UNIVERSITY OF ILORIN

THE TWO HUNDRED AND TWENTY-EIGHTH (228TH) INAUGURAL LECTURE

"MODULATING THE MEDIATORS OF LIFE PROCESSES: THE STRATEGIC PLACE OF ENZYMES IN HEALTH AND WELLNESS"

By

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The Vice-Chancellor

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My Lords, Spiritual and Temporal,
Distinguished Students of Biochemistry,
Members of my family, Nuclear and Extended,
Gentlemen of the Print, Electronic and New Media,
Esteemed Invited Guests, Friends and Relations,
Great Students of the University of Ilorin (Greatest Unilorites),
Distinguished Ladies and Gentlemen

Preamble

I give adoration and praises to God, for from Him and through Him and to Him are all things. To Him be honour and glory forever and ever. Blessed be the name of the Lord for not only sparing my life till today, but also for the grace He has given me to present the Two Hundred and Twenty Eighth Inaugural Lecture of the University of Ilorin, today, the 16th February, 2023. I am very humbled and privileged by your presence today as I deliver this Inaugural Lecture. An Inaugural Lecture is **an auspicious occasion for University to acknowledge the appointment or promotion of new Professors**, introduce them to the academic and non-academic community of the University, and provide opportunity for engagement with the larger community. The presentation of an Inaugural Lecture is a significant milestone in the career of an academic and provides a platform to share past research experience

and introduce new ideas to a diverse academic and non-academic audience.

Vice-Chancellor sir, before I do justice to this, kindly permit me to provide historical highlights of Inaugural Lectures that have been delivered from the Department of Biochemistry. The first Inaugural Lecture since the inception of the Department of Biochemistry in 1977, entitled "***The Essential Lipids: Life's Springboard****"*, was presented by Professor Adewale Agboola Odutuga (of blessed memory) on the 12th December, 1985, as the 20th in the University. The second (61st), entitled *"**Eat and Die by Little**"*,was delivered by Professor Musbau Adewumi Akanji on the 24th October, 2002 while the third (78th), entitled *"**All for the Love of Nutrients**"***,** was presented by Professor Hussein Oyelola Bukoye Oloyede on the 26th May, 2005. The fourth from the Department (102nd) entitled "***The Little Giants in Food****"*,was delivered by Professor Adenike Temidayo Oladiji, on the 22nd March, 2012 while the 5th (127th) entitled *"**The Invisible Behind and Beyond the Visible**"*,was presented by Professor Sylvia Omonirume Malomo on the 4th April, 2013. Furthermore, the 6th (146th) entitled "***Dreadable Unpaired Species:Biochemical Approach as Panacea****"*,was presented by Professor Elizabeth Abidemi Balogun on the 10th April, 2014 while the 7th (163rd) entitled *"**Knocking Down the Barriers to Four O'Clock Activities and Reproductive Inadequacies**"*,was presented by Professor Musa Toyin Yakubu on the 29th September, 2016 . All these lectures have addressed various aspects of basic and applied biochemistry which include Lipid, Nutrition, Toxicology, Food Biochemistry, Membrane Biochemistry, Enzymology and Reproductive Biochemistry.

Today, I feel highly honoured and privileged for the opportunity to deliver this 228th Inaugural Lecture of our great University, University of Ilorin, with the title: **"Modulating the Mediators of Life Processes: The Strategic Place of Enzymes in Health and Wellness"**. It is the 8th from the Department of Biochemistry, coming almost four years after my appointment as Professor of Biochemistry.

Introduction

My journey started about 50 years ago when I was born to the family of Joseph Jimoh Yaya Arise and Mary Ojusebinu Arise (both of blessed memory) of Oka-Akoko, Ondo State. May God grant their souls eternal rest (Amen). After my secondary school education at African Church Grammar School, Oka-Akoko, Ondo State, I worked briefly as a Laboratory Assistant in the same school from 1991 to 1992 because I didn't get my first choice course (Medicine) on my first attempt into the University. I was offered admission to study Biochemistry, but I declined the offer. In 1992, I was anxiously expecting my letter of admission for my first choice course from JAMB (my 2nd attempt), only to get to the Post Office, opened the box (Box 29) and found my admission letter among other mails. I was exhilarated! However, on unsealing the envelope, my letter of admission was for B.Sc. Biochemistry again. After series of advice and consultations, I took the offer since I did not know anything about Biochemistry then, but believed there must be a divine connection to Biochemistry according to God's purpose for my life as stated in **Proverbs 20:21** ***"It is the Lord who directs your life, for each step you take is ordained by God to bring you closer to your destiny. So much of your life, then, remains a mystery".***

After my National Youth Service Corp Scheme in Abakaliki, Ebonyi State, strongly backed and encouraged by my uncle and my living father figure, Alhaji Abdulfatai Bello, who paid for my application form and registration, I returned for my Master programme in Enzymology and Biochemical Toxicology at the Department of Biochemistry, University of Ilorin in October, 2000 under the supervision of Prof. Sylvia O. Malomo, the immediate past Deputy Vice-Chancellor (Academic) my academic mentor and mother. I was about rounding off my M.Sc. programme when I secured an appointment with Igbinedion University, Okada, Edo State as an Assistant Lecturer in the Department of Biochemistry, College of Health Sciences in 2001 under the leadership of my academic father, late Professor Adewale Agboola Odutuga. On the successful completion of my M.Sc., I furthered my academic pursuit by enrolling for a Ph.D. programme again under the supervision of Prof. Sylvia O. Malomo. It was during her tenure as

the Head of Department of Biochemistry that I applied to the Department of Biochemistry, University of Ilorin, as an Assistant Lecturer. She was the catalytic mediator of my move to the University of Ilorin on the 29th April, 2003, and has remained one of the positive modulators of my journey, growth and productivity till today.

Biochemistry

As the name may suggest, Biochemistry is a field of science that bridges the two traditional disciplines of Biology and Chemistry. If Chemistry is the science of matter, then Biochemistry is the science of *living* matter. It is the study of substances found in living organisms, the changes they undergo during development and life of the organism, and metabolism by which energy is made available for **life processes,** including synthesis of various complex molecules. The history of Biochemistry spans approximately 400 years. The word Biochemistry was coined around 1890 by the German chemist Ernst Hoppe–Seyler who established a journal and evoked the recognition of a new discipline called Biochemistry. Since then, Biochemistry which has evolved from organic, medicinal, physical chemistry and cell biology has also become a discipline that has paved the way for new ones. Certain branches of Chemistry, such as Biological Chemistry which studies the structural basis of living things, overlaps with Biochemistry. From a biochemist's perspective, the interest in Biological Chemistry is to identify the structure of living matter and relate them to their function while a chemist will go further in synthesizing these biomolecules to understand the chemical properties. Furthermore, Biochemistry and Molecular Biology are also interwoven with similar objectives. From a molecular biologist's point of view, the focus is to study the flow of **biological** information transfer by genetic material (RNA and DNA). This can be approached by recombinant DNA technology and molecular genetics, while a biochemist is interested in the structure and function of all biomolecules and energy relationships among them. Though Biochemistry exploits tools designed for chemical and physical measurements, certain biochemistry questions have required Molecular Biology techniques to answer them. Today, Biochemistry has developed to various specialties such as Biological Chemistry or

Chemical Biology, Structural or Descriptive Biochemistry, Enzymology, Bioenergetics, Metabolism, Clinical Biochemistry, Molecular Biochemistry, Endocrinology, Medicinal Biochemistry, Agricultural Biochemistry, Pharmacological Biochemistry, Analytic Biochemistry, Comparative Biochemistry etc

Biochemistry governs all living organisms and living processes. By controlling information flow through biochemical signaling and the flow of chemical energy through metabolism, biochemical processes give rise to the incredible complexity of life. Much of Biochemistry deals with the structures and functions of cellular components such as proteins, carbohydrates, lipids, nucleic acids and other biomolecules, although increasingly, processes rather than individual molecules, are the main focus. Over the last 40 years, Biochemistry has become so successful at explaining **life processes** that now almost all areas of Life Sciences from Botany to Medicine are engaged in it. Today, the main focus of pure biochemistry is in understanding how biological molecules give rise to the processes that occur within living cells, which in turn relates greatly to the study and understanding of whole organisms.

Among the vast number of different biomolecules are complex and large molecules (called polymers), which are composed of similar repeating subunits (called monomers). Each class of polymeric biomolecules has a different set of subunit types; for example, a protein is a polymer whose subunits are selected from a set of 20 or more amino acids. Biochemistry studies the chemical properties of important biological molecules, like proteins, and in particular the chemistry of enzyme-catalyzed reactions.

Biochemistry is one of the cornerstones of modern Medicine, Pharmacology, Pharmacy, Physiology, Nutrition, Genetics, Pathology, Toxicology and Microbiology, thus relevant to the definition of health and investigation of diseases. Furthermore, it is important to Zoology, Plant Biology and Agriculture as well as other Biological Sciences. The knowledge of Biochemistry is essential to all Life Sciences, and it is actually increasingly becoming their common language (Godwill, 2016).

Biochemistry has profoundly touched on man’s health and wellness and on our understanding of the catalytic or metabolic life processes taking place in living organisms. For example, the

relationship between diets and diseases was discovered in antiquity. Organ meat such as liver has long been known to cure night blindness. At that time, men wondered and marveled how this could be. Today, we know that liver is a good source of vitamin A. In the 18th century, cod liver oil was first used to treat rickets. Today, we know that cod liver oil is a good source of vitamin D. Juice of lemons was discovered to prevent the symptoms of scurvy (caused by vitamin C deficiency). Today, we know through improved knowledge of Biochemistry that lemon juice is a good source of vitamin C. Thus, Biochemistry as the chemistry of life, connotes that we must study and understand the chemical composition of life at the simplest structural and functional level - the Cell (Figure 1).

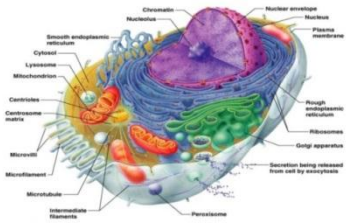

Figure 1: Structure of generalized Cell (The structural & functional unit of life)
Source: Koning (1994)

Life Processes and Enzyme Mediators

The cell is the structural and functional unit of life that is capable of independent existence and able to perform life processes. All living organisms possess specific characteristics, which differentiate them from non-living things. These characteristics are essential and they play a crucial role in the overall health of the organism, be it plants or animals, prokaryotic or eukaryotic organisms. These basic processes are known as **life processes** and include nutrition, metabolism, transportation, respiration, excretion and reproduction. All these processes are sustained by enzyme-mediated chemical reactions that take place inside living organisms. These enzyme-mediated chemical reactions are called biochemical

reactions. The sum of all the biochemical reactions in an organism is referred to as metabolism. Metabolism may be catabolic or anabolic reactions. Catabolic reactions break down molecules into smaller units and release energy. An example of a catabolic reaction is the breakdown of glucose during cellular respiration, which releases energy that cells need to carry out life processes. Anabolic reactions, on the other hand, absorb energy and build bigger molecules from smaller ones. An example of an anabolic reaction is the joining of amino acids to form a protein.All these processes function together in living organisms to maintain life and wellbeing. However, when these processes get disrupted and there is a change in their balance, it may result in diseased conditions.

Enzyme Mediators

An enzyme is a remarkable molecular entity that participates in or mediates several biological transformations in living organisms. Going through the historical lane to as early as the late 18th and early 19th centuries, the digestion of meat by stomach secretions and the conversion of starch to sugars by plant extracts and saliva were known. However, the mechanism by which these occurred was not understood.

Later in the 19th century, when studying the fermentation of sugar to alcohol by yeast, Louis Pasteur came to the conclusion that this fermentation was catalyzed by a vital force contained within the yeast cells called "ferments", which were thought to function only within living organisms. He wrote that "alcoholic fermentation is an act correlated with the life and organization of the yeast cells, not with the death or putrefaction of the cells."

In 1878, German physiologist, Wilhelm Kühne (1837–1900),coined the term *enzyme*, which comes from Greek *ενζυμον* "in leaven", to describe this process. The word *enzyme* was used later to refer to non-living substances such as pepsin, and the word *ferment* used to refer to chemical activity produced by living organisms. In 1897, Eduard Buchner began to study the ability of yeast extracts to ferment sugar despite the absence of living yeast cells. In a series of experiments at the University of Berlin, he found that the sugar was fermented even when there were no living yeast cells in the mixture. He named the

enzyme that brought about the fermentation of sucrose “zymase“. In 1907, he received the Nobel Prize in Chemistry “for his biochemical research and his discovery of cell-free fermentation”. This discovery that enzymes could be crystallized eventually allowed their structures to be resolved by x-ray crystallography. This was first done for lysozyme, an enzyme found in tears, saliva and egg whites that digest the coating of some bacteria. The structure was solved by a group led by David Chilton Phillips and published in 1965. This high-resolution structure of lysozyme marked the beginning of the field of Structural Biology and the effort to understand how enzymes work at an atomic level of detail.

