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RIVERS STATE UNIVERSITY
PORT HARCOURT

TINY LIVES AND FAMILIES, THE NEXUS BEFORE AND AFTER BIRTH: PHYTOMEDICINAL IMPACT

AN INAUGURAL LECTURE

BY

PROFESSOR TAMUNOTONYE WATSON JACKS

B.Med.Sc. (Uniport), M.Sc. and Ph.D. (Unimaid), FASN

Professor of Microscopic Anatomy

SERIES NO. 84

Wednesday 25th January, 2023

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DEDICATION

This 84th Inaugural Lecture is dedicated to the Almighty God who first gave me life, redeemed me by His Son, and sent His Spirit to teach me all things. It is also dedicated to the better part of me, my dear ST. It is further dedicated to my 'olive shoots', the heritage of the Lord, Boma, Belema and Ibim.

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PROTOCOL

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The Deputy Vice-Chancellor (Administration)

The Deputy Vice-Chancellor (Academics)

The Registrar and Secretary to Senate

The University Librarian
The Bursar
The Provost, College of Medical Sciences
The Dean, School of Postgraduate Studies
Deans of Faculties/Student Affairs
Directors of Centres/Institutes
Heads of Departments
Emeritus Professors
Distinguished Professors and other Members of Senate
All Academic, Administrative and Technical Staff
Students of this Great University
Respected Guests, Friends, Admirers, Associates, and Well Wishers
My Lords, Spiritual and Temporal
Gentlemen of the Press
Distinguished Ladies and Gentlemen

1.0 PREAMBLE

It is with a great sense of fulfillment and profound gratitude to God that I present this inaugural lecture. What was not possible many years ago is now being presented at the fullness of time. Scripture says "***He hath made everything beautiful in his time***" (Ecclesiastes 3:11). It has been a long journey from 15th November, 2012 when my professorship was retroactively announced by the Governing Council of the University of Maiduguri and backdated to 1st October, 2008, the effective due date. However, the insurgency in the Northeast of Nigeria was at its peak about the same period and discouraged any meaningful public academic gathering of that magnitude. The situation was unabated till September, 2017 when I took up appointment with this institution as one of the pioneer academics in our new College of Medical Sciences.

Furthermore, my initial inability to understand how the Senate Lectures Committee of RSU operates and the period I took ill early last year, further delayed my enlistment for presentation. However, I am particularly privileged to give the second inaugural lecture in the College of Medical Sciences of this great University. The first been presented by the Dean of the Faculty of Basic Medical Sciences, Professor Kenneth S. Ordu on the 24th November, 2021, with much glamour as the matrix that opened the College for inaugural lecture series. **I**t's now on record that the second inaugural lecture in the College is also presented by an Anatomist. I wish to specially thank the Provost of the College, Professor Chituru Orluwene, for the opportunity. The choice of the topic of this inaugural lecture "**Tiny Lives and Families: The Nexus Before and A**fter Birth; Phytomedicinal

Impact" was given by divine inspiration, in the light of many competing topics seeking my attention, for which I am eternally grateful to God.

2.0 INTRODUCTION

The term Anatomy is a Greek word, and like its Latin equivalent, *Dissectio* means "cutting up". It originally implied the study of the disposition of the different parts of the body, thus constituting gross or macroscopic anatomy or sometimes known as topographical anatomy. It also means the study of the science of the form and structure of the human body with a very long history, as old as creation itself. In the book of Genesis 1: 26 "And God said, let us make man in our image, after our likeness….." However, the documented period in history of the study of the human body dates back to the 5th century B.C. The ancient Egyptians were probably the first to have real knowledge of the form and structure of the human body, through their culture of preserving the dead. In their practice of embalming the dead, they removed most of the internal organs and thus learnt about the heart, liver, lungs, brain, uterus, intestines, etc. Herophilus and Hippocrates were famous in the 4th century B.C; Herophilus of Chalcedon was referred toas the founder of anatomy as a systematic learned discipline, while Hippocrates (460 – 377 B.C.), an ancient Greek physician, was regarded as the father of medicine with a scientific approach to anatomy. Andreas Vesalius (1514 – 1564) (Figure 1), a Belgian, is regarded as the father of modern anatomy. He distinguished himself through numerous dissections of the human body and thus studied the structure of the human body systematically for the first time.

Figure 1: Andreas Vesalius (1514 – 1564)

2.1 Sub-divisions in Anatomy

The science of Anatomy involves the study of the cells, tissues, organs and systems of the body. It also applies to the study of the regulations of the development of these structures in relation to functions and the external environment. In view of the structural complexity of the human body, anatomy can be studied in many different ways or sub-disciplines as follows (2020 classification by the International Federation of Associations of Anatomists, IFAA):

i. Gross Anatomy
ii. Developmental Anatomy/Embryology, including human genetics

iii. Microscopic Anatomy (including Histology, Cell and Molecular Biology, Tissue Engineering and Stem Cells)
iv. Neuroanatomy/Neuroscience
v. Radiological Anatomy, including imaging
vi. Clinical/Surgical Anatomy
vii. Physical/Biological Anthropology and Forensic Anatomy
viii. Veterinary and Comparative Anatomy
ix. Anatomy Education, including Digital Anatomy
x. History of Anatomy, including ART and Illustrations, and Medical Humanities
xi. Anatomical Services, Ethics, Anatomy and the Law

However, for the purpose of this lecture, anatomical study is divided into only three broad methods, namely gross anatomy, developmental anatomy and microscopic anatomy. The study of the spatial relationship of the tissues, organs and systems of the body with the naked eye is known as gross anatomy, while the study of early developmental stages of the cells, tissues and organs of the body from conception (at fertilization) to birth is called developmental anatomy (or embryology).On the other hand, the detailed study of the cells, tissues and organs of the body with the aid of the microscope is known as microscopic anatomy (or histology).

The relationship of these three blocks of anatomical sciences will be further highlighted in relation to the topic of the lecture, however, it is pertinent to emphasize that they represent the study of the same human body but divided into three streams based on differences in the method of study or examination

techniques. Furthermore, greater emphasis shall be placed on the area of my research interest, microscopic anatomy and especially phyto-histology, which is an important adjunct of microscopic anatomy, concerned with the application of plant medicinal substances and environmental impact on organisms and studying the effects on tissues and organs of the body by microscopic observation.

3.0 PRINCIPLES OF MICROSCOPIC OBSERVATION

To have a good understanding of this lecture, we may have to look at the study instrument, the microscope. Cellular structures can be identified using either the light or electron microscope (EM). The study of the cellular and tissue structures by the microscope is known as histology. The light microscope (fig. 2) has been modified in various ways, so that in addition to the common compound microscope, we now have available the Phase-Contrast microscope, Interference microscope, Polarizing microscope, Fluorescence microscope, Ultraviolet microscope, and confocal microscope. Each has its own advantages for special purposes. For example, the Phase-Contrast microscope can be used to directly observe living cells and tissues, like cell division, although the resolution may be poor. The electron microscope has two types; the transmission (fig.3) and scanning electron microscope.

3.1 Resolving Power (Resolution)

Let us imagine two points in a specimen viewed in a microscope. If the points are moved closer together, a certain critical distance of separation will be reached when the two points will appear to

merge and will be seen as one point only. The resolving power of a microscope is defined as the smallest distance by which two points on a specimen can be separated and still remain distinct as two points. The light microscope can resolve two objects as separate and distinct by about 0.2µm apart, while the electron microscope has a resolution of 0.0002µm or 0.2nm (2Å) (i.e., 1000 times better than the light microscope).

3.2 Magnification

Magnification is the ability of the microscope to increase the absolute size of the object being observed. The light microscope can magnify an object by 1000 times its original size, while the electron microscope can increase the size of an object by well over 200,000 times.

3.3 Contrast

The ability to distinguish the different components in a system due to differences in optical density is referred to as contrast. Naturally, the different components in cells and tissues are translucent and indistinct to observe as separate and distinct, and therefore coloured with biological dye (for light microscope) or stained with heavy metals like lead (for electron microscope). The electron microscope also gives a better contrast.

Figure 2: Light Microscope

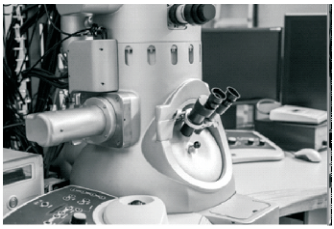


Figure 3: Transmission Electron Microscope

4.0 TINY LIVES AND FAMILIES BEFORE BIRTH

The anatomy of the unborn human being begins at conception or fertilization, which is a complex biological process by which the male sex cell/gamete (spermatozoon) fuses with the female sex cell/gamete (ovum) to form a single cell, the zygote (figure 4).Interestingly, of the millions of male sex cells(spermatozoa) that are deposited in the female genital tract with a single ejaculation, only one spermatozoon is required to fertilize an ovum. It is thought that enzymes present in a portion of the head of the spermatozoon (acrosomal cap) may assist in the penetration of the protective outer covering of the ovum (zona pellucida).Once the head of the spermatozoon has pierced the zona pellucida, the movement of the tail ceases, and the entire spermatozoon is engulfed and drawn into the cytoplasm of the ovum. Immediately following the penetration of the ovum by one spermatozoon, the permeability of the zona pellucida becomes altered so that though other competing spermatozoa become attached to the zona, they usually fail to penetrate the ovum.

4.1 The Female Sex Cell and Oogenesis

To form a mature ovum, meiosis must take place, which results in the reduction of chromosomes from 46 to 23; so that each ovum contains 22 autosomes and 1 sex chromosome. During early fetal development, primordial germ cells migrate from the embryonic yolk sac into the primitive gonads (ovaries) and begin to differentiate into oogonia (female sex cells). In the third

prenatal month, the oogonia (fig. 6) begin to increase in number by mitosis to form the primary oocytes (primitive ova), which immediately enter the prophase of their first meiotic division. From approximately 1,000sex cells (oogonia), they rapidly mitose to well over four million primary oocytes at 20 weeks gestation. The primary oocytes become surrounded by a single layer of flattened cells, granulosa cells and are then called primordial follicles. Many oogonia and primary oocytes degenerate during the fifth and sixth months of fetal life, and 4the surviving primordial follicles occupy the periphery of the ovarian cortex (figure 5).From this time on, the number of follicles continues to decline, so that at birth about700,000 are present in the two ovaries, and they are in the last stage of the prophase of their meiotic division. The number of follicles continues to diminish with age so that about 40,000 survive to puberty, and by 30 years of age approximately 10,000 follicles are left. At the time of menopause, only a few hundred follicles persist in the ovaries.

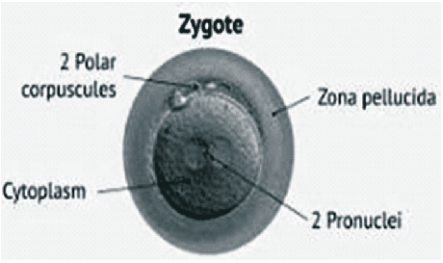


Figure 4: The Zygote

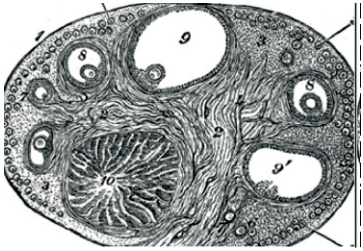


Figure 5: Maturation of an Ovarian follicle

From puberty, the ovarian cycles begin as a result of hormonal stimulation from the pituitary gland. During the reproductive life-span of the woman (between puberty – the age at which the reproductive organs are functionally active, and menopause – the end of the period of possible sexual reproduction, as evidenced by the cessation of menstrual periods), some follicles in both ovaries are chosen randomly each month to begin the final meiotic process. Of these follicles, usually only one reaches maturity and is ovulated, and subsequently undergoes the complete meiotic sequence. The remaining follicles degenerate and become atretic follicles. It has been estimated that only about 300 to 400 follicles reach full maturity and liberate their ova from the ovaries during the reproductive life of a woman. The mature ovum has a diameter of about 120μm.

4.2 The Male Sex Cell and Spermatogenesis

On the other hand, spermatogenesis (fig. 7) is the sequence of events by which the primordial male germ cells, spermatogonia, are transformed into the mature male reproductive cells, spermatozoa, within the testes. The spermatogonia are of two types, A and B. The type A are the stem cells which undergo mitotic division to form additional type A and a more differentiated type B spermatogonia. The type B then divide further by mitotic activity into primary spermatocytes, which migrate toward the middle zone of the seminiferous tubule and then undergo meiotic division into smaller secondary spermatocytes. The latter cells contain half the number of

chromosomes as the primary cells. The secondary spermatocytes further divide into even much smaller cells, spermatids, which become attached to the free surfaces of adjoining giant supporting or Sertoli cells. The spermatids then undergo a series of morphological changes and transform to become spermatozoa.

Like oogenesis, spermatogenesis begins at puberty or about 14 years of age. However, the process is delayed or completely stalled if the testis fails to descend into the scrotum from its original position in the abdomen. It is important to know that spermatogenesis can only thrive in a lower temperature outside the body than that within the body cavity. It is also of interest to know that neither all the seminiferous tubules, nor all the portions of the germinal epithelium within a single tubule are actively producing spermatozoa at the same time. At the end of spermatogenesis, the spermatozoa become detached from the Sertoli cells and lie free in the fluid of the seminiferous tubules. The average size of a spermatozoon is about 4 μm(Diameter of the head).

The average concentration of spermatozoa in an ejaculate is about 100 million per milliliter. Of this number, about 25 percent are non-motile, and about another 20 percent are morphologically abnormal, leaving only about 50 percent structurally and functional active spermatozoa, which are propelled forward by the undulating and rotatory movements of

their tails. On the other hand, as many as 10 percent of the spermatozoa in an ejaculate may be abnormal without loss of fertility. However, it has been estimated that about 10 to 20 percent of marriages are sterile, and in about one-third to one-half of such cases the male factor is responsible.

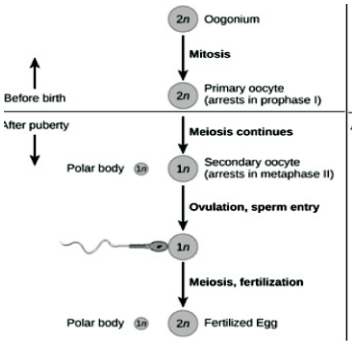


Figure 6: Oogenesis

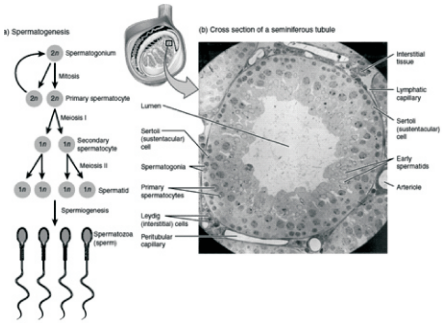


Figure 7: Spermatogenesis

4.3 Further Development of the Zygote

Chromosomes become organized in the center of the fertilized ovum (***zygote***) and the 23 paternal and 23 maternal chromosomes split longitudinally at the centromere in the first ***cleavage*** (mitotic) division. The zygote reaches the two-cell stage at about 30 hours after fertilization. The further rapid successive mitotic divisions of the zygote produce a large number of smaller cells, ***blastomeres***. Collectively, the blastomeres have the appearance of a mulberry and are called ***morula*** (fig. 8). As the cells continue to divide, the morula is gradually propelled down the uterine tube by the peristaltic contraction of the smooth muscle in its wall and the ciliary beating of its epithelial lining. The secretions of the glandular

epithelium also provide a fluid vehicle in the transport of the morula. The morula enters the uterine cavity at about the twelve- to sixteen-cell stage, within 5 to 8 days post ovulation. Glandular secretions of the uterine wall penetrate the zona pellucida and diffuse between the cells of the morula to form two groups of cells, a centrally placed ***inner cell mass*** which issurrounded peripherally by an ***outer cell mass***. (fig.8).The cells of the inner cell mass develop into the tissues of the embryo, while those of the outer cell mass form the trophoblast.

