UNIVERSITY OF NIGERIA

EXPLORING THE EXCITING WORLD OF THE WONDER AGENTS CALLED DRUGS

An Inaugural Lecture of the
University of Nigeria
Delivered on July 26, 2012

By

EMMANUEL CHINEDUM IBEZIM
Professor of Pharmaceutics
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1.0 PROTOCOLS

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Ladies and Gentlemen

It is with utmost humility and great delight that I stand here this 26th day of July 2012 to deliver this august 68th Inaugural lecture of our great University. I must say that I am greatly overwhelmed by this mammoth crowd that has gathered today in this dignified arena to hear the scientific story I have to tell. To me, it is a great honour, and I am the happiest for it.

As the name suggests, an Inaugural lecture in a university setting, is designed to enable persons, newly endowed to professorial chairs, introduce themselves to the university community and indeed the whole wide world. In other words, the *raison d'être* for this lecture is for the new professor to showcase, as it were, his or her research profile, expertise and focus. It also affords him or her, the opportunity to project to the world, his or her idea of what

an ideal professional practice in his chosen field should look like. Due to some exigencies however, this lecture has not always been coming up immediately upon announcement of the professorial endowment. In my own case, it is happening six years after.

Vice Chancellor Sir, Distinguished professors, esteemed audience, permit me at this point, to briefly feel the ebb and flow of history on an idyllic boat as I stroll leisurely through memory lane.

2.0 INTRODUCING THE INAUGURAL LECTURER

Born on 16th January 1964, to the humble home of two delightful and consistent Christians, Mr. Godson Onyemnado and Mrs. Justina Ukachi Ibezim, from Ogadama, Ogada, Atta, Ikeduru, Owerri, Imo State, little Master Emmanuel Chinedum Ibezim, grew up under strict Christian discipline and atmosphere of love. His stint with education started first at St Thomas Primary School Ogada, and later at Ogada Community School, Atta, Ikeduru.

At school, he was by every standard, too tiny and that earned him some, albeit, infamous derogatory names. For instance, one of his primary school teachers then, Mr. Iheriohanma, used to call him, *Nwa oke nga m* (my little rat). At the primary school, he proved his mettle and was consistently at the top of the class, to the admiration of his numerous teachers but, understandably, envy of a few of his class mates who did not see why such a 'tiny thing' should be ahead of them in class. Of course, this attracted beatings and other punitive treatments from the 'big boys'.

He later gained admission, in 1975, to the famous Amaimo High School, Ikeduru, for his secondary education, where the story was not different either. His small size attracted several other names – like 'atom', 'Tom boy' and the like. At a time, he was the smallest in the entire school and the Senior Prefect then, Mr. Jude Ugwoegbulem, when he wanted to emphasize that his announcement involves every student in the school, would always say, 'This announcement is for everybody - From the Senior Prefect to Emmanuel Ibezim'.

Back then at Amaimo High School, the little Emmanuel greatly got challenged by the academic prowess of his mates - Francis Ononogbo of Ubomiri, Cleopas Nwagwu of Ikembara, Ebenezer Emeribe of Umuoziri Inyishi, Nnamdi Nwachukwu of Umuri Amaimo and John Onuoha from Mbaise. Healthy rivalry later developed among these intelligent students that helped to model them and today, they are resounding professionals, making waves in their respective fields. Some teachers who greatly impacted Emma's life then included Mrs. Cordelia – Nee Mbawike (Chemistry teacher) and Mr. Iwuanyanwu (Biology teacher) both from Amaimo, Mr. Ikwueze (Igbo teacher) from Anambra, Mr. Boniface Nkwocha (Literature teacher) from Owerri, 'Ghana Pieces' (Maths teacher) from Uzoagba, Mr. Bruque (Physics teacher) and Mr. Oforha (Igbo Teacher). His principals, Mr. H. N. D. Ebonine and Mr. A. O. Nzerem also encouraged him a great deal.