Enzymes are very effective biological catalysts that accelerate almost all metabolic reactions in living organisms by up to 10^6–10^{18} folds. An enzyme generally works by reducing the amount of activation energy needed to start the reaction. Figure 2 shows the activation energy needed for glucose to combine with oxygen to produce carbon (iv) oxide and water. The overall reaction releases energy, but an initial activation energy is needed to start the process. The activation energy without an enzyme is much higher than the activation energy when an enzyme is used.

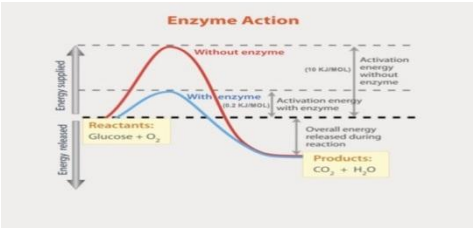

Figure 2: Enzyme Action
Source: Svendsen (2016)

This graph shows what happens when glucose combines with oxygen. A typical biochemical reaction that would take several days or even several years to occur without an enzyme is likely to occur in just a split of a second with the proper enzyme! Without enzymes to speed up biochemical reactions, life processes will be imperceptible.

Enzyme-deficiency Disorders

Enzyme deficiencies are inherited defects that result in a number of life-changing or life-threatening conditions in humans. In most of them, a single enzyme is either not produced by the body at all or is produced in a form that doesn't work. The missing or defective enzyme is like an absentee worker on the cell's assembly line. The absence of the normal enzyme means that toxic chemicals build-up or an essential chemical substance will not be made. Table 1 shows some examples of enzyme-deficiency disorders.

Table 1: Some enzyme deficiency disorders

Enzyme Deficiency Disorder	**Defective Enzyme**	**Symptoms/Description**
Phenylketonuria (PKU)	Phenylalanine hydroxylase	Small head below normal, hyperactivity, jerking limb movements, mental retardation, seizures, skin rashes, unusual urine odour due to high level of phenylalanine in urine.
Maple Syrup Urine Disease	Branched-chain α-keto acid dehydrogenase	Presents at the end of the first week of life with feeding difficulties, lethargy, coma, seizures, urine with characteristic odor resembling maple syrup (burned sugar).
Albinism	Tyrosinase	Albinism is a group of inherited disorders that results in little or no production of the pigment melanin which determines the colour of the skin, hair and eyes.
Alkaptonuria	Homogentisate oxidase	Homogentisic acid and its oxide - alkapton accumulate in the blood and are excreted in urine in large quantities; leading to damage to cartilage and heart valves, kidney stones.

Source: Chaturvedi *et al*. (2016)

Inhibition and Activation of Enzymes and their Applications

Enzyme inhibitors and activators that **modulate** the rate of enzyme reactions play important roles in the regulation of metabolic life processes. Enzyme activators (**positive modulators**) are chemical

compounds that increase the rate of enzymatic reactions. Their actions are opposite to those of enzyme inhibitors Examples of enzyme activators include ions, small organic molecules, as well as peptides, proteins, secondary metabolites and lipids. Enzyme inhibitors (**negative modulators**), on the other hand, are substances that reduce or supress the activity of an enzyme after binding to it. Due to their unique catalytic efficiency and fidelity, enzymes have wide range of applications in industries, diagnosis, molecular biology, therapy and drug designs.

Industrial Applications of Enzymes

The pharmaceutical, food and beverage, detergent, and biofuel industries have reaped the advantages of enzyme catalysis in commercial-scale applications, while other industries, such as natural gas conversion and fine chemical production, have more recently considered their use. Table 2 illustrates the broad applications of enzyme catalysis in various industries.

Table 2: Industrial applications

Sector	Enzymes	Applications
Pharmaceutical	Nitrile hydratase, transaminase, monoamine oxidase, lipase.	Production of active pharmaceutical ingredients.
Food Processing	Trypsin, amylase, glucose isomerase, papain, pectinase	Conversion of starch to glucose, production of prebiotics, debittering of fruit juice.
Detergent	Protease, lipase, amylase, cellulose	Stain removal, removal of fats and oils, color retention,
Biofuel	Lipase, cellulase, xylanase	Production of fatty acid methyl esters, decomposition of lignocellulotic material for bioethanol production
Paper and Pulp	Lipase, cellulase, xylanase	Removal of lignin for improved bleaching, improvement in fiber properties

Source: Chapman *et al.* (2018)

Enzymes as Manipulative Tools

In Molecular Biology, restriction enzymes, deoxyribonucleic acid (DNA) ligase and polymerases are used to

manipulate DNA for applications in Pharmacology, Agriculture, Medicine and Forensic Science.

Vice-Chancellor sir, the manipulation of DNA to achieve improved products was first recorded in the Holy Bible. ***"And God said; Let us make man in our image, after our likeness: and let them have dominion over the fish of the sea, and over the fowl of the air, and over the cattle, and over all the earth, and over every creeping thing that creepeth upon the earth. So God created man in his own image, in the image of God created he him; male and female created he them***" (Genesis 1:26-27). Also Genesis 5:2 reads "***Male and female created He them; and blessed them, and called their name Adam, in the day when they were created"***. With due respect and honour to our mothers, sisters, wives and daughters, the biblical account of the creation of man pointed out that in Adam was Eve. God did not create Adam and Eve, He created Adam but inside Adam, was Eve. Adam was an embodiment of male and female. ***"And the LORD God caused a deep sleep to fall on Adam, and he slept; and God took one of his ribs, and closed up the flesh in its place"*** (Genesis 2:21). We believe from this account that the rib donated by Adam served as the source from which the desired DNA for the cloning of Eve came from. God was the first to perform cloning (enzymatic manipulation of DNA) to bring about improvement to the living state of man at that time. Enzymatic manipulation of DNA of organisms will achieve enhanced structural and compositional qualities as well as value addition. It is no surprise then that women are fearfully, exceptionally and wonderfully made by God. "Whatever you give a woman, she will make it greater. If you give her sperm, she'll give you a baby. If you give her a house, she'll give you a home. If you give her groceries, she'll give you a meal. If you give her a smile, she'll give you her heart. She multiplies and enlarges what is given to her. So, if you give her any crap, be ready to receive a ton of shit!" Also, genetic cloning to obtain desired traits is known to be characterized by excessive manifestation of some of the desired attributes just like in the case of Dolly, the cloned sheep. This may explain why God gave women hairs and nails and they are now adding their own; He gave them ear and nose, they are piercing and adding their own;

God gave them eyes, skin and body, they are adding their own and changing the colour.

As we come back from the brief digression to the main topic, with due respect to our mothers, sisters, wives and daughters, it is incontestable that women remain the best, smartest and strongest of all the creatures of God.

Vice-Chancellor sir, application of enzymes as manipulative tools in Forensic Science involves techniques or tests used to investigate crime scene samples such as saliva, blood, urine, hair, sweat and other bodily substances. This is when crime scene investigators inspect/analyze such crime scene samples using enzymes. For example, blood, spit, sperm, sweat, hair and many more human secretions or parts can be tested to assess how a crime was perpetrated (An *et al*., 2012). Blood enzymes are used to identify individual's unique genetic markers leading to the determination of an individual's role in a crime. Also, saliva, composed of water, enzymes, mucus and epithelial cells from the inside of the cheeks, is an ideal body fluid for DNA profiling. Saliva, tissues or sperm is useful for forensic identification of rapists or perpetrators of related crimes because through the use of enzymes, it can be decided whose body fluid/tissue is found on the victim or the accused. We now know that through the use of enzymes as manipulative tools, disputed paternity can be resolved. There are new methods of DNA analysis and enzyme forensics that can identify a person of African/Caribbean decent; hair and eye colour, and even the age of a person (Branicki *et al*., 2011).

Application of Enzymes in Diagnosis

This aspect largely relates to Biochemical Toxicology, which involves the study of the adverse effects of chemical substances on living organisms and the practice of diagnosing and treating exposures to toxins and toxicants (Hodgson, 2010). The basic principle of using enzyme levels for diagnosing disease is based on comparing the changes in blood (serum or plasma) activity of enzymes with that of normal state (Table 3).

Enzymes are also very useful in the diagnosis or monitoring of the degree of deterioration, contamination or functional recovery of soil, vegetation and water bodies.

Table 3: Diagnostic Enzymes

Enzymes	Serum Level
	Elevated
Telomerase	In breast cancer, cervical cancer, colon cancer, liver cancer, lung adenocarcinoma, early prostate cancer, and biliary carcinoma
Aspartate aminotransferase	In myocardial infarction, acute viral or toxic hepatitis, cirrhosis, cholestatic jaundice,skeletal muscle disease and severe heamolytic anemia·
Alanine aminotransferase	In acute viral or toxic hepatitis, cirrhosis, cholestatic jaundice and skeletal muscle disease
Alkaline Phosphatase	In bone and liver diseases
Acid Phosphatase	In prostate cancer
Lactate Dehydrogenase	In liver, heart, skeletal muscle, kidney and hepatopoietic and neoplastic diseases.
Creatine Kinase	In skeletal muscle damage and myocardial infarction
Gama Glutamyl Transferase	In alcoholic hepatitis, cholestatic liver disorders
Amylase	In acute pancreatitis
Lipase	In pancreaticdisorders

Source: Ganesan and Xu (2017)

Enzyme Inhibitors and their Applications in Drug Design and Therapy

Substances that reduce or supress the activity of an enzyme after binding to it are known as enzyme inhibitors **(negative modulators).** The suppression of the activity is the result of the binding of inhibitor to the enzyme molecule leading to the arrest of catalytic reaction. In accordance with their mode of action, enzyme inhibitors may be divided into two different groups (reversible and irreversible inhibitors). Reversible inhibitors, in turn, may be grouped into four based on their kinetic behaviour (Malomo *et al*., 2022). Many cellular enzyme inhibitors are natural proteins or peptides that specifically bind to and inhibit target enzymes. Numerous metabolic life processes are modulated by these specific compounds.

Vice-Chancellor sir, it is important to recall that many living organisms are in a state of "chemical war." Fungi are fighting with bacteria for food using antibiotics. Most immobile organisms like plants and some sea invertebrates use different poisons to protect themselves from being eaten; some vertebrates (like snakes) and invertebrates (e.g., bees and wasps) use poisons not only for defense but also to get food. If we analyze the composition of these poisons, we can find in their content a lot of various enzyme inhibitors. Poisons of plants and invertebrates were used as medicine several years back. It, however, became clear in the twentieth century that the poisons contain various enzyme inhibitors as well as the blockers of some other biological structures (channels, receptors, etc.). For example, bee venom contains melittin, a peptide containing 28 amino acids. This peptide can interact with many enzymes to inhibit their activities (in particular, it binds with protein calmodulin that is an activator of many enzymes) (Katoka *et al*., 1989). Other examples of natural inhibitors are cardiotonic steroids that were found initially in plants (digoxin, digitonin, ouabain) and in the mucus of toads (marinobufagenin, bufotoxin, etc.) (Buckalew, 2015). These compounds are useful for the treatment of heart failure and atrial arrhythmias by irreversibly inhibiting the pumping function of Na^+/K^+-Adenosine Triphosphatase (Na^+/K^+-ATPase) and stimulating its signaling function (Buckalew, 2015).

Vice-Chancellor Sir, drug target is an old concept that was suggested at the end of the nineteenth and the beginning of the twentieth century by Ehrlich and Langley, who developed the idea that compounds display biological activity by binding to cellular constituents. Many pharmacological drugs are enzyme inhibitors. Some group of well-known pharmaceutical agents known as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), include inhibitors of the enzyme cyclooxygenase that catalyzes the first reaction step in the synthesis of biologically active compound- prostaglandins. The prostaglandins are responsible for the development of pain, inflammation, fever, contraction of smooth muscle, formation of blood clots and others life processes (Simon, 1996). NSAIDs (the most prescribed drugs in the world with the oldest among them being aspirin) have been successfully used for more than one

century around the world for treatment of fever, cardiovascular diseases, joint pain, etc (Simon, 1996). Among these drugs are enzyme inhibitors that slow down production of prostaglandins that control many aspects of inflammation, smooth muscle contraction and blood clotting.