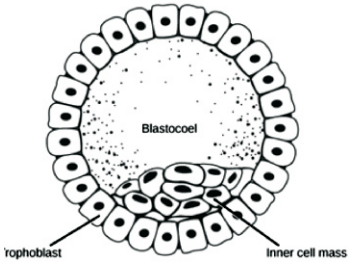


Figure 8: The Blastocyst

4.4 Reproductive Technology

The spermatozoa and the secretions of the accessory glands, which include those of the seminal vesicles, prostate, bulbourethral glands, and penile urethral glands constitute the seminal fluid or semen. When an ejaculate of spermatozoa is maintained in the environment of these natural secretions and stored below zero-degree temperature, a sperm bank can be obtained for artificial insemination. This is the realm of assisted reproductive technique. Medically assisted fertilization is becoming increasingly common. Intra-uterine insemination (IUI) and in vitro fertilization (IVF) are two frequently used

assisted reproductive techniques. During IUI, semen is inseminated into the uterus using a catheter with fertilization taking place inside the body. On the other hand, with IVF eggs are removed from the ovaries and fertilized in a laboratory (outside the body). The blastocyst is then implanted in the uterus.

5.0 TINY LIVES AND FAMILIES AFTER BIRTH

Almost all cells in the body evolve as free-living organisms and show some measure of specializations. However, natural selection favoured more complex communities of cells, where group of cells specialize during development to carry out specific functions as tissues and organs. Tissues are aggregates of cellular units which are adapted to perform a specific function in a coordinated manner, while organs are structural units brought together by more than one tissue, which performs a particular function. On the basis of their structure, most tissues are divided into four major types: epithelia, connective or supporting, muscular and nervous tissues.

5.1 Epithelia

Epithelial tissues are composed of closely aggregated cells that are in opposition over a large part of their surface with little intercellular spaces. In its simplest form, epithelium consists of a single continuous layer of cells of the same type covering the body surfaces or line the body cavities. However, multiple layers may develop and the cells may differentiate into two or more kinds. Epithelial tissues are characterized by a high cell density and a well-defined polarity with a basal end of the cell and a luminal end. The basal end sits on a basement membrane,

while the luminal end normally faces the surface, which is mostly hollowed surfaces such as intestinal, respiratory, urinary and reproductive lumen, or the bloodstream. Epithelial cells are joined in sheets by intercellular junctions. The basement membrane provides mechanical support and attachment for the epithelial cells. In the kidney, for example, the basal lamina also provides a barrier for the filtration of blood components during the formation of urine. Many epithelial cells have specializations of their luminal or apical surfaces, such as microvilli or cilia.

5.1.1 Origin and Distribution of Epithelium

Developmentally, epithelia are derived from all three of the germ layers of the early embryo. For example, the epidermis of the skin and the epithelium of the cornea, which cover the entire external surface of the body develop from the ectoderm. However, by invagination and proliferation, this outer covering epithelium gives rise to tubes or solid cords which form the glandular appendages of the skin, like the sudoriparous, sebaceous, and mammary glands. Similarly, the digestive tract is lined by epithelium of endodermal origin, while its associated glands (liver, pancreas, gastric and intestinal glands) arise by invagination and specialization of epithelial outgrowths from the lining of the primitive gut. Exocrine glands in the adult communicate with an internal cavity or an external surface by way of ducts that open unto the epithelium of the inner or outer surface layer from which it developed during embryonic life. Endocrine glands, on the other hand, normally lose their connection with the surface epithelium. Furthermore, there are

several lining layers and solid organs, such as the kidney and epithelia of the male and female reproductive tracts, which are derived from mesoderm. In addition, the linings of the peritoneal cavity and other serous cavities are termed mesothelial (mesodermal), while it is convenient and customary to refer to the linings of blood and lymph vessels as endothelial. Epithelia are specialized for a variety of functions, which include secretion, absorption, excretion, protection, transport, and sensory reception. Those that cover the outer surface of the body are adapted to protection of the organism against mechanical damage and loss of moisture. They are also involved in sensory reception, as they contain nerve endings that convey impulse of pain sensation. Others contain neural elements like taste buds and olfactory cells, which are chemical receptors.

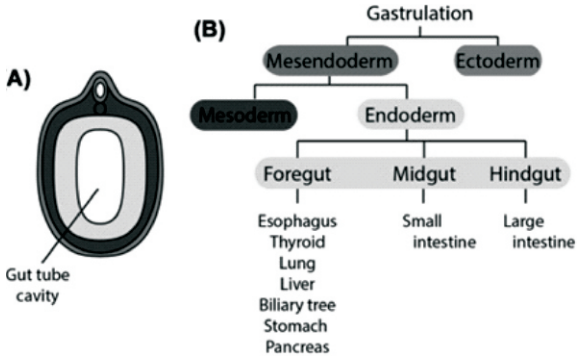


Figure 9: Germ Layers and Endoderm Cell Lineage

5.1.2 Classification of Epithelial Cells

Epithelia are classified and named according to the following criteria:

i. The number of cell layers. If there is one layer of cells, the epithelium is described as simple; if there are two or more layers, it is referred be stratified.
ii. The shape of their cells. The superficial cells may vary in shape from squamous (flattened), cuboidal, columnar or transitional.
iii. The type of surface specialization. The luminal surface could possess delicate vertical striations known as brush border or microvilli, or could possess motile processes called cilia or the covering epithelium keratinized.

Thus, a single layer of flat cells is a simple squamous epithelium (fig. 10). A single layer of tall prismatic cells is a simple columnar epithelium (fig. 10). The corresponding multiple layered cells are stratified squamous epithelium and stratified columnar epithelium. Within the same class of epithelium, especially among the columnar cells, the free surfaces may have motile cell processes and will be referred to as ciliated simple columnar epithelium or ciliated stratified columnar epithelium.

Similarly, the superficial cells in stratified squamous epithelium may accumulate keratin (a fibrous protein) in their cytoplasm and be reduced to scalelike lifeless residue of cells, keratinized stratified squamous epithelium. Another category among the columnar epithelia is the pseudostratified columnar ciliated type, where all the cells rest on a common basement membrane but are so arranged that the nuclei occur in two or more levels and the epithelium appear as stratified. Also among the stratified category are the transitional epithelium of the urinary tract,

where the cells assume different shapes depending on the activity of the tract.

5.1.3 Glandular Epithelial Tissue

When epithelial cells take up small molecules from the blood and transform them by intracellular biosynthetic mechanisms into a more complex product that is then released from the cell, it is known as secretion. Glandular epithelial cells store and secrete many compounds such as hormones and enzymes.

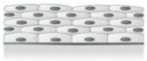
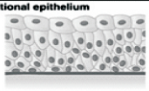
Cells	Location	Function
Simple squamous epithelium 	Air sacs of lungs and the lining of the heart, blood vessels, and lymphatic vessels	Allows materials to pass through by diffusion and filtration, and secretes lubricating substance
Simple cuboidal epithelium 	In ducts and secretory portions of small glands and in kidney tubules	Secretes and absorbs
Simple columnar epithelium 	Ciliated tissues are in bronchi, uterine tubes, and uterus; smooth (nonciliated tissues) are in the digestive tract, bladder	Absorbs; it also secretes mucous and enzymes
Pseudostratified columnar epithelium 	Ciliated tissue lines the trachea and much of the upper respiratory tract	Secretes mucus; ciliated tissue moves mucus
Stratified squamous epithelium 	Lines the esophagus, mouth, and vagina	Protects against abrasion
Stratified cuboidal epithelium 	Sweat glands, salivary glands, and the mammary glands	Protective tissue
Stratified columnar epithelium 	The male urethra and the ducts of some glands	Secretes and protects
Transitional epithelium 	Lines the bladder, uretha, and the ureters	Allows the urinary organs to expand and stretch

Figure 10: Epithelial Tissues

The simplest type of epithelial glands are the unicellular goblet cells, which secrete mucus into the intestinal lumen. Epithelial glands are either exocrine, which secrete either to the outside of the body or into luminal spaces through an excretory duct, endocrine, which are ductless and secretes directly into the blood or lymph for transport to another part of the body.

5.1.3.1 Exocrine Secretion

Exocrine glands have a secretory portion, where granules that accumulate precursors of their secretory product are stored, synthesized and released into the lumen of the gland, and an excretory portion consisting of a duct, which transports the secretory product to the outside. Exocrine glands are classified as unicellular or multicellular. The latter are further classified on the basis of their organization and geometry of the epithelial component, as tubular, alveolar, tubule-alveolar, or saccular. The most common example of unicellular gland is the goblet cell (fig. 16) found among columnar cells of mucous secreting epithelia in the digestive and reproductive tracts.

The simplest form of multicellular gland is a homogeneous sheet of secretory epithelial cells. The surface epithelium of gastric mucosa and the uterine lining at certain stages belong to this category, often referred to as a secretory sheet. Multicellular glands are designated as simple or compound depending upon whether their communication with the surface is branched.

A simple exocrine gland is one in which the excretory duct is

directly connected to the surface epithelium via an unbranched duct. Such glands are further categorized on the basis of their terminal secretory portion into simple tubular (intestinal glands of Lieberkuhn), simple coiled tubular (sweat glands), simple branched tubular (glands of the stomach and uterus, Brunner's gland), and simple alveolar/acinar (sebaceous glands of the skin and meibomian glands of the eyelids).

Compound exocrine glands: the duct of a compound exocrine gland branches repeatedly, and the gland is divided into units called lobes, which themselves are further subdivided into lobules. Thus, there are compound tubular (bulbourethral glands, and some Brunner's gland), compound alveolar/acinar (salivary gland, pancreas and glands of respiratory passages), compound saccular glands (mammary glands and prostate gland), etc.

5.1.4 Types of Secretion

There are three mechanisms by which cells discharge their secretory products.

Merocrine secretion; where the release is by exocytosis. Milk proteins of mammary glands are secreted by merocrine secretion.

Apocrine secretion; involves the loss of part of the apical cytoplasm along with the secretions inside it. In the mammary glands, milk lipids are secreted by apocrine secretion.

Holocrine secretion; where the entire cell disintegrates to release the stored product, or release of the whole cell into the excretory ducts. In sebaceous glands, the cells break down with an outpouring of their cytoplasm and accumulated lipids, while spermatozoa are released wholly from the seminiferous epithelium of the testis.

5.1.5 Endocrine Glands

Endocrine glands arise in the embryo as tubular evaginations or solid outgrowths from lining epithelium. However, in the course of development their connection with the surface is lost, and they are penetrated by blood vessels which form a very rich capillary plexus. The close proximity of the cells to a dense vascular bed favours release of secretory products into the blood. The principal endocrine glands are the hypophysis, thyroid, parathyroid, pancreas, adrenals, pineal, testis, and placenta.

Fully developed endocrine glands are normally dissociated completely from exocrine glandular tissues, but in a few cases, there is relatively little morphological separation between the two types. Examples are the islets of Langerhans (endocrine) scattered throughout the bulk of the exocrine pancreas. Similarly, the Leydig cells (secreting male sex hormone) are located in the interstitial tissue between the seminiferous tubules in the testis. Thus, in these mixed glands, one group of tissues secretes into the external duct system, while the group delivers its secretions directly into the blood.

5.2 Connective or Supporting Tissues

Connective or supporting tissues are derived from mesenchymal multipotent stem cells in the mesoderm. Traditionally, connective tissues consist of cells and extracellular fibers embedded in a matrix of amorphous ground substance, having the properties of a viscous solution or thin gel. The fibers are typically of three kinds, **collagenous**, **reticular** and **elastic**. However, collagenous and reticular fibers are simply different morphological expressions of the same fibrous protein. There are different types of cells in connective tissue, categorized into a relatively stable population of fixed cells and a population of motile wondering cells.

The fixed cells include **fibroblasts** (the principal cells of connective tissue), responsible for the production and long-term maintenance of the extracellular matrix (ECM), as well as **adipose** cells (for the storage of energy reserve). Fibroblasts produce the mature proteoglycans of the ECM and the precursors collagens (**tropocollagen**) and the elastins (**tropoelastin**). The wondering cells include:

Lymphoidcells- the smallest of the wondering cells are shown to recirculate from blood to lymph and back to blood. They are essential agents of the immune system by their ability to generate antibody forming cells, and effectors of cell-mediated immunity.

Freemacrophages- are cells of the immune system which can

phagocytose and digest bacteria, cell debris and other unwanted materials.

Eosinophils- are the as the eosinophilic leukocytes of the blood. They are abundant in the lamina propria of small intestine. They contain several enzymes which include peroxidase, ribonuclease, aryl-sulfatase, etc. It may increase in number in various parasiticinfections involving hypersensitivity, such as asthma and hay fever.

Plasma cells – are antibody-secreting mature B cells of the immune system.

Mast cells - are cells of the immune system that contain granules, some of which contain histamine and other mediators of inflammation, and can be released following exposure to environmental allergens.

The local structural requirements vary from one region to another, and determine the relative abundance of the various kinds of cells, fibers, and ground substance. The ground substance can be preserved by freeze-drying method, and gives a periodic acid-Schiff reaction for carbohydrates (**glycosaminoglycans** - a mucopolysaccharide) and stains metachromatically with toluidine blue. The ground substance also contains structural proteins such as **laminin** and **fibronectin**.

5.2.1 Classification of Connective Tissues

5.2.1.1 General Connective Tissue

Classification of connective tissues is difficult but descriptive terms are used to assign the phrase **g**eneral connective tissue to include areolar or loose connective tissue, where the fibers are loosely woven or dense connective tissue, when the fibers are densely packed. In the second category, when the fibers are arranged in an orderly parallel bundle (as in tendons and ligaments) or in flat sheets (as in aponeurosis), it is referred to as dense regular connective tissue, while disordered fibers as in the dermis of the skin or submucosa of digestive tract, constitute dense irregular connective tissue. Depending on the predominating feature, the following loose connective tissues are identified; mucous connective tissue, elastic tissue, reticular tissue, adipose tissue, pigment tissue, etc.

5.2.1.2 Specialized Connective Tissue

Apart from the general connective tissues, there are specialized connective tissues which include the blood, adipose tissue, cartilage, bone, and teeth.

5.2.1.2.1 Cartilage

It is solid but flexible and resists compression while allowing diffusion of water through the matrix. It lacks blood supply but allows metabolic substances to be exchanged by diffusion. Chondrocytes are the mature cartilage cells, which are usually trapped in cavities called lacunae within the ECM. Growing cartilage cells are the chondroblasts, which are metabolically

active and secretes proteins, and contain reserves in the form of lipids and glycogen. The ground substance contains large amounts of chondroitin sulphate and hyaluronic acid bound in a lattice of type II collagen. Depending on the relative abundance of the fibrous components, the following types have been identified; **Hyaline cartilage**(fig.11)–it contains primarily the type II collagen fibers and forms most the embryonic skeleton. In the adult, it forms the sternal part of the ribs, the cartilage of the trachea, larynx, and nose. It also forms the articular cartilages at the end of long bones.