The following uncles of his also made unrivalled impact in this his early formative life and he owes a great deal of his success in life to their wise counsels and encouragements:

Mr. Nathan Agubosim, Mr. Benjamin Agubosim, Mr. Emeka Agubosim, Ven Ephraim Onwubuariri, Late Mr. Jonathan Ibezim, Chief Longinus T. Ogide, Mr. Eddy Ogide, Mr. Clifford Onwubuariri, Mr. Raphael Uwakwe, Mr. Robert Ibezim, and Sir Remigius Nwaloka. His maternal grandparents, Mr. & Mrs. Felix and Abigail Agubosim (both of blessed memory) really showered him with great love and care.

Friends, they say, are like diamond, difficult to get, hard to mould but easy to lose. His five special childhood friends - Gozen (Nnadozie) Ekwueme, Ifeanyi Asiegbu, Dennis Ezirim, Nnamdi Nwachukwu and Linus Mmezu, like diamond, specially touched his life and he has been making efforts not to lose them.

Knowledge is the fortress that protects mankind from the tyranny of ignorance while ignorance is the dagger that pierced the soul of truth. It is the early realization of this fact that made Emma, in 1980, to seek and secure admission to study Education/Chemistry at Alvan Ikoku College of Education, Owerri, where he quickly got integrated and made special friends like Mr. Moses Njoku. His Head of Department then, Dr Mrs. Onyiuke (Now at Abia State University) had special influence on his life. His stay there was however short-lived as he immediately gained admission to read pharmacy here in the University of Nigeria, Nsukka, same year. He equally passed the interview for civil service job in Imo State, but had to, understandably, opt for further studies.

Late into his secondary school days, little Emma embraced Christ through the instrumentality of his friend, Nnamdi Nwachukwu (now Dr Nwachukwu). His Christian faith got strengthened during his brief stay at Alvan and blossomed when he entered UNN. The Student Christian Movement greatly shaped his Christian destiny at the University of Nigeria, Nsukka. Many thanks to his Christian friends – Late Pharm Ozioma Okoli, Mr. Chijioke Ezeofor, Bro (Now Prof) Augustine Ubachukwu, Mr. (Now Ven Engr) Emmanuel Olewuezi, Mr. Ngozi Emenogu, Mr. Amos Balami, Mr. Innocent Iorkyar and Mr. (Now Engr) Ozoemena Osiedo.

He graduated from the pharmacy school in 1985 and quickly left for General Hospital Owerri, where he undertook his one year mandatory Internship under the tutelage of Pharm Dr Atasie and Pharm Ann Chilaka. Thereafter, he proceeded to Jos for his one year National Youth Service Scheme where he worked with the Christian Health Association of Nigeria, Pharmacy (CHANPHARM) under Pharm. Dr Brown. The Christian Corpers' Fellowship which he served as National Drama Coordinator provided a great platform for Christian growth and evangelism. Christian friends like Nosa, Tope, Andrew, Hillary, Anderson, Foluke, Late Dr Erastus, Yinka, Funmi and Titi, were there to make the service year very memorable.

He later got a job at Bauchi after his NYSC and had just arrived at Bauchi to take it up when the Holy Spirit expressly told him not to. He had to leave the job and continued the search until he eventually pitched his career tent with JOMAF Pharmacy, Kaduna.

Career in the University of Nigeria

Emma, after working briefly with JOMAF Pharmacy in Kaduna decided to return to the University of Nigeria, Nsukka for a Masters Degree programme under the able and skilful supervision of then Dr. (Now Prof) Amarauche Chukwu, an academic icon. The programme was rounded off in record time and he was immediately offered appointment as Lecturer II in the Department of Pharmaceutics. Thanks to the untiring effort of his then Head of Department, Late Dr. C. O. Chiori. Emma thereafter, registered for Ph D under the supervision of the consummate pharmaceutical thesaurus of a sort, Prof O. K. Udeala, greatly assisted by Prof. A. Chukwu and in 1995, was conferred with a Doctorate degree in Physical Pharmaceutics.