There are many other groups of drugs that are, by their nature, inhibitors of some enzymes and do have very important therapeutic significances (Buckalew, 2015).

i. **Inhibitors of Angiotensin-Converting Enzyme (ACE):** ACE catalyzes the conversion of inactive decapeptide angiotensin I into angiotensin II by the removal of a dipeptide from the C-terminus of angiotensin I. Angiotensin II is a powerful vasoconstrictor. Inhibition of ACE results in the decrease of angiotensin I concentration and in the relaxation of smooth muscles of blood vessels. Inhibitors of ACE such as Captopril Enalapril/Enalaprilat, Fosinopril, Lisinopril, etc are widely used as drugs for treatment of arterial hypertension (Hsiao e*t al*., 2015).

ii. **Proton Pump Inhibitors (PPIs):** Proton pump (H^+/K^+-ATPase) is a membrane-bound enzyme that catalyzes acid secretion in gastric parietal cells of the stomach. Therefore, PPIs are acid-activated pro-drugs that are converted into drugs inside the organisms. The PPIs were introduced into therapeutic practice in the 8^{th} decade of the twentieth century (Jain *et al*., 2007). Since its introduction, PPIs such as omeprazole, rabeprazole, esomeprazole and dexlansoprazole have been successfully used for treatment of gastritis, gastric and duodenal ulcer and gastroesophageal reflux disease.

iii. **Anticancer Agents:**Certain enzyme inhibitors may slow tumour formation within weeks and could lead to treatments that retard or prevent recurrences of cancers. Telomerase is a unique reverse transcriptase enzyme, considered as a primary factor for diagnosis and treatment in almost all cancer cells (Table 3). If telomerase in tumour cells are inhibited, it shortens telomeres, which consequently slows the growth of tumours. Telomerase activity in cancer cells have been reported to be inhibited

by various natural products and this inhibition has been connected with the decrease of cell viability (Abliz *et al*., 2015). Methotrexate is another anticancer drug that inhibits dihydrofolate reductase with the consequent inhibition of nucleotide base synthesis (McGuire, 2003). New promising direction of anticancer therapy that is connected with the inhibition of protein kinases and the consequent control of the cellular response to DNA damage is now on the step of development (Lan-ya *et al*, 2021). Selective inhibitors of kinase enzymes are now being tested in clinical trials in cancer patients.

iv. **Antiviral Agents:** Nucleoside reverse transcriptase and protease inhibitors are enzyme inhibitors usually recommended for treatment of patients with Acquired Immune Deficiency Syndrome (AIDS) that is provoked by Human Immunodeficiency Virus (HIV) (Garrett and Collins, 2011).Coronavirus disease 2019 (COVID-19), a highly infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), spread swiftly throughout the world posing a global health emergency having infected more than 235 million individuals causing deaths of more than 4.8 million people worldwide (Zanganeh, 2021). Angiotensin Converting Enzyme 2 (ACE 2), as the essential receptor for binding to SARS-CoV-2, plays a significant role in the occurrence of this deadly disease. Finding treatments that target ACE 2 is an effective strategy for the treatment of COVID-19. Angiotensin-converting enzyme inhibitors (ACEI) and SARS-CoV-2 receptor blockers have been employed to confront COVID-19 infection (Zanganeh, 2021). The inhibition of α-glucosidase has also been linked to anti-viral therapy because viruses are dependent on the host endoplasmic reticulum-resident α-glucosidases to process the carbohydrate moiety in their envelope proteins, consequently affecting virus infectivity. Blocking the viruses from entering cells is the most direct approach to combat SARS-CoV-2 and other viral infections.As of June 3, 2022, there were 1,521 drugs and vaccines in the

pipeline targeting the coronavirus disease (COVID-19) (Tai *et al*., 2022).

v. **Aphrodisiacs:** An example of a medicinal enzyme inhibitor is sildenafil (Viagra), a common treatment for male erectile dysfunction. This compound is a potent inhibitor of the enzyme, phosphodiesterase, which degrades the signal ing molecule, cyclic guanosine monophosphate (cGMP) that is known to cause smooth muscle relaxation which allows blood to flow into the corpus cavernosum of the penis, thus leading to a stronger erection. The drug negatively modulates (inhibits) the activity of the enzyme that degrade cGMP, thus making penile erection to last for a longer period of time (Lopina, 2017).

vi. **Antibacterial Agents:** Some agents or substances are also used to inhibit enzymes needed for the survival of pathogens. For example, bacteria are surrounded by a thick cell wall made of a net like polymer called peptidoglycan. Many antibiotics such as penicillin and vancomycin inhibit the enzymes that produce and cross-link this polymer together. This causes the cell wall to lose strength and the bacteria to burst (Vellard, 2003).

Enzyme inhibition remains an integral part of modern drug discovery. The advent and refinement of new technologies and modalities, including enzyme informatics, activation or inhibition of enzyme functions by both synthetic and plant products, have stimulated a surge in drug discovery efforts targeting enzymes.

My Research Activities

Vice-Chancellor sir, I have had the triple role of teaching, conducting research and community service in more than three universities. And I have initiated and executed most of these research activities in collaboration with other colleagues for almost three decades of teaching Biochemistry to medical and non-medical students.

The modulation of **enzyme mediators** using **modulators** such as metal ions, plant extracts including proteins and peptides, natural and derivatized ligands largely form the focus of my

research efforts towards finding solutions to some chronic diseases and environmental health challenges.

MyResearch Contributions to Biochemical Toxicology

This section captures my contributions involving determinations of the activities of some enzyme mediators among others as indices of toxicity or cellular damage.

Vice-Chancellor sir, in the publication of *The Sun* Newspaper of 2nd December, 2022,a State Coordinator of the National Agency for Food and Drug Administration and Control (NAFDAC) said it has commenced its sensitization on dangers associated with drug abuse in the State**.** He described the spate of drug abuse among youths as "worrisome," adding that the agency embarked on the sensitization to address the menace, which has increased risks related to their well-being and health as well as the safety of the general populace. One of the abuse tendencies isthe common practice among alcohol drinkers to swallow antibiotics with ethanol or consume alcohol during antibiotic therapy. We **(Malomo, Arise, Olorunniji, Odutuga and Adebayo, 2004**) investigated the effects of co-administration of spectinomycin (an antibiotic widely used to cure gram negative infections) and ethanol on some biochemical parameters of rat kidneys. The result revealed a significant reduction in the rat kidney lactate dehydrogenase activity as well as elevated serum urea, total protein and cholesterol levels. We concluded that the concurrent intake of alcohol with antibiotics is toxic to the kidney and the body as a whole.

Arise and Malomo (2005) also investigated the effects of prolonged and repeated use of ivermectin and albendazole combination (usually administered for as long as 9 to 19 years in various programmes aimed at eradicating the co-endemicity of onchocerciasis and lymphatic filariasis) on the activities of rat kidney alkaline phosphatase and aminotransferases. We reported that the daily and oral administration of ivermectin and albendazole to rats for 15 days altered the activities of rat kidney alkaline phosphatase and aminotransferases. This revealed that the drug combination may be exerting some toxicity on the kidney.

As a follow up to the above finding, **Arise and Malomo (2006)** further investigated and compared the effects of ivermectin, albendazole and their combination in a series of study. In one of the

studies, we found out that the co-administration of ivermectin and albendazole led to a significant reduction in the rat hepatic microsomal enzyme activity and prolonged rat hexobarbital sleeping time (HST). Further investigation revealed that the structural differences and lipophilicty exhibited by the two drugs may be responsible for their differential effects and the negative synergistic modulation of the enzyme and other components of rat hepatic and brain endoplasmic reticulum **(Arise and Malomo, 2009a; Arise and Malomo, 2012).** In another related study, **Arise *et al.*(2012a)** reported significant alterations in the activities of acid phosphatase, lactase dehydrogenase, Na^+/K^+ - and Ca^{2+} /Mg^{2+}-ATPases of rat liver, kidney and brain following repeated and prolonged administration of ivermectin and albendazole. These findings suggest that the repeated and prolonged co-administration of ivermectin and albendazole may be toxic to the liver, kidney and brain cells.

In the light of the foregoing, **Arise *et al*. (2013)** further investigated and reported the potential of vitamin E at reversing the negative modulatory effects of the combined administration of ivermectin and albendazole in rats. The results provided evidence that vitamin E positively modulated the negative effects of the combined administration of ivermectin and albendazole in rats.

Vice-Chancellor sir, we investigated some medicinal plants commonly used for the management of some health conditions in order to provide a baseline safety data about their ability to either positively or negatively modulate metabolic life processes. The consumption of the crude extract of *Boungainvillea spectabilis* (paper flower)(Figure 3) leaves, particularly in the northern part of Nigeria as a remedy for diabetes, led us **(Malomo, Adebayo, Arise, Olorunniji and Egwim, 2006)** to investigate the effects of ethanolic leaf extract of *Boungainvillea spectabilis* on some liver and kidney function indices in rats. The results showed that consumption of the crude extract may negatively modulate (inhibit) liver and kidney functions.

Figure 3: *Boungainvillea spectabilis*

While *Eucaplytus globulus* (blue gum) (Figure 4) leaves contain high levels of phenol and terpenoids which may negatively modulate metabolic life processes, animals such as the Koala that eat *E. globulus* leaves have developed detoxyfing enzymes for these compounds in their liver (Whitman and Ghazizadeh, 1994) in addition to the presence of bacteria which degrade tannin-protein complexes. Most animals, however, do not possess these attributes. Thus, the resolve to determine the modulatory effects of aqueous extract of *E. globulus* on selected enzymes of rat liver. The results showed that acid and alkaline phosphatase and superoxide dismutase activities were significantly elevated in the liver at doses of 100 and 120 mg/kg b.w of the extract. **Arise *et al.* (2009b)** concluded that aqueous extract of *E. globulus* leaves (despite its acclaimed antidiabetic efficacy) may have negative modulatory effects on liver membrane structural and functional integrity.

Figure 4:*Eucaplytus globulus*

Yakubu and Bukoye (2009) had reported the secondary metabolite constituents of *Bambusa vulgaris* (bamboo) aqueous leaf extract; a plant that has been identified as a component of several formulae of medicinal importance ranging from anti-inflammatory to antihypertensive agents. **Arise *et al.* (2011a),** however, reported that the aqueous extract of *B. vulgaris* leaves may contain some toxic substances that may negatively modulate the endogenous detoxifying capacity of rat liver.

Arise *et al.* (2012b) also investigated the effects of aqueous extract of *Nauclea latifolia* (Figure 5), stem (known as "Egbo egbesi" in Yoruba; "Ubulu inu" in Ibo and "tabasiya" in Hausa) used in folk medicine for treatment of malaria, hypertension, diarrhea and tuberculosis, on some biochemical parameters of rat liver and kidney. The repeated administration of the extract for 28

days negatively modulated liver and kidney functions in a time and concentration dependent manner.

Figure 5: ***Nauclea latifolia***

We **(Adebayo, Igunnu, Arise and Malomo, 2011)** also investigated the modulatory effects of co-administration of antimalarial artesunate and amodiaquine on heart functions in rats. The results revealed that co-administration of artesunate and amodiaquine negatively modulated heart functions in rats. **Arise *et al*. (2012c)** further reported in a follow up study that single or combined repeated administration of artesunate and amodiaquine impacted negatively on rat liver membrane functions and integrity and consequently, distorted the ability of the liver to detoxify toxic molecules.

Vice-Chancellor sir, we also carried out studies on the toxicological potentials of some substances not only to emphasize their potential hazard and extent of modulation of metabolic mediators (enzymes), but also for toxicological information on organs such as the skin, liver and brain. It was also aimed at sensitizing the general populace for strict caution on the use of such substances. One of such substances is the eyeliner ("kwali" in Hausa, "tiro" in Yoruba and "uhie" in Igbo). Its use as a beautifying agent is an age-long practice. Apart from life style, living conditions and culture have influenced the application of eyeliners to the eyes. The pattern of results suggested harmful modulation of the structural and functional capacity of the eye, liver and brain caused by the eyeliner in a time and concentration dependent manner **(Arise *et al*., 2010).**

The other product investigated was spent engine oil, also known as used mineral-base crankcase oil. It is a brown to black

liquid produced when new engine oil is subjected to high temperature and high mechanical strain (ATSDR, 1997). The oil is released into the environment from the exhaust system during engine use and leaks. The attitude of auto mechanics in Nigeria to carelessly dispose and expose their skin to spent engine oil prompted this study aimed at evaluating the modulatory effect of topical application of spent-engine oil on the cellular and functional integrity of rat skin. The study established that repeated and prolonged exposure of skin to used lubricating oil have toxic potentials and may negatively modulate (disrupt) the protective and functional integrity of the skin **(Arise *et al*., 2012d).**

My Research Contributions to Drug Development

Vice-Chancellor sir, my research efforts in drug development can be categorized into two:

A. Search for modulators of some enzymes and other mediators that have been implicated in the pathogenesis of diabetes, peptic ulcer, hypertension, diarrhea and malaria.

