# UNIVERSITY OF PORT HARCOURT

## "LIFE UNDER ASSAULT: NOWHERE TO HIDE"

# An Inaugural Lecture

by

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## ACKNOWLEDGEMENT

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#### "LIFE UNDER ASSAULT: NOWHERE TO HIDE"

Mr. Vice-Chancellor, Deputy Vice-Chancellors, Members of Council here present, Principal Officers of the University, Provosts, Deans, Directors & Heads of Departments, My Academic Colleagues, Staff & Students, My Lords Spiritual & Temporal, Distinguished Friends of the University of Port Harcourt Distinguished Gentlemen of the Press, Ladies & Gentlemen.

#### PREAMBLE

This occasion couldn't have come at a better time than now when we are in the mood of triple celebrations - the centenary celebration as a nation, the celebration of the founders day of this great University of Port Harcourt founded some thirty eight years ago, and the last but not the least, celebrating the confirmation of my appointment this day as a faithful steward of this unique University. In all, it is a moment of sober reflection. To reflect on the past, assess the present, and offer the road map for sustainable development of the nation as well as to ascertain the actualization of the visions of the founding fathers of this most importantly, to reflect on the national institution, and educational developmental growth. On this premise, with great honour and pleasure, I count it a privilege, Mr. Vice-Chancellor to be enlisted among Professors to deliver this Professorial Inaugural Lecture today.

A perfect environment was divinely balanced to produce and preserve perfect mental and physical health. The Holy Book says "In the beginning.... "It was very good".... (Genesis 1:1, 31). Over the past decades, we live in a world tainted and corrupted by

an environment that is threatening the existence of human lives. This is achieved as an adverse reaction to potentially toxic unrelated chemicals of technological or natural (non-synthetic agents) origins or both in air, food (or water), at concentrations generally considered as harmless to the residents of the communities (as well as wildlife). We live in a 'toxic world' and every day, chemicals are hurting our bodies: it is against this back drop, Vice Chancellor Sir, ladies and gentlemen, that I have chosen the theme of my Inaugural lecture entitled: *"Life Under Assault: Nowhere to Hide"*.

#### 1.1. DEFINITION OF LIFE:

Life is not a tangible thing that we can touch. Medicine has apparently not been able to detect life under the microscope. The word for 'life' used in this lecture is *"blood*'. Suffice to quote the Greatest Physiologist who said ".... you shall not eat flesh with its "life" - its "blood". (Gen 9:4) "For "life" ....is in ..."blood"... (Leviticus. 17:11, 14). And according to a certain song writer "Jesus covered us with His life [blood]". Blood in every physiological system is not merely a fluid connective tissue that performs many functions in the body including regulating and/ or transporting medium; maintains its constituents within defined physiological normal range; and keep the body alive: but blood, - itself - is and contains "LIFE". Thus "LIFE" [or "BLOOD"] is under the assault of the "ENVIRONMENT" defined as:

- "All the biotic (internal) and abiotic (external) factors that act on an organism, (population, or ecological community) and influence its survival and development". "Biotic factors" include their food (hereafter shall be referred to as "chemicals of natural origin" or "natural medicine" i.e. non-synthetic or chemically produced agents) -the organisms themselves, and their interactions. While "Abiotic factor" (hereafter shall also be referred to "chemicals of technological origin" or "fugitive chemicals" i.e. non-synthetic or chemically produced agents) include such items as air, climate, pollution, sunlight, soil, and water; and Organism's response to changes in their environment by evolutionary adaptations in form and behaviour (The American Heritage Science Dictionary of 2005)
  - Biotic factor: Nutraceuticals also called botanical medicine, ergogenic aid, functional food, herbal medicine, medical food, or nutriceutical are, as defined by Merriam-Webster Dictionary and/or Jonas: Mosby's Dictionary of Complementary and Alternative Medicine (2005) Elsevier, as foodstuffs or any food supplement which provide health benefits in addition to their nutritional value. Or a food or naturally occurring food supplement thought to have a beneficial effect on human health (The American Heritage Medical Dictionary Copyright 2007).

#### 1.2. WHAT IS PHYSIOLOGY?

Aristotle, Greek thinker, (who lived between 384 and 323 B.C. in ancient Greece), the father of natural history, and also the world's first great biologist, was the person who actually created the word *physiology*. The word physiology is derived from a

combination of two Greek words, namely physis, which means 'nature' and logos, which means 'word'; and in Latin word *physiologia* meaning "natural" science.

Since some are just beginning the study of physiology, it is imperative to have some idea of what the field is. Human physiology is science of the mechanical, physical, biochemical, cell and organ functions of humans. As a discipline, it connects science, medicine, and health, and creates a framework for understanding how the human body adapts to stress, physical activity and disease.

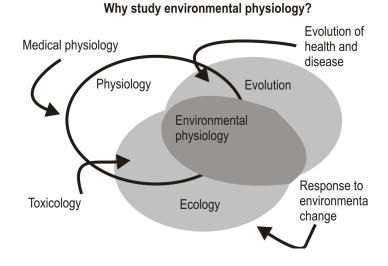


Fig. 1. Inter-relationship between Physiology and the Environment



Physiological studies of normal biological functions provide the basis for understanding the abnormal functions seen in human diseases (highly abnormal state of physiologypathophysiology) and for developing new methods for treating those diseases (translational research). Human physiology and anatomy are closely related- while anatomy is the study of form, physiology is the study of function and form, and these functions are intrinsically linked. Research in human physiology explores new ways to maintain or improve the quality of life, the development of new medical therapies and interventions, and the unanswered questions about how the human body works. Investigations in physiology often lead to a better understanding of the origins of diseases. In a simple term, physiology is the foundation upon which we build our knowledge of what "life" is, how to diagnose, treat disease, and how to cope with stresses imposed upon our bodies by new environments. It serves as the foundation of modern medicine.

Physiology is as old as man. The world's greatest "Physiologist" stated - "let us make man in our image and the Lord God...breathed into his nostrils the breath of "life" [contained in Blood]...;"(Genesis1:26; 2:7). Human (or mammalian) physiology is the oldest branch of the science of medicine and it is the bedrock of modern medicine dating back from 460 to 370 B.C. the time of Hippocrates, (who lived in Ancient Greece) the father of modern medicine. Experimental Physiology dates back to A.D. 130-200 the time of Claudius Galen, a philosopher and physician, often called the father of experimental physiology, who lived in Greece and later in Rome. He was the first person to perform experiments (control trials) on living animals like pigs, dogs, bears and apes. The use of modern version of animals as model for human anatomy and pathophysiology began with Claude Bernard in the 19<sup>th</sup> century. Bernard was a firm believer in the reductionist approach to medical science and that approach has indeed served biomedical science well for decades <sup>(1,47)</sup>

Traditionally, physiology is seen as a branch of biology. It is currently an interdisciplinary science that collaborates with other fields such as chemistry, computer science, engineering, linguistics, mathematics, medicine and allied disciplines, philosophy, physics, and psychology.

1.3. REDUCTIONISM AND COMPLEXITY: HOW CAN WE STUDY HUMAN BODY

Looking at the complexity of the human body and in order to fully understand the physiology of the complex living system, we can break it down patiently into simple pieces and then study the pieces. Accordingly, I shall focus this lecture on my activity to the study of the haematopoietic system- blood, still narrowing down to the study of its form elements, the red blood cells or erythrocytes in relation to body functions.

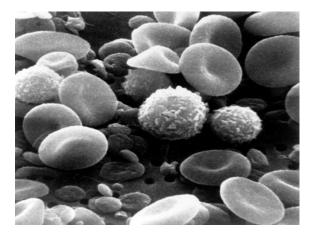


Fig.2 Photomicrograph of Red blood cells with white blood cells

Invariably I am studying life the smallest part of a living organism that retains the characteristics of a living thing. An adequate way to assess effects of environmental exposures on humans is to study effects on specific organs, tissues, etc. This also applies to testing effects in the human populations. In other words, by dividing a system into its parts and ascertain the functions of the parts of the system, one can deduce the function of the entire system. Claude Bernard stated: "Physiologists......deal with just one thing, the properties of living matter and the mechanism of life, in whatever form it shows itself. For them genus, species and class no longer exist. There are only living beings; and if they choose one of them for study, that is convenience in experimentation".

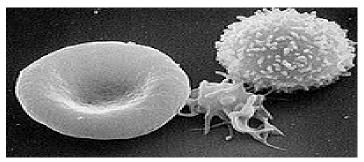
Erythrocytes were first described by a Dutch biologist Jan Swammerdam, who had used an early microscope in 1658 to study the blood of a frog. Unaware of this work, Anton van Leeuwenhoek provided another microscopic description in 1674, this time providing a more precise description of erythrocytes, even approximating their size, "25,000" times smaller than a fine grain of sand.

*R*eductionism basically is *divide* and *conquer*. It has led to many important scientific breakthroughs. Most of the Nobel Prize winners in medicine are Physiologists.

#### 1.4. BLOOD: A MODEL SYSTEM FOR STUDY.

The importance of blood to human life has been recognized since pre-history. Early humans knew that if enough blood leaves the body then life ceases to function. As a result of this blood has acquired mystic and religious significance throughout the ages. As stated by the father of homeostasis, American Physiologist, Walter B. Cannon (1929), coined the term homeostasis to describe one of the most basic concerns of physiology: *"how the varied components of living things adjust to maintain a constant internal environment that makes possible optimal functioning"*. Blood therefore is a physiological process which is nothing more than mechanisms for maintaining homeostasis; without it we will die. As a result, it is of huge importance clinically as a diagnostic aid because of its multifarious functions. An average adult has 5 to 6 quarts (4.7 to 5.6 litres) of blood, which is made up of plasma, red blood cells, white blood cells and platelets.

Fig. 3. Red blood cell, Platelet and White blood cell.



Red Blood Cell : Platelet: White Blood cell

And all of these cells are different in structure and function but they begin in the bone marrow from a common progenitor cell called the stem cell. Of the over 100 trillion cells in an average man, 25 trillion or one – fourth are erythrocyte. To understand the good thing about the use of blood for study, erythrocytes in particular, (which is part of my contribution to knowledge) for experimentations, we need to understand some specific established features of the cells which makes it unique in performing various functions in health and disease (1,7-9,11,19,25- $_{28,34,39,48)$ 

Erythrocytes in the presence and/or absence of chemotherapeutic agents at different trans-membrane and surface potentials heated in-vitro to 49°C instead of 50°C, does not show the expected dose response curve; the activities of ATPase and glycolysis are nearly optimal i.e. no metabolic lesions occurs.

- Charge-independent drug-specific properties can influence the distribution of drugs in the cell and can cause changes in the membrane or cytoskeleton or a combination of both.
- There is potential profile- zeta potential in the order of -15mV or less which is steep close to the outer surface of the cell and then remains relatively constant on approaching the bilayer. This potential gives the concentrations of the cations and anions at the surface of the bilayer to be 1.8 and 0.55 times the bulk concentrations respectively.
- The distribution of charged form of drugs across the cell membrane is in equilibrium with the distribution of chloride ion; i.e. there is Donnan equilibrium between the drugs and chloride.( the presence of membrane permeant drugs will modify the cell membrane potential equation to: E = 61.5 Log<sub>10</sub>{(Pcl[Cl<sup>•</sup>o] + P<sub>D</sub>[D<sup>•</sup>o] /(Pcl[Cl<sup>•</sup>i] + P<sub>D</sub>[D<sup>-</sup>i])} (Pcl and P<sub>D</sub> are the permeability coefficients for chloride and drug respectively)
- The erythrocyte membrane potential is in the magnitude of - 7.1mV while that for the sickle cell is + 16.5mV. at normal body temperature (37°C)( which it's accuracy can reasonably be given by the Nernst equation: E = 61.5 log<sub>10</sub>(r); where r is the activities of intracellular to extracellular chloride)

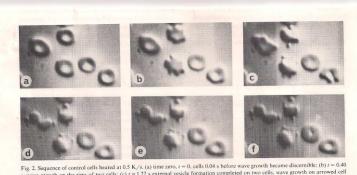


Fig. 2. Sequence of control cells heated at 0.5 K/s. (a) time zero, t = 0, cells 0.04 s before wave growth became discernible; (b) t = 0.40s, wave growth on the rims of two cells; (c) t = 1.22 s external vesicle formation completed on two cells, wave growth on arrowed cell without vesicle formation; (d) t = 6.0 s disturbance has subsided on the arrowed cell; (e) t = 6.0 s; (f) t = 7.2 s, cell (arrowhead) has internalized membrane at the cell dimple.

