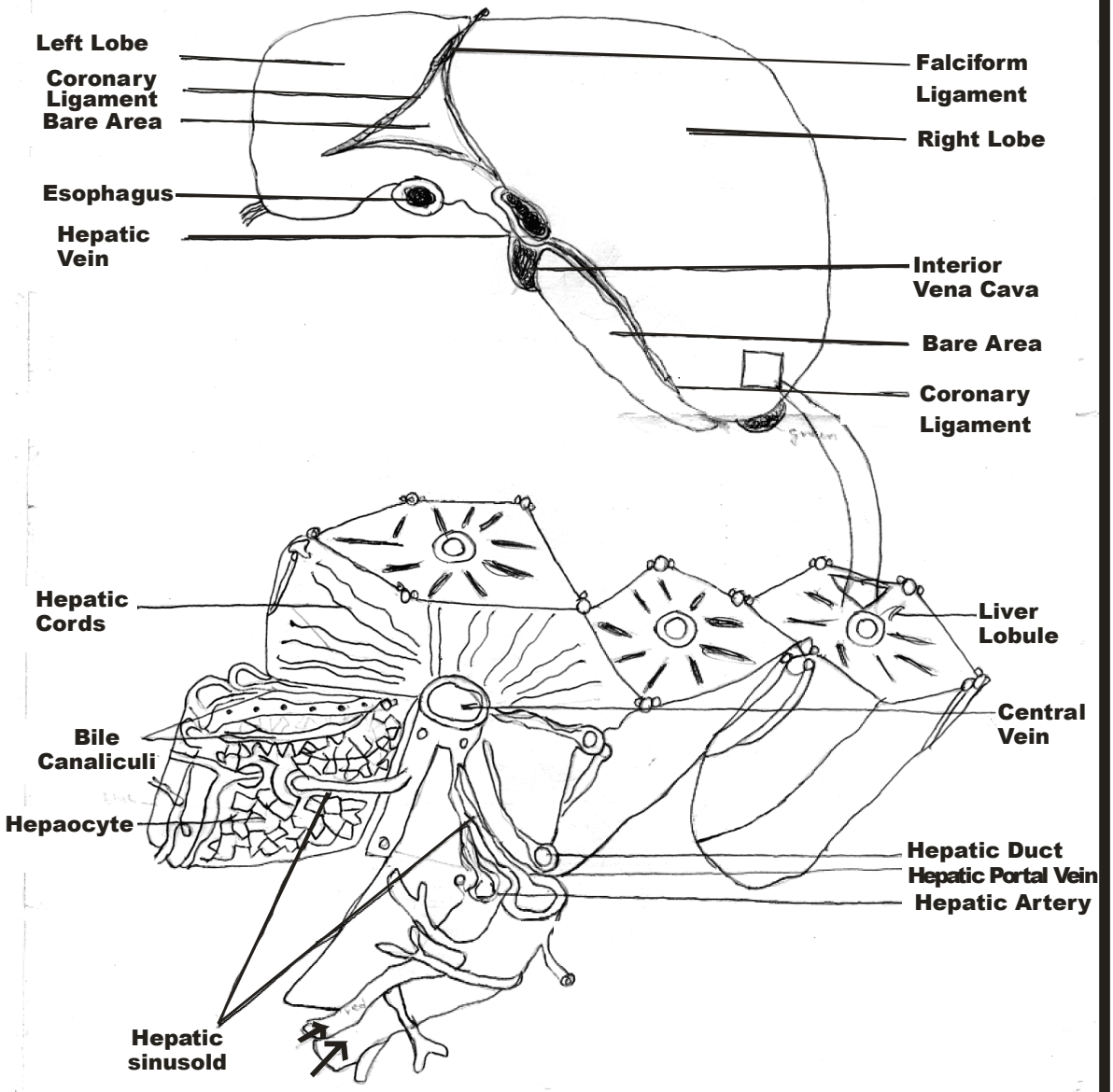
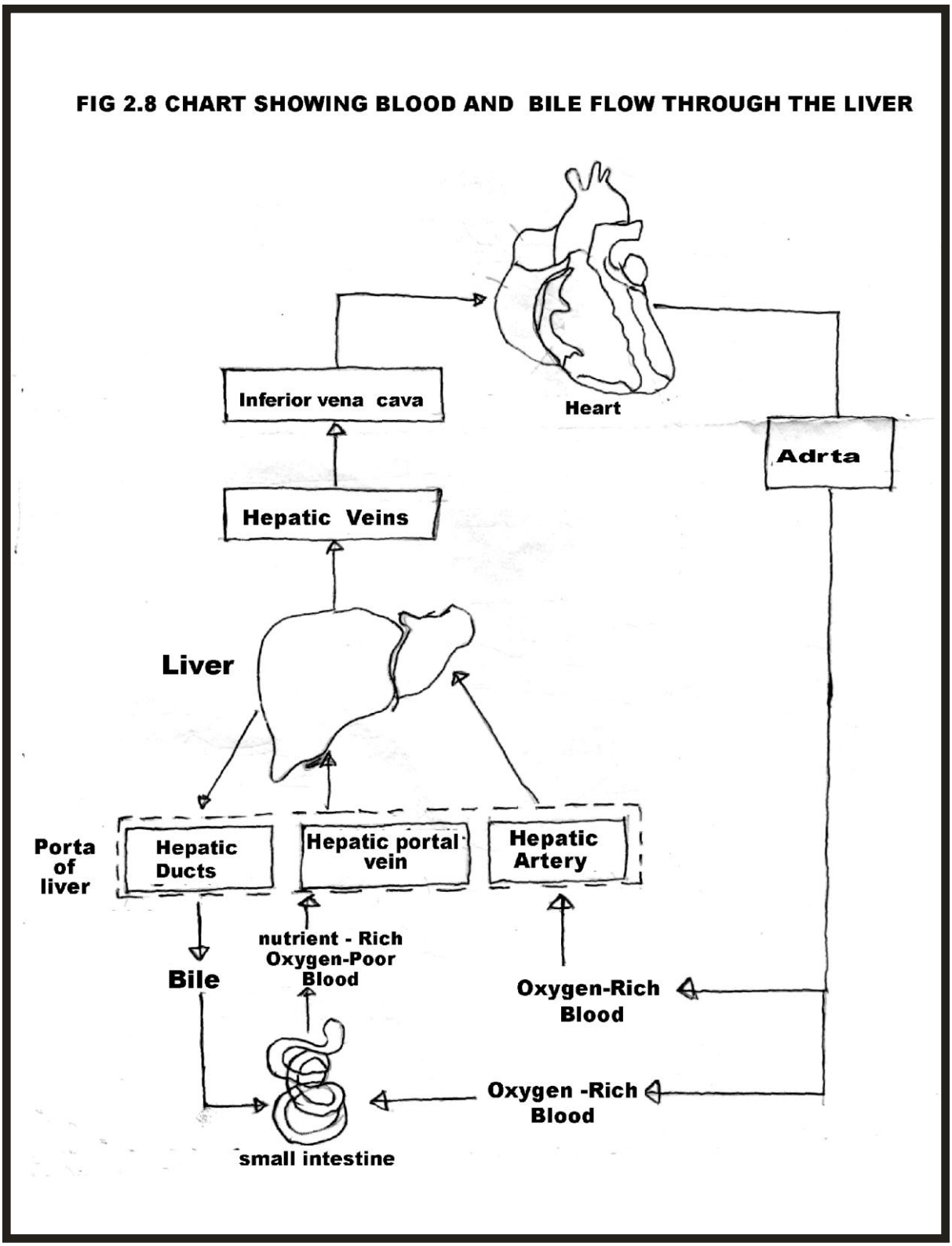