He rose through the academic ranks: Lecturer II (1989 – 1992); Lecturer I (1992 – 1995); Senior Lecturer (1995 – 2003); Reader (2003 – 2006); Professor (2006 to Date). In the course of his lecturing career, he has also had opportunity to offer his services on a part-time basis to the School of Nursing, Bishop Shanahan Hospital Nsukka; Science Laboratory Training Scheme, UNN, Akukris Pharmacy, Nsukka, to mention but these few.

He has held more than fifty (50) laudable academic positions in the university including two - time Headship of the Department of Pharmaceutics (2000-2002; 2006-2009); two time Associate Dean of the Faculty of Pharmaceutical

Sciences (2006-2007; 2007-2009); Chairman, Faculty Home Coming Committee; Faculty Representative at Senate; Faculty Representative at University Housing Committee; Head of Several Investigative Panels; Chairman, Faculty Continuing Education Committee; Coordinator, Faculty SIWES; Chairman, Faculty Silver Jubilee Anniversary; Faculty Representative at University Consultancy Management Board; Chairman, Faculty Curriculum Committee; Faculty Representative at NURUSDEF; Member, UNN/University of Toledo Pharmacy College Collaborative team; Member, UNN/SEDI Joint Working Committee, to mention but these.

He has successfully supervised about 22 postgraduate students at both Ph D and Masters levels and currently has about 30 others under his supervision. He has attended more than eighty-eight (88) international and national conferences, where he had presented not less than 120 scientific papers. He has published greater than one hundred and thirty-nine (139) papers in various national and international scientific journals of high repute and has authored six (6) professional books. He presently belongs to several professional bodies including: National Association of Pharmacists in Academia (where he had served as National Editor in Chief), Pharmaceutical Society of Nigeria, World Association of Medical Editors, International Society for Managing and Technical Editors, New York Academy of Sciences, Foundation for African Development through International Biotechnology and International Council of Science Editors. He has reviewed papers for more than 39 reputed national and international journals and is currently the Editor in Chief of a flourishing

internationally acclaimed journal as well as the immediate past editor of another and has in kitties, more than twenty four (24) international/national honours. Recreationally, he finds time to do some other things which are not strictly academic. Chiefly, he is deeply interested in writing Christian books (Has presently written about 10 of these), singing Christian songs and watching Christian movies. He also creates time to preach and teach the word of God, which he believes, is the only lasting food for the human soul.

Vice Chancellor Sir, Distinguished professors, Esteemed audience, permit me at this juncture, to get into the lecture proper.

3.0 THE LECTURE

It is not my intention, to make all of us pharmacists by virtue of this lecture. That would be attempting the impossible and an obvious contravention of some serious sections of our national edicts. It is rather my wish to demystify the subject of this wonder agent called drugs, and perhaps, stimulate some of us who are still intellectually young, to consider opting for a second degree – in pharmacy.

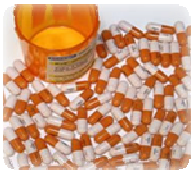
I will like to discuss this lecture titled – Exploring the exciting world of the wonder agents called drugs, under the following broad headings:

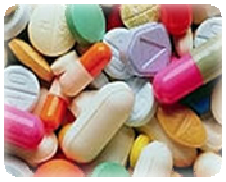
- Drugs: What are they?
- History of drugs
- Uses of drugs

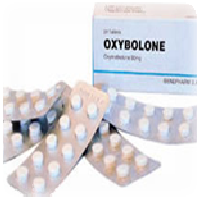
- ❖ Some peculiarities of drugs
- ❖ Drugs classified
- ❖ Drug administration
- ❖ Drug Active ingredients discovery
- ❖ Drug Excipients discovery
- ❖ Drug interaction studies
- ❖ Drug quality assessment

3.1 DRUGS: WHAT ARE THEY?

There is no single, precise definition of drugs, as there are different meanings in drug control law, government regulations, medicine and colloquial usage. A drug, broadly speaking, is any substance that, when absorbed into the body of a living organism, alters normal bodily function (WHO, 1969). A pharmaceutical drug, also referred to as medicine, medication or medicament, can loosely be defined as any





chemical substance intended for use in the medical diagnosis, cure, treatment, or prevention of disease. In pharmacology, a drug is ‘a chemical substance used in the treatment, cure, prevention or diagnosis of disease or used to otherwise enhance physical or mental well-being. Drugs may be prescribed for a limited duration, or on a regular basis for chronic disorders. Recreational drugs are chemical substances that affect the central nervous system, such as opioids or hallucinogens. They may be used for perceived beneficial effects on perception, consciousness, personality, and behavior (Merriam-Webster's Medical Dictionary, 2007). Some drugs can cause addiction and/or habituation.