B. Search for positive modulators or potentiators of some enzyme activities for improved protection against infections.

A. (i) In the Search for Antidiabetic Agents

Diabetes mellitus is a condition in which the body is unable to control blood glucose levels adequately, leading to high levels (hyperglycemia) resulting from defects in insulin secretion, insulin action, or both. The most common is type 2 diabetes, which occurs when the body becomes resistant to insulin or doesn't make enough insulin. In the past three decades, the prevalence of type 2 diabetes has risen dramatically (IDF, 2021). Type 1 diabetes, once known as juvenile diabetes or insulin-dependent diabetes, is a chronic condition in which the pancreas produces little or no insulin. In healthy individuals, fasting blood glucose levels range from 3.0-6.0 mmol/L (72-108mg/dL). This range is maintained by the action of insulin and glucagon as required after eating, during exercise or fasting. Without enough insulin, the cells of the body cannot absorb sufficient glucose from the blood into cells to be stored or used for

energy. If the glucose level in the blood remains high over a long period of time, this can result in long-term damage to organs, such as the kidneys, liver, eyes, nerves, heart and blood vessels. Complications in some of these organs can lead to death (Barcelo and Rajpathak, 2001).

Diabetes mellitus exists everywhere in the world and affects approximately 537 million people worldwide (IDF, 2021). The prevalence of diabetes mellitus is increasing with ageing and lifestyle changes associated with rapid urbanization and westernization. The WHO projects that diabetes will be the 7th leading cause of death by 2030 (IDF, 2021). According to the report, the number of people living with diabetes worldwide will increase from 537 to 552 million by 2030 unless action is taken. It has been predicted that the number of cases may jump by 90 percent in Africa.

An approach to control postprandial hyperglycemia apart from lifestyle changes with diets and exercise is to delay intestinal glucose absorption through the modulation of starch-digesting enzymes. In mammals, six enzymes (two α–amylasesand four α-glucosidases) are involved in the complete digestion of starch into glucose. α-Amylase inhibitors **(negative modulators)** inhibit mammalian alpha-amylases specifically, by forming a tight complex with α-amylase. The binding of the inhibitor to α-amylase leads to the blockage of the active site of the enzyme thereby reducing the breakdown of starch (Figure 6). In animals, alpha-amylase inhibitors lower the high blood levels of glucose that can occur after a meal by reducing the rate at which α-amylase converts starch into simple sugars (Bastaki, 2005). α-Glucosidase inhibitors **(negative modulators),** on the other hand, competitively inhibit α-glucosidase enzyme in the small intestine (Figure 6). This is important in people with type 2 diabetes, where low levels of insulin prevent extracellular glucose from being easily extracted from the blood.

The conventional treatment for diabetes mellitus is oral hypoglycemic agents/insulin therapy. However, these have been shown to have prominent side effects and they do not modify the course of diabetic complications (Rang and Dale, 1991; Bastaki, 2005).

The need to develop new antidiabetic drugs led us to the screening of some indigenous plants for their ability to modulate the activities of carbohydrate-digesting enzymes and other mediators.

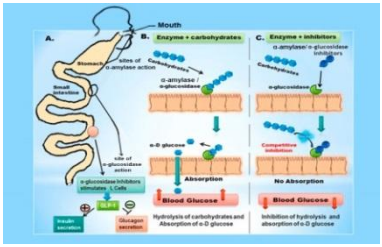

Figure 6: Role of α-amylase and α-glucosidase inhibitors in controlling postprandial hyperglycemia
Source: Hossain *et al.* (2020)

1. *Acacia ataxacantha*

Arise *et al.* (2014a and 2016a) investigated the lipid profile, blood sugar-modulatory, and antioxidant activities of extracts of stem bark and root of *Acacia ataxacantha* (also known as flame thorn in English and "ihun" in Yoruba) (Figure 7a) in streptozotocin – induced diabetic rats. The studies revealed that the normal modulation of blood-sugar and lipid observed may be due to the antioxidant properties of the extracts.

2. *Corchorus olitorius*

Also, **Arise *et al.* (2018a)** investigated the antidiabetic activity of ethanolic extract of *Corchorus olitorius* leaves (known as jute leaves in English and "ewedu" in Yoruba) (Figure7b) in diabetic rats. We concluded that ethanolic leaf extract *of C. olitorius* possesses normoglycemic property with no major side effects; hence, it could be considered safe for the management of diabetes.

3. *Moringa oleifera*

Arise *et al.* (2016b) also determined the antidiabetic and antioxidant effects of oral administration of ethanolic extract of *Moringa oleifera* (drum stick tree) (Figure 7c) flower in diabetic rats. Levels of blood glucose, serum lipids and lipid peroxidation as well as aspartate and alanine aminotransferases and alkaline

phosphatase activities were significantly reduced in the diabetic rats orally administered the ethanolic extract of *M. oleifera* flower. In addition, catalase and superoxide dismutase activities were significantly increased compared to controls. We concluded that the plant extract exhibited blood glucose lowering potential and improved lipid metabolism; thus it may be beneficial in preventing diabetic complications arising from oxidative stress.

(a) (b) (c)

Figure 7: (a) *Acacia ataxacantha* (b) *Corchorus olitorius* (c) *Moringa oleifera*

4.Water melon and Fluted Pumpkin Seeds

Vice- Chancellor sir, food proteins are of great interest in biochemistry due to their beneficial role to human health. Hydrolysis of food proteins became a subject of interest to scientists towards the end of the 20^{th} century because some of these bioactive peptides are more potent than the unhydrolysed protein (Moller *et al*., 2008). Food peptides with α - amylase and α -glucosidase inhibitory activities can serve as a safer and efficacious alternative for managing diabetes.

In another study, proteins from water melon seeds (Figure 8a) were isolated and hydrolyzed with the enzymes, pepsin, trypsin, and Alcalase for evaluation of their enzyme inhibitory property. **Arise *et al*. (2016c)** investigated the *in vitro*α-amylase and α-glucosidase inhibitory and antioxidant activities of protein hydrolysates enzymatically obtained from *Telfaria occidentalis* (Ugu) seeds (Figure 8b). The plant seed protein content was 86.5%

with 18 amino acids consisting of 10 essential amino acids. **Aburo and Arise (2022)** found out that *Telfaria occidentalis* (fluted pumpkin) seed protein hydrolysate was efficient at normalizing levels of blood glucose and lipids in diabetic and hyperlipidaemic rats. The hydrolysate also reversed and negatively modulated (inhibited) the increased congestion and proliferation of inflammatory cells in the pancreas of diabetic rats and we concluded that water melon and "ugu" seeds possess profound antidiabetic potential which can be explored as drug candidate for the management of diabetes.

(a)

(b)

Figure 8: **(a) Watermelon seeds (b)Fluted pumpkin (ugu) seeds**

(ii) In the Search for Antiulcer Agents

Peptic ulcer is one of the most common diseases of the gastrointestinal tract with prevailing incidence, which if not addressed, can increase mortality (Akah *et al*., 2020). Peptic ulcer has been attributed to several factors encountered during day-to-day life, such as stress, exposure to *Helicobacter pylori* infection, continuous use of non-steroidal anti-inflammatory drugs (NSAIDs) e.t.c. (Zhou *et al*., 2020). There are three types of peptic ulcers.

(i) Gastric ulcers: Ulcers that develop inside the stomach;
(ii) Esophageal ulcer: Ulcer that develop inside the esophagus;
(iii) Duodenal ulcer: ulcers that develop in the upper section of the small intestines, called duodenum.

Gastric ulcer is a deep necrotic lesion characterised by disruption of mucosal integrity, leading to local defect or excavation due to active inflammation. Reduction in gastro-protective factors (such as mucus, bicarbonate secretion, gastric mucosal blood flow and prostaglandins synthesis) and enhancement of aggressive factors (such as oxidative stress by reactive oxygen species, hyper

secretion of hydrochloric acid through H^+/K^+-ATPase action, blockade of cyclooxygenase enzyme system by NSAIDs in addition to *Helicobacter pylori* - mediated cytotoxicity) are responsible for gastric ulceration. Sustainable efforts and constant research have led to the development of several antiulcer drugs such as H^+/K^+-ATPase inhibitor (e.g omeprazole), histamine receptor blockers (e.g cimetidine) and *Helicobacter pylori* inhibitor (e.g amoxicillin). However, the majority of the drugs have been documented to pose problems of adverse effects (Zhou *et al*., 2020). Flowing from this, we screened some indigenous plants for their ability to modulate the activities of H^+/K^+-ATPase and cyclooxygenase among other mediators.

1. *Acacia ataxacantha*(flame thorn in English and "ihun" in Yoruba)

2. *Argemone mexicana*(Mexican poppy in English and "ahon-ekun" in Yoruba)

In our relentless search for potential modulators of the enzyme mediators implicated in the pathogenesis of peptic ulcer, **Arise *et al*. (2014b)** and **Idowu and Arise (2020),** in separate studies, investigated the modulatory potential of *Acacia ataxacantha* (Figure 7a) and *Argemone mexicana* (Figure 9a) leaf extracts on H^+/K^+-ATPase, cyclooxygenase and antioxidant enzyme activities,and on the growth of *H. pylori*. We concluded that *Acacia ataxacantha* and *Argemone mexicana* leaf extracts displayed ulcero-protective property by positively modulating production of mucus and glycoprotein and antioxidant enzyme activities in the mucosal membrane of gastric ulcer rat model. We **(Idowu, Saliu, Fakorede and Arise, 2021)** further revealed that the ethyl acetate fraction of the ethanolic leaf extract of *Argemone mexicana* demonstrated a more profound antiulcer activity than the butanol fractions.

3. *Cnidoscolus aconitifolius*

Adewale and Arise (2021) investigated the ulcer ameliorating principles of ethanolic leaf extract of *Cnidoscolus aconitifolius* (known as tree spinach in English and "efo Jerusalem" in Yoruba) (Figure 9b) in gastric ulcer rat model. Our findings revealed that the plant extract caused significant decrease in rat

gastric volume and acidity by negatively modulating H^+/K^+-ATPase and pepsin activities while it positively modulated mucosal prostaglandin E_2, mucus and nitric oxide production. We thus concluded that the plant leaf extract exhibited antiulcer activity and should be explored for the development of effective and safer antiulcer drugs.

(a)

(b)

Figure 9: **(a)** ***Argemone Mexicana*** **(b)** ***Cnidoscolus aconitifolius***

(iii) In the Search for Anti-hypertensive Agents

Vice-Chancellor sir, uncontrolled high blood pressure or hyprertension is one of the leading causes of disease and death worldwide. According to the current American College of Cardiology/American Heart Association (ACC/AHA) Hypertension Guidelines (2020), hypertension is now confirmed when systolic blood pressure is regularly ≥130 mm Hg and diastolic blood pressure ≥80 mm Hg.Uncontrolled high blood pressure can lead to complications accounting for 31% of all deaths. This implies that 17.7 million people die annually due to complications arising fromuncontrolled high blood pressure, and 80% of all deaths attributed to hypertension result from heart attacks and strokes (Morales-Camacho *et al*., 2019). Hypertension afflicts approximately a quarter of adults worldwide and more than 1 billion individuals in both developed and developing countries are considered hypertensive (Tian *et al*., 2018; Liao, 2019). The affected population is predicted to increase to more than 1.5 billion by 2025 (an increase of about 50%) and is estimated to result in 23.3 million deaths in 2030 (Courand and Lantelme, 2017; He *et al*., 2019). The inhibition of angiotensin converting enzyme (ACE), an important enzyme in the Renin-Angiotensin System (RAS), has remained an effective strategy in the management of hypertension. The blood pressure of mammals is chiefly regulated by the RAS.