FIG 2.7 LIVER LUBULES WITH TRIAS AT THE CORNERS AND CENTRAL VEINS IN THE CENTRE OF THE LOBULES

FIG 2.8 CHART SHOWING BLOOD AND BILE FLOW THROUGH THE LIVER



Functions of the Liver

The liver has many functions which are very important to human health. However, its most important function includes

- Biosynthesis of endogenous compounds and storage conversion and degradation of these compounds into extractable molecules. The liver is responsible for the biosynthesis degradation of almost all plasma protein.
- Production of urea (the main substance of urine)
- Production of certain amino acid (the building block of protein)
- Filtration of harmful substances from the blood (such is alcohol)
- Conversion of glucose to glycogen.
- It helps to maintain a proper level of glucose in the blood.
- Responsible for producing cholesterol, it produces about 80% of cholesterol in the body.
- Manufactures protein including albumin
- Metabolizes and store carbohydrate, which are used as the source for the sugar in the blood cells and the brain use.
- It forms and secretes bile that contains bile acids to aid in the intestinal absorption (taking in) of fats and fat soluble vitamins.
- The liver eliminates by metabolizing and or secreting the harmful biochemical products produced by the body such as bilirubin from the break down of old red blood cells and ammonia from the breakdown of old red blood cells and ammonia from the breakdown of proteins.
- Detoxification of toxic substances / compounds by bill transformation.
- The liver helps in the storage of vitamins and minerals (vit. A, D, K and B_{12})

- Excretion of substances with bile.

Liver Infections / Diseases

- Alcoholic Liver Disease: Alcoholic liver disease usually develops after years of excessive alcohol intake. The longer the period during which alcohol is excessively consumed and the greater the amount ingested, the higher the likelihood of developing alcoholic liver disease. (Hashmi et al., 1998)

Signs and symptoms

- Abdominal rain and tenderness
- Ascites
- Confusion
- Fatigue
- Jaundice
- Loss of appetite
- Nausea
- Difficulty concentrating
- Dry mouth / excessive thirst.