Drugs are usually distinguished from endogenous biochemicals by being introduced from outside the organism. For example, insulin is a hormone that is synthesized in the body; it is called a hormone when it is synthesized by the pancreas inside the body, but if it is introduced into the body from outside, it is called a drug. Many natural substances, such as beers, wines, and psychoactive mushrooms, blur the line between food and recreational drugs, as when ingested they affect the functioning of both mind and body and some substances normally considered drugs such as DMT (Dimethyltryptamine) are actually produced by the human body in trace amounts.

Legally, some governments define the term drug by law. In the United States, the Federal Food, Drug, and Cosmetic Act definition of "drug" includes "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals" and "articles (other than

food) intended to affect the structure or any function of the body of man or other animals" (Federal Food, Drug, and Cosmetic Act, 2007). Consistent with that definition, the U.S. separately defines narcotic drugs and controlled substances, which may include non-drugs, and explicitly excludes tobacco, caffeine and alcoholic beverages (USC sec 802, 2007).

3.2 HISTORY OF DRUGS

Drug use and abuse is as old as mankind itself. Human beings have always had a desire to eat or drink substances that make them feel relaxed, stimulated, or euphoric. Humans have used drugs of one sort or another for thousands of years. Wine was used at least from the time of the early Egyptians; narcotics from 4000 B.C.; and medicinal use of marijuana has been dated to 2737 BC in China.

As time went by, "home remedies" were discovered and used to alleviate aches, pains and other ailments. Most of these preparations were herbs, roots, mushrooms or fungi. They had to be eaten, drunk, rubbed on the skin, or inhaled to achieve the desired effect.

Drug is thought to originate from Old French "drogue", possibly deriving later into "droge-vate" from Middle Dutch meaning "dry barrels", referring to medicinal plants preserved in them (Chemical and Engineering News, 2011). Dispensing of medication is often regulated by governments into three categories—*over-the-counter* (OTC) medications, which are available in pharmacies and supermarkets without

special restrictions, *behind-the-counter* (BTC), which are dispensed by a pharmacist without needing a doctor's prescription, and *Prescription only medicines* (POM), which must be prescribed by a licensed medical professional, usually a physician. In the United Kingdom, BTC medicines are called pharmacy medicines which can only be sold in registered pharmacies, by or under the supervision of a pharmacist. These medications are designated by the letter P on the label (European Commission, 2008). The range of medicines available without a prescription varies from country to country.

Medications are typically produced by pharmaceutical companies and are often patented to give the developer exclusive rights to produce them, but they can also be derived from naturally occurring substances in plants called herbal medicines. Those that are not patented (or with expired patents) are called generic drugs since they can be produced by other companies without restrictions or licenses from the patent holder.

Ancient pharmacology

Using plants and plant substances to treat all kinds of diseases and medical conditions is believed to date back to prehistoric medicine. The Kahun Gynaecological Papyrus, the oldest known medical text of any kind, dates to about 1800 BCE and represents the first documented use of any kind of medication (Ruhoy and Daughton, 2008). It and other medical papyri describe Ancient Egyptian medical practices, such as using honey to treat infections. Ancient Babylonian medicine demonstrates the use of prescriptions in the first

half of the 2nd millennium BC. Medicinal creams and pills were employed as treatments.
On the Indian subcontinent, the Atharvaveda, a sacred text of Hinduism whose core dates from the 2nd millennium BCE, although the hymns recorded in it are believed to be older, is the first Indic text dealing with medicine. It describes plant-based medications to counter diseases (The Kahun Gynaecological Papyrus). The earliest foundations of ayurveda were built on a synthesis of selected ancient herbal practices, together with a massive addition of theoretical conceptualizations, new nosologies and new therapies dating from about 400 BCE onwards (Horstmanshoff *et al*., 2004). The student of Āyurveda was expected to know ten arts that were indispensable in the preparation and application of his medicines: distillation, operative skills, cooking, horticulture, metallurgy, sugar manufacture, pharmacy, analysis and separation of minerals, compounding of metals, and preparation of alkalis.