Elastic cartilage – it contains primarily elastic fibers. It forms the epiglottis and the pinna of the external ear.

Fibrocartilage – it contains type I collagen and has more compressibility than hyaline cartilage but with less matrix. It is found in areas with high pressure like the interverbal discs and the knee joint.

Perichondrium covers hyaline and elastic cartilages, and has chondroprogenitor potentials.

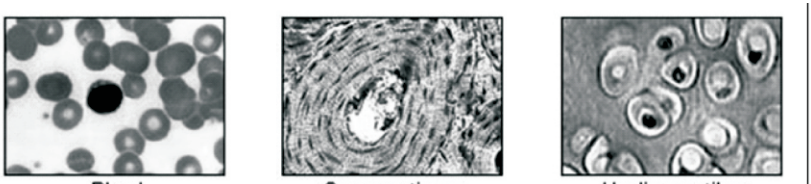


Figure 11 Specialized connective tissues

5.2.1.2.2 Bone Tissue

Bone and cartilage have similar structure, except that the extracellular matrix in bone is much compact with more of type 1 collagen fibers. Secondly, the matrix is highly mineralized in bone, thus making it a very rigid tissue that forms the skeleton of the body. The ground substance contains the glycoprotein, osteocalcin, which specifically binds to calcium. The bone cells are called osteoblasts, which produce the matrix osteoid and calcium phosphate.Crystals of calcium hydroxyapatite which are formed by the addition of hydroxide and bicarbonate ions to the amorphous calcium phosphate, accumulate around the immature bone cells, osteoblasts, which later converts to osteocytes.

Types of bone: There are basically two types of bone, namely spongy or woven and compact or lamellar.

Spongy bone – This is produced when the osteoid is secreted rapidly as in the embryo or during the early repair of a fracture. It is an immature form, that is relatively weak and has randomly organized collagen fibers.

Compact bone (fig. 11)–when the collagen is highly organized into layers or lamellae, then the spongy arrangement is remodeledinto compact bone. Compact bone apart from having a highly organized structure, is highly vascularized. Mature bone is continually being remodeled due to the activity of osteoclasts, which breakdown and osteoblasts, which replace it.

5.2.1.2.3Adipose Tissue

These are derived from the mesenchymal stem cells, and specifically from a common precursor cell, the preadipocyte. There are two types of adipose; white and brown.

White adipose tissue - White adipose tissue contains large adipocytes, whose entire cytoplasm are completely occupied by a single locule or droplet of fat. The nucleus is flattened and pushed to one side and the cytoplasm exists as a ring around the fat droplet. It is found throughout the body, and particularly under the skin and around abdominal organs. Adipose tissue serves as the body's most capacious reservoir of energy, containing about 80% triacylglycerol, and also function as a shock absorber and insulator. About 10% of the total body weight of an average man is fat. The distribution of adipose tissue varies with age and gender, it is much abundant in the female and typically increasing with age.

Brown adipose tissue- Brown fat is well differentiated as early as the twenty-eight weeks in the human fetus and in the newborn constitutes about 2 - 3% total body weight. However, it is less abundant in adult man and occurs only in certain specific areas, but are most abundant in hibernating species. It is highly vascularized and contains multiple droplets of fat that surround a large central nucleus. The cells contain large numbers of mitochondria that metabolize the fat without producing ATP. This uncoupling action of the mitochondria produces heat when

the cells are stimulated by the sympathetic autonomic nervous system. The colour of the large number of cytochromes (electron transport chain molecules) present in the mitochondria gave rise to the name.

5.2.1.2.4 Blood

Blood (fig. 11) is considered as connective because it is derived from the common germ layer as the others, mesoderm. Secondly, its cells (red blood cells, white blood cells, platelets) are also contained in a matrix, the blood plasma. However, unlike the other connective tissues, it does not provide mechanical support nor interconnect between tissues. Thirdly, blood contains the soluble protein fibrinogen, which is converted into insoluble fibers, fibrin during blood clotting. Platelets are important in controlling bleeding by plugging small holes in blood vessels, and their direct involvement in the clotting cascade (usually, more platelets are mobilized to the bleeding site and thrombin in the system acts to change fibrinogen into fibrin, thereby helping to stabilize the platelet plug). The different elements of blood provide metabolic support by carrying nutrients and waste materials, as well as immune production. They also transport white blood cells and antibodies around the body.

5.2.1.2.5 Teeth

The tooth is basically made of three parts or layers. The external surface of the tooth, crown, is covered by the enamel (the hardest

substance in the body). It consists primarily of calcium phosphate. The middle layer consists of the dentine, a mineralized matrix like bone, though without cells. The dentine contains the pulp cavity, which also contains the special cells, odontoblasts responsible for production of the dentine, as well as blood vessels and nerves that supply the teeth. A narrow channel at the root of each tooth, the root canal, provides the site for leaving or entry of nerves and vessels. Cementum, which is a thin layer of calcified tissue, covers the embedded part of the tooth into the jaw bone. It provides protection and anchor to the teeth.

5.3 Muscle Tissue

Muscle tissue consists of contractile cells. Though there are contractile cells which are not muscle tissue, for example pericytes that surround blood vessels. There are two main categories of muscle, smooth and striated. Striated muscle exhibits regularly spaced transvers bands along the length of the fiber. Striated muscle is further divided into two distinct types, skeletal and cardiac. Skeletal muscle fibers are syncytial, they are innervated by cerebrospinal nerves and contraction is voluntary. Cardiac muscle fibers are made up of separate cellular units, and their rhythmical contraction is involuntary. On the other hand, smooth muscle is composed of individual cellular units, and innervated by autonomic nervous system.

In general, the visceral musculature is made up of smooth

muscle, while the somatic musculature comprising the muscles of the body wall and the limbs is skeletal muscle. The muscle of the heart constitutes cardiac muscle. All muscle cells contain the contractile proteins, act in and myosin, although their arrangements differ among the different muscle types.

5.3.1 Smooth muscle

Smooth muscle consists of elongated spindle-shaped cells which taper at both ends. Each cell is longitudinally shorter than skeletal muscle cell, and contain a single elongated central nucleus. The muscle fibers are arranged in offset disposition, where the narrow tapering end of one aligns with the middle-expanded end of another. In transverse sections, smooth muscle therefore presents a mosaic of rounded or irregularly polygonal profiles varying from less than 1 μm to several micrometers. The cytoplasm of muscle cells is known as sarcoplasm. Under special staining and gentle maceration, fine longitudinal striations can be demonstrated running the full length of the cell, called myofibrils which are the contractile units or materials of the muscle cell. They are doubly refractile under polarizing microscope but no banding profile as in skeletal muscle.

Smooth muscles are specialized to produce relatively slow, low force contraction with little energy requirement. However, under certain conditions such as during labour, it can produce very forceful contractions. Muscle contraction is usually spontaneous and may be affected by the influence of the

autonomic nervous system, hormones and other local factors like stretching. Smooth muscle fibers have the potential to divide and hypertrophy in response to increased stress. This is usually a problem in hypertension, where the blood vessels respond to increase in blood pressure by increasing the thickness of the smooth muscle layer. This in turn reduce the diameter of the lumen and further increase the resistance to blood flow, with a facultative increase in blood pressure.

5.3.2 Skeletal muscle

The histological unit of skeletal muscle is the muscle fiber, which is a long cylindrical multinucleated cell, between 10μm to 100μm in diameter and sometime extending the whole length of the muscle, as in the **sartorius** muscle. The nuclei are located at the periphery of the fiber immediately beneath the **sarcolemma**. As might be expected in a multinucleate syncytium, there are also multiple small Golgi bodies, which are located near one pole of each nucleus throughout the muscle fiber. Mitochondria are also abundant near the poles of the nuclei, immediately beneath the sarcolemma, and in the interior between the myofibrils. Large numbers of parallel muscle fibers are grouped into **fascicles**, which are visible to naked eye in fresh state. The entire muscle is enclosed by a connective tissue layer called **epimysium**. Thin collagenous septa extend inward from the epimysium to surround each fascicle called **perimysium**, from which extend delicate reticulum that invests the individual fibers know as **endomysium**.

They have a distinct banded appearance, which is due to the regular arrangement of the myosin and actin filaments into repeating units called sarcomeres. It is this banded appearance that is referred to as striated. The **myofilaments** which make up the **sarcomeres** are arranged in cylindrical myofibrils, which are grouped together to form the muscle fibers. The shortening of muscles during contraction occurs because of the overlap between the thin actin and the thick myosin filaments, a process which is triggered by calcium release from within (intracellular reserve). These calcium stores of **sarcoplasmic reticulum** form a network of flattened sacs surrounding the sarcomeres and are connected to the surface via **T-tubules**. Contraction of skeletal muscle is controlled by the central nervous system through specialized nerve junction called **neuromuscular junctions**.

Muscle fibers are adorned with muscle precursor cells known as **satellite cells**, which are usually quiescent but can quickly resume proliferation and increase the muscle mass when there is damage or stress to the muscle, as it occurs in weight lifters or body builders. This phenomenon is referred as **hypertrophy of use**. Conversely, the fibers may become thinner in muscles immobilized for long periods, as in the treatment of fractures called **atrophy of disuse**.

5.3.3 Cardiac muscle

Cardiac muscle is the muscle of the heart, and consists of striated muscle fibers which differ in several respects from those of

skeletal muscle. (a). The fibers are not in syncytium but made up of separate cellular units which are joined end-to-end by special surface specializations, intercalated discs that run across the fiber. (b). The fibers are not simple cylindrical units, but branch or bifurcate and connect with adjacent fibers to form a three-dimensional complex. (c). The elongated nuclei of the muscle fibers are usually deep in the interior of the cell instead of being peripheral. (d). The major physiological difference between the two are the spontaneous nature of the beat of cardiac muscle and its rhythmical contraction that is involuntary.

The intercalated discs have large numbers of gap junctions, that allow electrical communications between the cells, and adhering junctions which bind the cells together to form a network of electrically and mechanically interconnected cells. In the repeating pattern of cross striations, the intercalated discs occur at the level of the I band and can be demonstrated by iron-hematoxylin or phosphotungstic acid-hematoxylin preparations. Due to their high metabolic demands, the muscle fibers have large numbers of mitochondria and a rich blood supply. Specialized regions of the heart are electrically unstable and form pacemaker areas. Such areas could trigger rhythmic muscular contractions in the absence of nervous input, which are then transmitted throughout the heart via low resistance pathways to ensure coordinated contraction of different areas of the heart. This intrinsic rhythm could be modified by both nervous and hormonal actions. There are no stem cells in cardiac

muscle, hence recent research is investigating if stem cells from other parts of the body can be injected into the heart and subsequently induced to replace damaged cardiac muscle. However, heart muscle can also hypertrophy due to an increase in the size of cells and the addition of myofibrils.

5.4 Nervous Tissue

The nervous tissue is comprised of the **central nervous system** (CNS) and the **peripheral nervous system** (PNS). The CNS consists of the brain and spinal cord, while the PNS is made up of all nervous tissues located outside the brain and spinal cord. The unit or principal cell of the nervous system is the **neuron**. Another type of cells that are found both in the CNS and PNS are the **neuroglia**. Other minor cell types present in the brain are the **ependymal cells**, which are epithelial cells that lines the cavities or ventricles of the brain and **choroid epithelial cells** which are involved in the secretion of cerebrospinal fluid.

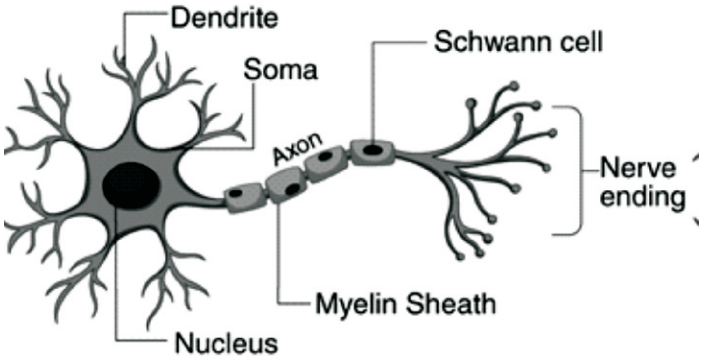


Figure 12: The Neuron

5.4.1 Neurons

The neuron (fig. 12) is the brain cell that receives signals, processes them and transmit the appropriate response to another neuron or an effector cell (a secretory cell or a muscle). The neuron has the following components, the cell body (**perikaryon**) and numerous nerve processes. The nerve cell body contains the nucleus and other intracellular organelles concerned particularly with protein biosynthesis and secretory processes. Large numbers of ribosomes associated with rough endoplasmic reticulum are present as darkly staining **Nissl bodies**. **Dendrites** are branching processes that receive stimuli and conduct the neurons impulses so generated toward the nerve cell body.Most stimuli affecting nerve cells are chemical messengers or transmitters that are secreted from one neuron to another adjacent neuron. The **axon** (**axis cylinder**) is a single unbranched nerve process that conducts impulses away from the perikaryon to other parts of the nervous system or a muscle tissue or a secretory gland. At the start of an axon is an area called the **axon hillock** or **trigger zone** where electrical signals, known as action potentials, can be generated. These are then propagated along the axon.

Neurons can be classified majorly into three different types, based on the position and number of dendrites and the position of the axon hillock namely, multipolar neurons, bipolar neurons, and pseudo-unipolar neurons. Neurons in general have a very high metabolic rate, they therefore need a continuous source of oxygen and glucose. Any interruption in the supply is critical

and may lead to the death of deprived neurons. During development epithelial cells lining the neural tube give rise to neuroblasts, that divide mitotically to produce amitotic neurons of the brain. The mature brain does not contain neurons which can divide. Thus, neurons that die cannot usually be replaced. The implication of this is that brain tumours associated with neurons are rare and occur only in children as neuroblastomas. However, neural stem cells have now been isolated from both fetal and adult brains. These cells do not normally divide in adults but current research is focusing on the possible conditions that can stimulate these 'stem cells' to divide in order to replace damaged brain tissue.

5.4.2 Glial cells

Glial cells make up about half the brain mass and outnumber neurons by about 10 times. In addition to many other functions, glial cells provide structural and metabolic support, electrical insulation and immune activity. Three types of glial cells have been identified, namely **astrocytes**, **oligodendrocytes** and **Schwann** cells, and **microglia**. The first two are collectively called macroglia, and like the nerve cells, are ectodermal in origin, while microglia are said to originate from mesodermal cells of the pia mater but migrate into the central nervous system along the blood vessels.

5.4.2.1 Astrocytes

They are of two varieties, protoplasmic and fibrous astrocytes. The protoplasmic astrocytes have a larger nucleus than

oligodendrocytes and microglia, abundant granular cytoplasm and numerous thick processes, and are found mainly in the grey matter. Fibrous astrocytes contain large numbers of filaments and are found in the nerve bundles of the white matter of the brain. They have a number of fine processes that surround neurons, capillaries and ependymal cells lining the ventricles. These astrocytic end-feet do not touch the capillaries but release factors that induce blood-brain barrier in the capillary endothelial cells. Astrocytes are also important in regulating K^+ levels around neurons and a store of glycogen, in the form of lactate. Astrocytes control the distribution of neurotransmitter substances from neurons, first by restricting the diffusion and secondly by transporting them into the astrocytes, where they are metabolized or recycled. The precursors of astrocytes are the radial glial cells, which span the cerebral cortex to form scaffolding for the migration of new nerve cells early in development.