Fig. 4. Plates showing sequence of events in heated human erythrocytes

- At 50°C, the thermal denaturation temperature of spectrin - cell's cytoskeletal protein that plays the critical role in regulating membrane mechanical function, undergoes progressive morphological changes.( which can be explained by Murphy's law of interfacial instability at cell surface)
- Haematological markers- erythrocyte counts (RBC), haemogolobin concentration[Hb], or corpuscular haemoglobin (MCH), platelet distribution width(PDW) and mean platelet volume (MPV) remains unchanged at 50°C.
- While the following haematological markers- mean corpuscular volume (MCV), haematocrit (PCV), red cell distribution width (RDW), platelet count and eosinophiles

are significantly high and mean cell haemoglobin concentration (MCHC) decreases.

- Cautions the therapeutic use of urea fragments erythrocytes without temperature increase in time concentration dependent fashion
- Modern technological advances, ranging from the simple to differential interference scanning and electron microscope to ultra-high-technology computerized scanning devices, can be used for investigating the functioning components of human body, specifically erythrocytes in its life-like manner that could not ordinarily be observed with the naked eyes.
- Erythrocytes survive in the circulation for approximately 120 days; approximately 1% is replaced each day. This equates to a cell turnover of between 2- 3 million per second.
- In the average man, about 2,000 gallons (7,572 litres) of blood travel daily through about 60,000 miles (96,560 kilometers) of blood vessels, perfuse all of the body's organs and carry toxic (and infect itself as well as other organs) and/or beneficial substances around the body. And this is the mean thrust of the expository.
  - I will principally make use of the above definitions how changes in the physical environment are tools for investigating physiological and pathophysiological processes in humans.

- Focusing on the mechanisms available for response to environmental challenges (including different responses at different time scales)
- General mechanisms frequently involved in a variety of physiological responses and incredible physiological responses to environmental challenges of technological and /or natural origins in a way that is not usually entertained.

This expository lecture tailored alongside the above definitions will be detailed but in a format that is suitable enough for the benefit of this mixed audience, regardless of their academic backgrounds or fields of study. It will not only describe facts and events but will also provide accurate explanations on the mechanisms - curative - of "how an individual's present state of health is affected by their previous residences" and not the usual epidemiological studies - symptoms, "mobility"; it allowed the unique advantage to identify and evaluate original exposure. (2, 4, 6, 13)

Given the complexity of the factors that influence human health, assessing health impacts related to the environmental factors poses a difficult challenge. This is as a result that potentially dangerous relatively new chemically unrelated substances be it natural or artificial, which are potentially dangerous, are being introduced into the environment all the time. Their effects on living things may not be known until many years after their release.<sup>(3,4,6,13)</sup> Mr. Vice Chancellor Sir, permit me to say that information about environmental challenges and its risks to humans is a complex and rapidly changing area of human endeavour. Today, a great number of chemically unrelated substances are released into our environment with its concomitant rude effects of human life-span brevity. These various chemically unrelated substances may enhance or have an antagonist effects on each other. Thus, comparison or balance between human activities and ecological sustainability will be misguiding.

## 2.0. ENVIRONMENTAL INSULTS OF TECHNOLOGICAL ORIGINS -VULNERABILITY AND ADVERSE HEALTH IMPLICATIONS ON EXPOSED POPULATION (Figures 5-9).

In the first part of this lecture we will examine the effect of environmental toxins on physiological processes in humans (and in experimental animal models which may effectively address issues of importance in understanding the underlying causes of human diseases). In the wake of industrial revolution, many tonnes of man-made unrelated chemicals of technological origins are produced by oil and gas exploration and exploitation and released into the environment. The fugitive natural gas emissions contain many contaminants. Chronic -low -levels and prolongedexposure comes with a terrible cost on human health. The cost is not for the workers on site, though they are affected. It is to men, women and children, the aged and the unborn, the teachers and doctors and self-employed, chiefs and priests who live away from but in proximity to a flare or spilled site. Of particular concern to the public – and that which understandably generates the most outrage – is the involuntary subjection of certain groups of the population 24 hours/day, 7 days/week to the emissions of gas flaring base-stations, when they are insensitively sited near to homes, schools and hospitals.



Fig 5. Serene Environment being polluted by gas flares.

The communities are unprotected by Labour - code statutes about exposure because they live at home and are exposed where they sleep and eat as wind carries the plume of combustion products - the excessive concentration of foreign matter in the air which travels slowly but surely from source towards residential areas.

The potential adverse human health impact and implications are the direct effect on the natural environment and natural habitat of blood (haematopoietic system) which is the most important system in all organisms in states of both health and diseases. Cells transport materials along crowded, complex and busy intercellular "highways" that is vital to the survival of cells and organs, failure of which exposes the system to a variety of diseases and cancer such as: cardiovascular, respiratory , reproductive, neurodegenerative, kidney dysfunctions ..... This list of diseases measures is by no means exhaustive.

"This means that the blood environment is the most dangerous environment on earth to inhabit since blood (erythrocyte) has little or no legal protection".

Ideally in both states of health and disease there are a triangular relationship between three role-players – the environment, the blood and other body organ systems. While the environment is the pivotal role-player, this triangular relationship sets up accountability structures of both states of health and disease.

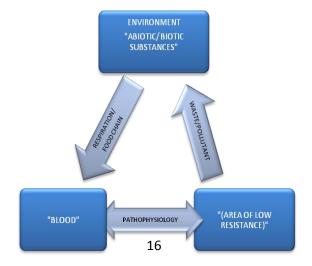


Fig.6. Relationship between environmental challenges and physiological processes

- Exposure to potentially toxic chemically unrelated compounds in the environment enters the body to the bloodstream through the skin, lungs or gastrointestinal track. By these mechanisms, chemically unrelated compounds affect the health of human (as well as wildlife) populations by upsetting the normal physiological balance and/ or functioning of blood, thereby give rise to blood cancer- a combination of disorders that affect the way the body produces blood and fights off other diseases.
- The abnormal cells act by interfering with the production of healthy blood cells; and that is the etiology of the many of the chronic diseases. In other words, blood keeps traffic flowing smoothly along the busy transporting body network that is vital to the survival of the cells which the failure of the system leads to a variety of diseases.

According to World Bank "one of the planet's major environmental problems" is the huge plumes of flame resulting from burning of unwanted natural gas during oil production". A flare has been defined as a "toilet up-side-down at the end of a pipe 30 feet in the air with a flame to keep the seat warm". Unlike the situation in the more developed countries of the world the disposing of waste gas and oil and co-produced sea-water is at an elevation above the ground varying from 15 to 75 or more meters.  $^{(4,5)}$ 



Gas flare at Refinery

Figure 7. Polluted environment at night by gas flares.

The elevation is to disperse the combustion products and throw them away from the work site to make assault on life less noticeable by dispersing it. The situation in Nigeria, particularly,



in the Niger Delta region is different.

Fig. 8. Polluted scene ravaged by fire.

The flares in the Niger Delta are at sea level, so the environmentally exposed groups live with gas flares that roar continuously, turning night into day, and polluting the air and ground thereby creating extremes of temperature and climate change and global warming with concurrent exacerbation ofenvironmental associated increases

Country Home covered by Black Cloud in the Night



Country Home at Night Totally Taken over by Black Cloud



in disease and cancer.

Fig, 9. Gas flares endanger the neighbourhood communities at night.

Living and working close to the oil and gas extractions increases the likelihood that people will be exposed to the hazardous chemical emissions and pollutants associated with these industrial activities - the environment of these people are effectively and permanently polluted - pollution from which there is literally *'nowhere to hide'* 

"The venting of the fugitive natural gas is scaring, for it is hard to measure because it is invisible and the concentration in the air is far below their threshold for smell - the substances are present but we have no warning( i.e. there is no early mechanisms of warning). Hitherto, the health risks are not detectable by sufferers until the damage is done - they are effectively involuntary subjects in a mass experiment".

This totally unacceptable state of affairs raises serious ethical questions, in that it is these local populations in the setting of oil and gas extractions that will eventually reveal the degree or the seriousness of the health problems associated with exposure to low- level- chronic hazardous substances which the threshold levels are not necessarily surpassed, over a period – information that is not currently available particularly for Nigerians in the Niger Delta region and which will be presented.

2.1. OIL AND GAS CONTAMINANTS - "CHEMICALLY UNRELATED COMPOUNDS OF TECHNOLOGICAL ORIGIN" AND HEALTH

"Open path" air quality laser monitoring techniques have provided conclusive evidence that oil and gas contaminants can arise from (a) Industrial processing sites (b) Greenhouse gases effect and (c) Automotive exhaust chemicals.

Path	ogen Inventory
Industrial processing sites (>	
thousand Chemicals)	
Particulates	PM10 (diameter = 10 microns)</td
	PM2.5(diameter = 2.5 microns)</td
	Ultrafine particles (diameter = 1</td
	microns)
Nitrous oxide (NOx)	
Sulphur oxides (SOx)	
Ozone (O <sub>3</sub> )	
Dioxin	
Hydrogen Sulphide(H <sub>2</sub> S)	
Volatile organic Compounds	BTEX (Benzene, Toluene, Ethyl
(VOC)	benzene, Xylene) Methylene Chloride;
	Tetrachloroethene; Trichloroethene;
	1,4-dichlorbenzene; m,p-xylenes; 2-
	hexanone
Diesel fuel/exhaust chemicals	
Metals	Arsenic; Barium; Cadmium; Chromium;
	Lead; Mercury; Selenium; Zinc
Polycyclic aromatic	(>100 organic chemicals)
hydrocarbons (PAH)	
Radiations	Radon; Radium; Uranium
Greenhouse Gas Effect	

Table 1. Contaminants of oil and gas flared

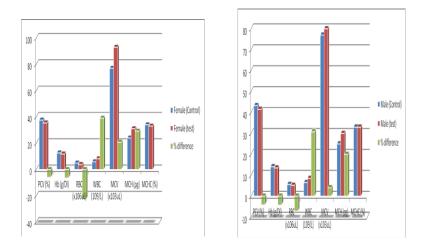
## PART ONE: ENVIRONMENTAL INSULTS OF CHEMICALS OF TECHNOLOGICAL ORIGIN: RELATED HEALTH IMPACT AND IMPLICATIONS

The focus in this section is on lifetime prolonged exposure assessment of residents in communities in close proximity to oil and gas flaring and disease stemming from chronic exposure, specifically on the haematopoietic system. Proximity is defined as from 0.2 km up to 10+ km.

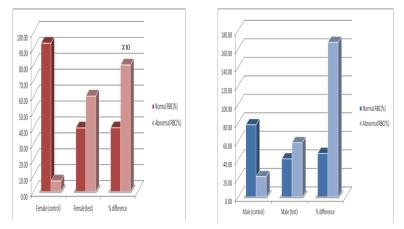
- Subjects (volunteers) under the same atmospheric pollution levels (normally staying in the Niger Delta Region-Rivers/Bayelsa States).
- Same physical activity patterns socioeconomics, nutritional status and anthropometric determinants (Age, sex, height, weight, race)

## 3.1 EFFECT ON HAEMATOLOGICAL INDICES:

The environmental effect, though frightening, is that prolonged exposure (*involuntary*) to gas and oil flared pathogens adversely affects the haematological parameters which are more pronounced in females than in males (Figs 10 to 14). Chronic exposure leads to a drastic decrease in the following blood parameters - packed cell volume (PCV), haemoglobin concentration [Hb], and red blood cell count (RBC) compared to none residents of the gas flaring environment <sup>(5, 6)</sup>



Figures 10 and 11. Comparison of variations in hematological parameters in both sexes relative to the control.