Primary Liver Cancer

Primary liver cancer is a growing liver problem and generally remains undetected until it has reached the advanced stages because most people do not exhibit symptoms earlier on by protecting yourself from cirrhosis and hepatitis (Rod et al., 1998)

Signs and symptoms

- ✓ Yellow colouration of the skin and whiteness of the eye
- ✓ Abdominal swelling
- ✓ An enlarged liver
- ✓ General weakness and fatigue
- ✓ Loss of appetite
- ✓ Nausea and vomiting
- ✓ Weight loss

Liver Cirrhosis

Liver cirrhosis is generally considered to be the 4th stage of alcoholic liver disease, a progressive condition causing liver damage. The most common cause of liver cirrhosis is chronic alcoholism which accounts for approximately 40% of 20,000 people who died from the disease. (Rod et al., 1998).

Cirrhosis is characterized by the replacement of healthy tissue with fibrous tissue regenerative nodules and liver scarring (song et al., 2004).

Signs and symptoms

- ✓ Abdominal pain
- ✓ Abnormal accumulation of fluid in the abdominal cavity (Ascites)
- ✓ Bleeding from engorged veins in the oesophagus
- ✓ Dark, cola-coloured urine
- ✓ Fatigue
- ✓ Liver cancer

- ✓ Liver failure

Liver Cyst

Also known as a hepatic cyst, a simple liver cyst is a thin waved bubble, a fluid – filled cavity in the liver. Liver cyst may grow large enough to cause pain or discomfort in the upper right part of the abdomen (song et al., 2004).

Signs and symptoms

Liver cyst do not normally produce any signs or symptoms. They are sometime detected by chance during other types of testing.

Fatty Liver Disease

The exact cause of fatty liver disease is unclear many researcher however believes that metabolic syndrome of cluster of disorder that increase the risk of diabetes heart disease and stroke. It is also caused by excessive alcohol consumption, chronic hepatitis and overweight individual (Rod et al., 1998).

Signs and Symptoms

You may have fally liver disease without any signs or symptoms. If there are symptoms, they are normally vague and non-specific. In early stages you may experience fatigue, malaise or a dull ache in your upper right abdomen.

Other symptoms are:

- Lack of appetite
- Nausea
- Swelling of your legs and feets
- Weakness.

Liver Fibrosis

Liver fibrosis is characterized by the formation of fibroid or fibrous tissue, regenerative nodules and liver scarring, all of which impede blood circulation and lead to progressive loss of liver function. It is commonly cause by alcoholism and hepatitis.

Signs and Symptoms

- Abdominal pains
- Abnormal accumulation of fluid in the abdominal cavity.
- Fatigue
- Dark coloured urine
- Easy bruising
- Loss of interest in sex.

Hepatitis

Hepatitis is a gastroenterogical disease. It means inflammation of the liver. Hepatitis is not one but many diseases. Hepatitis A to E in which the liver becomes inflamed and its cells are damaged as a result of inflammatory chemicals being produced and released in the liver. Chronic hepatitis B infection increases a persons chance of developing liver cancer. It is the most common type of hepatitis. (song et al., 2004).

Signs and Symptoms

- Abdominal pains
- Dark urine

- Diarrhea
- Enlarged liver
- Fatigue
- Fever
- Headache
- Jaundice
- Joint aches

Primary sclerosing Cholanditis (PSC)

Cholangitis is inflammation of the bile duct of the liver, sclerosing is inflammation that leads to the extensive formation of fibrous and scar tissue. In primary sclerosing cholangitis. The bile duct inside and outside the liver have become inflammed and scarred.

Signs and Symptoms

- Bile duct infections
- Fatigue
- Intense itching
- Malabsorption
- Severe jaundice
- Signs of cirrhosis

Gallstone

Cholesterol and bile pigment in the bile stones in the bladder, where bile is stored, if present for a long time they may damage the gall bladder and prevent.

It from working properly, it can also block the duct that drawn bile from the gall bladder. This can lead to feeling of bloating, fever, etc.

Liver Cancer

Liver cancer (hepatocellular carcinoma) is a cancer arousing from the liver. It is also known as primary liver cancer or hepatoma. The liver is made up of different cell types, (for example bile ducts, blood vessels and fat storing cells). However, liver cells (hepatocytes) make up of 30% of the liver tissue. Thus; the majority of primary liver cancer cover 90% - 95%) arises from liver cells and is called hepatocellular cancer, however hey are often referred to cancer that has spread o the liver, having originated from other organs more specifically, this type of liver cancer is called metastatic liver cancer or secondary liver cancer. (Song et al., 2004)

Liver Enzymes / Functions

Liver enzymes are those enzymes that play important role in the liver. Among the sensitive and widely used liver enzymes are the amino transferases. They include aspartate amino transferase (AST) and alanine aminotransferase (ATL). These enzymes are normally contained within liver cells. If the liver is injured to cell spill the enzymes into blood raising the enzyme levels in the blood ad signaling the liver damage (Robbins, et al., 1993).