5.4.2.2 Microglia

They are small cells with long spiny processes. The nucleus is small and surrounded by scant protoplasm. Early in development, they act as macrophages removing debris produced by the programmed cell death that occur at this stage, in addition to releasing growth factors. In adult life, they are relatively quiescent, except in times of injury or insult to the nervous system, when they revert to their phagocytic role as macrophages.

5.4.2.3 **Oligodendrocytes** and **Schwann cells**

They electrically insulate nerve axons in the central nervous system (oligodendrocytes) and peripheral nervous system (Schwann cells). Many peripheral nerve axons are encased in a wrapping of multiple lipid bilayers of their plasma membranes, myelin sheath (Schwann sheath).Each Schwann cell contributes myelin to one segment (or internode) of the axon, between two adjacent Schwann cell internodes is a small gap called the node of Ranvier. Some fibers have no myelin sheath but retain a single wrapping of cytoplasm from Schwann cells, and are referred to as unmyelinated. In the brain and spinal cord, cell bodies and unmyelinated axons occupy the grey matter, while the white matter is predominantly made up of myelinated axons.

Schwann cells have a role in the regeneration of peripheral axons following injury. When the tip of the broken axon makes contact with a Schwann cell, it stimulates mitoses in the Schwann cell, which then extends processes towards the growth zone of the axon. The axon at the rate of 2mm to 5mm per day along the Schwann cell, which also re-myelinate the new axon.

Oligodendrocytes can myelinate more than one axon and the cell body lies between them. Damaged neurons in the CNS do not seem to regenerate successfully because CNS glial cells release factors that specifically inhibit axon growth. In the experimental treatment of Parkinson's disease, the application of fetal cells or neural stem cells may be useful, which is the new direction of current research.

5.5. Organs and Systems

Organs consists of two or more tissues, and form distinct structural units with specific functions. A few examples of organs include the heart, lungs, liver and kidney. Many activities of the body are performed by more than one organ. For example, the **urinary system** requires the kidneys, urinary bladder, and the genital organs, the **cardiovascular system** requires the heart and blood vessels, operating in a coordinated fashion. On the order hand, the endocrine system coordinates all hormone-secreting organs and are stimulated by feedback from almost all other organs of the body.

6.0 TINY LIVES AND FAMILIES: THE NEXUS

The term "tiny lives" refers to the building blocks of tissues, organs and organ systems, which are the cells (fig. 13)). On the other hand, "families" refer to the composite tissues, organs and organ systems of the human organism. Therefore, the phrase "tiny lives and families" refers to the cells and their aggregate components which become tissues, organs and organ systems of the organism. The detailed study of the structure, special arrangement and functions of these building blocks and its organized tissues constitutes the realm of histology or microscopic anatomy, and thus forms the common factor connecting the life before birth and that after birth. There are estimated 70 trillion cells in the average human body. The average age of a cell in the human body is 7 years. Approximately 1 million cells die every second. Brain cells can

die if deprived of oxygen for more than three minutes, while muscle cells can live on for several hours. Bone and skin cells, on the other hand, can stay alive for several days. The size of a typical human cell ranges from 10 to 100 micrometer (μm). The ovum is the largest cell in the human body, measuring about 0.1mm, while the smallest cell is the spermatozoon, which is about 4 – 5 μm., which is the same size as the granule cell of the cerebellum.

Early developmental cells could either be totipotent, or pluripotent, or multipotent. Pluripotent cells are capable of developing into different cells, while a totipotent cell has the potential to divide until it creates an entire, complete organism. Embryonic stem cells (ESCs) are an example of pluripotent cells, similar to a type of "lab made" stem cells called "induced pluripotent stem cells (IPS cells). Embryonic stem cells are obtained from the embryo, which is the stage of the organism between the zygote and fetus. At this point the embryonic stem cells have the ability/capacity to both self-renew and give rise to differentiated cells of any part of the body (blood, nerve, muscle, bone, etc.) It is this ability to become any type of cell in the body that is called pluripotency. Pluripotent stem cells can divide into most, or all, cell types in an organism, but cannot develop into an entire organism on their own.

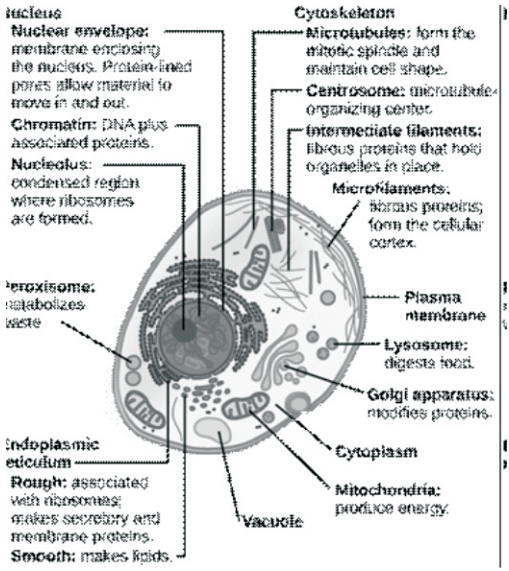


Figure 13: A Typical Eukaryotic cell

Stem cells research originated in the context of two major embryological questions of the 19th century: the continuity of the germ-plasm and the origin of the haemopoietic system. Theodor Boveri and Valentin Hacker used the term to describe cells committed to give rise to the germline, while other scientists used it to describe a proposed progenitor of the blood system. Stem cells provide an opportunity to investigate the mechanisms that regulate embryonic development, cellular differentiation, and organ maintenance. Given their proliferation and differentiation capacities, stem cells have great potential for the development of novel cell-based therapies. In addition, recent

studies suggest that dysregulation of stem cell properties may be the origin of certain types of cancer. Totipotent cells can form all the cell types in the body, including extraembryonic and placental cells. Embryonic cells within the first couple of cell division, after fertilization that are capable of forming the entire human body, are the only cells that are totipotent, so called because its potential is "total". On the other hand, multipotent cells can develop into more than one cell type, but are more limited than pluripotent cells; adult stem cells and cord blood stem cells are considered multipotent.

There are about 200 different types of cells in the human body. The main cellular components of the human body include:

Cell Types	Percentage (%) Cell Count
Erythrocytes	84.0
Platelets	4.9
Bone marrow cells	2.5
Vascular endothelial cells	2.1
Lymphocytes	1.5
Hepatocytes	0.8
Neurons and glial cells	0.6
Bronchial endothelial cells	0.5
Epidermal cells	0.5
Respiratory interstitial cells	0.5
Adipocytes (fat cells)	0.2
Dermal fibroblasts	0.1
Muscle cells	0.001
Other cells	2.0

6.1 The Germ Layers

During gastrulation of the blastula three primary germ layers are formed, namely: Ectoderm (dorsal layer),Mesoderm (intermediate layer), and Endoderm (most inner or ventrally-located layer).

6.1.1 Cells Derived Primarily from Ectoderm

Exocrine Secretory Epithelial Cells include: Salivary gland mucous cell, Salivary gland serous cell, Von Ebner's gland cell in tongue (washes taste buds), Eccrine sweat gland dark cell (secretes glycoprotein), Eccrine sweat gland clear cell (secretes small molecule), Apocrine sweat gland cell (secretes odoriferous substance, sex-hormone sensitive), Gland of Moll cell in eyelid (specialized sweat gland), Mammary gland cell (secretes milk), Lacrimal gland cell (secretes tear), Ceruminous gland cell in the ear (secretes earwax), Sebaceous gland cell (secretes lipid-rich sebum), Bowman's gland cell in the nose (washes olfactory epithelium), Hormone-Secreting Cells, Anterior/intermediate pituitary cells (Corticotropes, Gonadotropes, Lactotropes, Melanotropes, Somatotropes, Thyrotropes), Magnocellular neurosecretory cells (secretes oxytocin and vasopressin), Parvocellular neurosecretory cells (secretes thyrotropin releasing hormone (TRH), corticotropin-releasing hormone (CRH), vasopressin, oxytocin, neurotensin, and prolactin), Chromaffin cells (adrenal gland). Outer ectoderm give rise to epidermis of skin, and epidermal derivatives such as hair, nails, sebaceous glands, olfactory epithelium, mouth epithelium (anterior pituitary, tooth enamel,

cheek epithelium), lens, cornea.Neural ectoderm gives rise to the central nervous system, neural pituitary, spinal cord, motor neurons, retina, and neuroglia.Neural crest ectoderm/cells give rise to dorsal root ganglia, autonomic ganglia, peripheral nervous system (Schwann cells, neuroglial cells, sympathetic and parasympathetic nervous system), adrenal medulla, facial cartilage, odontoblasts, melanocytes, APUD cells.

6.1.2 Cells Derived Primarily from Mesoderm

Further in development, the mesoderm is divided into four subregions, namely: Chordamesoderm which forms the notochord (a transient organ whose major functions include inducing the formation of the neural tube and establishing the anterior-posterior body axis. Paraxial mesoderm, which gives rise to the forming somites in the body and the unsegmented mesoderm of the head region.Intermediate mesoderm, which gives rise to the urogenital system.Lateral plate mesoderm (comprised of splanchnic and somitic mesoderm), which contributes to the heart progenitors, blood vessels and blood cells of the circulatory system.Each of these gets segmented and further gives rise to different tissues as shown in figure 14 below. The most prevalent mesodermal derivatives are the supporting tissues, including connective tissues, skeletal muscles, bones and cartilage. Other derivatives include the smooth muscles, walls of the heart, blood and lymph vessels, blood and lymph cells, adrenal cortex, dermis of skin, kidneys, gonads and their corresponding ducts, and spleen.

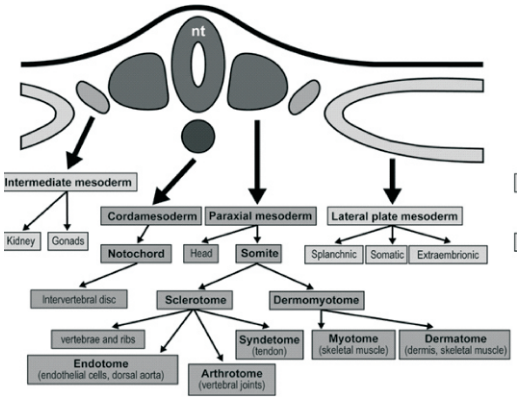


Figure 14: Derivatives of Mesoderm

6.1.1 Cells Derived Primarily from Endoderm

Exocrine Secretory Epithelial Cells include: Brunner's gland cell in the duodenum (enzymes and alkaline mucus), Stomach - foveolar cell (mucus secreting), Chief cell (pepsinogen secretion), parietal cell (hydrochloric acid secretion), Paneth cell of small intestine (lysosome secretion), Insulated goblet cell of respiratory and digestive tracts (mucus secretion), Pancreatic acinar cell (bicarbonate and digestive enzyme secretion), Type II pneumonocyte of lung (surfactant secretion), Club cell of lung, Barrier Cells, Type I pneumonocyte (lung), Gall bladder epithelial cell, Centro acinar cell (pancreas), Intestinal brush border cell (with microvilli), Hormone Secreting Cells, Enteroendocrine cells, K cell (secretes gastric inhibitory peptide), L cell (secretes glucagon-like peptide-1, peptide, oxyntomodulin, and glucagon-like peptide-2), I cell (secretes cholecystokinin, CCK), G cell (secretes gastrin), Enterochromaffin cell (secretes serotonin), Enterochromaffin-

like cell (secretes histamine), N cell (secretes neurotensin), S cell (secretes secretin), D cell (secretes somatostatin), M /Mo cell (secretes motilin), Other hormones secreted: vasoactive intestinal peptide, substance P, alpha and gamma endorphin, bombesin.Thyroid gland cells (Thyroid epithelial cell and Parafollicular cell). Parathyroid gland cells (Parathyroid chief cell and Oxyphil cell). Pancreatic Islets (Islet cells of Langerhans) which include: Alpha cell (secretes glucagon), Beta cell (secretes insulin and amylin), Delta cell (secretes somatostatin), Epsilon cell (secretes ghrelin), PP cell /gamma cell (secretes pancreatic polypeptide).

6.2 Cell-Cell Communication

Cells need to be able to communicate with each other effectively in order to perform a number of functions. For example, imagine a situation where the brain could not tell the leg muscles to contract to bring about the action of walking, or the urinary bladder could not tell the brain that it was full and about to void, or an infection had been contracted and the immune system had not been contacted. Some cell-to-cell interactions are transient, such as the interactions between cells of the immune system and the interactions that direct white blood cells to sites of tissue inflammation. In other cases, stable cell-to-cell junctions play a key role in the organization of cells in tissues.

The most common method of cell-to-cell interaction/ communication is through the use of chemicals called signaling molecules. The cell secretes these molecules out. Other cells detect the presence of the signaling molecules through receptors

present on their surface.There are four basic categories of chemical signaling found in multicellular organisms, as follows:

- paracrine signaling, cells that are near one another communicate through the release of chemical messengers (ligands that diffuse through the space between them). This kind of signaling over a relatively short distance is paracrine. Estrogens produced in the ovaries are good examples of paracrine hormones, and are crucial for the maturation of ovarian follicles.
- autocrine signaling; where a cell targets itself, releasing a signal that can bind to receptors on its own surface to initiate signal transduction. An example of autocrine signals is cytokine interleukin-1 in monocytes. Autocrine signal is an amplifier or a brake for message transmission.
- endocrine signaling; unlike autocrine and paracrine hormones, endocrine hormones are secreted into the blood stream and act on distant target cells, not self or local cells. Endocrine signaling is also relatively slower because it relies on blood flow. Examples are estrogen and testosterone.
- signaling by direct contact.

  There are some other types of cell-to-cell interactions, some of which are meant for big molecules that enter and exit the cell, vis endocytosis (entering the cell) and exocytosis (exiting the cell). For smaller particles such as ions, amino acids, water and other solutes, there are different types of direct contact between the cells, which are:

- tight junctions (occluding junctions or zonula occludens), are the connections that form when cells compact together. The cell membranes are connected together but the contents of each cell are not connected in any way. There are no tubes but an impermeable membrane between the cells, and are found in places which contains certain fluids like the urinary bladder, or the intestines or the kidney.
- adhering junctions (zonula adherens). Epithelial cells are held tightly together by strong adhering junctions. On the epithelial cell boundaries just below the zonular occludens, the membranes diverge to a distance of 150-200 Å. In the space between the cells, there is a protein known as cadherin – a cell membrane glycoprotein, which interact to 'zipper' up the two cells together.