The Hippocratic Oath for physicians, attributed to 5 th century BCE Greece, refers to the existence of "deadly drugs", and ancient Greek physicians imported medications from Egypt and elsewhere (Atharvaveda XIX.34.9). The first drugstores were created in Baghdad in the 8 th century CE. The injection syringe was invented by Ammar ibn Ali al-Mawsili in 9 th century Iraq. Al-Kindi's 9 th century CE book, *De Gradibus*, developed a mathematical scale to quantify the strength of drugs (Zysk, 1998).
The Canon of Medicine by Ibn Sina (Avicenna), who is considered the father of modern medicine (Heinrich, 1989), reported 800 tested drugs at the time of its completion in 1025 CE. Ibn Sina's contributions include the separation of

medicine from pharmacology, which was important to the development of the pharmaceutical sciences (Felix Klein-Frank, 2001). Islamic medicine knew of at least 2,000 medicinal and chemical substances (Cas Lek Cesk, 1980).

Medieval pharmacology

Medieval medicine saw advances in surgery, but few truly effective drugs existed, beyond opium and quinine. Folklore cures and potentially poisonous metal-based compounds were popular treatments. Theodoric Borgognoni, (1205–1296), one of the most significant surgeons of the medieval period, was responsible for introducing and promoting important surgical advances including basic antiseptic practice and the use of anaesthetics. Garcia de Orta described some herbal treatments that were used.

Modern medicines

For most of the 19th century, the now burgeoning entity called drugs were not highly effective, leading Oliver Wendell Holmes, Sr. to famously comment in 1842 that "if all medicines in the world were thrown into the sea, it would be all the better for mankind and all the worse for the fishes" (Bashar Saad *et al.*, 2005).

During the First World War, Alexis Carrel and Henry Dakin developed the Carrel-Dakin method of treating wounds with an irrigation, Dakin's solution, a germicide which helped prevent gangrene. In the inter-war period, the first anti-bacterial agents such as the sulpha antibiotics were developed. The Second World War saw the introduction of widespread and effective antimicrobial therapy with the development and mass production of penicillin antibiotics, made possible by the pressures of the war and the

collaboration of British scientists with the American pharmaceutical industry.

Medicines commonly used by the late 1920s included aspirin, codeine, and morphine for pain; digitalis, nitroglycerin, and quinine for heart disorders, and insulin for diabetes. Other drugs included antitoxins, a few biological vaccines, and a few synthetic drugs. In the 1930s antibiotics emerged: first sulfa drugs, then penicillin and other antibiotics. Drugs increasingly became "the center of medical practice" (Bashar Saad *et al.*, 2005). In the 1950s, other drugs emerged including corticosteroids for inflammation, rauwolfia alkaloids as tranquilizers and antihypertensives, antihistamines for nasal allergies, xanthines for asthma, and typical antipsychotics for psychosis. As of 2008, thousands of approved drugs have been developed. Increasingly, biotechnology is used to discover biopharmaceuticals. Recently, multi-disciplinary approaches have yielded a wealth of new data on the development of novel antibiotics and antibacterials and on the use of biological agents for antibacterial therapy (Hadzović, 1997).

In the 1950s new psychiatric drugs, notably the antipsychotic chlorpromazine, were designed in laboratories and slowly came into preferred use. Although often accepted as an advance in some ways, there was some opposition, due to serious adverse effects such as tardive dyskinesia. Patients often opposed psychiatry and refused or stopped taking the drugs when not subject to psychiatric control.