The key pathogenesis of high blood pressure in humans is the dysregulation of the RAS (Aluko, 2015). Inhibition of ACE reduces vasoconstriction and artery stiffness among others (Boutouyrie *et al*., 2011) while extreme ACE activity leads to elevated amounts of angiotensin II, causing a high vasoconstriction rate and therefore resulting in high blood pressure (Aluko, 2018). Hence, the management of blood pressure requires the use of compounds (negative modulators) that inhibit ACE (mediators) activities, thereby producing and maintaining the homeostatic amount of angiotensin II. Nonetheless, the usage of synthetic ACE inhibitors like perindopril or ramipril has numerous adverse effects like low blood pressure, dry cough and swelling underneath the skin (Martin *et al.*, 2019). Thus, the need for natural, safer and effective modulators of these enzyme mediators.

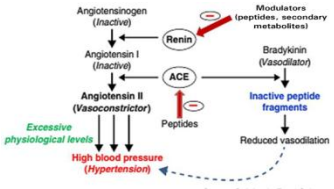

Figure 10:The RAS-induced Hypertension and Enzyme Targets for Negative Modulation (Inhibition) by Antihypertensive Drugs
Source: Aluko (2015)

In our continuous search for safer, effective and endogenously related negative modulators (inhibitors) of angiotensin-1 converting enzyme, we investigated the *in vitro* antihypertensive, antiradical and hydrogen peroxide scavenging properties of enzymatically obtained protein hydrolysates from the seeds of:

1. ***Citrullus lanatus*** **(watermelon)**
2. ***Moringa oleifera*** **(drum stick tree)**
3. ***Luffacylindrica*** **(vegetable sponge; "kankan-ayaba" in Yoruba)**
4. ***Anarcadium occidentale*** **(cashew)**
5. ***Azadirachta indica*** **(neem; "dogoyaro" in Yoruba)**

Arise *et al.* (2016d) and Arise *et al.* (2019a) reported that water melon (Figure 8a) and *Moringa oleifera* seed (Figure 11a)

protein hydrolysates contain bioactive peptides that may be exploited as potential food sources of antioxidant and antihypertensive agents. **Arise *et al.* (2019b)** concluded that *Luffa cylindrica* seed (Figure 11b) protein hydrolysate contain peptides that may play critical and indispensable role as bio-tools in hypertension treatment. **Arise *et al.* (2021a)** also reported that cashew nut (Figure 12a) protein hydrolysates typify germane sources of novel blood pressure and sugar regulating biopeptides for enhanced wellness and as alternative sources of essential amino acids.

(a)

(b)

Figure 11: **(a) *Moringa oleifera seeds* (b) *Luffacylindrica* seeds**

Furthermore, **Arise *et al*. (2019c)** also found out that neem seed (Figure 12b) protein isolate is rich in peptides that could offer protection to the heart, thus may be formulated as nutraceutical for managing oxidative stress-related diseases including hypertension.

(a)

(b)

Figure 12: **(a) Cashew nuts (b) Neem seeds**

6. Cocoa pod husks

Vice-Chancellor sir, the increase in production of cocoa has favored the proliferation of undesirable residues, such as cocoa pod husks.Consequently, specific applications are needed to use these raw materials in the most efficient way possible in the production process. The concepts of “wealth-generating waste” and “recyclable materials” are important for building a sustainable and healthy

environment through the efficient use of these waste resources.Cocoa pod husk has, however, remained under-exploited despite its richness in dietary fiber, lignin and bioactive antioxidants, such as polyphenols (Lu *et al*. 2018). **Arise *et al*. (2021b)** embarked on the investigation of *in vitro* antioxidant and angiotensin-1 converting enzyme modulatory properties of peptides and polyphenols contained in cocoa pod husks (Figure13) and concluded that enzymatically derived cocoa pod husk protein hydrolysates and polyphenol-rich fraction may be an effective source of natural angiotensin -1 converting enzyme inhibitors and antioxidants with potential blood pressure regulating activity which may be explored for the development of antihypertensive drugs.

Figure 13: **Cocoa pod husks**

In the light of our studies on the discovery of potent modulators of angiotensin-1 converting enzyme with antioxidant properties, we **(Adeoye, Joel, Igunnu, Arise and Malomo, 2021)** published a review article of some African spices and seeds with antihypertensive potential in the Journal of Food Biochemistry by Wiley, wherein we emphasised the bioactive compounds present in them and their ability to negatively modulate (reduce) plasma angiotensin-1 converting enzyme activity better than simvastatin (a standard angiotensin-1 converting enzyme inhibitor). We further emphasized that studies have revealed that some of the spices/seeds such as scent leaves, garlic, ginger, turmeric, African locust beans and thyme may be used as safer dietary alternative therapy alongside common antihypertensive medications.

(iv) In the Search for Antidiarhoeal Agents
Annona senegalensis

Diarrhea is a major health threat to people in the tropical and sub-tropical countries. Diarrhea occurs when there is an imbalance between absorption and secretion of water and electrolytes in the gastrointestinal tract (GIT). It is an alteration inthe movement of electrolytes and water in the intestine. Active extrusion of Na^+ across the basolateral membrane is mediated by the sodium pump (Na^+/K^+ -

ATPase) (Sandle, 1998). Na^+/K^+ - ATPase maintains the electrochemical gradient required for Na^+ absorption and eventually water re-absorption. The activity of the pump is negatively modulated (inhibited) in all types of diarrhea. Also, cyclooxygenase is the key enzyme responsible for the synthesis of prostaglandins. Prostaglandins elicit net secretion of fluid by inhibiting sodium absorption. Prostaglandin is also known to cause inflammation. Inflammation causes inflammatory bowel disease (IBD) whose symptoms include diarrhea.

Vice-Chancellor sir, we **(Ahmed, Arise and Sudi, 2020) and (Ahmed, Arise, Umaru and Mohammed, 2022)** investigated the potential of stem and root bark extracts of *Annona senegalensis* (popularly known as African custard apple in English; "gwandar daaji" in Hausa; "uburu-ocha" in Igbo and "abo" in Yoruba) (Figure14) to positively modulate (activate) the activity of Na^+/K^+-ATPase and some antioxidant enzymes while negatively modulating cyclooxygenase II. We concluded that the extract exerted its anti-secretory activity via anti-oxidation, negative modulation (inhibition) of prostaglandin synthesis and positive modulation (stimulation) of Na^+/K^+-ATPase activity. **Ahmed, Arise and Umaru (2022)** further concluded that *A. senegalensis* root bark is rich in bioactivities that may be employed in the prevention of diarrhoea through stimulation of Na^+ absorption and negative modulation (inhibition) of cyclooxygenase activity.

Figure 14: ***Annona senegalensis***

(v) In the Search for Antimalarial Agents

Vice-Chancellor sir, malaria remains the major cause of morbidity and mortality among tropical Africans, South Asians, Central and South Americans, the Caribbeans, the middle Easterners and Oceanians. It is estimated that over 241 million cases of malaria infection occur annually while over 627,000 people die of the disease (especially children below age 5 and pregnant women) with over 90% from Sub-Sahara Africa (WHO, 2022). In our continuous search for

safer, effective antimalarial modulators, we screened the mixtures of the under listed plants for their antimalarial activity.

1. ***Caricapapaya* and *Alstonia broonei***
2. ***Tithonia diversifolia* and *Morinda lucida***

Arise *et al*. (2012e) and Arise *et al*. (2013a) investigated the antimalarial property of the methanol extracts of mixtures of *Caricapapaya* - pawpaw leaves (Figure 15a) and stem bark of *Alstonia broonei*, known as stoolwood in English and ahun in Yoruba (Figure 15b); leaves of *Tithonia diversifolia*, known as shrub sunflower in English and "sepeleba" in Yoruba (Figure 16a) and *Morinda lucida* known as brimstone tree in English and "oruwo" in Yoruba (Figure 16b), respectively, in animal models. We concluded that methanolic extracts of the plant parts mixtures possess considerable anti-malarial activity but may potentiate some level of toxicity with prolonged administration.

(a)

(b)

Figure 15: **(a) *Caricapapaya* (b) *Alstonia broonei***

(a)

(b)

Figure 16: **(a) *Tithonia diversifolia* (b) *Morinda lucida***

As part of the team of Prof. Obaleye on co-ordination of mefloquine and quinine with metals, we (**Obaleye, Tella and Arise, 2009**) synthesized, characterised and investigated the antimalarial activity of metal complexes of mefloquine and quinine in *Plasmodiumberghei*-infected mice. Our findings revealed that four of the metal complexes $(MeFH^{+})_2[Fe(SO_4)_2]^{2+}$, $(MeFH+)_2CuCl_4.4H_2O$,

$[Fe(QUIN)Cl_2.H_2O]SO_4.3H_2O$ and $[Zn(QUIN)ClSO_4]$ exhibited significantly higher antimalarial activity than chloroquine and their parent ligands with no modulation of any sort on rat liver, kidney and serum alkaline phosphate activity. We concluded that the complexes are non-toxic and possess more profound antimalarial activity than chloroquine.

Also, **Tella, Owalude, Simon and Arise (2015**) embarked on the green synthesis of tetrachlorometallate salts of amodiaquine and investigated their antimalarial efficacy on *Plasmodiumberghei*-infected mice. Our findings showed enhanced activity of the synthesized antimalarial as evidenced by improved suppression of parasitemia in established infection. **Arise *et al.* (2016e)** further investigated the antimalarial efficacy and safety of mechanically induced solventless synthesized lumefanthrine-copper complex and found out that pure lumefanthrine attained parasite clearance of 88.52%, chloroquine 91.95%, and lumefanthrine-copper complex, 95.10%. **Arise *et al.* (2016f)** found out that mechanical green synthesis of trimethoprim-Cu improved trimethoprim antimalarial activity. We further reported the mechanochemical synthesis and characterization of Zn^{2+} complex with amodiaquine as well as its improved antimalarial efficacy and safety in *plasmodium berghei*-infected mice. **Arise *et al.* (2017)** reported that coordination of Zn^{2+} with amodiaquine may not be completely safe for prolonged and repeated use as an oral anti-malarial remedy. **Arise *et al.* (2018b)** revealed that lumefanthrine-trimethoprim-copper complex demonstrated higher antimalarial activity than lumefanthrine or trimethoprim but exhibited negative modulation (inhibition) of rat liver alkaline phosphatase, alanine and aspartate aminotransferase activities. The observed effects suggest that lumefanthrine-trimethoprim-copper complex may not be safe.

B. Search for positive modulators or potentiators of certain enzyme activities for improved protection against infections

Vice-Chancellor sir, in our search for immunomodulatory agents (i.e substances that can boost and improve immune responses and protection against infections), we focused on the membrane bound enzyme – alkaline phosphatase. Alkaline phosphatase is present in most parts of the body and is richly expressed at sites (e.g lungs and gastrointestinal tract) where antigens, such as lipopolysacharide may likely enter blood circulation. In order to understand the role of this

enzyme and the potential for overall improved effect when two different modulators are bound to an enzyme mediator; we **(Malomo, Olorunniji, Arise, Adebayo, Adedosu and Odutuga, 2003)** investigated the possible synergistic effects of two linear inhibitors (vanadate and phenylalanine) on rat liver alkaline phosphatase activity and discovered that the combined effect of the two inhibitors were mutually enhanced. Furthermore, our findings revealed that Mg^{2+}, either as an activator (positive modulator) at optimal concentration or inhibitor (negative modulator) at supra-optimal level, exerted its action via a V_{max} effect **(Arise *et al.*, 2005)**. We **(Olorunniji, Igunnu, Adebayo, Arise and Malomo, 2007)** also found out that there was synergistic interaction between Mg^{2+} and Zn^{2+}, which is helpful in promoting the up-regulation of kidney alkaline phosphatase activity. **Arise *et al.* (2008a & b)** reported the positive modulatory (activatory) effect of Co^{2+} and Mg^{2+} on alkaline phosphatase activity, and suggested thatCo^{2+} may be employed as a better cofactor than Mg^{2+} in clinical and diagnostic applications.

In order to fully elucidate the mechanism of modulation of alkaline phosphatase activity, we **(Igunnu, Arise, Adebayo and Malomo, 2012 & 2014)** investigated the time-dependent modulatory effects of Mg^{2+} and Zn^{2+} on monoesterase activity of Ca^{2+}- inhibited calf intestinal alkaline phosphatase. We concluded that the modulation of Ca^{2+} - inhibited calf intestinal alkaline phosphatase activity by Mg^{2+} and Zn^{2+} may be explored in the treatment and prevention of disorders of bone mineralization.