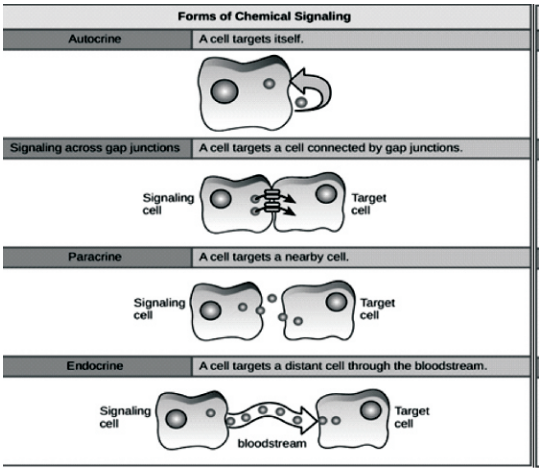


Figure 15: Cell Signaling

- Desmosomes (macula adherens),where the cell membranes are inter-connected with thread-like substances across the space between the cells. The cell surfaces are 150 to 200 Å apart. Similar to tight junctions, desmosomes physically hold the cells together, but do not allow fluids or materials to pass from the inside of one cell to the next. In addition, desmosomes are attached to the cytoskeleton of the cells for structural support. The space in-between allows free flow of water and solutes freely between the cells. This is convenient for areas of the body that experience high stress like the skin or intestines
- gap junctions, these are essentially tubes that join two cells together, that allows the transport of ions and water to and from the connecting cells. In thin sections, the normal intercellular space is about 20 Å. The tubes also help to spread electrochemical signals that are produced by action potentials which occur in neurons and cardiac cells.

6.3 Cell Surface Specializations

The free surface of epithelial cells sometimes bears motile extensions of the cell surface that sweep materials past the cell, called **cilia**(fig. 16) or **flagella**. Cilia and flagella are membrane-bound, centriole-derived, motile and sensory projections from the cell surface, and contain a microtubule cytoskeleton.In some cases, like the male reproductive cell (spermatozoon), the flagellum (singular) propels the entire cell through a liquid medium, and thus provide the means of locomotion. Cilia and flagella have different beating patterns, but their internal

structure is the same. It is composed of a long cylinder of nine pairs of microtubules enclosing a central pair (axoneme of 9+2) with dynein arms. There are also axonemes of 9+0 non-motile primary cilia found in epithelial cells of kidney tubules, and non-epithelial cells of chondrocytes, fibroblasts and neurons. Ciliary membranes of all cilia contain specific receptors and ion channel proteins that are initiate signal transduction and growth factor.

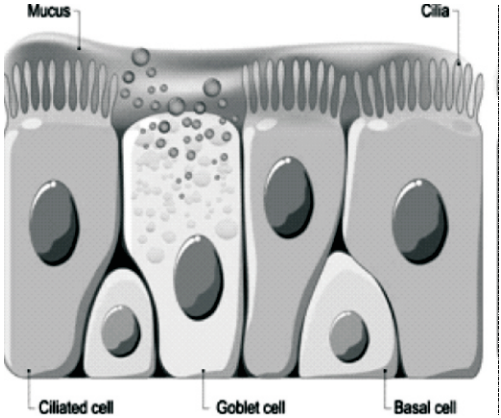


Figure 16: Pseudostratified Ciliated Epithelial Cells

In the lining epithelium of the intestine, the apical surfaces present orderly arrays of finger-like projections, **microvilli**(fig. 17), which increase the surface area for absorption. The surface area can be increased as much as 20- to 30-folds. In these absorptive cells, the glycocalyx is thicker than in most cells, and presents a complex of microvilli and glycocalyx in the light microscope as brush or striated border.

Stereocilia are long apical processes of the cell in the absorptive epithelial lining of epididymis and ductus deferens. They are longer, branched and less motile than microvilli. Stereocilia increase the surface area and facilitate movement of molecules into and out of the cells.

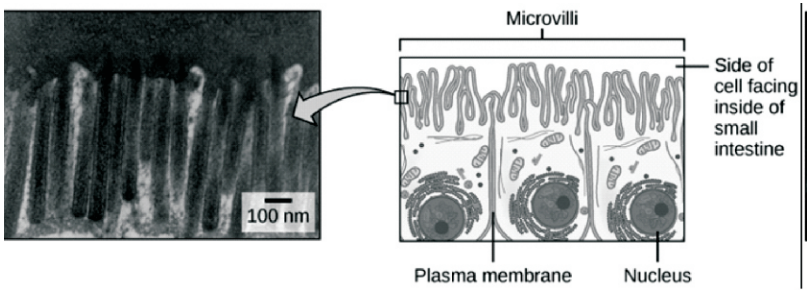


Figure 17: Microvilli in small intestine

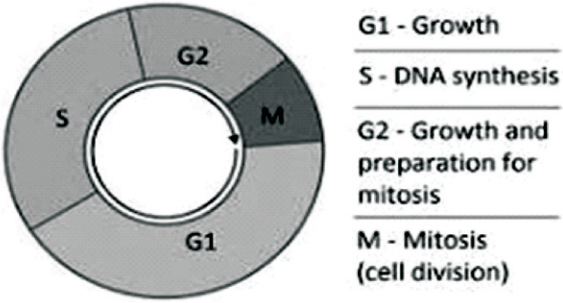


Figure 18: The Cell Cycle

6.4 The Cell Cycle

The ordered sequence of events that occur in a cell in preparation for cell division is the cell cycle. The cell cycle can be thought of as the life cycle of a cell. It is the series of growth and

development steps a cell undergoes between its 'birth' and 'reproduction'.To divide, a cell must complete some important tasks; it must grow, copy its genetic material (DNA), and physically split into two daughter cells. Cells perform these tasks in an organized, predictable series of steps that make up the cell cycle. The stages of the cell cycle can be divided into two major phases: interphase and mitosis (M) phase.During interphase, the cell grows and makes a copy of its DNA.During the mitotic (M) phase, the cell separates its DNA into two sets and divides its cytoplasm, forming two new cells.

Preparations for cell division happens in three steps:
G1 phase, also called the first gap phase, when the cell grows physically larger, copies organelles, and makes the molecular building blocks it will need in later steps.

S phase, in which the synthesizes a complete copy of the DNA in its nucleus. It also duplicates a microtubule-organizing structure called the centrosome, which helps separate DNA during M phase.

G2 phase, or the second gap phase, in which the cell grows more, makes proteins and organelles, and begins to re-organize its contents in preparation for mitosis. G2 phase ends when mitosis begins.
The stages G1, S, and G2 make up the interphase, which accounts for the span between cell divisions. Depending on the stimulatory and inhibitory messages a cell receives, it may decide whether to enter the cell cycle and divide or not.

M phase, or mitotic phase, the cell divides its copied DNA and cytoplasm to make two new cells. M phase involves two distinct division-related processes; mitosis and cytokinesis. In mitosis, the nuclear DNA condenses into visible chromosomes, and is pulled apart by the mitotic spindle (made out of microtubules). Mitosis takes place in four stages; prophase, metaphase, anaphase, and telophase. In cytokinesis, the cytoplasm of the cell is split in two, making two new cells.

The proteins that stimulate cell division can be categorized into four types, namely growth factors, growth factor receptors, signal transducers, and nuclear regulatory proteins (transcription factors). For a stimulatory signal to reach the nucleus and "turn on" cell division, the following steps are required: (a) A growth factor must bind to its receptor on the cell membrane. (b) The receptor must become temporally activated by this binding event. (c) This activation must stimulate a signal to be transmitted, or transduced, from the receptor at the cell surface to the nucleus within the cell. (d) Transcription factors within the nucleus must initiate the transcription of genes involved in cell proliferation.

Transcription is the process in which DNA is converted into RNA. Proteins are subsequently made according to the RNA blueprint, which makes transcription crucial as an initial step in protein biosynthesis.

Cells use special proteins and checkpoint signaling systems to ensure that the cell cycle progresses properly. Checkpoints at the end of G1 and at the beginning of G2 are designated to assess

DNA for damage before and after S phase. Similarly, a checkpoint during mitosis ensures that the cell's spindle fibers are properly aligned in metaphase before the chromosomes are separated in anaphase. If abnormalities in spindle formation or a damage in DNA is detected at these checkpoints, the cell is forced to undergo programmed cell death (apoptosis). On the other hand, the cell cycle and its checkpoint systems can be sabotaged by defective proteins or genes that may cause malignant transformation of the cell, leading to the manifestation of cancer cells.

6.5 The Plasma Membrane

The plasma membrane or plasmalemma is a phospholipid bilayer with embedded proteins with carbohydrate patches, that separates the internal contents of the cell from its surrounding environment. The phospholipid is a lipid molecule with two fatty acid chains and a phosphate-containing group. The second lipid in the membrane is sterol (generally cholesterol). Both lipid types dissolve readily in organic solvents. In addition, both have a region that is attracted to and soluble in water. This amphiphilic property (having a dual attraction, containing both a lipid-soluble and water-soluble region) is basic to the role of lipids as building blocks of cell membranes.

The membrane proteins are of two types, extrinsic and intrinsic proteins. The extrinsic proteins are loosely attached by ionic bonds or calcium bridges to the electrically charged phosphoryl surface of the bilayer, while the intrinsic proteins are firmly embedded within the phospholipid bilayer. Both the extrinsic proteins and glycolipids embedded in the outer lipid layer, as

well as the carbohydrate group (glycocalyx) act as enzymes to facilitate interaction with the cell's environment, either for cell adhesion or exchange or signal transduction. The plasmalemma controls the passage of organic molecules, ions, water, and oxygen into and out of the cell. Waste materials such as carbon dioxide and ammonia also leave the cell by passing through the plasma membrane.

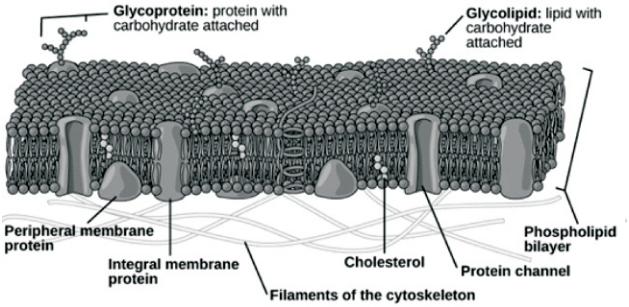


Figure 19: Plasma Membrane

7.0 CURRENT RESEARCH FOCUS

7.1 PHYTOMEDICINAL IMPACT

7.1.1 The Free Radicals Factor

Oxidative stress is a phenomenon caused by an imbalance between the production and accumulation of oxygen reactive species (ROS) also known as free radicals in the cells and tissues, and the antioxidant defense system of the body. This imbalance can lead to cell and tissue breakdown, and may play a role in certain illnesses and conditions like diabetes. Superoxide radicals (O_2^-), hydrogen peroxide (H_2O_2), hydroxyl radicals (-OH), and singlet oxygen ($^1O_2$) are commonreactive oxygen

species (ROS), which are generated as by-products of oxygen metabolism. In addition, environmental stressors such as UV, ionizing radiation, pollutants, and heavy metals, as well as xenobiotics (i.e., antiblastic drugs) contribute to greatly increase ROS production.Free radicals can chemically interact with cell components such as DNA, protein or lipid and "steal" their electrons in order to become stabilized. This in turn, destabilizes the cell component molecules, which then seek and "steal" an electron from another molecule, and thus trigger a large chain of free radical reactions.

Antioxidants, on the other hand, are molecules present in cells that prevent these reactions by donating an electron to the free radicals without becoming destabilized themselves. Cells deploy antioxidant defensive system based mainly on enzymatic components such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPX), to protect themselves from ROS-induced cellular damage. Several antioxidants have also been exploited exogenously for their actual or supposed beneficial effect against oxidative stress, namely vitamin E, flavonoids, and polyphenols. Oxidative stress occurs naturally and plays a role in the aging process. Oxidative stress is known to activate multiple intracellular signaling, which induces apoptosis or cell overgrowth, leading to organ dysfunction.

7.2 Use of Medicinal Plants

Medicinal plants are of economic importance as potential sources of drugs. They are used locally for the treatment of various ailments in the developing world, including Nigeria.

Within the Sahel savanna, crude extracts of plants are used without purification, standardization, or concern as to what the active principles are. WHO (1992) advocates that such plants need to be evaluated and developed in order to improve their efficacy, safety, availability, and wider application, as they also play a major role in the health care of about 80% of world's population (Farnsworth et al., 1985). Ethno-medicine and traditional pharmacology have gained increased recognition in human and veterinary medicine.Drugs are generally poisonous but their therapeutic use is based on the fact that they do more good than harm to the sick (Okogun, 1992). The majority of the active chemical substances are in the roots and bark of trees and shrubs. Most of the active chemical principles of many of these plants are now known.

7.2.1 Ameliorative Effects of *Leptadenia hastata on* Oxidative Stress and Serum Biochemical Parameters

Jacks and others (2020) investigated the oxidative stress causing potential of diabetes mellitus and the ameliorative effect produced by *Leptadenia hastata* leaves. Diabetes mellitus is a major health problem and is characterized by hyperglycemia and disturbances in carbohydrate, fat and protein metabolism. Treatment of diabetes has always included the administration of insulin and oral hypoglycemic agents in conjunction with lifestyle modifications. These treatments offer effective glycemic control; however, they present limitations about availability, affordability and side effects. Ethno-botanical information revealed that Leptadenia hastata (Pers) is used

locally for the treatment of diabetes mellitus, but also have antimicrobial and hypo-lipidemic effects (Aliero and Wara, (2009), Bello et al. (2011). Diabetes mellitus was induced in 20 Wistar rats using a single injection of streptozotocin (50 mg/kg i.p.). The rats were divided into four groups (3-6) of 5 rats each. Rats in groups 3-6 received olive oil, 100mg/kg of extract, 200mg/kg of extract and insulin (6IU/kg), respectively. In addition, 10 non-diabetic rats were grouped into 1 and 2. They received olive oil and 200mg/kg of in rats with 100 and 200 mg/kg of n-hexane extract of *L. hastata* extract, respectively for 28 days. Rats in all groups were sacrificed by injecting with ketamine hydrochloride, blood was collected from the heart chambers by cardiac puncture and centrifuged. The serum was analyzed for biochemical parameters. The liver was quickly removed and homogenized in 5mls chilled phosphate buffer. The homogenate obtained was centrifuged and the supernatant collected and used for analysis of oxidative stress enzymes. The experimental procedures were conducted in accordance with the ARRIVE guidelines (reporting of in vivo experiment), and the National Institute of Health (NIH) guide for the CARE and use of laboratory animals (NIH Publications No. 8023, revised 1978). The results showed that the extract reduced ($p<0.001$) blood glucose level, prevented diabetic weight loss which was evident in the untreated diabetic rats and significantly decreased serum levels of AST ($p<0.05$), ALP ($p<0.001$), ALT ($p<0.05$), TG ($p<0.01$) and TC ($p<0.001$) as well as creatinine ($p<0.001$). It had no effect on SOD and CAT levels of liver homogenate but significantly increased ($p<0.001$) GSH levels and reduced ($p<0.05$) MDA level.

Table 1 Effect of hexane extract of *Leptadenia hastata* on AST, ALT and ALP in groups.

Groups	Treatment	AST(µ/L)	ALT (µ/L)	ALP (µ/L)
I	Olive Oil	62.6 ± 7.0^{a}	46.6 ± 11.2^{b}	124.6 ± 1.6^{a}
II	Extract (200mg/kg)	65.2 ± 0.5^{a}	29.4 ± 1.1^{b}	155.6 ± 1.3^{c}
III	Olive Oil	164.4 ± 7.7^{c}	72.4 ± 1.3^{a}	230.8 ± 3.9^{b}
IV	Extract (100mg/kg)	115.8 ± 16.9^{b}	33.2 ± 2.3^{b}	164.6 ± 2.2^{a}
V	Extract (200mg/kg)	115.9 ± 16.9^{b}	29.8 ± 3.2^{b}	121.2 ± 4.7^{a}
VI	Insulin	173.2 ± 1.3^{b}	45.6 ± 6.5^{b}	225.0 ± 4.9^{b}

The values are expressed as mean ± S.E.M expressed (n = 5). Values in the same column with different superscript are significantly different at $P<0.05$. Values in the same column with same superscript are not significant. AST-aspartate aminotransferase; ALT-alanine aminotransferase; ALP-alkaline phosphatase. I – Non-diabetic and untreated with extract, II – non-diabetic but extracted treated, III – diabetic and untreated, IV – diabetic and treated with 100mg/kg extract, V – diabetic and treated with 200mg/kg of extract, VI – diabetic andtreatedwithinsulin.