Figures 12 and 13. Comparison of variations in Red blood cells in both sexes relative to the control.

There is a drastic increase in white blood cell count (WBC), which is an indication of degenerative disease condition principally malfunctions of the human immune system. Such weakened human immune system (damaged to CD4 cells or Tcells) may account for the preponderance of HIV/AIDS and chronic illnesses and infections in the Niger Delta region. Increases in erythrocyte indices such as mean cell volume (MCV), and mean cell haemoglobin (MCH) are indications that people in the gas flaring communities suffer various forms of anaemia (deficient red blood cell production); invariably they have shorter erythrocyte lifespan.

# 3.1.1 SENSITIVITY OF HUMAN ERYTHROCYTES TO ENVIRONMENTAL TOXINS

The potential human health hazard emanating from the prolonged exposure of human erythrocytes to the potentially toxic substances in the environment is an increase in abnormal red blood cells <sup>(6,10, 50)</sup> (Fig 14).

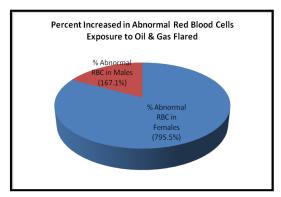


Fig. 14.Percentage differences of the abnormal red blood cells in both sexes

People at particular risk are women who are more vulnerable or more sensitive to chronic chemical *odor* exposures of diverse structural classes (Multiple Chemical Sensitivity) than men giving male to female ratio of 1:5. The women have detoxification mechanisms that have been seriously compromised from the environmental insults and obviously would develop environmental illness that could be known as "*oil and gas related problem" or "petroleum disease"* (*which* the treatment may not be immediately known). It means that they will become ill after prolonged exposure to a small but significant dose of chemicals when leaving in a heavily oil and gas extraction environment with oil and gas pathogens.<sup>(4,6,10,23,30,50)</sup>

#### 3.1.1.1 POSSIBLE MECHANISMS OF ACTION

The synthetic chemical antigens are not always or easily eliminated from the body and are lodged in the fatty tissues, and they remain continual irritants in the blood system and the whole body at large. This probably can be contributed to the differences in the levels of the enzymes in males and females:

(1) Alcohol dehydrogenase that detoxifies carbohydrates, sugar, alcohol, and chemicals and/or

(2) Butyl cholinesterase which scavenge chemicals, which both are much lower in females than in males and/or additionally,

(3)Women, apart from having a greater total percentage of body fat which stores chemicals, their immune systems are more complicated because they need to accept and protect a 'foreign' foetus in the womb.

When once a person is sensitized to such a substance, future exposures to low-level chemicals may lead to increasingly severe and debilitating reactivity which "spreads" so that the body now either reacts to a wider range of chemicals over time or develops dysfunction in more organ systems or restricts blood flow to the brain during chemical exposure. <sup>(10)</sup>

The low-level environmental chemicals gain access to the central nervous system via the olfactory and limbic pathways in the brain (the blood brain barrier may be made more permeable and chemical exposure create hypersensitivity in the neurons in the brain). So, its disruption could easily lead to induction or sensitization of lasting changes in nerve tissues and alter a broad spectrum of behavioural and physiological functions to produce adverse health effect or abnormal reactions (The limbic system is the part of the brain stem which is involved in regulating emotional/ survival behaviours and motivational drives aggression, sleep, eating.)

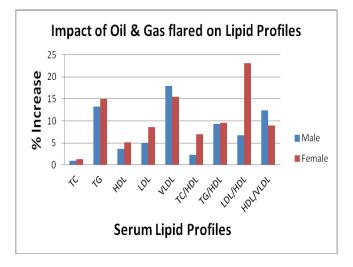
As the fugitive natural gas are carried through the bloodstream they disproportionately affects residents of communities exposed to toxic oil and gas pathogens and significantly contribute to multiple non-cancer and cancer endpoints. Some of the human risks are Presented below (because of time constraint not all the effects are presented –John 21:25):

26

#### 3.2. BIOCHEMICAL VICIOUS CYCLE ACTIVITIES

Pathogenic substances resulting from prolonged low-level exposures to oil & gas apparently accumulates in the soft tissues of the body longer, making it more toxic and increases lipid levels possible by controlling hydrolysis of certain lipoproteins and their selective uptake and metabolism by different tissues.

The cardiovascular disease risk assessing factorsatherogenic index, the ratio of LDL-C (low density lipoprotein- bad cholesterol) and HDL-C (high density lipoprotein- good cholesterol), coronary risk index, fasting blood glucose level, and lipid parameters except very low density lipoprotein (VLDL-C) fraction are significantly also increased in females compared with males (Fig 15 to 16). The male and female ratio of LDL-C / HDL-C gave male to female ratio of 1:5.



#### Fig 15. Serum lipid profiles in male and female compared

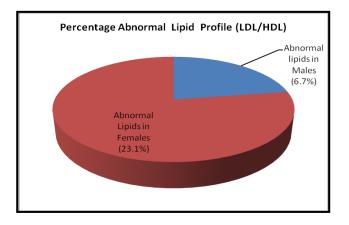


Fig 16.Percentage abnormal lipid profile in male and female compared.

#### 3.2.1 POSSIBLE MECHANISMS OF ACTION

The chemicals caused generation of free radicals and consequently induction of oxidative stress -related lipid peroxidation which subsequently reduces the body antioxidant defense mechanisms – and women being more prone to developing environmental - chemical - induced stress than males. This probably may be due to the fact that the domiciled females at home as house wives and/or are mainly farmers and spend most of their time in the gas flared environment are more predisposed to developing environmental chemical AIDS, and idiopathic environmental associated illness than the more migratory males. The avoidance of pollutants/toxicants is the best protection, which extremely is hard to achieve (for those in the Niger Delta region)

## 3.3. EFFECTS ON THE CARDIOVASCULAR SYSTEM: RAISED LEFT VENTRICULAR HYPERTROPHY RISK

The fugitive natural gas and the myriad of other pollutants that are also in the air together with the corrupted blood or cancerous blood are also carried through the heart and exact their toxic effects in the heart ( and as well as affects the metabolism of other body organs- pancreas, kidney etc) as they are carried by the bloodstream.

Electrocardiographic (ECG) analysis of the heart revealed unprecedented high prevalence of left ventricular hypertrophy (LVH) - an independent cardiovascular (CV) risk factor, and other related cardiovascular abnormalities on ECG among hypertensive and normotensive type 2 diabetics in Nigerians in the Niger Delta region. <sup>(24,30)</sup>

Comparison of some Ph	ysiological char	nges in Norma	otensive and Hypert	ensive Diabetics
Blood Pressure	Normotensive Diabetes		Hypertensive Diabetes	
(mmHg)	Systolic	Diastolic	Systolic	Diastolic
Normal range: SBP< 120,& DBP<80	35(17.5%)	45(22.5%)	Nil	Nil
Pre-hypertension: SBP:120-139 & DBP:80-89	67(33.5%)	31(15.5%)	Nil	Nil
Stage one hypertension: SBP:140-159 & DBP:90-99	Nil	26(13.0%)	36(18.0%)	55(27.5%)
Stagetwohypertension:SBP:>160DBP:>100	Nil	Nil	62(31.0%)	43(21.5%)
Mean blood pressure (mmHg)	117.64+10.5	77.75+10. 8	154.95+15.24	154.94+12.58
Mean arterial blood pressure (mmHg)	91.04+	9.67	111.91	+11.31
Mean body mass index (m/kg <sup>2</sup> )	25.90-	+3.60	26.17+3.47	
Normal ECG Pattern[with no detectable abnormality]	29(14.5%)		29(14.5%)	
Prevalence rate of Left ventricular hypertrophy (LVH)	26(13	.0%)	33(16.5%)	
Prevalence rate of Right ventricular hypertrophy (RVH)	21(10	-	33(16.5%)	
Dros	Prevalence rate	e of type 2 dia	betes 7 - 9% etes 18.9% - 41%	
FIE		ugnosed alab	eles 10.9/0 - 41%	

Table 2. Comparison of some Physiological changes in Normotensive and Hypertensive Diabetics

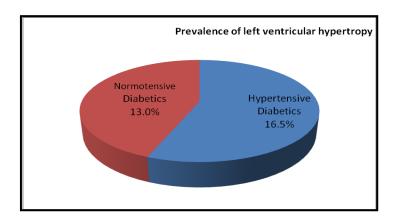


Fig 17. Prevalence of left ventricular hypertrophy

Although initially thought to be rare, it has now become clear that cardiovascular diseases (CVD) and associated complications and diabetes, raised cholesterol level, blood pressure, heart attacks, strokes ,obesity (and many kinds of cancer) are on the rise among Nigerians, in particular, those in the Niger Delta region.(<sup>24,30)</sup>

### 3.3.1 POSSIBLE MECHANISMS OF ACTION

The abnormal conditions cannot be easily be associated with the classical risk factors (Westernized lifestyles) but could likely be attributed to the impact of the harmful effects from prolonged exposure to potentially relatively chronic – low – levels of the chemically unrelated oil and gas pathogens in the environment.

Which leads to the manifestations of a pattern of underlying effects of oil and gas flared chemical - free radical - induced abnormal endothelial functions or metabolic syndrome that gives rise to such conditions as raised body fat and predisposition to development of atherosclerosis. In other words, the abnormal conditions are probably due to reactive oxygen species (ROS) production or oxidative stress damaged induced by the toxic agents in the environment. <sup>(30,45)</sup>

- (Free radicals are atoms or molecules that lack an electron in the outer shell. They are unstable molecules that are highly destructive as they move around seeking an electron to attach to form balance.
- They can attach to cell membranes or to the organelles inside the cell. By so doing, the cells degenerate casing abnormal physiology- aging, diseases and cancers.
- Antioxidants on the other hand, are such substances like vitamin C, A, E (and can also be provided by a healthy diet that includes a variety of fruits and vegetables - see section 2) that supply the missing electrons to the free radicals and balance them - antioxidants are therefore potent free radical quenchers (Table 3).

Variables	Table 3.Antioxidant Activities of Vitamins on Lead Poisoning in Animal Models- (Sub-acute toxicity study - lead acetate -				
	10mg/mL/day/rat for 28 days)				
	Control	Control Lead alone Lead + Lead +			
			Vitamin C	Vitamin E	
Initial body	203.3+_29.4	210.0+10.54	200.0+0.01	190.0+10.54	
weight (g)	2				
Final body	245.8+29.42	230.0+35.0	234.0+24	225.0+26.35	
weight (g)					
Body	20.70	9.50	17.0	19.0	
weight					
gain (%)					

Antioxidants protect the cells from damage caused by the unstable molecules – the free radicals.

Antioxidants interact with and stabilize free radicals and prevent some of the damage the free radicals might otherwise cause)

# 3. 4 ENVIRONMENTAL TOXIN EFFECTS ON THE RESPIRATORY FUNCTION

The continuous and the prolonged exposure to low-levels of the environmentally unrelated chemicals led to diminution in respiratory indices - lung volumes and peak expiratory flow rates (lung cancer risk - independent of smoking status etc) (Fig.18). The mean peak expiratory flow rate (PEFR) value - the caliber of the airways which serves as valuable tool for diagnosis and treatment of lung functions for Nigerians cohort in the Niger Delta region are less than the international and national values. This is an indication that people living nearest to and downwind of the site of the oil and gas extraction environments are at increased risk of having respiratory and pulmonary disorders related to exposure to "petroleum diseases" or "oil and gas flared problems"<sup>(4,10,12,49)</sup>

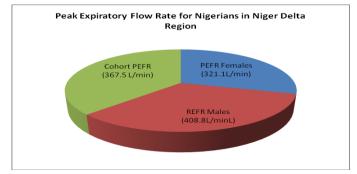


Fig 18. PEFR of Nigerians in Niger Delta regions.