Governments have been heavily involved in the regulation of drug development and drug sales. In the U.S., the Elixir Sulfanilamide disaster led to the establishment of the Food and Drug Administration, and the 1938 Federal Food, Drug,

and Cosmetic Act required manufacturers to file new drugs with the FDA. The 1951 Humphrey-Durham Amendment required certain drugs to be sold by prescription. In 1962 a subsequent amendment required new drugs to be tested for efficacy and safety in clinical trials (Bashar Saad *et al.*, 2005). Until the 1970s, drug prices were not a major concern for doctors and patients. As more drugs became prescribed for chronic illnesses, however, costs became burdensome, and by the 1970s nearly every U.S. state required or encouraged the substitution of generic drugs for higher-priced brand names. This also led to the 2006 U.S. law, Medicare Part D, which offers Medicare coverage for drugs.

As of 2008, the United States is the leader in medical research, including pharmaceutical development. U.S. drug prices are among the highest in the world, and drug innovation is correspondingly high. In 2000, U.S. based firms developed 29 of the 75 top-selling drugs; firms from the second-largest market, Japan, developed eight, and the United Kingdom contributed 10. France, which imposes price controls, developed three. Throughout the 1990s, outcomes were similar.

The Nigerian story is not significantly different from the above, as drug development has followed a similar historical pattern culminating in the establishment of the National Agency for Food and Drug Administration and Control, National Drug Law Enforcement Agency and the like.

3.3 USES OF DRUGS

These days, drugs can be found everywhere, and it may seem like everyone is using them. Lots of people are tempted by the excitement or escape that drugs seem to offer. But learning the facts about drugs can help one see the risks of chasing this excitement or escape.

Attributable to rigorous medical and drug research, there are thousands of drugs that help people in several ways. Antibiotics and vaccines have, for instance, revolutionized the treatment of infections. Drugs can lower blood pressure, treat diabetes, and reduce the body's rejection of new organs. They can cure, slow, or prevent disease, helping man to lead healthier and happier lives. But there are also lots of illegal, harmful drugs that people take to help them feel good or have a good time.

How do drugs work? Drugs are chemicals or substances that change the way the body works. When one takes them into the body (often by swallowing, inhaling, or injecting them), drugs find their way into the bloodstream and are transported to parts of the body, such as brain. In the brain, drugs may intensify or dull the senses, alter the sense of alertness, and sometimes decrease physical pain. A drug may be helpful or harmful. The effects of drugs can vary depending on the kind of drug taken, how much is taken, how often it is used, how quickly it gets to the brain, and what other drugs, food, or substances are taken at the same time. Effects can also vary based on the differences in body size, shape, and chemistry.

Although substances can feel good at first, they can ultimately do a lot of harm to the body and brain. Drinking alcohol, smoking tobacco, taking illegal drugs, and sniffing glue can all cause serious damage to the human body. Some drugs severely impair a person's ability to make healthy choices and decisions. Teens that drink, for example, are more likely to get involved in dangerous situations, such as driving under the influence or having unprotected sex. The various uses of drugs are hereby summarized:

As medication

A *medication* or *medicine* is a drug taken to cure and/or ameliorate any symptoms of an illness or medical condition, or may be used as preventive medicine that has future benefits but does not treat any existing or pre-existing diseases or symptoms.

Spiritual and religious use

The spiritual and religious use of drugs has been occurring since the dawn of our species. Drugs that are considered to have spiritual or religious use are called entheogens. Some religions are based completely on the use of certain drugs. Entheogens are mostly hallucinogens, being either psychedelics or deliriants, but some are also stimulants and sedatives.

Self-improvement

Nootropics, also commonly referred to as "smart drugs", are drugs that are claimed to improve human cognitive abilities. Nootropics are used to improve memory, concentration, thought, mood, learning, and many other things. Some nootropics are now beginning to be used to treat certain

diseases such as attention-deficit hyperactivity disorder, Parkinson's disease, and Alzheimer's disease. They are also commonly used to regain brain function lost during aging or accidents. Similarly, drugs such as steroids improve human physical capabilities and are sometimes used (legally or not) for this purpose, often by professional athletes.