The amino transferases catalysze chemical reaction in the cell in which an amino group is transferred from a donor molecule to a recipient molecule. Aside from AST and ATL alkaline phosphatase is also one of the liver enzymes.

Alanine Transaminase (AIT)

Alanine transaminase (ALT) is also called serum glutamic pyrurate transaminase (SGPT) or Alanine amino transferase (ALAT). It is an enzyme present in hepatocytes (liver cells) when a cell is damaged it leaks this enzymes into the blood. Where it is measured, AIT rises dramatically in acute liver damage such as viral hepatitis or paracetamol (acetaminophen) overdose. Elevations are often measured in multiples of the upper limit of normal (ULN).

Alanine transaminase when released into the blood stream it also indicates hepatocellular disease active cirrhosis, metastatic liver tumor, infection or toxic hepatitis, severe burns, pancreatitis trauma, acute hemolytic anemia etc.

AIT helps to metabolize protein. (Robbins et al., 1993)

Aspartate transaminase (AST) is also called serum Glutamic Oxaloacetic transminase (SGOT) or Aspartate amino transferase (ASAT). It is similar to AIT in that it is another enzyme associated with the liver paranchymal cells. It is raised in acute liver damage, but is also present in red blood cells, cardiac and skeletal muscles and is therefore not specific to the liver. The ratio of AST to AIT is sometimes useful ion differentiating between causes of liver damage, elevated AST levels are not specific for liver damage and AST has been used as a cardiac marker.

Aspartate transminase plays important role in the metabolism of the amino acid alanine. An increase level of AST may indicate hepatocellular disease, active cirrhosis, metastatic liver tumor pancreatitis, heart attack, trauma and

shock.

Alkaline Phosphatase (AIP)

Alkaline phosphatase (AIP) is an enzyme in the cells lining the biliary ducts of the liver. AIP levels in plasma will rise with large bile duct obstruction intrahepatic cholestesis or infiltrative diseases of the liver. Alkaline phosphates (AIP) is also present in bones and placental tissue, so it is higher in growing children (as their bones are being remodeled) and elderly patients with paget's disease.

AIT is needed in small amount to trigger specific chemical reactions.

Total Bilirubin (TBIL)

Bilirubin is a breakdown product of heme (a part of heamoglobin in red blood cells). The liver is responsible for clearing the blood of bilirubin is taken up into hepatocytes, conjugated (modified to make it water soluble) and secrete into the bile, which is excreted into the intestine. Increased total bilirubin causes jaundice and a signal a number of liver problems.

Direct Bilirubin (Conjugated Bilirubin)

The diagnosis is narrowed down further by looking at the levels of direct bilirubin is normal, then the problem is on excess of unconjugated bilirubin and the location of the problem is up stream of bilirubin excretion. Hemolysis, viral hepatitis or cirrhosis can be suspected.

If direct bilirubin is elevated, then the liver is conjugating bilirubin normally, but is not able to excrete it. Bile duct obstruction by gallstone or

cancer should be suspected.

Gamma Glutamyl Transpeptidase (GGT)

Although reasonably specific to the liver and a more sensitive marker for cholestasis damage then AIP, Gamma transpeptidase (GGT) may be elevated with even minor, sub clinical levels of liver dysfunction. It can also be helpful in identifying the cause of an isolated elevation in AIP (GGT) is raised in chronic alcohol toxicity.

5'Nucleotidase (5NTD)

5'Nucleotidase is another test specific for cholestasis or damage to the intra or extra hepatic biliary system and in some laboratories is used as a substitute for GGT for ascertaining whether an elevated AIP is of biliary or extra biliary origin.

Lactate Dehydrogenase (LDII)

Lactate dehydrogenase is an enzyme found in many body tissues, including the liver elevated levels of Lactate dehydrogenase may indicate liver damage.

PHYTOCHEMICALS

Phytochemicals are the compounds that are of plant origin. They are chemicals extracted from plants which are non-nutritive but with protective or disease preventive properties. They are non-essential nutrients, meaning that they are not required by the human body for sustaining life. It is well–known that

plants produce these chemicals to protect themselves but recent research demonstrates that they can also protect human against disease. These chemicals are classified as primary or secondary constituents depending on their role in plant metabolism. Primary constituent include the common sugars, amino acids, proteins purines and pyramidines of nucleric acids. Chlorophyll's etc. secondary constituents are the remaining plant chemicals such as alkaloids (derived from amino acids) terpenes (a group of lipid) and phenolic; (derived from carbohydrates).

There are more than thousands known phytochemicals some of the well known phytochemicals are saponins, tanins, lycopene in tomato and flavonoids in fruits.