Table 2 Effect of hexane extract of *Leptadenia hastata* on triglyceride, total cholesterol, total protein, high density lipoprotein and low-density lipoprotein.

Groups	Treatment	TP (g/L)	TG(mg/dl)	TC(mg/dl	HDL(mg/dl	LDL(mg/dl)
I	Olive Oil	63.0 ± 0.4^{a}	21.2 ± 2.9^{a}	44.3 ± 0.4^{i}	21.9 ± 1.7^{a}	19.8 ± 1.6^{a}
II	Extract (200mg/kg	61.8 ± 1.2^{a}	22.3 ± 0.5^{a}	38.2 ± 1.0^{i}	14.4 ± 0.8^{a}	20.5 ± 1.2^{a}
III	Olive Oil	61.4 ± 3.3^{a}	31.7 ± 2.3^{b}	68.4 ± 5.4^{i}	16.6 ± 6.7^{a}	26.6 ± 1.3^{a}
IV	Extract (100mg/kg	55.6 ± 2.3^{a}	21.9 ± 1.7^{a}	37.4 ± 3.6^{i}	19.8 ± 3.0^{a}	19.4 ± 2.9^{a}
V	Extract (200mg/kg	53.0 ± 4.8^{a}	20.2 ± 1.7^{a}	35.1 ± 4.7^{i}	18.8 ± 5.4^{a}	18.7 ± 5.4^{a}
VI	Insulin	51.6 ± 0.2^{b}	19.8 ± 1.6^{a}	27.0 ± 3.2^{l}	19.8 ± 1.6^{a}	16.9 ± 0.7^{a}

Data is presented as mean ± S.E.M. of 5 animals per group. Values with different superscript down the column and different alphabet across the column indicate significant difference ($p < 0.05$). Values with the same superscript across the column indicate no significant difference at $P<0.05$. TP- total protein, TG- triglycerides, TC- total cholesterol, HDL- high density lipoproteins,LDL- low density lipoproteins.I – Non-diabetic and untreated with extract, II – non-diabetic but extracted treated, III – diabetic and untreated, IV – diabetic and treated with 100mg/kg extract, V – diabetic and treated with 200mg/kg of extract, VI – diabetic and treated with insulin.

Groups	Treatment	Albumin (g/dl)	Creatinine(mg/dl)	Urea (mmol/l)
I	Olive Oil	32.6 ± 2.2^{a}	0.7 ± 0.07^{a}	5.8 ± 0.1^{a}
II	Extract (200mg/kg)	29.6 ± 1.2^{a}	0.7 ± 0.06	7.0 ± 0.3^{a}
III	Olive Oil	33.8 ± 2.9^{a}	1.5 ± 0.03^{b}	9.1 ± 1.3^{a}
IV	Extract (100mg/kg)	29.8 ± 0.9^{a}	0.7 ± 0.01^{a}	6.3 ± 0.6^{a}
V	Extract (200mg/kg)	27.8 ± 3.2^{a}	0.8 ± 0.05^{a}	8.7 ± 1.3^{a}
VI	Insulin	33.8 ± 1.3^{a}	0.8 ± 0.05^{a}	7.4 ± 0.2^{a}

Table 3 Effect of hexane extract of *Leptadenia hastata* on serum albumin, urea and creatinine levels.

Data is presented as mean ± S.E.M. of 5 animals per group. Values with different superscript down the column and different alphabet across the column indicate significant ($p<0.05$) difference. Values with the same superscript across the column indicate no significant difference at ($p>0.05$). I – Non-diabetic and untreated with extract, II – non-diabetic but extracted treated, III – diabetic and untreated, IV – diabetic and treated with 100mg/kg extract, V – diabetic and treated with 200mg/kg of extract, VI – diabetic and treated with insulin.

Groups	Treatment	CAT (µg/ml)	GSH (µg/ml)	MDA (µmol/mg protein)	SOD (µ/ml)
I	Olive Oil	21.4 ± 1.7^{a}	17.04 ± 0.6^{i}	48.12 ± 3.1^{a}	23.4 ± 1.1^{a}
II	Extract (200mg/kg)	21.3 ± 0.3^{a}	26.36 ± 0.5^{l}	50.96 ± 1.2^{a}	26.5 ± 0.6^{a}
III	Olive Oil	25.1 ± 3.4^{a}	19.68 ± 0.9^{i}	63.8 ± 6.5^{b}	23.5 ± 1.3^{a}
IV	Extract (100mg/kg)	22.8 ± 2.8^{a}	22.96 ± 1.3^{l}	50.3 ± 2.9^{a}	24.4 ± 1.7^{a}
V	Extract (200mg/kg)	21.9 ± 0.9^{a}	17.66 ± 0.3^{i}	47.7 ± 2.1^{a}	25.0 ± 0.5^{a}
VI	Insulin	26.8 ± 1.7^{a}	22.08 ± 1.0^{l}	54.4 ± 0.4^{a}	22.1 ± 1.04^{a}

Table 4 Effect of n-hexane Extract of Leptadenia hastata on Oxidative Stress Parameters

The values are expressed as mean ± SEM (n=5). Values in the same column with different superscript are significantly different at $P<0.05$. Values in the same column with same superscript are not significant. CAT- catalase, GSH- Glutathione reductase, MDA- malondialdehyde, SOD- superoxide dismutase. I – Non-diabetic and untreated with extract, II – non-diabetic but extracted treated, III – diabetic and untreated, IV – diabetic and treated with 100mg/kg extract, V – diabetic and treated with 200mg/kg of extract, VI – diabetic and treated with insulin.

7.2.2 Onion Peel Quercetin Attenuates Ethanol induced Liver Injury

Jacks et al. (2022) examined the role of onion peel quercetin (OPQ) on oxidative stress, liver function and steatosis in ethanol-treated mice over a two-phase period (protective and therapeutic). Alcoholic liver disease (ALD) is a histological abnormality of the liver that ranges from steatosis to fibrosis/cirrhosis. In each phase, 25mice were divided equally among five groups (n=5). In both phases, groups 1 and 2 received vehicle and ethanol, respectively, for 8 days. In the protective phase, groups 3-5 received 50mg/kg OPQ, 100mg/kg OPQ and 100mg/kg sily marin, followed by ethanol for 8 days. Mice in these groups were euthanized on day 9. In the therapeutic phase, groups 3-5 received ethanol for 8 days and were then treated with 50mg/kg OPQ, 100mg/kg OPQ and 100mg/kg sily marin for an additional 8 days before being euthanized on day 17. The results reveal significant decreases in ALT, AST, and ALP serum levels in mice that received OPQ and sily marin compared to mice that received ethanol ($p<0.05$).The catalase activity of mice treated with 50mg/kg OPQ was significantly higher than in controls ($p<0.05$). OPQ treatment significantly improved MDA levels relative to controls ($p<0.05$).Hepatocyte degeneration, steatosis, and increased lipidperoxidation were observed in ethanol-treatedmice.OPQsignificantlydecreased ALP, ALT, and AST serum levels compared with ethanol treatment ($p<0.05$). We conclude that OPQ can be used as an antioxidant to delay the onset and progression of liver disease by preventing lipid peroxidation, regulating liver function, and promoting albumin synthesis.

Table 5:Protective phase of onion peel quercetin and ethanol administration in mice (n=5)

Groups	Treatment	NumberofDays
1	5ml/kg of tween 80 indistilledwater	8
2	5ml/kg of 50% ethanol	8
3	50 mg/kg of onion peel quercetin + 5 ml/kg of 50% ethanol	8
4	100 mg/kg of onion peel quercetin + 5 ml/kg of 50% ethanol	8
5	100mg/kgofSilymarin+5ml/kgof50% ethanol	8

Table 6:Therapeutic phase of onion peel quercetin and ethanol administration in mice (n = 5)

Groups	Pre-treatment(8days)	Post-treatment(8 days)
1	5ml/kg tween 80 in distilled water	Nil
2	5ml/kg of 50% ethanol	Nil
3	5ml/kg of 50% ethanol	50mg/kg of onion peel quercetin
4	5ml/kg of 50% ethanol	100mg/kg of onion peel quercetin
5	5ml/kg of 50% ethanol	100mg/kg of Silymarin

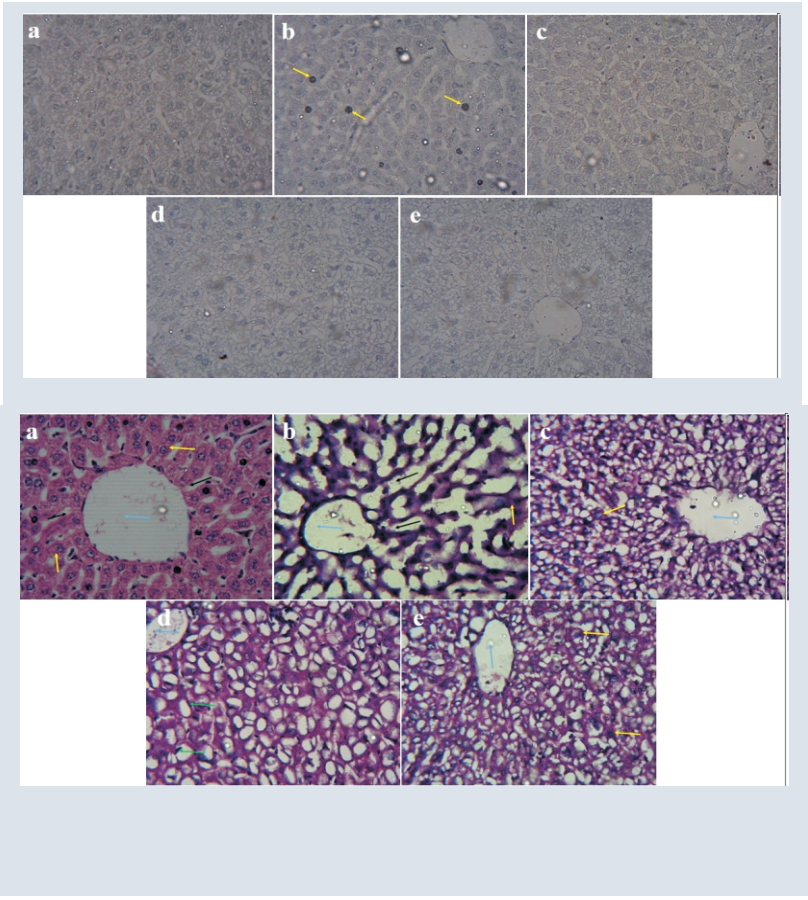


Figure 21: Photomicrographs of the liver in OPQ and ethanol treated mice (therapeutic phase) showing hepatocytes (yellow arrows), central vein (blue arrows), sinusoids (black arrows) and pyknosis (green arrows).
a=control,b=ethanol,c=ethanolplus50mg/kgOPQ,d=ethanolplus100mg/kgOPQe=ethanolplus silymarin. H&E stain, x200 magnification

7.2.3 Histological and Morphometric Assessment of Cutaneous Wound Healing in Streptozotocin Induced Diabetic Rats

Jacks et al. (2019) assessed the histological and morphometric effects of *Leptadenia hastata* on cutaneous wound healing in diabetic and non diabetic rats. A wound can bedefinedasalossorbreakingofcellular,anatomical,orfunctional continuity of living tissues. Diabetes may delay the process of wound healing leading to development of chronic wounds. Healing impairment of diabetic wounds presents serious clinical problems for both diabetic patients and physicians worldwide. Diabetes mellitus was induced in twenty Albino rats using a single injection of streptozotocin (50mg/kg,i.p.). The rats were divided into four groups (III–VI) consisting of five rats each. In addition, ten non diabetic rats were grouped into I and II.

Full-thickness excision wounds extending to the subcutaneous tissue were made on the mid-dorsal region, and rats in Group III–VI had their wounds treated with olive oil,100mg/kgofextract,200mg/kgofextract,andprocainepenicillin,respectively.RatsinGroups I and II received olive oil and 200 mg/kg of extract, respectively, for 28 days. Wound areas were calculated, and histological sections of the wound area were analyzed. Data were statistically analyzed using Graph Pad In Stat software using one-way analysis of variance and expressed as mean± standard error of mean and percentage followed by Bonferroni multiple comparisons test. Analysis of the results of wound area in all groups revealed that the extract promoted wound healing in the diabetic rats by significantly ($P < 0.05$) increasing the thickness of the epithelial layers and stimulated

collagen synthesis.

We conclude that the extract enhanced diabetic wound healing by reducing inflammation, increasing wound contraction and epithelialization.