Vice-Chancellor sir, the continued and synergized efforts of our team in understanding the role of alkaline phosphatase in endotoxemic (bacterial) injury protection led to the investigation of the effect of taurine (an amino acid) on the activity of L-phenylalanine (also an amino acid)-inhibited rat intestinal alkaline phosphatase. **Arise *et al.* (2015a)** thus concluded that the activation of rat intestinal alkaline phosphatase modulated by taurine in the presence of L-phenylalanine may be an alternative immunological mechanism against endotoxemic injury. In other related studies, we reported how taurine and vitamin E protected against cigarette smoke – induced changes in lung alkaline phosphatase, Na^{+} / K^{+} - ATPase and Ca^{2+}/Mg^{2+}- ATPase activities among other mediators **(Arise *et al.*, 2021c)**. **Arise *et al.* (2022)** also found out that enhancement in the activity of intestinal alkaline phosphatase by

taurine and sodium butyrate may further emphasise the role of alkaline phosphatase in attenuating bacterial lipopolysaccharide-mediated diseases. The implication of this is that regular and moderate intake of foods rich in taurine, L-phenylalanine and vitamin E such as chicken, eggs, yoghurt, almond and cashew nuts will help to synergistically up-regulate intestinal alkaline phosphatase activity towards offering protection against bacterial and other microbial assaults.

Arise *et al.* (2019d) also investigated the hepatoprotective and antioxidant activities of aqueous extract of *Moringa oleifera* flowers on carbon tetrachloride-induced (CCl_4) toxicity in rats and found that aqueous extract of *M. oleifera* flower possesses remarkable hepatoprotective potential underlining its ability to prevent and reverse CCl_4 - induced liver injury in experimental animals. In a related study, we **(Malomo, Yakubu, Amira, Dosumu, Igunnu, Oluwaniyi, Arise and Adebayo, 2014)** reported that ethyl acetate and methanolic extracts of *Celosia argentea* leaves (known as Lagos spinach in English and "soko yokoto" in Yoruba) (Figure 17a) possess antioxidant activity and have modulatory capabilities to protect and attenuate the effects of cadmium-related toxicity in rats.

Arise *et al.* (2019e) also reported the protective effect of ivermectin on mono-sodium glutamate-induced excitotoxicity in male rats and found out that co-administration of monosodium glutamate with ivermectin for 21 days did not cause any modulation in the activities of brain glutathione-S-transferase, nitric oxide synthase, superoxide dismutase, catalase, Na^+/K^+-ATPase, Ca^{2+}/Mg^{2+}-ATPase, alkaline and acid phosphatases compared to the observed opposite with the administration of monosodium glutamate for 21 days. This result suggested that ivermectin may offer protection against monosodium glutamate-induced excitotoxicity.

(a)

(b)

Figure 17:(a) *Celosia argentea* (b) *Talinium triangulare*

My Research Contributions to Bioremediation

Vice-Chancellor sir, some aspects of my research efforts are also focused on the modulation of enzyme mediators among others towards finding solution to some environmental health challenges. These aspects fall under bioremediation, which uses bacteria, fungi, green plants or their enzymes to return contaminated environment to its natural healthy state (Megharaj *et al*., 2014). In order to provide useful indicator to monitor levels and extents of water pollution as well as the role of co-factor containing effluent, **Arise *et al*. (2011b)** investigated and reported the presence of alkaline phosphatase, Zn^{2+} and Mg^{2+} in Agba River water and concluded that this may be one mechanism by which water pollution, through phosphorus-containing contaminants such as detergents, fertilizers and animal wastes from homes, industries and farmlands, are removed or reduced. We **(Osioma, Akanji and Arise, 2013)** and **Arise *et al*. (2013b)** revealed modulation (alteration) in the hepatic activities of glutathione-S-transferase, superoxide dismutase, catalase and lactate dehydrogenaseof *Clarias gariepinus* from swamps around Kokori-Erhoike petroleum exploration area in Delta State, suggesting that the fish were under stress in their natural habitats and thus could be employed as biomarkers of contamination in environmental monitoring of crude oil pollution. **Arise *et al*. (2015b)** also investigated the biochemical changes in *Lumbricus terrestris* (earthworms) and *Talinium triangulare* (water leaves) (Figure 17b) remediation of heavy metals from Ugberikoko petroleum flow swamps of Delta State, Nigeria, and concluded that the earthworm enzymes may be good candidates for the assessment of soil pollution; and that *Talinium triangulare* could be used for commercial and environmentally friendly phytoremediation. **Arise *et al.* (2015c)** also reported, in another related study, the level of cadmium, acid and alkaline phosphatase in the soil around Odo-efo River, Ilorin, Kwara State. Also, **Arise *et al.* (2021d)** reported the biochemical alterations in *Lumbricus terrestris* and remediation capacity of *Azadirachta indica* plant from industrial effluent discharge locations in Challawa and Kura village of Kano State and concluded that *Azadiracha indica* may be useful for extraction and stabilization of heavy metals in polluted soils while the changes in earthworm enzymes may serve as sensitive bioindicators of soil contamination.

Arise *et al*. (2019f) also investigated the *in vivo* effects of zinc oxide-*Chromolaenaodorata* nano particle-treated Oyun River water. Our findings, among many others, revealed that liver alanine and

aspartate aminotransferase and acid phosphatase activities of rats maintained on zinc oxide-*Chromoleana odorata* nanoparticle treated-Oyun River water were positively modulated (elevated). We concluded that zinc oxide-*Chromoleana odorata*-treated water impacted negatively on rat liver and kidney functional enzymes; hence, zinc oxide-*Chromolaena odorata* nanoparticle-treated water may not be safe as drinking water.

Vice-Chancellor sir, the increasing concern about pollution that occurs from agricultural and industrial wastes, posing environmental health challenge, stimulated our interest in the conversion of waste materials into commercially valuable products such as enzymes. We isolated peroxidases (useful in biotechnology, biomedicine, pharmacy and agriculture) from *Eichhornia crasspies* and *Pistia stratiotes* leaves (Figures 18a&b). *Eichhornia crasspies* also widely known as water hyacinth is an aquatic plant that is considered to be one of the world's persistent weed used as an indicator of heavy metal pollution (Gonzalez *et al*., 1989) while *Pistia stratiotes* (known as water lettuce in English, and "Oju oro" in Yoruba) is a freshwater macrophyte with evasive characteristics similar to *Eichhornia crasspies*. **Arise *et al.* (2016g) and Arise *et al*. (2018c)** reported the isolation, purification and characterisation of peroxidases from water hyacinth and lettuce leaves with the conditions and factors which could identify the enzyme prospects for industrial applications and the consequent removal or reduction of these weeds from water bodies or ways.

Arise *et al.* (2020) also embarked on the isolation, partial purification and characterisation of invertase from watermelon (Figure 8a) rind (that is usually discarded as waste) and found out that invertase isolated from watermelon rind was purified to 46.94 folds with 23.19% yield and was competitively inhibited by Fe^{2+}, Cu^{2+}, Mg^{2+} and Ag^{+} while Co^{2+} positively modulated(activated) its activity. Thus, we recommended that watermelon rind may be employed as a local source of invertase for applications in the production of jams, candies, non-crystallizing creams, artificial honey, lactic acid, ethanol, confectionaries, digestive aid tablets, powder milk for infants and other infant foods with consequent remediating effects on the environment.

(a) (b)

Figure 18:(a) *Eichhornia crasspies* (b) *Pistia stratiotes*

Current Research in Molecular Biology and Enzyme Informatics

Vice-Chancellor sir, one of the duties of molecular biologists is the organisation and utilisation of the wealth of information available on computer databases to answer basic biological questions. Bioinformatics integrate knowledge in molecular biology with computer and programming skills essential for success in life sciences. Molecular biologists and bioinformatists are able to solve a variety of important biological challenges facing the society such as diagnosis and treatment of diseases, management of environmental degradation and production of stable food supply.

In July 2015, the then Vice-Chancellor, Prof AbdulGaniyu Ambali approved my training and certification in Molecular Biology and Bioinformatics at New England Biolabs, Boston, Massachusetts, U.S.A. The training and exposure sharpened my skills and at the end of the training, I was able to clone a *Caenorhabitis elegan* - bearing mouse RNA (Figure 19) in collaboration with Professor Steve Williams, a Gates Professor of Biological Sciences and Biochemistry at Smith College and the University of Massachusetts, Boston, U.S.A.

One of the importance of cloning C. *elegans*-bearing mammalian genes is to be able to carry out studies involving enzyme modulation targeted at drug discovery for humans. *C. elegans* represents an ideal model system in which one can study gene expression patterns. *C. elegans* is transparent and this facilitates live imaging of gene expression throughout development, which unequivocally allows for identification of cells in which specific genes are being expressed. This is possible because the *C. elegans* genome is relatively small, yet it contains a surprisingly large number of genes (approximately 20,000) of which nearly 40% show homology to those of other multicellular animals (CSC,1998).

Figure 19:Cloned *C. elegans* bearing mouse liver ribonucleic acid (RNA)

We are currently focusing on identification of renin and ACE inhibitors with improved efficacy with little or no side effects by exploring the available structural renin- and ACE-inhibitor data via ligand and structure-based pharmacophore modeling. At present, we have docked a total of 207,062 compounds against renin using a screening workflow. We are hopeful that the results, which will be obtained from this study and related ones, would provide important data for the rational design of novel antihypertensives with improved pharmacokinetic and pharmacodynamics properties.

Conclusion

The phenomenon of enzymatic catalysis makes possible biochemical reactions necessary for all life processes; and the living cell is the site of tremendous biochemical activities called metabolism that characterise "life". Enzymes are the mediators or facilitators of these life processes. Without enzymes, life will be imperceptible or inconceivable because these chemical reactions would have been taking place at a rate far too slow for the pace of metabolism. Any disruption or modulation in the activities of these mediators or facilitators of life processes may result into a diseased or improved health condition. I have shown how biochemistry is influencing man's health and wellness and the modulation of the catalytically mediated life processes in pursuant of healthy living and promotion of well-being for all. Our contributions in the areas of biochemical and environmental toxicology involving the basic principle of using enzyme levels for diagnosis of disease and environmental health as well as potential harms of some antibiotics were highlighted. I also delved into how we used plant extracts, proteins and peptide for blood pressure and sugar modulation, employing angiotension-1 converting enzyme, α-amylase and α- glucosidase among others, and not leaving out peptic ulcers, diarrhea and malaria. Our works on alkaline phosphatase and nitric

oxide synthase modulation emphasized their role in protection against infections and cellular damage. We are currently using molecular biology and enzyme informatics as tools to predict potential modulators and enzyme targets for hypertension and diabetes among others. As a way of contributing to the attainment of United Nations Global Goals, I have been employing **modulators** like metal ions, plant extracts including proteins and peptides and other ligands to **modulate the mediators or facilitators (enzymes) of life processes as a strategy** to achieving health and wellness.

Recommendations

The following are recommended for:

A. The General Public

Let your food nutrients be your medicines (the enzyme modulators)

1. Our common indigenous fresh vegetables, fruits and nuts are very rich in antioxidants, short peptides and micronutrients; and studies have shown that, they are good modulators of relevant enzymes with potentials to prevent and protect against diseases like diabetes, hypertension and ulcer. *Corchorus olitorius* leaves (ewedu) have potent blood sugar modulatory and immune boosting activities. I therefore recommend its increased, regular and general consumption.
2. The general public is hereby advised against the practice of concurrent intake of drugs such as antibiotics with alcohol, and the use of galena (tiiro) as well as exposure of skin to used lubricating oil because of the danger or harms inherent in the practice.
3. The inclusion of fresh *Telfaria occidentalis* (fluted pumpkin; ugu) fruits and leaves and water melon seeds as components of fresh vegetable salads especially for pre-diabetics and diabetics because of their potent and safe blood sugar-modulatory ability is hereby recommended.
4. The general public is enjoined to cultivate the regular intake of cashew nuts both at home and offices because of its blood sugar and pressure modulatory capacity as well as eggs, yoghurt and foods that are good sources of taurine, L-phenylalanine and vitamin E because of their synergistic enhancement of alkaline phosphatase activity for improved

immunological response and protection against microbial infections.

B. The Researchers

5. There is the need for specific research geared towards application of detailed mechanistic enzyme kinetics for the characterisation of enzyme targets; the design and prosecution of assays for effective profiling of compound properties and insight into the mechanism of action required for drug efficacy; combining information from enzyme kinetic studies with that derived from biophysical methods.
6. Researchers should embark on more collaborative research efforts with industries as well as clinical and representative studies so that most of the research outputs will not be left to gather dust on the shelves but developed into beneficial products.

C. The Industries

7. Industries (Pharmaceutical, Food and Drinks etc) should fund research as part of their corporate social responsibility.