Functions of phytochemicals

- **Antioxidants**

Most phytochemicals have antioxidat activity and protect our cells against oxidative damage and reduce the risk of developing certain types of cancer. Phytochemicals with antioxidant activity: allyl sulphides (onions, leeks, garlic) carotenoids (fruits, carrots) flavonoids (fruits,vegetables) polyphenols (tea, grapes).

- **Hormonal Action**

Isoflavonos, found in soy, imitate human oestrogen and help to reduce menopausal symptoms and osteoporosis.

- **Stimulation of Enzymes**

Indoles, which are found in cabbages, stimulate enzymes that make the oestrogen less effective and could reduce the risk of breast cancer. Other phytochemicals, which can interfere with enzymes are, protease inhibitor (Soy and beans), terpenes (Citrus fruits and cherries).

Interference with DNA Replication

Saponin found in beans interferes with the replication of the cells DNA, thereby preventing the multiplication of cancer cells. Capsaicin, found in not peppers, protects DNA from carcinogen.

- **Anti – Bacterial Effect**

  The phytochemical allicin from garlic has anti-bacterial properties.

- **Physical Action**

  Some phytochemicals bind physically to cell walls there by preventing the adhesion of pathogens to human cell walls. Proanthocyanidins are responsible for the anti-adhesion properties of cranberry. Consumption of cranberries will reduce the risk of urinary tract infections and will improve dental health.

Phytochemicals are of over 900 that have been identified and characterised. Phytochemical screening revealed the presence of tannins, phenolic compounds, saponins alkaloids, steroids and flavonoids which could be subsumed to be responsible for its varied biological and pharmacological properties.

Phytochemicals commonly known as follows

- **Tannins**: the word tannins is very old and it reflects traditional technology

"tannin" (water proofing and preserving) was the word used to describe the process of transforming animal hides into leather by using plant extracts from different parts of the plan species. It is a term that is un duly applied to any large polyphenoptic compound containing sufficient hydrolysis and other suitable groups to form strong complexes with protein and other macro-molecules to have molecular weight range from 500 to over 9,000.

Tannis are incompatible with alkalis, gelatin, heavy, tals, iron, lime water. Metallic salt, zinc, sulphate; it is divided into two which include; hydrolysable and condensed Tannins. It can also be located in the vacuoles or surface waxed the plants. The tannin which is also a phenolic compounds interferes with iron absorption through a complex formation with iron when it is in gastrointestinal lumen which decrease the bioavailability of iron large intake of tannins may cause kidney irritation, liver damage, irritation of the stomach and gastrointestinal pains. But food rich in vitamin C help in neutralizing the negative effect of tannins on iron absorption. It is used to pull out poisons from oak causing instant relief.

- **Flavonoids:** The flavonoids are diverse group of polyphenolic compound that is duly distributed in the plant kingdom. There are more than 6,400 known flavonoids compounds. Flavonoids contribute to the flavor and pigmentation of the fruits and vegetables in the human diet. They also have important roles in plant growth, production and pathogen and predator resistance. It is present in plants either as aglycones or aglycoside conjugate. It may be divided into

8(eight) different classes (flavones, flavonol, flavonone, catechina, anthocyanidins, isoflavones, dihydro-flavonols and chalcones). Others such as the anticyanidins from billbery, purple cabbage and grapes may help protect the lens of the eyes from cataract.

- **Alkaloids:** A large number of drugs are being produced from this class of phytochemical constituents. Alkaloids are basic containing one or more nitrogen in a heterocyclic … most alkaloids are known for their pharmacological nature. They usually have physiological action on man and other animals.
- **Saponins:** Saponins glycosides are divided into two types: the neutral saponina and the acid saponins.

Based on the chemical structure of saponins aglycones (sapogenin) lytic presaponinson hydrolysis yields an aglycone known as "Sapogenin"

Saponins = sugar + sagogenin

(glycone) (aglycone)

Neutral saponins are derived from steroids with spiroketal side chains. The acid saponins possess tritetpenoids structures. The plant material containing saponins have long been used in the world for their detergent properties. They also have haemolytic properties and when injected into the blood stream, which are highly toxic, but orally, saponins are comparatively harmless.

Saponins are used in injection because of its pharmacological reputation. It results in the lysis of the blood cells haemolysis like all detergents and therefore highly toxic.

Medical Uses;

There a re tremendous, commercially driven promotion of saponin dietary supplement and nutriceuticals. There is evidence of the presence of saponin in traditional medicine preparation where oral administration might be expected to lead to hydrolysis of glycoside from terpenoid. But it is often the case with wide ranging therapeutic chains for natural products.

- **Carotenoids**: These are the major classes of phytochemical found in fruits and vegetables. The carotenoids are found in carrots, tomatoes, mango, sweet potatoes, sweet corn etc. examples of carotenoids are; lycotene α – carotene β – carotene, y – carotene, phytoene, xanthrophyll (lutein), phytofluene and neurosprene.