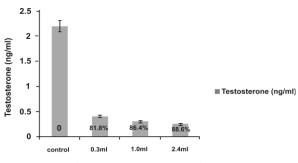
These are reasonably strong evidence that Nigerians in the Niger Delta region are exposed to potentially dangerous chemicals in their environment. The increases in such pollutants as nitrogen oxides, sulphur dioxide, and ozone exposures along with other air pollutants from oil and gas exploration activities are significant contributors to chronic obstructive pulmonary diseases.

- Air- pollution and sedentary lifestyles in the population of Nigerians in the Niger Delta region may be the probable reasons for the decline in respiratory performance.
- 3.5. ENVIRONMENTAL TOXINS AND REPRODUCTIVE HEALTH

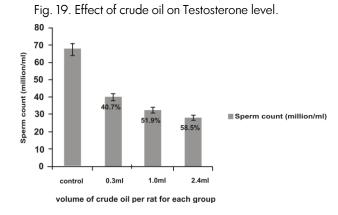
An attempt has been made here and elsewhere to elucidate the impact of unrelated chemicals in the environment be it of technological or natural origins on reproductive systems admitting that the scientific data came from experimental animals which the conclusions cannot be applied to humans easily. It should be emphasized that animal models are often employed in scientific investigations owing to its convenience, reproducibility, and availability. So, it is aimed at presenting available scientific information, highlighting the relationship between the impact of environmental toxins carried by the blood stream and human health in order to stimulate re-evaluation in identifying how the chemicals in the environment can be either environmentally friendly or unfriendly.<sup>(18)</sup>

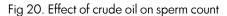
Apart from air pollution, environmentally contaminated feed (20g feed mixed with known concentrations of crude oilshort term -2- weeks) can also affect reproduction by causing a decrease in a dose- dependent manner, the weight, hormones (Testosterone, Leutenizing hormone, and follicle stimulating hormone), semen parameters compared to control (Figs 19 -22)- indicating that a man's polluted diet can affect his fertility and sexual life quality - sperm quality determined by :

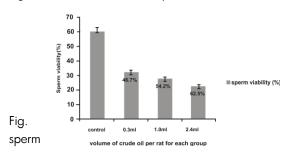
- $\Rightarrow$  The total number of sperm cells productions (sperm count)
- $\Rightarrow$  Their physical attributes (morphology)
- ⇒ Their ability to move properly once ejaculated (motility) all which are demonstrated with the exception of
- $\Rightarrow$  (the integrity of their DNA ?); as shown











21. Effect of crude oil on viability.

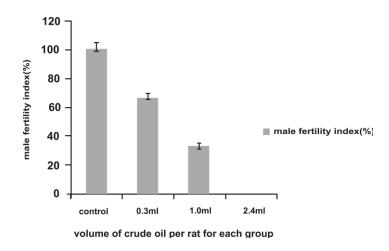


Fig. 22. Effect of crude oil on male fertility index.

Following the withdrawal of the crude oil contaminated feed, the weight of the offspring from the males mated with virgin females as well as the male fertility indices also decreased respectively. The chemical substances disrupted the hormonal balance of the body; it disrupted the action of the important male sex hormone, testosterone, their action in the male (as well as in female) reproductive system and male (as well as female) fertility is of great interest in that the chemicals are hazardous to human biology and health, particularly in uterus and in developing children. The decrease in reproduction indices is also an indication that exposure of males (as well as females) to Nigerian bonny light crude oil adversely affected male(as well as females) reproductive system. This implies possible reproductive health hazards to humans (and for animals) that are exposed to environment polluted feed, especially in areas where oil spill is a common feature. <sup>(18)</sup>

## 3.5.1. POSSIBLE MECHANISMS OF ACTION: HYPOTHALAMUS - PITUITARY AXIS

Infertility is a major clinical problem affecting people medically, psychologically, and economically, peace and harmony. In many infertile couples, no apparent cause of infertility can be found even after thorough examination. Exposure of blood cells to environmental endocrine disrupter chemicals affected hormone concentration and reproduction and have adverse effects on the reproductive indices. Thus some cases of unknown infertility may be explained by the action of these chemical substances in the environment.

Histological examinations did not detect abnormal testicular physiology (Figs 23-26)

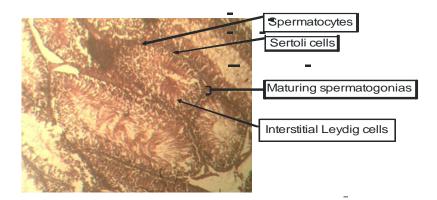


Fig. 23 Testicular section from control rats showing normal spermatogonic cells and interstitial cells

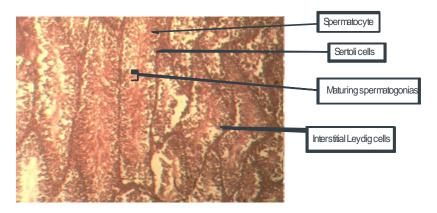


Fig. 24 Testicular section from test groups (0.3ml/rats/day) showing normal spermatogonic cells and interstitial cells

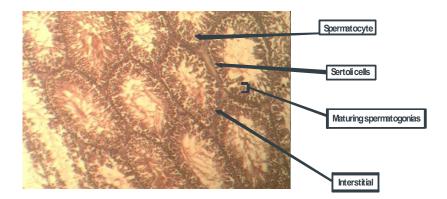


Fig. 25 Testicular section from test groups(1.0ml/rats/day) showing normal spermatogonic cells and interstitial cells

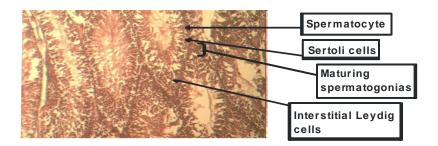


Fig. 26 Testicular section from test groups (2.4ml/rats/days) showing normal spermatogonic cells and interstitial cells

From this, it is evident that the brain's mechanisms are especially important because it's there that the problem begins. The hypothalamus part of the brain may be "turned off" when triggering the pituitary glands to produce testosterone. The outcome would be that, men (younger men) with low testosterone or hypogonadism (as against andropause- the natural decline of testosterone that results from aging) levels may be predisposed to developing erectile dysfunction, and may be also at a higher risk of developing heart disease, obesity or increased body fat, type - 2 diabetes and high cholesterol level as well as decrease in sexual endurance, or metabolic syndrome and many more. What's more, low testosterone levels can slow or stop sexual maturation- the males (teenagers) could grow up to be inadequate in sexual performance and also in terms of fertility. The poor sperm quality perhaps may be associated with environmental - toxin - induced - elevation in oxidative stress in sperm cells in males.<sup>(30,43)</sup>

This perhaps may account for the expected decrease in the population or decrease in the fertility rate in the developing countries like Nigeria, particularly, Niger Delta where exposure to oil spill or oil and gas flared environment is the norm of the day (Fig.27)



#### Fig. 27. Vulnerability and societal pathogens

## 3.6. PATHOPHYSIOLOGY: VULNERABILITY AND SOCIETAL PATHOGENS

underlying the The possible mechanisms etiology of pathophysiological conditions related to exposure to chronic lowlevels of the chemically unrelated substances generated from oil and gas pathogens in the environment involves the modulation of the normal physiological functions of blood. Unfortunate, humans (as well as wildlife) have not evolved physiological mechanisms or biochemical pathways to detoxify and excrete these chemical substances. They are stored and accumulated in the body lipids and fatty tissues, and raise rare disease risk in residents in the annihilated areas both young and old as well as exacerbate communicable and/or non-communicable chronic diseases included:

- Cardiovascular disease- prevalence of cardio-vascular disease (CVD) risk factors (including increase in cholesterol level and hypertension/high blood pressure, heart disease, stroke) left and / or right ventricular hypertrophy
- Respiratory disease- prevalence of lung volume abnormalities/impairment of respiratory disorders, asthma
- Dermatological toxicity- Including occupational contact dermatitis.

- Haematological disorder-including humeral and cell mediated immunity, altered levels of immunoglobulin ,abnormal blood cell indices
- Metabolic syndrome -reduced antioxidant capacity, increase oxidative stress, pancreatic dysfunction ( diabetes) in youth and adolescents
- Renal dysfunction
- Prevalence of hypogonadism or low testosterone in youth and adolescents.
- Sexual promiscuity and associated diseases- increase rates in HIV/AIDS - low CD4 count.
- Potential cancer patients and malformations compromised immune system and many cases of unknown etiology.
- Increased in daily Morbidity and mortality rate
- Risk to endocrine-reproductive systems The endocrine disrupter chemicals present in the environment of blood affect hormone concentrations and reproduction - the function of oestrogen and progesterone and /or the hypothalamic-hypophysial - increased risk of spontaneous abortion in women; spermatozoa may have molecular or biochemical disorders resulting in an inability for fertilization though their mobility and morphology may be normal.<sup>(18)</sup>
- The placenta cannot prevent the environmental chemicals from entering the embryonic circulation. The foetus is exposed to endocrine disrupting chemicals (i.e. exogenous hormones) during the period of organogenesis,

which depends on hormone balance. At birth, exposure continuous via lactation, so that the infant has already a burden of endocrine disrupting chemicals within the first months of its life. Every child lost is a loss to the nation.

- Rare genetic disease prevalence and aetiology of fetal congenital abnormalities in the population - prominent presence of autosomal recessive disorders (sickle cell disease, glucose 6 phosphate dehydrogenase deficiency, thalassaemia) and anomalies caused by the complex interaction between the genetic constitution of the individual and environmental degradation. Haemoglobinopathies HbSC and HbCC with prevalence rate of about 0.5% have been predicted to be the expected haemoglobin genotype of newborn into the population in the next decade<sup>.(42)</sup>
- Environmental -Associated- Neurodegenerative Indices:  $\geq$ Such environmental chemically unrelated associated challenges in blood physiology no doubt may be the contributing factors to our understanding of the pathophysiology of behavioural dysfunction, particularly as manifested in behavioural changes evident in societal pathology as breeding frustrated population, establishing hostilities, agitations, anti-government stances or tendencies, socio-political and socio-economic instability; and manifestations of a pattern of underlying yet unidentified societal problems [ as envisaged in the South-South Niger Delta region of Nigeria ]. (21)

- Exposure to chronic -low-levels of the oil and gas  $\geq$ pathogens (biomarkers) carried by the cells in the blood vessels produce toxic changes in the brain which may contribute to the development and cause of explosion of abnormalities of such conditions as Alzheimer's disease. (This is an irreversible, progressive brain disease that slowly destroys memory and thinking skills and even the ability to carry out the simplest tasks, and/or also known as Type 3 brain diabetes. This is so in that cells in the blood vessels in the brain are also insulin dependent. As such, their metabolisms could be altered by blood flow to the brain secondary to the development of diabetes which could alter brain functions and potentially lead to Alzheimer's disease). Alzheimer's disease is the most common causes of dementia (prevalence rate is about 9%) - loss of cognitive functioning - thinking, remembering, as well as mood and behavioural changes, problems with communication and reasoning. and (Despite these possibilities the oil and gas industries or government have failed to take reasonable steps to protect these families and communities, particularly, Niger Delta).
- Normal Base Line Values: This expository tend to suggest the need to the establishment of a separate "normal physiological base line values" for Nigerians in the Niger Delta region

#### PART TWO: ENVIRONMENTAL INSULTS OF NATURAL MEDICINE: HEALTHCARE MANAGEMENT AND ECONOMIC DEVELOPMENT

### 4.0. ENVIRONMENTAL IMPACT OF NATURAL MEDICINE: WORLD HEALTH ORGANIZATION CONCERN

As a result of the rapid emergence of oil and gas extractions globally over the past decades, particularly in Nigeria where there is little or no control or monitoring of gas and oil contaminates, (because there is little or no concerned and effective effort on the part of the government, let alone the oil industry operators, to control the environmental problems) it is triggering public reactions ranging from annoyance to allegations of serious health consequences for the communities associated with the industry. Most of the populace in desperation for survival from infectious and chronic so - called "20th century illness", "environmental illness" "environmental AIDS" who attempts to stave off such serious illnesses amidst an environment rife with fear and unprecedented poverty are turning to physiologically unproven and untested natural products [natural medicines] nutraceuticals as food and medicine for treatment and prevention of diseases or for primary healthcare, for many reasons, included are:

- dissatisfaction with drug costs and the conventional healthcare,
- With the public perception that "nature is good" therefore they must be harmless,

- That the chemicals produced in nature are better than the same products synthesized in chemical laboratories,
- > The desire for personalized medicines and
- Distrust between traditional and conventional physicians.