Table7: Quantitative assessment of the healing process

Groups	Treatment	Days					
		1	3	5	10	15	20
I	-	240.0[a]	258.0±7.3[a]	291.8±2.1[a]	243.8±11[a]	89.7±8.6[a]	38.8±1.9[a]
II	Extract (200 mg/kg)	240.0[a]	301.6±4.0[b]	292.0±8.5[a]	284.4±11[a]	86.2±2.6[a]	41.8±4.4[a]
III	-	240.0[a]	260.0±0.9[a]	298.8±2.5[a]	258.6±12[a]	105.3±2.5[b]	97.6±1.8[b]
IV	Extract (100 mg/kg)	240.0[a]	285.6±5.0[b]	288.8±0.5[a]	135.9±3.9[b]	91.36±3.4[a]	83.0±1.4[b]
V	Extract (200 mg/kg)	240.0[a]	328.8±5.5[b]	284.8±4.2[a]	143.4±4.6[b]	89.2±7.6[a]	73.6±3.2[b]
VI	Insulin	240.0[a]	233.2±3.6[b]	280.4±6.9[a]	212.2±3.0[b]	121.9±14[a]	96.5±2.9[b]

The values are expressed as mean±SEM.Values in the same column with different superscript are significantly different at $P<0.05$. Values in the same column with the same superscript are not significant. The unit for the above measurements is mm^2. SEM-Standard error of mean

Table8:Therateofwoundcontraction

Groups	Treatment	Percentage change in wound diameter (%)				
		Day3	Day 5	Day10	Day 15	Day20
I	-	−7.5±4.6[c]	−21.5±6.5[c]	−1.25±3.6[c]	62.6±2.1[a]	83.8±2.6[a]
II	Extract (200 mg/kg)	−25.4±2.6[c]	−21.6±4.3[c]	−18.5±4.2[c]	64.0±2.6[a]	82.5±4.1[a]
III	-	−8.5±6.63[c]	−24.1±4.4[c]	−7.4±4.5[c]	56.0±3.4[a]	59.3±4.8[a]
IV	Extract (100 mg/kg)	−19.0±5.1[a]	−20.0±3.6[c]	43.8±3.2[a]	61.9±2.1[a]	65.0±6.6[a]
V	Extract (200 mg/kg)	−36.6±6.3[c]	−18.3±5.5[c]	40.4±4.2[a]	62.8±3.0[a]	69.5±3.2[a]
VI	Insulin	2.9±7.2[a]	−16.6±6.6[c]	11.6±4.6[a]	49.2±2.6[a]	59.8±4.4[a]

The values are expressed as mean± SEM. Values in the same column with different superscript are significantly different at $P<0.05$. Values in the same column with the same superscript are not significant. SEM- Standard error of mean

Table 9::Themorphometric findings of the skin

Groups	Treatment	SB (µm)	SS (µm)	SG (µm)	SC (µm)	CF(µm)	FN (µm)
I		9.0±1.0[a]	33.5±7.5[a]	7.9±1.1[a]	8.5±3.0[a]	12.5±0.8[a]	5.5±0.9[a]
II	Extract (200 mg/kg)	2.5±0.0[b]	9.0±0.6[b]	5.5±0.9[a]	10.5±2.0[a]	14.5±1.6[a]	5.5±0.9[a]
III	-	2.5±0.0[b]	12.0±3.9[b]	6.0±1.0[a]	16.0±3.9[b]	7.0±0.9[b]	6.5±1.0[a]
IV	Extract (100 mg/kg)	14.0±2.2[c]	76.5±14.7[c]	19.0±3.1[b]	26.0±4.2[b]	11.0±2.9[a]	6.2±0.5[a]
V	Extract (200 mg/kg)	2.5±0.0[b]	23.5±6.2[a]	4.0±1.0[a]	6.5±0.6[a]	13.5±1.3[a]	3.5±0.6[b]
VI	Insulin	5.5±0.9[b]	24.0±1.3[a]	14.0±1.3[b]	29.5±4.0[b]	10.0±1.1[a]	6.0±0.6[a]

Data are presented as mean±SEM. The values are expressed as mean±SEM expressed (n=5). Values in the same column with different superscript are significantly different at P<0.05. Values in the same column with same superscript are not significant. SB-Stratumbasale, SS-Stratumspinosum, SG-Stratumgranulosum, SC - Stratum corneum, CF - Collagen fiber thickness, FN - Fibroblast nucleus, SEM - Standard error of mean

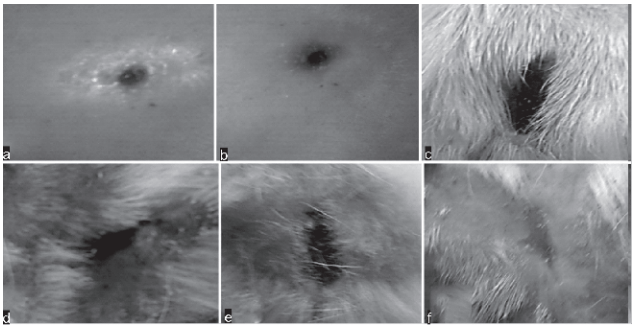


Figure23: Woundareasonday20inexperimentalanimals.
Normal control (a), non diabetic experimental (b), diabetic control (C), 100mg/kg (d), 200mg/kg (e), and procainepenicillin (f) wound areas

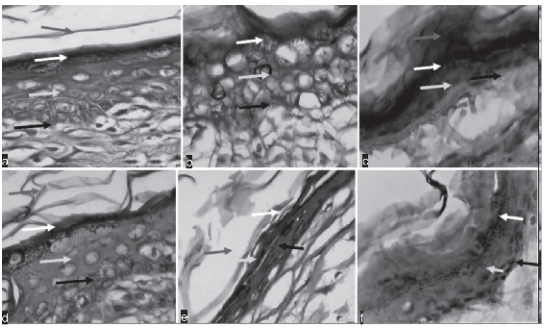


Figure 24: Photomicrographs of skin from wound areas in rats in all groups after 28-days treatment.

Red arrow–stratum corneum,White arrow–stratum granulosum,Yellow arrow – stratum spinosum, Black arrow – stratum basale. Groups I (a), II (b), III (c), IV (d), V (e), and VI (f). H and E, ×400

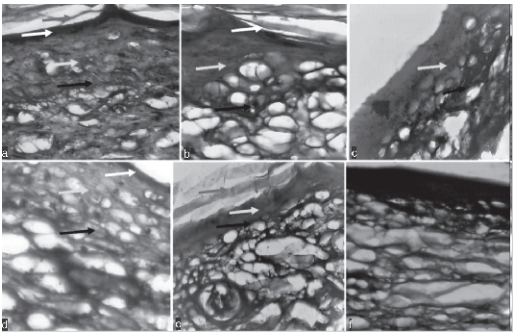


Figure24: Photomicrographs of skin from wound areas in rats in all groups after 28-day oral toxicity.

Red arrow–stratumcorneum, white arrow–stratumgranulosum, yellow arrow – stratum spinosum, Blackarrow – stratum basale. Groups I (a), II (b), III (c), IV (d), V (e), and VI (f). MT, ×400

7.2.4 Evaluation of Acute Oral Toxicity Induced By N-Hexane Extract of *Leptadenia Hastata* Leaves on the Histology of the Pancreas and Spleen

Jacks et al. (2019) evaluated the oral acute toxicological profile of then-hexane extract of *Leptadenia hastata* after acute administration on the histology of the pancreas and spleen of albino rats.

A total of seventeen (17)albino rats were used for the study. For theacutetoxicitystudy, Lorke'smethod wasadopted.Twelve rats were grouped into two major phases, comprising of six rats each. Rats in phase one were further divided into three groups of two each (I-III), and received a dosage of 10mg/kg, 100mg/kg and 1000mg/kg, respectively. The second phase consisted of three groups of two rats each (IV-VI)and were administered a dose of 1600mg/kg, 2900mg/kg and 5000mg/kg, respectively. Five rats were given, each 1000mg/kg, 2000mg/kg, 3000mg/kg, 4000mg/kg and 5000mg/kg of n-hexane extract of *Leptadenia hastata* to determine the effect of the extract on the pancreas and spleen at these concentrations. The rats were observed for general behavioral changes, adverse effects and mortality up to 7 days post-treatment. Body weight, food intake and water intake were monitored throughout the experimental period and the pancreas and spleen were removed and evaluated at the end of the experiment. In the acute toxicity study, there was no mortality nor significant behavioural changes observed after administering the highest dose (5000mg/kg). Histological analysis showed no significant changes when compared with the control in the pancreatic and splenic tissues at a dosage of3000mg/kg and below. These results demonstrate that the extract may not have toxic effect. The Ld_{50} was greater than 5000

mg/kg. However, at tissue level, there was observable heamolysis at a concentration above 3000mg/kg.

Table-10. Outcome of first phase (a) and second phase (b) acute oral toxicity study

(a)

Dose(mg/kg)	NumberofRatsUsed	Mortality(%)
10	2	0 (0.0)
100	2	0 (0.0)
1000	2	0 (0.0)

(b)

Dose(mg/kg)	NumberofRatsUsed	Mortality(%)
1600	2	0 (0.0)
2900	2	0 (0.0)
5000	2	0 (0.0)

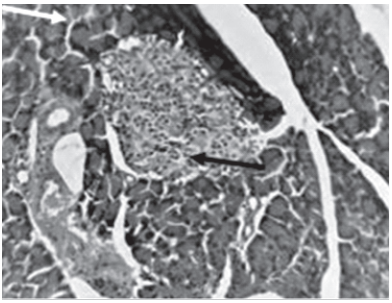


Figure-25. Micrograph of pancreas of rats exposed to acute toxicity study. A- 1000mg/kg, Islet of Langerhans (black arrow), pancreatic acinar cells (white arrow), H & E X100

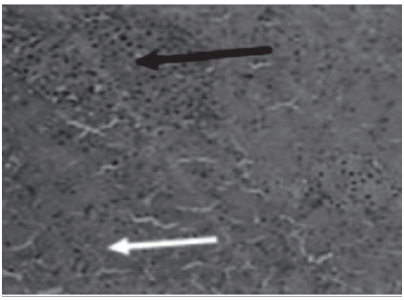


Figure-26. Micrograph of pancreas of rats exposed to acute toxicity study. 4000mg/kg, Islet of Langerhans (black arrow), pancreatic acinar cells (white arrow), H & E X100

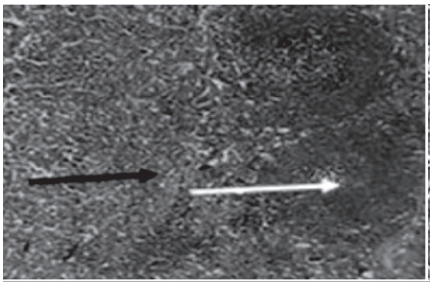


Figure-27. Micrograph of spleen of rats exposed to acute toxicity study. 2000mg/kgof extract. White pulp (white arrow), Red pulp (black arrow). H & E stain, ×100.

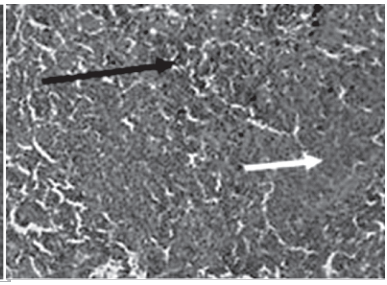


Figure-28. Micrograph of spleen of rats exposed to acute toxicity study. 3000mg/kg of extract. White pulp (white arrow), Red pulp (black arrow). H & E stain, ×100.

6.2.5 Analysis of Pancreatic Morphology and Morphometryin Streptozotocin-induced Diabetic Rats

Jacks et al. (2019) analyzed pancreatic morphology and morphometry in streptozotocin-induced diabetic rats administered with n-hexane extract of *Leptadenia hastata* leaves.

Diabetes mellitus was induced in 20 Wistar rats using a single injection of streptozotocin (50 mg/kg) administered intraperitonially. The rats were divided into four groups (3-6) of 5 rats each. Rats in group 3-6 received olive oil, 100mg/kg of extract, 200mg/kg of extract and insulin (6IU/kg), respectively. 10 non-diabetic rats were grouped into 1 and 2.Theyreceived olive oil and 200mg/kgofextract, respectively for 28 days. At the end of the study, the pancreas was removed and processed for paraffin sectioning. Sections were stained with hematoxylin and eosin.

The results showed an improvement in the area of pancreatic islets in the groups that received the extract and insulin. The islet cells in the diabetic group were atrophied with pyknotic and karyolitic cells. The mean number of pancreatic islets, pancreatic diameter and number of beta cells in the extract treated groups were significantly ($P<0.05$) increased when compared to the untreated diabetic rats.

n-haxane extract of *Leptadenia hastata* was found to have anti-diabetic and hypoglycemic properties and was also shown to improve the number and size of pancreatic islets in treated animals.

Table 11: Morphometricanalysis of the pancreas

Groups	Treatment	MeanNumberofIslets	PancreaticIsletAre(μm)	NumberofBetaCells
I	-	26± 5.0$_a$	192.2±7.2$_a$	248.2±7.5$_a$
II	Extract(200mg/kg)	23±2.0$_a$	145.2±10.8$_b$	233.3±4.4$_a$
III	-	13±3.0$_c$	110.2±8.7$_c$	59.9±3.5$_b$
IV	Extract(100mg/kg)	19±7.0$_a$	170.4±14.1$_a$	165.3±2.6$_c$
V	Extract(200mg/kg)	17±2.0$_b$	152.4±10.1$_b$	125.5±7.1$_c$
VI	Insulin	17± 2.0$_b$	163.2±11.5$_b$	169.3±1.6$_c$

The values are expressed as mean± SEM. The values are expressed as mean±S.E.M expressed (n=5). Values in the same column with different superscript are significantly different at $P<0.05$. Values in the same column with same superscript are not significant.

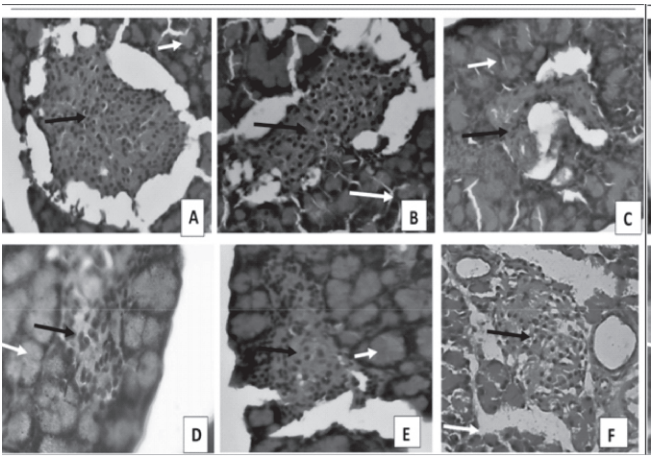
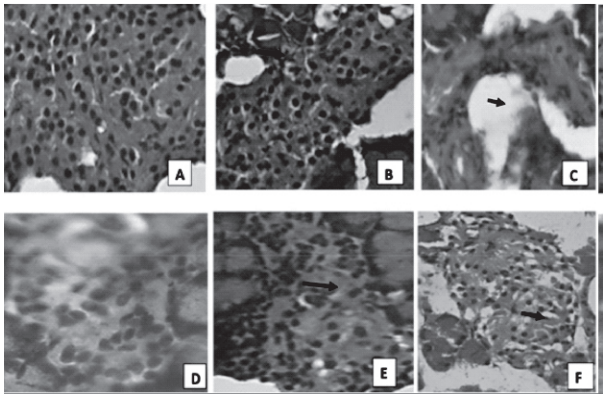


Figure29:The micrographs of pancreas in rats after 28-day oral toxicity study. Shows islet of Langerhans (blackarrow) and pancreatic acinar cells (whitearrow) Groups I (A), II (B), III (C), IV (D), V (E) and VI (F). H & E ×100

Figure30:Photomicrographs of pancreas in rats after 28-day oral toxicity study. Shows beta cells in the pancreatic islets. Black arrow–Beta islet cell. Groups I(A), II (B), III (C), IV (D), V (E) and VI(F). Modified Aldehyde Fuschin ×200.



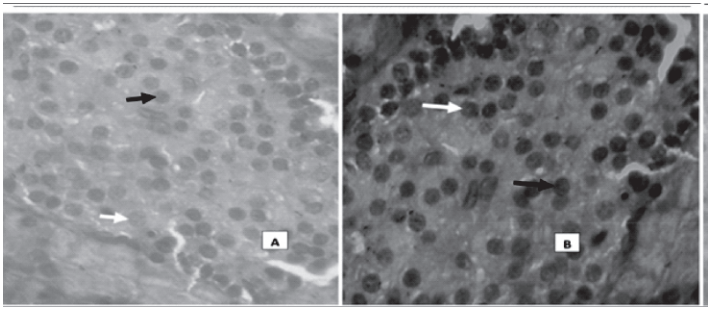


Figure 31: Photomicrographs of pancreatic tissue from control group. Stained with modified aldehydefuchsin (A) and Hematoxylin and Eosin (B) showing alpha cells (white arrows) and beta cells (black arrows) X400

7.2.6. Hypoglycemic and Anti-Diabetic Properties of N-Hexane Extract of *Leptadenia Hastata* Leaves

Jacks et al. (2019) investigated the hypoglycemic and anti-diabetic properties of n-hexane extract of *Leptadenia hastata* leaves in streptozotocin-induced diabetic rats.