D. The Government

8. Government agencies such as NAFDAC, SON and other relevant agencies should do more in their regulatory efforts to subject new products to standard toxicological evaluation procedures.
9. More than half of all known drugs act by inhibiting or modulating enzymes. Therefore, understanding the structures and functions of enzymes is important for drug design and target prediction. To take advantage of this science with a resolve to enhancing drug discovery efforts by utilizing as raw materials our vast medicinal plants, there is a need to adequately fund the provision of essential facilities and training of more biochemists in mechanistic enzymology and enzyme informatics.

E. The University

10. Biochemistry is the pivot of all life sciences. The equipment for teaching, training and research are capital intensive. Thus, there is a need to adequately fund and equip the laboratories and classrooms with the state of the artequipment andfacilities that will enhance teaching, training and research.

11. Biochemistry is a service Department to other programmes like Medicine, Pharmacy, Nursing, Veterinary Medicine, Anatomy, Physiology, Medical Laboratory Science, Optometry and Vision Science, Microbiology, Plant Biology, Zoology and Agriculture. The Department of Biochemistry, University of Ilorin, has always been saddled with the responsibility of teaching biochemistry students, medical students and others. I believe that the best brains and hands to teach biochemistry to medical students and others should be biochemists that major in the subject, because you can only give what you have. The situation where we now have non-core biochemists teaching biochemistry to our medical students should be looked into and corrected. Biochemists with special interest in Clinical and Medical Biochemistry should be engaged to teach biochemistry to medical students. That is when the chemistry of life processes would have been correctly modulated by the right mediators.

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Peradventure, I have inadvertently left some people or groups out due to constraint of space and time, kindly accept my unreserved apology.

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References

Abliz, G., Mijit, F., Hua, L., Abdixkur, G., Ablimit, T., Amat, N. and Upur, H. (2015). Anti-carcinogenic effects of the phenolic-rich extract from abnormal *Savda Munziq* in association with its cytotoxicity, apoptosis-inducing properties and telomerase activity in human cervical cancer cells (SiHa) *BMC Complement. Altern. Med.* 15, 23.

Aburo, O.R. and **Arise, R.O**.(2022):Antidiabetic activity of peptic *T. Occidentalis* seed protein hydrolysate in streptozotocin-induced diabetic rats. *Pharma-Food Congress*, 091, 85.

Adebayo, J.O., Igunnu, A., **Arise, R.O.** and Malomo, S.O. (2011). Effects of co-administration of artesunate and amodiaquine on some cardiovascular disease indices in rats. *Food and Chemical Toxicology*49,45-48.

Adeoye, R.I., Joel, E. B., Igunnu, A., **Arise, R.O.** and Malomo, S.O. (2021). A review of some common African spices with antihypertensive potential. *Journal of Food Biochemistry* 46(1), e14003.

Adewale, A.A. and **Arise, R.O**.(2021). *In silico* identification of H^+/K^+-ATPase and *H. pylori* virulent CagA and VacA proteins inhibitors in ethanolic leaf extract of *Cnidoscolus aconitifolius. NISEB Conference*, EP3 052, 109.

Ahmed, M.U., **Arise, R.O.** and Sudi, I.Y. (2020). Evaluation of the anti-diarrhoeal activity of aqueous root and stem bark extracts of *Annona senegalensis. International Journal of Life Sciences and Biotechnology*. 3(1), 1-17.

Ahmed, M.U., **Arise, R.O.** and Umaru, I.J. (2022). Identification and biochemical characterization of anti-enteropooling compounds from Annona senegalensis root bark. *Scientific African*, 15, e01128.

Ahmed, M.U., **Arise, R.O.,** Umaru, I.J. and Mohammed, A. (2022). Antidiarhoeal activity of catechol and ethyl 5, 8,11,14,17 – Icosapentanoate-rich fraction of *Annona senegalensis* stem bark. *Journal of Traditional and Complementary Medicine*, 12(2),190-194.

Aluko, R. E. (2015). Structure and function of plant protein-derived antihypertensive peptides. Current Opinion in Food Science, 4, 44–50.

Aluko, R. E. (2018). Food protein-derived peptides: Production, isolation, and purification. In R. Y. Yada (Ed.), *Proteinsin Food Processing*(Second Edition), (pp. 389-412). Sawston Cambridge: Woodhead Publishing.

An, J. H., Shin, K.-J., Yang, W. I., Lee, H. Y. (2012). Body fluid identification in forensics. *BMB Reports* 45, 545-553.

Arise, R.O. and Malomo, S.O. (2005). Effect of separate and combined administration of ivermectin and albendazole on the activities of alkaline phosphatase and aminotransferases of rat kidney. *Nigerian Journal of Pure and Applied Sciences* 20,1774-1780.

Arise, R.O. and Malomo, S.O. (2006). Effects of ivermectin and/ or albendazole on some hepatic microsomal components and lipid

peroxidation in rat. *NigerianJournal of Biochemistry and Molecular Biology* 21(1), 47-54.

Arise, R.O. and Malomo, S.O. (2009a). Effects of ivermectin and albendazole on some liver and kidney function indices in rats. *African Journal of Biochemistry Research* 3(5) 190-197.

Arise, R.O. and Malomo, S.O. (2012). Albendazole potentiates the neurotoxic effect of ivermectin in rat. *International Journal of Biological and Chemical Sciences (IJBCS)* 6(1), 317-327.

Arise, R.O., Aboyewa, J.A. and Osioma, E. (2015b). Biochemical changes in *Lumbricusterrestris* and phytoaccumulation of heavy metals from Ugberikoko Petroleum Flow Station Swamps, Delta State, Nigeria. *Nigerian Journal of Basic and Applied Sciences* 23(2), 141-155.

Arise, R.O., Aboyewa, J.A. and Osioma, E. (2015b). Biochemical changes in *Lumbricusterrestris* and phytoaccumulation of heavy metals from Ugberikoko Petroleum Flow Station Swamps, Delta State, Nigeria. ***Nigerian Journal of Basic and Applied Sciences*** 23(2), 141-155.

Arise, R.O., Aburo, O.R, Farohunbi, S.T. and Adewale, A.A. (2016b): Antidiabetic and Antioxidant Activities of Ethanolic Extract of Dried Flowers of *Moringa oleifera* in Streptozotocin-induced Diabetic Rats. *Acta Facultatis Medicae Naissensis* 33(4), 259-272.

Arise, R.O., Acho, M.A., Yekeen, A.A., Omokanye, I.A., Sunday-Nwaso, E.O., Akiode, O.S. and Malomo, S.O. (2019c). Kinetics of angiotensin -1 converting enzyme inhibition and antioxidative properties of *Azadirachta indica* seed protein hydrolysates.*Heliyon* 5, e01747.

Arise, R.O., Adetiwa, O.M., Adeoye, R.I. and Malomo, S.O. (2022).Synergistic enhancement of rat intestinal alkaline phosphatase activity by taurine and sodium butyrate protects against endotoxin-induced bowel inflammation. *Food Biochemistry* 46(7), e14123.

Arise, R.O., Akapa, T., Adigun, M.A., Yekeen, A.A. and Oguntibeju, O.O. (2016a). Normoglycaemic, normolipidaemic and antioxidant effects of ethanolic extract of *Acaciaataxacantha* root in streptozotocin-induced diabetic rats. *Notulae Scientia Biologicae*8(2), 144-150.

Arise, R.O., Akapa, T.C., Olajide, O. J. and Ikusemoro, I. T. (2014b). Ulcero-protective potentials of methanolic extract of *Acacia ataxacantha* leaves in indomethacin and stress induced gastric ulcer models. *International Journal of Biochemistry Research & Review*, 4(4), 12-321.

Arise, R.O., Akintola, A.A., Olarinoye, J.B. and Balogun, E.A. (2012b) Effects of aqueous extract of *Nauclea latifolia* stem on lipid profile and some enzymes of rat liver and kidney. *International Journal of Pharmacology* 8(5), 389-395.

Arise, R.O., Akiode, S.O, Igunnu, A. and Malomo, S.O. (2012c). Effect of artesunate and amodiaquine on rat hexobarbital sleeping time and some hepatic biochemical parameters. *Nigerian Journal of Pure and Applied Sciences* 25, 2385-2393.

Arise, R.O., Alabi, A.B., Maccarthy, O.S., Olurombi, T.M., Olufemi, O., Farohunbi, O.S. and Anthony, T.O. (2019f). *In vivo* effects of zinc oxide-*Chromolaena odorata*nanoparticle-treated Oyun River water. *Sri Lankan Journal of Biology***,** 4(2):13– 31.

Arise, R.O., Arise, A.K., Malomo, S.O. and Oyewole, I.O. (2019e): Ivermectin protects against monosodim glutamate-induced excitotoxicity in the rat. *Acta Facultatis Medicae Naissensis*36(1),38-47.

Arise, R.O., Basiru, D.I., Olufemi, O. and Adeoye, R.I. (2021d). Biochemical transmutation in *Lumbricus terrestris* and phytoextraction of heavy metals from the swamp of Challawa industrial layout, Kano, Nigeria. *Springer Nature Applied Sciences* 3**,** 362.

Arise, R.O., Bolaji, F.F., Jimoh, O.A., Adebayo, J.O., Olorunniji, F.J. and Malomo, S.O. (2005). Regulatory effects of divalent cations on rat liver alkaline phosphate activity: How Mg^{2+} activates (and inhibits) the hydrolysis of p-nitrophenylphosphate. *Biokemistri***.** 17, 129-136.

Arise, R.O., Davies, F.F. and Malomo, S.O. (2008a). Cobalt reverses vanadate inhibition of rat kidney alkaline phosphate. *Scientific Research and Essay***,** 3 (12), 613-620.

Arise, R.O., Davies, F.F. and Malomo, S.O. (2008b). Independent and interactive effects of Mg^{2+} and Co^{2+} on some kinetic parameters of rat kidney alkaline phosphatase. *Scientific Research and Essay* 3(10), 488-494.

Arise, R.O., Farohunbi, S.T. and Ayilara, H. O. (2021b):Blood Pressure Regulating and Antioxidant Potentials of *Theobroma Cacao* Pod Husk Protein Hydrolysates. *Avicenna Journal of Medical Biochemistry*9(1), 26-36.

Arise, R.O., Idi, J.J., Mic-Braimoh, I.M., Korode, E., Ahmed, R.N. and Osemwegie, O. (2019b). *In vitro* angiotesin-1-converting enzyme, α-amylase and α-glucosidase inhibitory and antioxidant activities of *Luffa cylindrical* (L.) M. Roem seed protein hydrolysate. *Heliyon*5, e01634.

Arise, R.O., Idowu, O.A., Farohunbi, S.T., Abubakar, F.A. and Aboyewa, J.A. (2015c). Levels of Some Metals and Earthworm Phosphatase Activities in the Soil around Odo-Efo River, Ilorin, Kwara State**.** *Centrepoint Journal* (Science Edition)21,88-105.

Arise, R.O., Idris, B. I., Aburo, O. R., Adewale, A. A. (2019d): Hepatoprotective and antioxidant activities of aqueous extract of *Moringa oleifera fl*ower on CCl_4- induced toxicity in rats.*Ife Journal of Science*, 21(1), 205-213.

Arise, R.O., Igunnu, A., Olajunyin, A. and Olatomiwa, O.A. (2015a). Activation of rat intestinal alkaline phosphate by taurine may be an alternative mechanism of endotexmic injury protection. *Nigerian Journal of Basic and Applied Sciences* 23(1), 55-64.

Arise, R.O., Igunnu, A., Olajunyin, A. and Olatomiwa, O.A. (2015a). Activation of rat intestinal alkaline phosphate by taurine may be an

alternative mechanism of endotexmic injury protection. *Nigerian Journal of Basic and Applied Sciences***,** 23(1), 55-64.

Arise, R.O., Malomo S.O. and Bolarinwa, O.A. (2013). Comparative antimalarial and safety attributes of methanolic extract of leaves of *Tithoniadiversifolia* and *Morindalucida* in animal models. *American Journal of Drug Discovery and Development*3(3), 140-148.

Arise, R.O., Malomo S.O. and Bolarinwa, O.A. (2013a). Comparative antimalarial and safety attributes of methanolic extract of leaves of *Tithoniadiversifolia* and *Morindalucida* in animal models. *American Journal of Drug Discovery and Development*3(3), 140-148.

Arise, R.O., Malomo, S.O. and Akiode, S.O. (2011b). Influence of Zn^{2+} and Mg^{2+} on Some kinetic parameters of alkaline phosphatase in Agba river water. *Nigerian Journal of Biochemistry and Molecular Biology*26(2), 88-98.