Chemically, carotene is a terpene synthesized biochemically from 8 isoprene units. It is used for several related compounds having the formular ($C4OH_{56}$). As hydrocarbon carotenes are fat soluble, carotenes are carotenoids having no oxygen in their molecular formular while xanthrophylls are carotenoids containing oxygen.

Carotenes are orange photosynthetic pigment important for photosynthesis. They are responsible for orange colour of carrot and any fruits and vegetables. They contribute to photosynthesis by transmitting light energy. They absorb to chlorophyll. Carotene protects plant cells from the destructive effects of ultra – violet light (UV – light). B – Carotenes are the antioxidants.

CHAPTER 3

MATERIALS AND METHODS

MATERIALS

Animals

Male and female albino wistar rats were used for this experiment. The rats were purchased from Ogbete Main Market in Enugu State. The animals were kept under standard conditions for 3 days with water and food freely so as to allow them for acclimatization before starting up the experiments.

Magani buranthashi stems

The stems of Magani burantashi plant were purchased from an agent in Maiduguri, Borno State (northern Nigeria).

Instruments/Equipment

Some of the instrument/equipment used for this study include:

Water bath	Gallenkamp, England
Chemical balance	Gallenkamp, England
Test-tubes	Pyrex, England
Conical Flasks	Pyrex, England
Hot box	Gallenkamp, England
Centrifuge (3,500 rpm)	PIC, England
Syringe (1ml and 5ml)	DANA JET, Nigeria
Digital Photo Colorimeter	EI (312 Model), Japan
Adjustable micropipette	PERFECT, USA

Refrigerator	Kelvinator, Germany
Beakers	Pyrex, England
Soxhlet extractor	Gallenkamp, England
Thermometer	Lexington, USA

Capillary tubes

Cuvettes (1cm light path)

Sample Bottles

Rat cages

Chemicals and Reagents

The chemicals used in this study were of analytical grade and products of May and Baker, England; Darmstadt, Germany; BDH, England. They were sourced from Onitsha Main Market in Anambra State.

The reagents used for all the assays were commercially prepared kits and products of RANDOX, Biosystem Reagents and Instruments, USA.

Preparation of Normal Saline

A quantity, 0.9g of sodium chloride was weighed and dissolved in a little quantity of distilled water. The volume was finally made up to 100ml.

Preparation of reagents for phytochemical analysis

5% Ferric Chloride solution

A quantity, 2.5g of ferric chloride was dissolved in 50ml of distilled water.

Ammonium Solution

The volume of 375ml of the stock concentrated ammonium solution was dissolved in 62.5ml of distilled water and made up to 1000ml.

Aluminium Chloride solution

To prepare this, 0.5g of aluminium chloride was dissolved in 100ml of distilled water.

Dilute tetraoxosulphate (iv) acid

A known volume of 10.4ml of concentrated tetraoxosulphate (iv) acid was mixed with 5ml of distilled water and made up to 100ml.

Lead acetate solution

To prepare this, 45ml of 15% lead acetate solution was dissolved in 20ml of absolute ethanol and 35ml of distilled water.

Wagner's reagent

Exactly 2g of iodine crystals and 3g of potassium iodide were dissolved in 100ml of distilled water.

Mayer's reagent

To prepare this, 1.35g of mercuric chloride was dissolved in 60ml of distilled water. Also, 5g of potassium iodide was dissolved in 20ml of distilled water. The solution was mixed and the volume made up to 100ml.

Dragendorff's reagent

Exactly 0.85g of bismuth carbonate was dissolved in 100ml of glacial acetic acid and 40ml of distilled water to give solution called solution A. Another solution called solution B was prepared by dissolving 8.0g of potassium iodide in 20ml of

distilled water. Both solutions were then mixed to give a stock solution called Dragendorff's reagent.

Molisch reagent

To prepare this, 2ml of concentrated hydrochloric acid was dissolved in distilled water and made up to 100ml.

Experimental Design

A total of twenty-five male and female albino rats were used for this study. However, about sixteen survived to the end of the experiment. The rats were acclimatized and housed in separate cages according to their groups and in mixed sexes. Soon after, the rats were divided into four groups of six animals (n=6).

Group 1 was rats given 300mg/kg ethanol extract (E) of magani buranthashi stem orally.

Group 2 was rats given 300mg/kg of the aqueous extract (E) of magani buranthashi stem orally.

Group 3 was rats given 100mg/kg of sildenafil citrate orally.

Group 4 was rats given normal saline only.

The experiments continued and lasted for a period of four (4) weeks. At the end of the experiment, the surviving rats were sacrificed and their blood collected for the various and specific analyses. The analyses carried out on the rats include the liver function tests on the liver enzymes.