N-hexane extract of the leaves of *Leptadenia hastata* was prepared bysoxhlet extraction using maceration method. The extract was evaluated for anti- diabetic effect in streptozotocin-induced diabetes in rats. The serum glucose levels were assayed as indices of diabetes.

The results showed that treatment of streptozotocin-induced diabetes in rats with 100 and 200 mg/kg of n-hexane extractof *L. hastata* reduced significantly ($p<0.001$) blood glucose level and prevented diabetic weight loss, which was evident in the untreated diabetic rats.

The results of the study affirm the efficacy of *Leptadenia hastata* leaves in the treatment of diabetes mellitus.

Table-12. Effect of n-hexane extract of Leptadenia hastata on fasting blood glucose in experimental rats

Group	Treatment	Initial	FastingBloodGlucoselevels(mg/dl)				
			Day1	Day7	Day14	Day21	Day28
I	-	105.2 ± 4.3 ^{a}	100.2 ± 3.3 ^{a}	96.5 ±7.4 ^{a}	99.9 ±6.9 ^{a}	92.3 ±3.5 ^{a}	110.6 ±12.6 ^{a}
II	Extract (200mg/kg)	108.3 ±6.6 ^{a}	112.3 ±4.8 ^{a}	114.2 ±5.5 ^{a}	108.8 ±8.1 ^{a}	119.2 ±7.3 ^{a}	105.0 ±9.3 ^{a}
III	-	120.2 ±4.1 ^{a}	420.2 ±5.2 ^{b}	444.8 ±8.7 ^{b}	547.0 ±4.2 ^{c}	567.8 ±2.4 ^{c}	539.0 ±8.5 ^{c}
IV	Extract (100mg/kg)	108.0 ±8.8 ^{a}	4 50.0 ±6.9 ^{b}	494.0 ±3.6 ^{b}	414.2 ±3.3 ^{b}	124.6 ±12.9 ^{a}	180.7 ±8.7 ^{b}
V	Extract (200mg/kg)	116.8 ±5.4 ^{a}	440.8 ±5.6 ^{b}	446.0 ±4.7 ^{b}	391.4 ±4.7 ^{b}	214.4 ±6.3 ^{b}	93.4 ±8.9 ^{a}
VI	Insulin	113.4 ±3.7 ^{a}	462.4 ±6.8 ^{b}	441.0 ±9.3 ^{b}	374.4 ±3.3 ^{b}	291.7 ±6.0 ^{b}	222.4 ±3.0 ^{b}

The values are expressed as mean±SEM (n=5). Values in the same column with different superscripts are significantly different at $p<0.05$. Values in the same column with the same superscripts are not significant.

Table-13. The Effect o fn-hexane Extract of *Leptadenia hastata* on Body Weight

Group	Treatment	Bodyweight(g)					Differencebetween Day28 -Day1(%)
		Day1	Day7	Day14	Day21	Day28	
I	-	160.5 ±2.9^{a}	160.3 ± 2.9 ^{a}	186.8 ± 3.6^{a}	187.1 ± 3.1^{a}	182.4 ± 3.0^{a}	13.7
II	Extract (200mg/kg)	150.0 ±2.2^{a}	171.54 ± 1.4 ^{a}	197.2 ± 1.7^{a}	180.1 ± 2.6^{a}	177.1 ± 2.6^{a}	18.0
III	-	190.2 ±1.4^{b}	133.8 ± 2.4 ^{b}	110.8 ± 2.4^{b}	123.6 ± 2.0^{b}	123.7 ± 1.9^{b}	-35.0
IV	Extract (100mg/kg)	143.5 ±2.1^{b}	140.6 ± 2.0 ^{b}	140.6 ± 1.6^{b}	131.8 ± 1.2^{b}	129.0 ± 1.2^{b}	-10.1
V	Extract (200mg/kg)	135.6 ±1.8^{b}	135.6 ± 1.8 ^{b}	130.9 ± 1.3^{b}	129.8 ± 1.2^{b}	131.5 ± 1.2^{b}	-3.0
VI	Insulin	138.2 ±4.2^{b}	138.1 ± 3.4 ^{b}	136.5 ± 3.3^{b}	152.0± 3.0^{a}	153.8 ± 3.0^{b}	10.7

The values are expressed as mean ± SEM (n=5). The values are expressed as mean ± SEM.Values in the same column with different superscript are significantly different at $p<0.05$. Values in the same column with the same superscript are not significant.

7.2.7 Testicular Enhancement Activity of Aqueous Extract of *Pausinystalia Macroceras* Stem-back

Jacks et al. (2007) investigated the testicular enhancement potentials of *Pausinystalia macroceras* (Pierre ex Beille), family Rubiaceae, a tall forest tree with medicinal properties. Aqueous extract of the stem-bark *P. macroceras* (0.1 – 0.4g/kg) was administered oro-gastrically to male Wistar rats once daily for 28 days. Light microscopic study revealed that the extract produced significant ($p \leq 0.5$) increase in the volume of germ cells (80/20µm), and in the size of Leydig cells (about 20µm in diameter) relative to the control. Ultrastructural observation of the testis showed abundance of branching and anastomosing tubules of smooth-surfaced endoplasmic reticulum in the Leydig cells, Sertoli cells exhibited very large and ovoid nuclei, numerous mitochondria, with several spermatids and spermatozoa associated with it. The results indicate that the plant extract could enhance testicular activity.

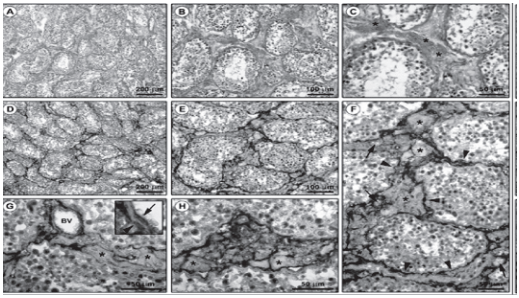


Figure 32. Light micrograph of testis of rats administered with different doses of *Pausinystalia macroceras*. A – C are normal control, Scale bar = 200µm, 100µm, and 50µm, respectively. D – F were given *P. macroceras* (0.1g/kg), shows marked increases in the volume of germinal epithelium, Scale bar = 200µm, 100µm, and 50µm, respectively. G & H were given *P. macroceras* (0.4g/kg), showsseveral Leydig cells (asterisks) in the interstitial tissue, basement membrane of seminiferous tubule (arrow), and blood vessel (BV).Scale bar = 50µm. H & E, ×100.

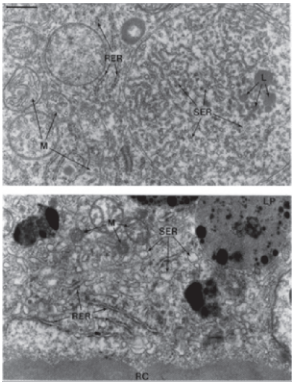


Figure 33. Electron micrograph of Leydig cells in testis of an extract-treated rat (0.1g/kg).
Shows abundance of anastomosing tubules of smooth-surfaced endoplasmic reticulum (SER),and several spherically-shaped mitochondria (M). (×50,000).

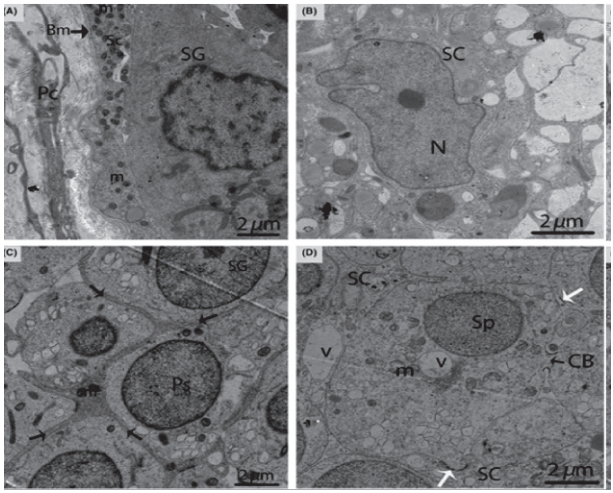


Figure 34. Electron micrograph of Sertoli Cell in Seminiferous tubules of extract treated rat (0.1g/kg).Shows (A) Sertoli cell between the basal membrane (Bm) of spermatogonia (SG);(B) An oval-shaped nucleus (N) in the Sertoli cell (SC); (C) The thick process of Sertoli cell wraps around the spermatogonia (SG) and primary spermatocytes (Ps); (D) Sertoli cell (SC), spermatids (Sp), cytoplasmic bridge (CB), vesicles (v), mitochondria (m). Scale bar = 2µm, ×20,000.

8. 0 CONCLUSION AND RECOMMENDATIONS

8.1 Conclusion

Cells are the building blocks of tissues, organs and organism. Stem cells are the ancestors of all cells in the body, from simple skin cells to complex cells like neurons. Stem cells could be pluripotent, multipotent, or totipotent, and provide an opportunity to investigate the mechanisms that regulate embryonic development, cellular differentiation, and organ maintenance or repair.Stem cells are important in assisted reproductive technology. Cells communicate with each other either directly through different occluding junctions or through the use of chemicals (signaling molecules).The internal contents of the cell are separated from its surrounding environment by the cell membrane, a phospholipid bilayer.

Oxygen reactive species (ROS) or free radicals are by-products of cellular activity, produced mainly by the mitochondria (intra-cellular organelle), that must be detoxified by the immune system of the cells. However, there is often an imbalance in favour of ROS, causing oxidative stress, which could lead to cell death (apoptosis). Oxidative stress occurs naturally and plays a role in the aging process. Certain factors could increase a person's risk of long-term oxidative stress, including obesity, diets rich in fat, exposure to radiation, tobacco smoking, alcohol consumption, pollution, etc. Ways of body defense against oxidative stress include, exercise, good sleep, stress reduction, limiting alcohol consumption, quitting smoking, eating healthy (anti-oxidant rich diets).

8.2 Recommendations

The following recommendations will help in the study and research activities in the morphological sciences:

i. Provision of a central research laboratory where relevant high-tech equipment like the Electron Microscope will be available. It can also serve as a referral laboratory for postgraduate training, particularly Ph.D. programme.

ii. Training of technical staff with requisite knowledge and skills to manage equipment in the central laboratory.

iii. More funding for staff in collaborative and multi-disciplinary research.

iv. Renaming of the Department of Human Anatomy to "Department of Anatomical Sciences" in response to recent agitation to properly name the Department because of the multi-disciplinary nature of the science of Anatomy.

9.0 ACKNOWLEDGMENTS

I give all the glory to God Almighty who first gave me life and dueling in a world of darkness, had also redeemed me into His marvelous light. May His name forever be praised for granting me the grace, strength and wisdom to accomplish this feat.

Perhaps, I might begin by apologizing to all those who have contributed in both small and big ways to the accomplishment of my academic ascension, including this inaugural lecture but whose names did not appear here, in what looks like roll call, for

want of space. Please bear with me but remember that your labour of love will not go un-rewarded. Thank you very much. I celebrate you all.

In keeping with the university tradition, I wish to sincerely appreciate the Vice Chancellor of this great institution, Professor Nlerum S. Okogbule, for giving me the singular opportunity to present this inaugural lecture, a debt every Professor owe the university system. Permit me to also appreciate your lieutenants, the Deputy Vice Chancelor (Administration), Prof Nnamdi S. Okoroma and the Deputy Vice Chancellor (Academic), Prof Valentine Omubo-Pepple, for their continued and relentless support to your administration. I will not forget to appreciate other members of the Management team, the Registrar, Dr. Sydney C. Enyindah, the Librarian, Dr. (Mrs.) Jennifer N. Igwela, and the Acting Bursar, Mr. James O. Ebere, for their contributions to the development of this University.

I wish to specially thank the former Vice Chancellor, Professor Blessing C. Didia, whom the Lord used to rescue me out of the camp of Boko Haram in the northeast of Nigeria to this institution. It is interesting to know that Prof. Didia, is also an Anatomist and one of my admired teachers during my undergraduate days at the University of Port Harcourt. Incidentally, it was the same Prof. Didia that I succeeded in 2014 as the President of the Anatomical Society of Nigeria (ASN). It was Prof. Didia who first appointed me as Head of Department of Human Anatomy in this University in 2018. I deeply appreciate you sir; your labour of love shall not be forgotten by God. May I also appreciate the former acting Vice Chancellor, my respected sister, Prof. (Mrs.) Opuenebo B. Owei for her

caring and unassuming disposition, throughout the period she was in office.

I wish to deeply appreciate the Provost of the College of Medical Sciences, Professor Chituru G. Orluwene, for moving the College into an enviable and lofty heights, since he assumed office. I also wish to thank him sincerely for the cordial working atmosphere in the College that has made it easy for me to present this inaugural lecture, another Anatomist, after my colleague and Dean, Faculty of Basic Medical Sciences, Prof. Kenneth S. Ordu gave the debut College inaugural lecture. May I also express my gratitude to the former Provost, Professor Raphael Oruamabo, a father with a large heart, highly disciplined, hardworking, and visionary. So much to learn from him. He laid the academic foundation of the College and received me when I joined in 2017 to continue the "building". I won't forget to mention that Prof. Ordu was appointed the pioneer Head of Department of Human Anatomy in 2016 at a time when the entire College was run like a Faculty (the College was established in 2015). I succeeded Prof. Ordu as Head of Department in 2018, while he was appointed pioneer Dean of the Faculty of Basic Medical Sciences. Prof. Ordu and I had had a very cordial and friendly working relationship because we both flow together in the spirit. May I also appreciate other Deans in the College, Prof. Kaladada Korubo, the Dean, Faculty of Basic Clinical Sciences and Prof. Solomon Elenwo, Dean, Faculty of Clinical Sciences, whom I have enjoyed working as members of the College Academic Board.

My gratitude goes to the Chairman, Senate Lecture Committee, Professor Nkalo H. Ukoima and other members, Prof. Jones M.

Jaja, Prof. John Ohaka and Prof. N. H. Nwafor for their great support and assistance. May I also appreciate my colleagues, Dr. Tonye Korubo-Owiye (my teacher at the undergraduate level at the University of Port Harcourt), the Head of Department of Human Physiology, Prof. Ahamefula Ezekwe, Head of Department of Medical Biochemistry and his predecessor. Dr. (Mrs.) Christine Brisibe, and Dr. (Mrs.) Janet E. Peter, Head of Department of Nursing Science and her predecessor Dr. (Mrs.) Elizabeth Okankwo, for their enduring support and cooperation. May I also use this privilege to deeply appreciate members of the "Anatomy family" for the tremendous support I have received from each person as Head of Department.

My sincere thanks and appreciation go to Professor Ibrahim Njodi, the former Vice Chancelor of the University of Maiduguri, who painfully released me on Leave of Absence to this University (January,2018 – December, 2019), and Professor Aliyu Shugaba, the current Vice Chancelor, University of Maiduguri, who freely signed my transfer to this great institution in January, 2020. My deepest appreciation also goes to Prof Samuel A. Asala, my teacher and supervisor of my Ph.D. Thesis, Prof. J. Prasad, Prof. H. C. Varma and Prof P. Shukla, my teachers at the postgraduate level (M.Sc. and Ph.D.), the later three are of blessed memory. They taught me hard work, diligence, tolerance and patience at the University of Maiduguri. Others include late Prof Oluwale J. Ogunranti, who supervised my undergraduate work at the University of Port Harcourt and later became a dear friend.

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