Arise, R.O., Malomo, S.O. and Akiode, S.O. (2011b). Influence of Zn^{2+} and Mg^{2+} on Some kinetic parameters of alkaline phosphatase in Agba river water. *Nigerian Journal of Biochemistry and Molecular Biology*26(2), 88-98.

Arise, R.O., Malomo, S.O. and Lawal, M.M. (2012e). Comparative antimalarial and toxicological effects of artemisinin with methanoloic extract of *Carica papaya* leaves and bark of *Alstonia broonai* in animal models.*Advances in Natural and Applied Science*: 6(2), 116-123.

Arise, R.O., Malomo, S.O. and Oyewole, O.I. (2012a). Histological changes in selected tissues of ivermectin and/or albendazole-treated rats. *International Journal of Toxicology and Applied Pharmacology*2(1), 1-5.

Arise, R.O., Malomo, S.O., Adebayo, J.O. and Igunnu, A. (2009b). Effects of aqueous extract of *Eucalyptus globulus* on lipid peroxidation and selected enzymes of rat liver. *Journal of Medicinal Plants Research* 3(2), 077-081.

Arise, R.O., Olapade, E.O., Olufemi, O. and Yekeen, A.A. (2021c). Taurine and Vitamin E Protect against Pulmonary Toxicity in Rats Exposed to Cigarette Smoke. *Scientific African* 13,e00923.

Arise, R.O., Olawoye, D.O., Acho, M.A., Olufemi, O., Adewale, A.A., Alejolowo, O. and Nwonuma, C. (2020):Kinetic characteristics of partially purified invertase from *Citrullus lanatus* Rind *Ceylon Journal of Science*49(1), 61-69.

Arise, R.O., Omokanye, I.A., Yekeen, A.A., and Malomo, S.O. (2019a): Angiotensin-1 converting enzyme-inhibitory and *in vitro* antioxidant activities of *Moringaoleifera* seed protein hydrolysates. *Science Research Anals***,** 9(1):67-74

Arise, R.O., Osioma, E. and Akanji, M.A. (2013b). Assessment of water quality parameters from swamps around Koriko-Erhoike Petroleum Flow Station in Delta State, Nigeria. ***Der Chemica Sinica*** 4(1), 155-161.

Arise, R.O., Osundahunsi, B.O. and Adewale, A.A. (2018c): Stability profile of *Pistia stratiotes* leaf peroxidase. *Nigerian Journal of Basic and Applied Sciences* 26(1), 96-

Arise, R.O., Osundahunsi, B.O., Farohunbi, S.T. and Yekeen, A.A. (2016g). Catalytic and kinetic properties of purified *Eichhorniacrassipes* leaf peroxidase. *Environmental and Experimental Biology* 14, 83-90.

Arise, R.O., Sunday-Nwaso, E., Farohunbi, S.T., Nafiu, M.O. and Tella, A.C. (2017): Mechanochemical Synthesis, In vivo Anti-malarial and Safety Evaluation of Amodiaquine-zinc Complex. *Acta Facultatis Medicae Naissensis*34(3), 221-233.

Arise, R.O., Taofeek, O.O., Babaita, K., Adeoye, R.I. and Osemwegie, O. (2021a). Blood pressure and sugar regulating potentials of *Anarcadium occidentale* nut globulin and albumin hydrolysates. *Heliyon* 7(3), e06384.

Arise, R.O., Tella, A.C., Akintola A.A., Akiode, O.S. and Malomo, S.O. (2012d) Toxicity evaluation of crankase oil in rats. *Excli Journal* 11, 219-225.

Arise, R.O., Tella, A.C., Igunnu, A. and Malomo, S.O. (2010). Elemental analysis of a local galena-based eyeliner and its effects on some enzymes of rat liver and brain. *International Research Journal of Biotechnology*, 1(4), 59-64.

Arise, R.O., Tella, A.C., Iyiola, O.A., Ayeni, O.M., Farohunbi, S.T. and Yekeen, A.A (2016e). Solventless synthesis, antimalarial and toxicity evaluation of lumefantrine-copper complex in Swiss mice. *Notulae Scientia Biologicae* 8, 292-300.

Arise, R.O., Yekeen, A.A. and Ekun, O.E. (2016c): *In vitro* antioxidant and α-amylase inhibitory properties of watermelon seed protein hydrolysates.*Environmental and Experimental Biology* 14(4), 163–172.

Arise, R.O., Yekeen, A.A., Ekun, O.E. and Olatomiwa, O.J. (2016d). Angiotensin-I converting enzyme-inhibitory, antiradical and hydrogen peroxide-scavenging properties of *Citrullus lanatus* seed protein hydrolysates. *Ceylon Journal of Science*45, 39-52.

Barceló, A. and Rajpathak, S. (2001). Incidence and prevalence of diabetes mellitus in the Americas. *Rev Panam Salud Publica* 10(5), 300-308.
of wheat gluten hydrolysates. *Food Chemistry*277, 655–663.

IDF (2021). *International Diabetes Federation. IDF Diabetes Atlas*, 10th edn. Brussel Belgium: International Diabetes Federation.

Idowu, O.A., Saliu, O.A., Fakorede, C.N. and **Arise, R.O.** (2021). Antiulcerogenic efficacy of leaf fractions of Argemone mexicana against indomethacin-induced ulceration in rats. *Asian Journal of Emerging Research* 3(2),129-136.

Idowu, O.A. and **Arise, R.O.** (2020). Ameliorative and safety characteristics of Argemone mexicana in indomethacin-induced peptic ulcer. *Pharmaceutical Fronts* 2(3), e133-e142.

Igunnu, A., **Arise, R.O.,** Adebayo, J.O. and Malomo, S.O. (2012). Metal displacement effects on monoesterase activity of calf intestinal alkaline phosphatase. *Nigerian Journal of Biochemistry and Molecular Biology* 27(1), 13-19.

Igunnu, A., **Arise, R.O.**, Adebayo, J.O., Olorunniji, F.J. and Malomo, S.O. (2014). Catalytic cofactors (Mg^{2+} and Zn^{2+}) influence the pattern of vanadate inhibition of the monoesterase activity of calf intestinal alkaline phosphatase. *Biokemistri*26(2), 36-42.

Li, L., Guan, Y., Chen, X., Yang, J., Cheng, Y. (2021). DNA Repair Pathways in Cancer Therapy and Resistance, *Frontiers in Pharmacology* 11, 1-13.

Liao, S.M., Liang, G., Zhu, J., Lu, B., Peng, L.X., Wang, Q.Y., Wei, Y.T., Zhou, G.P. and Huang, R.B. (2019). Influence of Calcium Ions on the Thermal Characteristics of α-amylase from Thermophilic Anoxybacillus sp. GXS-BL. *Protein Pept Lett*. 26(2),148-157.

Lopina, O. D. (2017). *Enzyme Inhibitors and Activators.* In (Ed.), Enzyme Inhibitors and Activators. IntechOpen. https://doi.org/10.5772/67248

Malomo, S.O., **Arise, R.O.,** Adebayo, J.O., Igunnu, A. and Adeoye, R. A. (2022). *Proteins and Enzymes*. Ilorin: University of Ilorin Library and Publications & Unilorin Press.

Malomo, S.O., **Arise, R.O.**, Olorunniji, F.J., Odutuga, A.A. and Adebayo, J.O. (2004). Effects of co-administration of spectinomycin and ethanol on some biochemical parameters of rat kidney. *NigerianJournal of Biochemistry and Molecular Biology* 19(1), 51-55.

Malomo, S.O., **Arise, R.O.**, Olorunniji, F.J., Odutuga, A.A. and Adebayo, J.O. (2004). Effects of co-administration of spectinomycin and ethanol on some biochemical parameters of rat kidney. *NigerianJournal of Biochemistry and Molecular Biology,*19(1), 51-55.

Malomo, S.O., Olorunniji, F.J., **Arise, R.O.**, Adebayo, J.O., Adedosu, O.T. and Odutuga, A.A. (2003). Synergistic interaction between two linear inhibitors on a single enzyme: vanadate and L-phenylalanine inhibition of rat liver alkaline phosphatase. *Biokemistri*13, 23-30.

Malomo, S.O., Yakubu, M.T., Amira, O.J. Dosumu, O.O., Igunnu, A., Oluwaniyi, O.O., **Arise, R.O.** and Adebayo, J.O. (2014). Antioxidant activities of ethyl acetate leaf extract of *Celosiaargentea* (Var Cristata). *Nigeria Journal of Biochemistry and Molecular Biology*, 29 (2), 42-51.

Martín, C., Jun, G., Schurhammer, R., Reina, G., Chen, P., Bianco, A., Ménard-Moyon, C. (2019). Enzymatic Degradation of Graphene Quantum Dots by Human Peroxidases. *Nano Small* 15(52), 1905405.

McGuire, J.J. (2003). Anticancer antifolates: current status and future directions. *Curr Pharm Des*. 9(31),2593-613.

Megharaj, M., Venkateswarlu, K. and Ravi, N. (2014). Bioremediation. In: *Encyclopedia of Toxicology.* Vol. 1, 3rd Chapter: Bioremediation.

Möller, C.C., Mangos, S., Drummond, I.A., and Reiser, J. (2008) Expression of trpC1 and trpC6 orthologs in zebrafish. Gene expression patterns: *GEP*. 8(5), 291-296.

Morales-Camacho, W.J., Molina-Díaz, J.M., Ortiz, S.P., Plata Ortiz, J.E., Morales-Camacho, M.A. and Calderón, B.P. (2015). Childhood

obesity: Aetiology, comorbidities, and treatment. *Diabetes Metab Res Rev*,35(8), e3203.

Obaleye, J.A. Tella, A.C. and **Arise, R.O.** (2009). *In vivo* antimalarial activity and toxicological studies of some quinoline methanol metal complexes. *Advances in Natural and Applied Sciences*3(1), 143-48.

Olorunniji, F.J., Igunnu, A., Adebayo, J.O., **Arise, R.O.** and Malomo, S.O. (2007). Cofactor interactions in the activation of tissue non-specific alkaline phosphatase: Synergistic effects of Zn^{2+} and Mg^{2+}. *Biokemistri* 19,43-48.

Osioma, F., Akanji, M.A. and **Arise, R.O.** (2013). Hepatic enzyme markers and proteins in serum and some selected tissues in *Clariasgariepinus* from swamp around Kokori-Erhoike oil field Nigeria. *Journal of Research in Biology* 3(4), 984-992.

Rang, H.P. and Dale, M.M. (1991). *The Endocrine System Pharmacology.* Harlow: Longman.

Svendsen, A. (2016). *Understanding Enzymes: Function, Design, Engineering and Analysis.* 1st Edition, https://doi.org/10.1201/b19951.

Tai, D.B.G., Shah, A., Doubeni, C.A., Sia, I.G. and Wieland. M.L. (2021). The Disproportionate Impact of COVID-19 on Racial and Ethnic Minorities in the United States. *Clin Infect Dis*. 72(4),703-706.

Tella, A.C., Owalude, O.S., Simon, N and **Arise, R.O.** (2015). Solid state synthesis of isostructural tetrachlorometallate salts of Amodiaquine: crystal structure of ($CdCl_4$) ($C_{20}H_{24}CIN_3O$) *Medicinal Chemistry Research.* 24, 3949-3957.

Tien, J., He, G. and Liu, C. (2015). Effects of postprandial starvation on mRNA expression of endocrine-, amino acid and peptide transporter-, and metabolic enzyme-related genes in zebrafish (*Danio rerio*). *Fish Physiology and Biochemistry* 41(3), 773-87.

Vellard, M. (2003): The enzyme as drug: application of enzymes as pharmaceuticals. *Curr. Opin. Biotechnol.* 14, 444–450.

Whitman, B.W., Ghazizadeh, H. (1994). Eucalyptus oil (from *Eucalyptus spp*. including *E. globulus*): therapeutic and toxic aspects of pharmacology in humans and animals. *J. Paediatr. Child. Health* 30(2), 190-191.

Yakubu, M.T. and Bukoye, B.B. (2009). Abortifacient potentials of the aqueous extract of *Bambusa vulgaris* leaves in pregnant Dutch rabbits. *Contracept.* 80, 308-313.

Zanganeh, S. (2021). Potential COVID-19 therapeutic approaches targeting angiotensin-converting enzyme 2; an updated review. *Reviews in Medical Virology* 32(4), e2321.

Zhou, L., Liu, S., Shen, H., Zhao, M., Xu, L., Xing, A. and Fang, J. (2020). Soil extracellular enzyme activity and stoichiometry in China's forests. *Functional Ecology* 34(7),1461-1471.