Notwithstanding, phytotherapy has existed since prehistoric times. And according to World Health Organization (WHO) the use of medicinal plants flourishes today as the primary form of medicine for primary health care for perhaps as much as 80% in some Asian and African countries. Since "human poverty," "illness", "environmental degradation" and rapid emergence of "natural medicines" are interrelated, WHO, taking cognizance of the claims of natural medicine benefits, accessibility and availability, is strongly encouraging the integrations of traditional medicine (TM) and medical practices referred to as complementary or alternate medicine (CAM) into national healthcare system. But the Great Physiologist stated "...every seed - bearing plant on the face of the whole earth and every tree that has fruit with seed in it ... will be yours for food ..... but of the fruit of the tree which is in the midst of the garden...ye shall not eat of it ....lest ye die" (Genesis 2:29, 3:3).

⇒ This is a clear manifestation that natural substances do not contain only medicinally beneficial constituents, but may also contain harmful bioactive ingredients, and like fugitive oil and gas chemicals, are potential environmental pollutants. And when consumed, the environment and the natural habitat of "*blood*" will be effectively and permanently polluted - pollution from which there is literally '*nowhere to hide*"

As the use of phyto-therapy practices are rapidly adopted by new populations because of the new focus on preventive medicine, and also as good starting points for the discovery of bioactive molecules for drug development, there are challenges to the medical sciences, particularly, physiologist.

More worrisome, in Africa, Nigeria in particular, natural medicines are taken in many circumstances such as in pregnancy, by those likely to become pregnant, by breastfeeding mothers, as medication or by those under medical supervisions and their children. Thus potential harm can occur via inherent toxicity of natural medicines, as well as from contamination, plant misidentification, and interactions with other natural medicinal products or pharmaceutical drugs. Some can have abortive effects on pregnant women or should not be consumed by children - babies could be born with malformations – Fig. 28. Birth defects

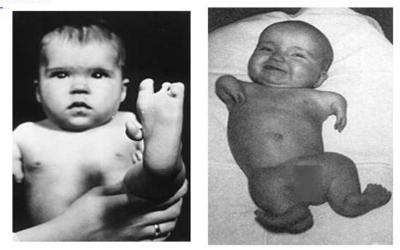


Fig. 28 Birth defects induced by drug in pregnancy

The environment of blood and therefore the normal blood physiology will equally be affected, making the blood environment and the natural habitat of blood the most dangerous environment on earth to inhabit since blood (erythrocyte) has little or no legal protection, which lethally *"nowhere to hide"*.

What must be understood is that the claims of these nutritional supplements may not be supported by research and either the traditional physician and/or the patient may not have any idea of the physiological (and pharmacological) mechanisms of action of the "natural medicine" (which can include hundreds of natural constituents) in nature's cure in regard to health problems.

# 4.1. NATURAL MEDICINES IN THE 21<sup>ST</sup> CENTURY: XYLOPIA AETHIOPICA

There are many species of flowering plants, listed below, and it is estimated that only 8% have been systematically studied in terms of constituents. Nevertheless, approximately 7,000 substances of pharmaceutical importance have been isolated from plants known for their medicinal properties, and several constituents have been processed into pharmaceuticals <sup>(22,23)</sup>

List of Some Medicinal Plants that have undergone preliminary studies in our laboratory.<sup>(13-17,21-22,29-32,36,44)</sup>

- Allium sativum (Garlic),
- Chrysophyllum albidum (Udara)
- Cocus nucifera (Coconut)
- Cola acuminate/ nitida (Kola nut),
- Gongronema latifolium (utazi),
- Lycopersicon esculentum (Tomatoe)
- Momordica angustisepalis (Waghara-waghara)
- Moringa oleifera
- Nature cure bitters
- Ocimum gratissimum(scent leaf),
- Phyllanthus amarus (stone breaker, black pepper)
- Piper nigrum (Uziza)
- Rauwolfia vomitoria (Akanta)
- Solanum melongena (garden egg leaf),
- Telfaria occidentalis (Pumpkin leaf)
- Vernonia amygdalina (Bitter leaf)

- Vigna unguiculata(Cowpea)
- Yoyo bitters
- Zingiber officinale (Ginger)
- Xylopia aethiopica (Uda, Erunji, Atta, Kimbara, Okada) (Fully characterized and presented)
- Psidium guajava (guafa). (Awaiting full, detailed characterization from South Africa).
- Cnidoscolus aconitifolia (Efo jerusalem -yoruba) (awaiting full, detailed characterization from South Africa).
- In contrast to the situation in developed countries, in Africa, Nigeria in particular, knowledge of tradition medicine are passed through generations by oral communications and indigenous practices and little or no exhaustive data on the constituents let alone scientific evidence of its physiological effects on the body functions which is of clinical and/or commercial interest are available.

In this second part of the expository it will explore and / or provide rare opportunities of the environmental insults / *in-vivo* state-of -the -art - of the mechanisms of action of one of the most commonest and economically important indigenous versatile wonder nutritional and medicinal plant drug "*xylopia aethiopica (Dunal) A. Rich, (Annonaceae)* or ( "Africa pepper" "Ethiopian pepper" "Guinea pepper" or "Negro pepper' (Fig 29; Voucher No .UUH 1819).

#### Medicinal Plant: XYLOPIA AETHIOPICA



Fig. 29 Dried fruits of Xylopia Aethiopica

It is acclaimed locally to possess indeed a mile range of both medical and nutritional values viz:-.

- Lower cholesterol or reduced heart disease- high blood pressure ,heart problems and obesity
- As a postpartum tonic to relieve delivery pains and inflammation
- > To heal after birth wounds, improve the immune system and enhance mood
- > To terminate unwanted pregnancy (obstetric potential)
- As anti-malarial, antifungal, antiviral and antimicrobial agent.

- > To treat gastrointestinal problems
- ➢ To treat cancer,
- To treat other medical conditions, including cure of blood anaemia, common cold, diabetes(as blood glucose control), applied to the eyes to treat corneal ulcers, The list is much longer.

Xylopia aethiopica have been part of our culture and are widely consumed in special local preparations by both sexes, old or young named <u>"pepper soup"</u> in the Southwestern and Southern parts of Nigeria .<sup>(22)</sup>

This study will provide the mechanisms of action of natural chemicals in the body which are of paramount importance in clinical practice. This is of central importance in medicine as it will provide valuable physiological (and pharmacological) information about the status of a patient or provide clues about the underlying pathophysiology of a patient's disease process. Modeling of physiological (and pharmacological) activities of natural substances will help the clinician conceptualize the processes involved; in order to better diagnose and treat the patient.

⇒ Thereafter you will think for yourself, and decide how best to integrate natural substances into your condition and you'll learn how - in terms of your health - when natural chemicals become either environmentally friendly or unfriendly and/or experimenting with the unknown, or little - known, can be risky.

### 4.1.1. PHYSICO-CHEMICAL AND PHYTOCHEMICAL CHARACTERISTICS OF XYLOPIA AETHIOPICA: HEALTH CARE IMPLICATIONS

#### 4.1.1.1 Phyto-Medicine Constituents

Following WHO guideline to ensure the use of safe, effective, and quality products and practices, based on scientific evidence (preclinical testing of herbs), novel innovative strategic methodology of formulation of xylopia aethiopica (and which could be used to test any other natural substances of medicinal/nutritional significance) has been developed. Crude extracts or purified compounds obtained by fractionation of the medicinal plant can be also evaluated by these formulations. This was based in accordance with the local methods of handling finished herbal medicine products and practices and it was employed in the isolation and characterization of the powdered functional nutritional/medicinal plant based materials for routine practice. The formulation was made of hydro-alcoholic (hydro-methanolic, 1:4,v/v; and hydro-ethanolic, 1:4,v/v) extractability of the bio-active constituents of the medicinal plant. <sup>(20,44)</sup>

The novel formulation increases the solubility of the water insoluble phytochemical/physicochemical constituents and fat in an aqueous solution. This is because phyto-constituents are amphiphilic substances composed of both a hydrophobic and hydrophilic functional groups. In addition to being a promising way to extract polar as well as non polar phyto-constituents by modifying mixing bahaviour of oil and water, it showed tremendous potential to enhance solubility of different solutes and selective extraction of bioactive compounds on a commercial scale.<sup>(20,44)</sup> The water-alcohol- solvent extractive values of the natural medicinal plants assessed in accordance with the methods for medicinal plant materials of World Health Organization revealed variations and statistically significance differences in the phytochemical and physicochemical compositions of xylopia aethiopica compared with the standard methods of extraction of medicinal plants (Tables 4 – 6)

Table 4. Comparison of the phytochemical	extractability potential of the
various formulations	

S/N O	Bio-active Components(%)	Hydro- methanolic	Hydro- ethanolic	Methanolic	Ethanolic	Aqueous
1	ALKALOIDS (%)	66.7	66.7	33.3	33.3	33.3
2	SAPONINS (%)	-	-	-	-	-
3	FLAVONOIDS (%)	66.7	33.3	33.3	66.7	66.7
4	TANNINS (%)	66.7	33.3	33.3	33.3	33.3
5	BORNTRAGER'S					
I	ANTHRAQUINONE	33.3	-	33.3	-	-
li	COMBINED ANTHRAQUINONE	66.7	-	33.3	-	-
6	GLYCOSIDES					
Ι	LIEBERMAN'S (%)	100 (Terpene)	100	66.7	33.3	33.3
li	SALKOWSKI'S(%)	100	100	100	66.7 (sterols)	33.3
111	KELLER KILIANI'S(%)	100	100 (Deoxy- Sugar)	33.3	-	33.3
	Total Constituent (%)	75%	54%	45.8%,	29%	29%

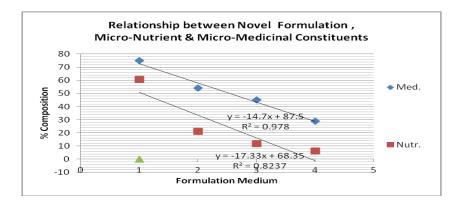
Mineral elements(mg)	Hydro-methanol	Hydro-ethanol	Methanol	Ethanol
Iron (Fe)	129.00 ±0.00	0.11 ± 0.00*	4.00 ±0.00*	2.00 ± 0.00*
Magnesium (Mg)	40.11 ± 0.00	32.11 ± 0.00*	17.11 ±0.00*	10.00 ± 0.00*
Manganese (Mn)	35.00 ± 0.00	26.32 ± 0.00*	20.11 ± 0.00*	10.02 ± 0.00*
Calcium(Ca)	30.10 ± 0.00	23.10 ± 0.00*	5.00 ± 0.00*	2.00 ± 0.00*
Potassium(K)	$2.70\pm0.00$	0.41 ± 0.00*	0.11 ± 0.00*	0.21 ± 0.00*
Zinc (Zn)	$1.40\pm0.00$	0.61 ± 0.00*	0.12 ± 0.00*	0.00 ± 0.00 *
Sodium(Na)	$1.12\pm0.00$	0.91 ± 0.00*	0.00 ± 0.00*	0.01 ± 0.00 *
Phosphorus(P)	$0.31\pm0.00$	0.20 ± 0.00*	0.00 ± 0.00*	0.02 ± 0.00*
Lead(Ld)	$0.004 \pm 0.00$	0.01 ± 0.00*	0.11 ± 0.00*	0.01 ± 0.00*
Total Mineral content (mg %)	60.79%	21.25%	11.81%	<b>6.15%</b> 46

Table 5: Comparison of the physicochemical constituents in the various formulations

### Table 6. Proximate Composition and Anti-Nutrient Minerals

Physio-chemicals- Proximate	% Composition
Composition	
Carbohydrate	72.5 - 77.7
Protein	12 - 14.7
Fiber	2.99 - 5.97
Ash Value	2.45 - 3.92
lipid/fat	1.47 - 2.33
Moisture content	0.98 - 1.96.
Physico-Chemicals - Anti-Nutrient	
Minerals	
Tannin	86.96
Oxalate	12.03
Hydrogen cyanide	0.93
Phytates	0.08.