METHODS

Extraction Procedures

Preparation of the ethanol extract

The stems of magani buranthashi plant were gathered and dried under room temperature for two weeks. The dried stems were divided into two parts. The first part was pulverised into coarse form. About 500g of the powdered stems were soaked in 1000ml of 99% ethanol. The mixture was left to stand for twenty-four hours with occasional stirring. The mixture was later extracted using a soxhelet extractor to obtain the ethanol extract. The extract was concentrated over a water bath at a temperature range of 25^{o}C to 30^{o}C to obtain 34.32g (yield = 18.28% w/w) ethanol extract.

Preparation of the aqueous extract

The second part of the dried stems were also pulverised into coarse form. About 500g of the powder were soaked in 100ml of distilled water and left to stand for twenty-four hours with occasional stirring. The pulverised leaves were later extracted to get the water (aqueous) extract. Later, the extract was concentrated over a water bath at a temperature of 30^{o}C to 35^{o}C to obtain 25.73 (yield = 8.87% w/w) of aqueous extract.

Determination of the concentration of extracts

To determine the concentration of the extracts, a known weight of both extracts were determined separately. The weight of dry crucible was also determined. Later, known weights of both extract were put into the dry crucible, respectively,

and their weight determined before heating. The crucible with its content was heated to constant weight. After the heating, the crucible was weighed with its heated content and the weight recorded. The concentration of both extracts was then calculated from the various weights.

PHYTOCHEMICAL ANALYSIS

The preliminary phytochemical analysis involved tests for the presence or absence of the following constituents: alkaloids, acidity, carbohydrates, fats and oil, proteins, glycosides, reducing sugar, flavonoids, terpenoids, steroids, resins, tannins, and saponins.

Test for Alkaloids (General Tests)

About 2ml of 5% tetraoxosulphate (iv) acid in 50% ethanol was added to 5ml of the methanol and water extracts, respectively. The different mixtures were brought to heat on a boiling water bath for 10 minutes. They were cooled and filtered.

To 2ml of each filtrate was added few drops of:

Mayer’s Reagent (Potassium mercuric iodide solution)

Dragendorff’s Reagent (Bismuth potassium iodide solution)

Wagner’s Reagent (Iodine in potassium iodide solution)

Picric acid solution (1%)

The remaining filtrates were placed separately in 100ml separator funnels and made alkaline with dilute ammonia solution. The aqueous alkaline solution, of each extract, was separated and extracted with two 5ml portions of dilute

sulphuric acid. Both extracts were tested with a few drops of Mayer's, Wagner's, and Dragendorff's reagents. Alkaloids showed up as milky precipitate with one drop of Mayer's reagent and a reddish brown precipitate with one drop of Wagner's reagent.

Test for Acidity

About 0.1g of both extracts were placed in clean dry test tube and sufficient water poured into the mixtures. The mixtures were warmed in a hot water bath and allowed to cool. A wet blue litmus paper was dipped into each of the mixture and the colour change observed. A colour change to red indicated acidity.

Test for Carbohydrate (Molisch's Test)

One gram of each extract (methanol and water extracts) was boiled with 2ml of distilled water and then filtered. Concentrated sulphuric acid was gently poured down the sides of each test tube to form a lower layer. A purple interface of ring indicated the presence of carbohydrates.

Test for Fats and Oils

One gram of each extract was pressed between a clean filter paper. The filter paper was observed for translucency which indicated the presence of oils in the extracts.

Test for Proteins (Million's Test)

Two drops of Million's Reagent were added, respectively, to both extracts in a test tube. The formation of white precipitate indicated the presence of proteins.

Test for Glycosides (Fehling's Test)

About 5ml of a mixture of equal parts of Fehling Solutions I and II were added to about 5ml of each extract and then heated on a water bath for 5 minutes. A brick red precipitate showed the presence of reducing sugar.

Test for Reducing Sugars (Fehling's Test)

About 1g of both extracts were shaken vigorously with 5ml of distilled water and later filtered. The filtrate was used for the Fehling's test.

Fehling's Test: To 1ml portion of the filtrate were added equal volumes of Fehling's Solutions I and II and boiled on a water bath for few minutes. A brick red precipitate indicated the presence of reducing sugars.

Test for Saponins (Fehling's Method)

About 20ml of water was poured into 0.25g of both extracts in a 100ml beaker and boiled gently on a hot water bath for 2 minutes. Both mixtures were respectively filtered out and allowed to cool. The filtrates were used for the Fehling's test. A reddish precipitate indicated the presence of Saponins.

Test for Tannins (Ferric Chloride Method)

One gram of both extracts was boiled respectively with 50ml of distilled water. Each was filtered and the filtrate used for the test. To about 3 ml of the respective filtrate, few drops of ferric chloride solution were added. A greenish black precipitate indicated the presence of tannins.

Test for Flavonoids (Ammonium Test Method)

About 10ml of ethylacetate were added to 0.2g of both extracts. Both mixtures were treated on a water bath for 3 minutes. Each mixture was cooled, filtered and the filtrate used for the ammonium test.