Recreational drug use

Recreational drugs use is the use of psychoactive substances to have fun, for the experience, or to enhance an already positive experience. The cigarette is the common pharmaceutical form of tobacco – one of the world's best selling drugs.

Cannabis

Cannabis is another commonly used recreational drug (Lingeman, Penguin Dictionary). National laws prohibit the use of many different recreational drugs and medicinal drugs that have the potential for recreational use are heavily regulated. Many other recreational drugs on the other hand are legal, widely culturally accepted, and at the most have an age restriction on using and/or purchasing them. These include alcohol, tobacco, betel nut, and caffeine products in the west and in other localized areas of the world drugs such

as Khat are common. Because of the legal status of many drugs, recreational drug use is controversial, with many governments not recognizing spiritual or other perceived uses for drugs and classing them under illegal recreational use.

3.4 SOME PECULIARITIES OF DRUGS

- Drugs in small doses are effective therapeutic agents, but in large doses are poisons
- A minor mistake made in the computation of formula or preparation of a drug by a single pharmacist can lead to the death of millions of persons.
- Drugs are effective in very minute amounts
- Most drugs are subjects of abuse, misuse and overuse while some are habit forming with the accompanying dependence
- Most drugs have side effects which are most of the time unpleasant to the person taking them. Some side effects may include the induction of a different sickness
- Drugs are foreign bodies to the human system, hence we should be careful stuffing our bodies and lives with them.
- Wrong use of drugs or taking of incomplete doses of drugs, especially the antibiotics, can lead to a very terrible therapeutic problem termed drug resistance
- Drugs, like policemen, are our friends, but can be deadly if wrongly approached

3.5 CLASSIFICATION OF DRUGS

Drugs can be classified in various ways, such as by chemical properties, mode or route of administration, biological system affected, or therapeutic effects. An elaborate and widely used classification system is the Anatomical Therapeutic Chemical Classification System (ATC system). The World Health Organization keeps a list of essential medicines. A typical example of classification based on the biological properties is as follows:

Trentyxicyls: reducing headache (sexual appetite/erectile dysfunction); *Antipyretics*: reducing fever (pyrexia/pyresis); *Analgesics*: reducing pain (painkillers); *Antimalarial drugs*: treating malaria; *Antibiotics*: inhibiting germ growth; *Antiseptics*: prevention of germ growth near burns, cuts and wounds.

Another classification, based on the site of action is as follows:

(i): For the *gastrointestinal tract (digestive system)*

- Upper digestive tract: antacids, reflux suppressants, antiflatulents, antidopaminergics, proton pump inhibitors (PPIs), H_2-receptor antagonists, cytoprotectants, prostaglandin analogues
- Lower digestive tract: laxatives, antispasmodics, antidiarrhoeals, bile acid sequestrants, opioid

(ii) For the *cardiovascular system*

- General: β-receptor blockers ("beta blockers"), calcium channel blockers, diuretics, cardiac glycosides, antiarrhythmics, nitrate, antianginals, vasoconstrictors, vasodilators, peripheral activators

- Affecting blood pressure (antihypertensive drugs): ACE inhibitors, angiotensin receptor blockers, α blockers, calcium channel blockers
- Coagulation: anticoagulants, heparin, antiplatelet drugs, fibrinolytics, anti-hemophilic factors, haemostatic drugs
- Atherosclerosis/cholesterol inhibitors: hypolipidaemic agents, statins.

(iii) For the *central nervous system*

Drugs affecting the central nervous system include: hypnotics, anaesthetics, antipsychotics, antidepressants (including tricyclic antidepressants, monoamine oxidase inhibitors, lithium salts, and selective serotonin reuptake inhibitors (SSRIs), antiemetics, anticonvulsants/antiepileptics, anxiolytics, barbiturates, movement disorder (e.g., Parkinson's disease) drugs, stimulants (including amphetamines), benzodiazepines, cyclopyrrolones, dopamine antagonists, antihistamines, cholinergics, anticholinergics, emetics, cannabinoids, and 5-HT (serotonin) antagonists.