- Scientific quantitative and /or qualitative of phytochemical and /or physio-chemical evaluation of the plant extract provided information regarding various types of the phyto/ physio -constituents in the tissue.
- The novel formulation revealed that xylopia aethiopica may be essential sources of mineral supplements, amino acids and antioxidants, and are fashioned naturally clinically to perform specific or diverse biochemical and /or physiological /pharmacological functions in the body included: control and regulation of blood pressure, diabetes and wide spectrum of biological activities of physiological significance discussed below.
- Aside, the stock or liquid in which the natural food is cooked is safe for consumption as the micro- antinutrient- mineral cyanide (2.95mg), may be



volatilized as hydrogen cyanide (HCN) during cooking.

Fig. 30. Scattered diagram showing relationship between micro nutrient & micro medicinal constituents.

- It implied that the novel hydro-methanolic (1:4, v/v) formulations yielded more medicinal/nutritional biomarkers/constituents than the conventional methods and ranked the percentage yield as hydro-methanolic > hydroethanolic > methanolic > ethanolic = aqueous.
- The novel hydro-methanolic formulation therefore is highly recommended for future analysis, isolation, and characterization of physicochemical/phytochemical compounds of clinical relevance.

### 4. 1.1.2. PHYSIOLOGICAL – PHARMACOLOGICAL BIOACTIVE CONSTUTIENTS OF XYLOPIA AETHIOPICA: PURE SAMPLES

High-Performance Thin-layer Chromatographic (HPTLC) analysis, isolation, and characterization of xylopia aethiopica in hydromethanolic chloroform fractions identified eighty one (81) chemically unrelated compounds which obviously may be responsible for the multifarious environmental insults<sup>(46)</sup>

Table 7 Physicotherapeutic Constituents		Composition (%)
Terpenes		44.3
Flavonoids		30.9
Alkaloids		22.2
Carbohydrate	(1,4:3,6-Dianhydro-α-d-	1.3
glucopyranose)		

Phyto-steroid (γ-Sitosterol)	1.3
FATTY ACIDS	
Unsaturated	54.3
Saturated	22.2
Others ( protein/amino acids etc)	23.5

HPTLC also revealed that *xylopia aethiopica* contains fifty-eight (58) normal natural pharmacological agents which forty-seven (47) are medicinal while eleven (11) are non-medicinal.

Table 8 Physico-Pharmacological Functions	Composition	
(MEDICINAL)	(%)	
Anti-microbial/Anti-bacterial/Plague	36	
Anti-inflammatory / Analgesics	31	
Anti- tumor/Anti-carcinogenic /Prevents degenerative	28	
diseases		
Anti-parasitic (nematodes, helminthes)	20	
Anti-diuretic agent	1	
Phyto-Pharmacological Activity (NON-MEDICINAL)		
Pesticides/Insecticide/Acaricidal/Termiticide	16	
Flavourings	14	
Fragrance/Perfumes	13	
Deodorant/Perspirant /Desiccants	5	
Antiseptic/Disinfectant	1	

The analysis of these isolated phyto-medicinal/phytomineral constituents are necessitated/recommended to understand the physiological and therapeutic implications of xylopia aethiopica (and many other natural substances of medicinal significance) utilizations.

Furthermore, the presence or absence of a particular type of physio/phyto-constituent (a marker compound) in the plant of interest may be helpful, partly, in the development of analytical profile or medicaments which included the efficacy and safety of natural medicines and in the development of future medicines and treatments and treatment guidelines - suitable dosage forms and stability.

4.2 POSSIBLE MECHANISMS OF ACTION OF NATURAL MEDICINAL SUBSTANCES

4.2.1. EFFECT ON THE PHYSIOLOGY OF REPRODUCTION IN FEMALES

*Xylopia aethiopica,* in-*vivo* significantly caused a decline in the vital female reproductive blood hormonal levels of:

- ⇒ The gonadotropins- (Luteinizing hormone, LH and Follicle stimulating hormone, FSH),
- ⇒ Sex- steroids hormones (progesterone & oestrogen) necessary for implantation;
- ⇒ Prolactin (for stimulating, regulating and supporting both the female reproductive cycle and pregnancy) in a dose dependent fashion (similar effects were also evident in male reproductive hormones) and
- ⇒ Significantly caused reduction (p>0.05) in the number of litters delivered compared to control which inevitably caused risk to reproductive health.

⇒ Nevertheless, the anti-fertility effects of the natural chemicals contained in xylopia aethiopica are transient and reversible.<sup>(26,27)</sup>

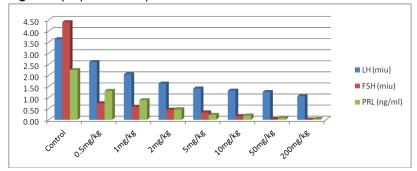
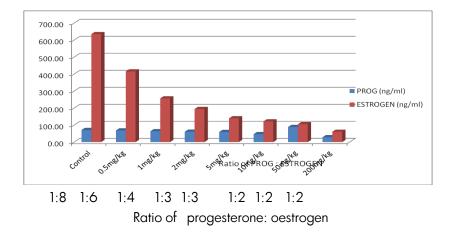


Fig. 31 Xylopia Aethiopica Effects on Hormonal Profiles



The natural chemicals contained in xylopia aethiopica acted as endocrine disrupter by interfering with the functions of the highly sensitive female reproductive system - by altering both the hormone concentrations and the menstrual cycle of the female animals as well as their fertility:

- Produced adverse effect on maturation and ovulation of follicles with resultant impairment on fertility and conception in females.
  - Pollution of the natural environment of the unborn; especially the environment of embryonic foetus in females and this is the first assault on early foetus life.
  - Inhibits the lining of the womb, the natural habitat of the unborn, and make hostile to implantation. The environment of the womb then becomes uninhabitable and the new foetus life dies

- Caused reduction in gestation period as well as the number and weight of neonates thereby producing antifertility effects.
- In-vitro evoked contraction of the uterus, similar to that produced by oxytocin. The implication if given to pregnant women can induce spontaneous and premature contraction of the uterus, which would eventually lead to abortion and premature deliveries.
  - Such effects exhibited abortifacient type of action; anti-implantation and anti-oestrogenic activities respectively.
  - ✓ It provided our understandings on the mechanic of herbal contraceptive, including maternal and child health use with the view of developing truly new orally active non -toxic, yet potential, broad spectrum anti-inflammatory non-steroidal compounds having anti-implantation property<sup>(28)</sup>
- ⇒ Scientific Challenge: The relationship between progesterone and oestrogen could lead to development of the use of xylopia aethiopica in etiology, prognosis, management and treatment of fibroid since this abnormal growth in females are known to be associated with progesterone and oestrogen activities. It may therefore, be considered for use by persons who are at risk of having fibroid such as those with family history of fibroid in the first degree relative at older age (> 45 years)

### 4.2.2. EFFECT ON PHYSIOLOGY OF REPRODUCTION IN MALES

Xylopia *aethiopica*, in-vivo, in males induced a decline in

- Sperm count,
- Sperm motility and
- Sperm viability with corresponding
- Increase in abnormal sperm morphology in a concentration dependent fashion compared to control (figs 32 - 35). However, similarly to the situation in the females, the anti-fertility effects of the natural chemicals were transient and reversible.

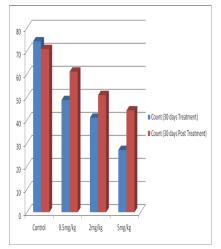


Fig. 32. Effect on sperm motility.

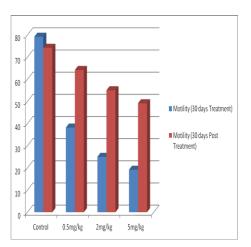


Fig.33 Effect on sperm count

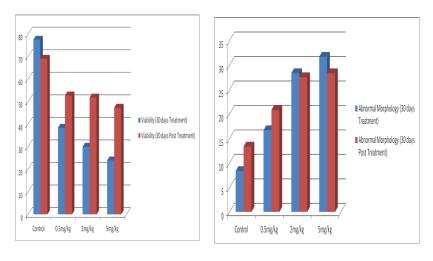


Fig.34. Effect on Viability.

Fig.35. Effect on the morphology

#### 4.2.2.1 POSSIBLE MECHANISMS OF ACTION

Fertility or infertility is a major clinical problem, affecting people medically, psychologically economically, and family instability. According to World Health Organization infertility affects about 8 to 12 % of the world's population and in about half of the cases men are either the single cause of it or contribute to the couple's infertility. Male factor contributes 40%, females factor 40%, both male and female 15% and unknown factors 5% of causes of infertility.

Natural chemicals as evident can affect reproductive physiology, by upsetting the balance of the endocrine system through modulation of the physiological functions of blood- hormonal levels, and can account for some of the cases of unknown infertility in many infertile couples where no apparent cause of infertility can be found even after thorough medical examination.

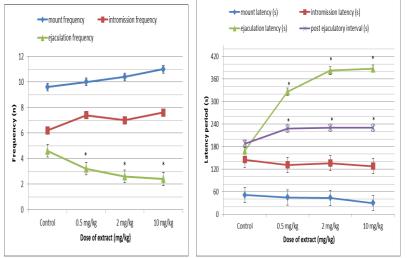
It is possible that the phytoestrogens *in-vivo* acted in the control of fertility by interfering with the feedback mechanisms on the hypothalamic-pituitary- gonadal axis ,bringing about oxytocinlike type of contractions of the uterus (as in females) or impair reproductive capabilities in males either by hindering the release of semen, reduced sperm quality or affect the testes resulting to formation of orchites or inflammation consequently lowering the survival and development of offspring controlled by blood hormonal level. It could be suggested also that xylopia aethiopica be added to the number of the existing known environmental pollutants that affect fertility included as sexually transmitted infections, anabolic steroid use, ionizing radiation, environmental related oil and gas pathogens (such as crude oil) just to mention but a few which are not known some 50 years ago.