Ammonium Test: A quantity, 4ml of each of the filtrates were shaken with 1ml of ammonia solution. The layers were allowed to separate and the yellow colour in the ammoniacal layer indicated the presence of flavonoids.

Test for Resins (Precipitation Test)

About 0.2g of both extracts was washed with about 15ml of 95% ethanol and the mixture poured into 20ml distilled water in a beaker. The formation of a precipitate indicated the presence of resins.

Test for Steroids and Terpenoids

About 9ml of ethanol was poured into 1g of the extract. It was refluxed for a few minutes and then filtered. The filtrate was concentrated to 2.5ml on a boiling water bath and 5ml of hot water was added. The mixture was allowed to stand for 1 hour and the waxy matter filtered off. The filtrate was extracted with 2.5ml chloroform using a separating funnel.

Later 1ml of concentrated sulphuric acid was poured into about 0.5ml of the chloroform extract in a test tube. The appearance of a reddish-brown interface showed the presence of steroids.

Another 0.5ml of the chloroform extract was evaporated to dryness on a water bath and heated with 3ml of concentrated sulphuric acid for 10 minutes on a water bath. A grey colour indicated the presence of terpenoids.

CHAPTER 4

RESULTS

YIELD OF THE EXTRACTS

As shown in Table 3.1, extracting 500g of the stems of magani burantashi gave 34.32g of the ethanol extract and 25.73g of the aqueous extract. Their extractive yields are 18.28% w/w and 8.87% w/w respectively.

Table 3.1: Extract yield of ethanol extract and aqueous extract

Weight of plant material (g)	Total weight of extract (g)	Extractive yield (% w/w)
500	34.32 ethanol	18.28
25.73 aqueous	8.87	

PHYTOCHEMICAL DATA

Phytochemical analysis showed that the aqueous extract tested positive to carbohydrates, proteins, glycosides, reducing sugars, flavonoids, terpenoids, steroids, resins, tannins, and saponins while the ethanol extract gave positive reactions to alkaloids, carbohydrates, glycosides, reducing sugars, flavonoids, terpenoids, steroids, resins, and tannins (Table 3).

Table 3: Phytochemical properties of extracts

Constituents	Aqueous extract	Methanol extract

Alkaloids	-	++

Extract	Dose	Concentrations (mg/dl) in weeks	
Carbohydrates		+++	+++
Fats and Oils		-	-
Proteins		++	-
Glycosides		++	+++
Reducing Sugar		++	++
Flavonoids		+++	++
Terpenoids		+	++
Steroids		++	++
Resins		+++	+++
Tannins		++	++
Saponins		+	-

Legend:

+	Present in trace concentration
++	Present in moderately high concentration
+++	Present in very high concentration
-	Absent

EFFECT OF EXTRACTS ON SOME LIVER FUNCTION ENZYMES OF WISTAR RATS

		Alanine transaminase	Aspartate transaminase	Total bilirubin	Blood glucose
Ethanol	500	113.58 ± 3.13	73.58 ± 3.13	65.88 ± 2.98	63.67 ± 1.97
Aqueous	500	121.38 ± 3.49	81.25 ± 3.60	73.13 ± 5.24	60.38 ± 4.41
Control		134.21 ± 2.53	163.67 ± 4.52	179.21 ± 2.08	193.04 ± 1.93

The ethanol and aqueous extracts significantly ($P<0.05$) affected the examined liver function enzymes in the wistar rats.

CHAPTER FIVE

DISCUSSION AND CONCLUSION

DISCUSSION

Burantashi was first discovered and used by the pygmies and Bushmen in West Africa, where it grows wild. The Bantu speaking tribe of West Africa still use and praise Burantashi for its powerful and aphrodisiac effects. But these West African tribes considered it a treatment of fever, leprosy and cough. It has also been used to dilate pupil, for heart disease and as a local anesthetic. It has a more recent history of use as aphrodisiac and as a hallucinogen (Sahelian, 2010).

In the 19th century, some German missionaries discovered Burantashi while in West Africa and brought it back to Europe where it quickly became very popular. The Burantashi tree was nicknamed “love tree” and the bark extract was inserted into delicious little candies. These “love candies” as they were appropriately named, were a popular gift among European lovers. The burantashi stem / seed is also phosphodiesterase – 5’(PDE-5) inhibitor used to treat erectile dysfunction.

CONCLUSION

This descriptive analysis suggests erection sufficient for penetration and intercourse completion was achieved within 0.25 hours and lasted for 6 hours after dosing with Burantashi 10mg in these men with mostly moderate to severe erectile dysfunction and a history of non response to sildenafil and who chose to

make attempts during those intervals. The herbal drug was generally well tolerated. Also, the results obtained on the acute toxicity effect of Burantashi stem / seed shows that the liver can tolerate it in moderate consumption.

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