4.2.3 SEXUAL BEHAVIOUR EFFECT OF XYLOPIA AETHIOPICA At the concentrations used for the study and for the 30 minutes duration of the study, xylopia aethiopica induced sexual motivation and performance in male rats which correspondently did not improve fertility indices because the ejaculation frequency and hence the quantity of semen available for fertilization decreased <sup>(14,16,41)</sup>

- The mount frequency- the animal assumes the copulatory position on top of the female and grasps her flanks and the mount latency-the time that elapses between introducing the male to the female before the male mounts the female,
- the intromission frequency- the male mounts the female and inserts its penis and the intromission latency- the time between successive mounts as well as the ejaculation latency increased (i.e. the time it took the male rats to reach exhaustion (satiation) was much longer compared to control),
- the ejaculation frequency after intromissions decreased (fig. 36a).
- Thus xylopia aethiopica enhances sexual performances since the mount frequencies and intromissions are increased while ejaculation frequencies decrease. This is also suggestive that xylopia aethiopica may be acting at the high centres in the brain.

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Fig.36 Effect of xylopia aethiopica on some sexual behavioural parameters



#### 4.3 EFFECTS ON HAEMORHEOLOGICAL INDICES

Xylopia aethiopica *in-vivo* insignificantly and/ or slightly increased the following haematological parameters: packed cell volume (PCV), haemoglobin concentration [HB], and red blood cell count (RBC) compared with control. It slightly decreased erythrocyte sedimentation rate (ESR) and coagulation factors (activated partial thrombin time, APTT and prothrombin time, *PT*). It caused an increase in white blood cell (WBC) and platelet productions (Fig 37).

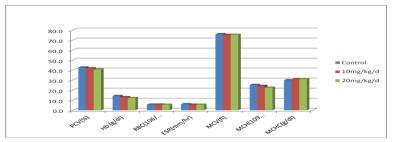


Fig. 37. Haemorheological activities of novel *xylopia aethiopica* formulation

#### 4.3.1 POSSIBLE MECHANISMS OF ACTION

The extract acted as immune- stimulating, thrombopoietin and /or erythropoietin - potentiating factor which possibly stimulated erythropoietin production or acted directly by stimulating increase in red blood cells which is required to carry the much needed oxygen by the body to make energy.<sup>(44)</sup>

- This is not surprising that of the 60.8% phyto-mineral elements, iron accounted as high as 32.7% (Table 2) which nutritionally is beneficial as it could explain its local use as post partum tonic in women who have given birth newly.
- This probably may aid in energy production, or improve oxygen delivery to muscles, boost the immune system and cell functions as well as increase haematocrit (% of blood volume that is red cell mass) and the total cell mass in the body.
- The high iron content could also significantly contribute to reduction of anaemia caused by iron deficiency

(management of anaemia) and correspondingly lead to the production of high oxygen blood level and transport. Interestingly, iron is the only nutrient for which women have a higher daily requirement than men. The U.S. Recommended Daily Allowance (RDA) of iron for men is 10 milligramms or less and 15-18 milligrams for women and the average child while pregnant and nursing women need about 50-60 mg per day.

*Scientific challenge*: It follows that synthetically:

- Xylopia aethiopica could be produced for use as a treatment for persons with certain types of anemia (low blood count) or used to correct anaemia by stimulating red blood cell production in the bone marrow in these conditions.
- it could be a novel blood-oxygen stimulating substance used as a pharmacological performance (sport)enhancing substances since the overall oxygen delivery system (blood oxygen levels, as well as heart stroke volume, vascularization, and lung function) is one of the major limiting factors to muscle's ability to perform endurance sports -race walking, boxing, cycling, and distance running. This is so since the primary reason why athletes use drug enhancing performance is to improve oxygen delivery to muscles, which directly improves their endurance capacity. <sup>(44)</sup>

## 4.4 NEUROLOGICAL ACTIVITIES: IMPLICATION IN PAIN AND INFLAMMATION

Neurological function analysis using Analgesy-meter and plethysmometer (Ugo Basile, Italy) respectively revealed that *xylopia aethiopica* can modulate neurological activities by exploiting the body's built-in mechanisms in the brain that controls pain- the *analgesia system*<sup>(45)</sup>. (The fundamental concept of the neurological function tests is to apply increasing force to an inflamed rodent paw and to measure the force that causes the rodent to withdraw its paw based on the method first described by Randall and Selitto in 1957.)

- It showed that the novel xylopia aethiopica formulation significantly exhibited analgesic and anti-inflammation activities in rodent models of both sexes by inhibiting paw jumping that were either comparable or better than those of standard drug, piroxicam (figs. 38)
- Importantly, females appear to endure more pains than males in the ratio male: female of 1:2 in agreement with the Holy Book, which says, ..."upon the woman .... "I will greatly multiply your pain....."(Genesis 3:16).

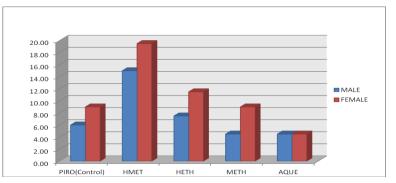


Fig. 38 Percent analgesic activities induced in both sexes by novel xylopia aethiopica formulation

*Scientific challenge*: The study provided the development of a truly non-toxic, yet potent, broad spectrum anti-inflammatorynon-narcotics for integration into the healthcare delivery system as well as for economic development. This is so as a wide variety of the available orthodox or synthetic analgesics and anti-inflammatory agents are not without adverse side effects such as respiratory depression, addiction and gastrointestinal irritations.

Nonetheless, it is evident in its local applications as pain relieving tonic for nursing mothers. The analgesic and antiinflammatory potency of xylopia aethiopica may be attributable to the presence of flavonoids as well as the glycoside sitosterol in the plant extract.

### 4.5 EFFECT ON CARDIOVASCULAR SYSTEM: IMPLICATIONS IN BLOOD PRESSURE CONTROL

Blood pressure recording using non-invasive technique from the tail cuff of un-anesthetized rodent model (Ugo Basil, Italy) revealed that *xylopia aethiopica* in*-vivo*, in a dose -related manner, insignificantly affected systolic blood pressure (SBP) and diastolic pressure (DBP, Fig 39). This perhaps might be attributable to the presence of appreciable quantities of glycosides, antioxidants which are capable of modulating the cardiovascular system and hence normalized normal blood pressure. On the contrary, the animal's pulse assessed in real time by a pulse counter which picks up the signal from the pulse transducer showed increased pulse rate in a dose -related manner.<sup>(44)</sup>

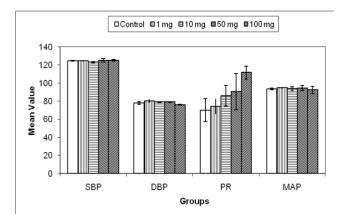


Fig.39.Normalization of Blood Pressure activities of novel xylopia aethiopica formulation

*Scientific challenge:* Based on the available evidence and understanding these relationships, specific clinical trials may help us to understand whether xylopia aethiopica medication , a natural occurring agent, might probably help to reduce the risk of metabolic conditions such as heart disease, stroke, hypertension/ high blood pressure, diabetes, obesity, lung cancers , cognitive decline and Alzheimer's disease.

#### 4.6. BIOCHEMICAL ACTIVITIES: POTENTIAL ANTIOXIDANTS

Treatment with Xylopia aethiopica showed a dose dependent reduction in blood serum total cholesterol (TC), triglycerides (TG), and low density lipoprotein-cholesterol (LDL-C) levels but caused an increase in the levels of high density lipoprotein cholesterol (HDL-C). This is an indication that xylopia is capable of controlling the hydrolysis of certain lipoproteins and their selective uptake and metabolism by different tissues.

The increase in the HDL levels is an indication of its antioxidant activities in lowering cardiovascular decreases; similarly, xylopia aethiopica also caused a decrease in the following biochemical parameters: ALP, ALT, AST levels and an increase in albumin, direct bilirubin, total bilirubin and total protein levels. Xylopia aethiopica treatment caused a significant improvement in the atherogenic indices, the ratios of LDL/HDL and HDL/TC as well as the changes in the biochemical profiles indicating atheroprotective/ cardiopropective efficacy - i.e. intake of xylopia aethiopica can cause normalization of lipid and biochemical profiles and hence reduced cardiovascular related disease.

*Scientific challenge:* It therefore finds clinical application in treatment of dyslipidaemia in diabetic patients as well as in the control of cardiovascular risk factors. This could largely be attributable to the presence of the free radical-scavenging antioxidant defense mechanisms (that act against molecular damage from reactive oxygen species produced by arterial wall microphages) of the phenolic compounds (flavonoids or glycoside -sitosterol) in the extract of xylopia aethiopica. <sup>(20,46)</sup>

- It is evident that the body's tuned mechanisms (holistically) are carefully balanced to withstand a variety of environmental insults.
- Exposure to chronic-low-levels either chemical of technological or natural origins without a complete understanding of all of their effects may disrupt these balances.

5.0 WHERE DO WE GO FROM HERE: CREATING THE FUTURE Currently, with the number of environmental associated health problems continuing to grow, particularly in the Niger Delta region of Nigeria, and throughout Nigeria and the world at large, a serious health challenge faces the physio-medical professions and the health system. Therefore, there is the need to address the unraveled fundamental etiology, anti-environmental related drug development, lifestyle modification, disease treatment and complication control as well as exploring collaborative chances and evaluate emerging technologies to combat environmental insults both nationally and globally.

Novel Family Planning Commodities- Contraceptives for  $\geq$ Couples: fertility control is becoming an issue of global and national public health concern. Current methods of contraception are resulting in an unacceptable rate of unwanted pregnancies. In Nigeria, for instance, this might be as a result of fear or ignorance due to limited formal education, high cost of drug or non-availability of orthodox method or because of cultural, moral or religious belief. Interest in the use of natural medicine in contraception has thus attracted much attention in the last decade. Considering the importance of fertility control and side effects of the existing modern/ orthodox contraceptive methods or anabolic steroid use, research should be advanced toward reproductive health physiology potential of xylopia aethiopica because of the presence of Phyto-steroid (y-Sitosterol the only natural hormone) since it is co-friendly in nature and can interfere natural patterns of reproduction physiology. with Pharmacological formulations therefore should be undertaken

- as a source of potent non-steroidal natural contraceptive with the highest possible level of safety and efficacy for *birth control* in family planning for both sexes
- Natural medicine local to our environment should be checked to exploit the physio-therapeutic potentials nutritional and medicinal properties for further drug development in the future rather than its adverse effect.
- The innovative formulation perhaps will be alternate way to compensate for some perceived deficiencies in orthodox pharmacotherapy as well as provide scientific credence regarding safety and efficacy to back up the continued therapeutic application of natural medicines.
- The novel formulation will not only provide valuable resources for new pharmaceutical products but novel compounds or precursors in drug development and utilization of isolated compounds for curative, investigative, evaluative and other research tools in drug development and testing processes.
- Based on the environmental -associated chemical challenges emanating from either technological or natural origins, it has become apparent that physiological normal values be established for Niger Delta region..
  - Scientific challenge : Research should be advanced toward developing some form of protection devices for the communities in the oil and gas flaring vicinity similar to pharmacological strategy of attempting to protect against malarial infection, for example, by taking anti-malarial

drugs, to fortify the immune system, rather than by wearing a protective net to simply reduce the intensity of the malarial field to which a person is exposed

Government policy: Based upon scientific knowledge, assessment, and acceptable public health principles the government should implement a modern, comprehensive chemical policy in line with current scientific knowledge on human health

# 6.0 COOPERATION BETWEEN RESEARCH AND COMMERCIAL ORGANIZATION

Because of societal responsibilities, centre for Health Assessment and Translation should be established especially in the Niger Delta region, to serve as physio-medicinal environmental health resource to the public and to regulatory and health agencies. The centre shall conduct evaluations (researches) to assess the evidence that environmental substances cause adverse

health effects and to provide opinions on whether these substances may be of concern given what is known about human exposure levels. The centre also will organize workshops or stateof-the-science evaluations to address the environmental challenges besetting this area bearing in mind that no University outside the Niger Delta Region can help accomplish this; it must be done by

this university located within the Niger Delta Region and not any other university within Nigeria or outside. Government alone cannot provide the necessary fund for sustainable research. It is advocated that like in developed economies, for example, where research is an engine for national development, individuals, religious groups, businesses, joint-public and private-sector (Public Private Partnerships (PPPS) funding partnership should support the institution to contribute in no small measures in the fields of scientific research feats and education that leverages national development.

#### CONCLUDING REMARKS

Finally , Mr. Vice Chancellor sir, Distinguished Ladies & Gentlemen, I have examined *in-vivo* mechanisms of action of environmental chemical challenges of natural or technological origins in health or disease, focusing principally on the contributions that the haematopoietic system make because of its strategic position in quality life. Dysfunction of any magnitude in normal blood physiology can lead to increased susceptibility of the body to various health concerns. This infers that since erythrocytes has little or no "legal protections" are the most important target/vulnerable system to various assaults in human lives with "Nowhere to hide": a situation we must all take responsibility for. As the saying goes - "your life is in your hand; to live or not to live: that was the question" "...people are destroyed for lack of knowledge" (Hosea 4:6)

Thank you for listening

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#### CITATION ON



#### Professor Arthur Nwafor

Prof Arthur Nwafor rose from a humble beginning. He was born in the mid 50's to late *Emere* Titus Chu Nwafor and *Emere-Owa* Comfort Yeye Chu Nwafor in Acharama Obiningwa Community in Okuebemere Royal Family of Alode Clan, Eleme Local Government Area of Rivers State, Nigeria. Born into a 'military' cum Christian home that instilled in him discipline and the fear of God, young Arthur Nwafor grew with great courage to face various life challenges. His father a 2<sup>nd</sup> world - war veteran in Bombay and who had seen at firsthand how much transformation and development that a good education could bring to an individual and the community at large, developed an ideology of starting the education of his son at a very tender age even when the boy's hand could not cross over his head to reach the ear - a measure used for admission at that time. To give a boost to that ideology, his late uncle Headmaster I.O.K Eyi who also insisted that Arthur Nwafor be enrolled into the primary school, enrolled him at the famous Seventh-day Adventist Primary School, Nichia Eleme (now State Primary School, Alesa) his tender age notwithstanding. Later, he continued his secondary school education career at Ascension High School Eleme which was truncated by the Civil War in the country.

During the Nigeria - civil war, his father presented him for conscription into the Biafra army- the opposing side of the war. So Arthur Nwafor became a 'child- soldier'. He distinguished himself and exhibited such military gallantry that earned him a promotion to the rank of *lance corporal* under the commandership of the war veteran, Lieutenant Geoffrey Odigor, from Delta State of Nigeria.

Following the cessation of the internecine war in 1970, young Arthur Nwafor resumed his educational pursuit with more vigor having in mind the dream of his parents about the empowerment Western education could afford. Determined to realize his academic ambition Professor Arthur Nwafor braved the trauma of trekking through the woods from his village in Eleme to St Pius Secondary School Bodo, Ogoni, in Gokana Local Government Area – with his school bag on his head- to and fro on bare foot! While in that school he held the positions of a Dormitory and Dining hall prefect under the principals Archbishop Uche Akaralu (*late*) and Chief Philip Badom respectively when his first article, titled "THE POWER HOUSE" was published. Between 1972 and 1975 he was employed by the Rivers State Government as X-ray attendant and as clerical officer at Okrika General Hospital respectively. The man Arthur Nwafor, was still in the making.

Professor Arthur Nwafor is unassuming, quiet and calculative, sound-minded and dogged; he does not just easily give up on academic puzzles: perhaps, the death of his father in 1973 could have dimmed his academic ambition, but this is far from it; his child's trust in God soon paid off and he had no difficulties obtaining his higher qualifications in record time. The Rivers State Government sponsored his Higher School education at South Glamorgan Institute of Higher Education Cardiff, through his undergraduate programmes at the University of London, Portsmouth from 1975-1980, and the Federal Government (1980-1984) and Welcome Trust (London,1982-1984) for the postgraduate education at the University of Wales, Cardiff, all in the United Kingdom.

Professor Arthur Nwafor is a multi-disciplinary researcher scientist whose interest is in the move of research products from a university-based-research laboratory to a commercial biotechnology or pharmaceutical development laboratory for the service of humanity. His seminal works under the tutelage of Professor W.T. Coakley at the University of Wales *"Effect of Amphipaths on Erythrocyte Shape"* had led to the development in our understanding of the relationship between transmembrane potential and surface potential as well as penetration of chemo-therapeutic agents on the suitability of the state – of – the – art – mechanics that the heat generated from ultra-sound and scanning devices or ultra-modern hightechnology computerized scanning devices for studying internal body functions in health care management, and microwaves oven used for warming blood and blood products, does not pose risk for human survival. Additionally, it showed that the use of stream bath at temperatures of the application in the order of 45°C, Whole Body Hyperthaermia (WBH) at 42°C or even climate change, does not even pose risk to erythrocyte survival. The seminal provided therapeutical modeling of biological membranes as probe in health and disease for the management and treatment of diseases such as diabetics, sickle cell diseases, cardiovascular diseases various forms of cancers etc without the usual intraperitoneally /intramuscularly administration of drugs.

Professors A.A Obouforibo (late) and John O. Ibu sought him from Britain. After the mandatory service to his father land (NYSC) in 1986 at the School of Health Technology Aba, Abia State he confirmed his services at the University of Port Harcourt, March 11, 1986.

Professor Arthur Nwafor is an academic scientist and an administrator par excellence. His unique and outstanding administrative qualities stood him out as a desirable colleague in close cooperation with successive administration in the University from Vice Chancellor Professor Sylvanus J.S Cookey to the current amiable Vice Chancellor Professor Joseph Atubokiki Ajienka. His landmark achievements have remained indelible in the institution's records book as he diligently executed his various assigned responsibilities, viz:- Associate Dean, Student Affairs Department 1991-1993, Director, Central University Community Service Programme 1994-1998, Director, School of General Studies 2006 – 2010, and Head, Department of Human Physiology, 1988-1989, 1989-2004, and 2011 to date.

It is also on record that Professor Arthur Nwafor among others positioned the School of General Studies to reach heights -GES examinations were conducted using Optical data capturing methods (OMR), GES 300 (Entrepreneurship) was introduced, and backlog of results were cleared. Above all, the mysteries surrounding the so called "outstanding", "missing" "carry-over" or "sorting" of results were demystified, and the performance of the students greatly improved. As Head of the department, the department received donations /gift items to boost teaching, learning and research. Furthermore, the department was to represent the University and the country at international Medical School Physiology Student Quiz competition in Malaysia which the University was unable to provide the necessary logistics. Still, under his leadership, the department is nurturing "MR. IDEAL NIGERIA" - an outstanding skill - minded entrepreneurial youth who will be representing Rivers State and the country at Mr. Africa international competition in London.

Professor Arthur Nwafor has served either as chairman or member in a number of College of Health Sciences and University boards and committees including board of enquiries. He is a Senate member and has been Senate representatives also on boards of the University of Port Harcourt. He is a member of NUC and Medical and Dental Council of Nigeria accreditation committees. He represented the Vice-Chancellor/Leader of University of Port Harcourt contingent to NUGA 1992 at University of llorin, Kwara State.

In 1984 Professor David Lloyd, a Briton and Head Department of Microbiology, University College, Cardiff, Wales, stated: "......It is evident that we have a very high regard of Dr Nwafor's (now Professor) ability as a research scientist and feel sure that his diligence, conscientiousness and careful approach will stand him in good stead in his scientific research....... I have, therefore, every confidence in his all-round ability in research and teaching, and feel sure that he will make an excellent academic" Professor Nwafor rose from the ranks to the enviable position of (pioneer) Professor of the Department of Human Physiology (June 9, 2005). He is an erudite scholar completely dedicated to the field of physiology and continuing medical education. And he has a gigantic impact on the education of countless medical scientist some of whom are professors with him in his department as well as other departments in the Faculty of Basic Medical Sciences and Clinical Sciences - Professors O.A Georgewill, Deputy provost College of Health Sciences and former head dept of Pharmacology, H.B. Fawehinmi Dean Faculty of Basic Medical Sciences and former Head department of Human Anatomy, DV Dapper former Dean Faculty of Basic Medical Sciences and head department of Human Physiology, I.M Siminialayi, former Head department of Pharmacology, CA Nwauche former Head

Haematology, Immunology and blood transfusion, PC Stanley former Head Psychiatry In addition to training Medical/Dental, Pharmacy, Nursing and Professionals Allied to Medicine students. He has under his supervision produced four PhD students (subject to senate approval). He has turned out a number of M.Sc, PGD graduates in Human Physiology and many internationally registered scientists in various countries in America, Europe etc. Professor Arthur Nwafor is an external examiner to B.Sc. and MB;BS students in many of the medical schools across the width and breadth of this country. As well, he has also assessed M.Sc, and PhD students, Associate Professors and Professors.

Indeed Professor Arthur Nwafor is an Experimental core Physiologist that had developed and maintained a rare understanding of the field of physiology. Since his 'adventure' into higher education, he has had over fifty (50) original articles published in indexed, learned and reputable journals worldwide, over thirty (30) conference proceedings and a book and chapters in books. With his objective of distilling a complex subject into a concise presentation, this have paved the way for his scientific findings to have been consistently ranked No. 1 among the top twenty publications in the domain of articles by the world renowned literature-monitoring service providers America BiomedLib Journal (www.BioMedlib.com). His internalization of the University through research and publication has earned the Department, College of Health Sciences and the University well deserved recognitions by:

- LabArchives (USA) that introduced him to a powerful new tool that will help to
  - > Better organize the laboratory
  - Protect data and intellectual property
  - Collaborate with colleagues inside the lab or across the globe
  - Publish results
- Labome Exact Alest. Organization (USA),
- The Research and Development Network of the International Research and Development Institute, Nigeria.

Prof Arthur Nwafor is a member of a number of local and international organizations including:

- Vice President Physiological Society of Nigeria 2007 - date
- Financial Secretary, Physiological Society of Nigeria 1999 - 2005
- Chairman, Local Organizing Committee, 25<sup>th</sup> Annual Sci. Conf. of the Physiological Society of Nigeria 2005
- > American Physiological Society.
- American Society for Bioethics and Humanities –
- > (EGOS) European Group for Organizational Studies -
- International Professors Project –
- American Association for the Advancement of Science, and a number of others.

He has travelled the world - Europe, Far East etc and had attended a number of scientific conferences both locally and internationally. He is an assistant editor as well as a member of editorial advisory board to many renowned journals.

Prof Arthur Nwafor is an ordained Elder of the Seventh-day Adventist Church. He has ascended to Jerusalem, the Holy City of God and he is a Jerusalem Pilgrim (JP), impacting positively on his community. He has been the chairman that dialogued to site the Ibru group of companies in his community as well as the chairman that negotiated the establishment of the current fertilizer company in his community, and many more.

Professor Arthur Nwafor is married to Mrs. Joyce Nwafor, BSc Catering and Diploma, Labour Law (London). Currently, Mrs. Joyce Nwafor is the Chief Catering Officer, Rivers State Government House. Between them are four children, Engr. Njubemere, Mrs. Owate Faith Mmom (nee Nwafor), Engrs. Nyimeochen Chu and Elera Gomba and grand children and son and daughter in-laws.

Having attempted to go through the flavourig pedigree, I have the privilege and singular honour, Mr. Vice Chancellor, ladies and gentlemen, to present to you this humble man of rare resilience with astute perception and ardent determination, a man of truth and faith, a man of hard work and dedication, an accomplished and erudite scholar, a reliable representative and faithful steward of the unique Uniport, friend, mentor, and professional colleague - time has come for him to deliver his Inaugural Lecture – No. 102 in the series – he is no other than Elder (Professor) Arthur Nwafor (JP)

Professor Datonye Victor Dapper Department of Human Physiology Faculty of Basic Medical Sciences University of Port Harcourt

ORATOR