(iv) For *pain and consciousness (analgesic drugs)*

The main classes of painkillers are non steroidal anti-inflammatory drugs (NSAIDs), opioids and various orphans such as paracetamol, tricyclic antidepressants and anticonvulsants.

(v) For *musculo-skeletal disorders*

The main categories of drugs for musculoskeletal disorders are: NSAIDs (including COX-2 selective inhibitors), muscle relaxants, neuromuscular drugs, and anticholinesterases.

(vi) For the *eye*

- General: adrenergic neurone blocker, astringent, ocular lubricant

- Diagnostic: topical anesthetics, sympathomimetics, parasympatholytics, mydriatics, cycloplegics
- Anti-bacterial: antibiotics, topical antibiotics, sulfa drugs, aminoglycosides, fluoroquinolones
- Antiviral drugs
- Anti-fungal: imidazoles, polyenes
- Anti-inflammatory: NSAIDs, corticosteroids
- Anti-allergy: mast cell inhibitors
- Anti-glaucoma: adrenergic agonists, beta-blockers, carbonic anhydrase inhibitors/hyperosmotics, cholinergics, miotics, parasympathomimetics, prostaglandin agonists/prostaglandin inhibitors. nitroglycerin

(vii) For the *ear, nose and oropharynx*

These include the sympathomimetics, antihistamines, anticholinergics, NSAIDs, steroids, antiseptics, local anesthetics, antifungals, cerumenolyti

(viii) For the *respiratory system*

They include the bronchodilators, NSAIDs, anti-allergics, antitussives, mucolytics, decongestants corticosteroids, Beta2-adrenergic agonists, anticholinergics, steroids

(ix) For *endocrine problems*

Androgens, antiandrogens, gonadotropin, corticosteroids, human growth hormone, insulin, antidiabetics (sulfonylureas, biguanides/metformin, thiazolidinediones), thyroid hormones, antithyroid drugs, calcitonin, vasopressin analogues

(x) For the *reproductive system or urinary system*

Antifungal, alkalizing agents, quinolones, antibiotics, cholinergics, anticholinergics, anticholinesterases,

antispasmodics, 5-alpha reductase inhibitors, selective alpha-1 blockers, sildenafils, fertility medications

(xi) For *contraception*

- Hormonal contraception
- Ormeloxifene
- Spermicide

(xii) For *obstetrics and gynecology*

NSAIDs, anticholinergics, haemostatic drugs, antifibrinolytics, Hormone Replacement Therapy (HRT), bone regulators, beta-receptor agonists, follicle stimulating hormone, luteinising hormone, LHRH gamolenic acid, gonadotropin release inhibitor, progestogen, dopamine agonists, oestrogen, prostaglandins, gonadorelin, clomiphene, tamoxifen, diethylstilbestrol

(xiii) For the *skin*

Emollients, anti-pruritics, antifungals, disinfectants, scabicides, pediculicides, tar products, vitamin A derivatives, vitamin D analogues, keratolytics, abrasives, topical antibiotics, hormones, desloughing agents, exudate absorbents, fibrinolytics, proteolytics, sunscreens, antiperspirants, corticosteroids

(xiv) For *infections and infestations*

Antibiotics, antifungals, antileprotics, antituberculous drugs, antimalarials, anthelmintics, amoebicides, antivirals, antiprotozoals

(xv) For the *immune system*

Vaccines, immunoglobulins, immunosuppressants, interferons, monoclonal antibodies

(xvi) For *allergic disorders*

Anti-Allergics, antihistamines, NSAIDs

(xv) For *nutrition*

Tonics, iron preparations, electrolytes, parenteral nutritional supplements, vitamins, anti-obesity drugs, anabolic drugs, haematopoietic drugs, food product drugs

(xvi) For *neoplastic disorders*

Cytotoxic Drugs, therapeutic antibodies, sex hormones, aromatase inhibitors, somatostatin inhibitors, recombinant interleukins, G-CSF, erythropoietin

(xvii) For *diagnostics*

contrast media

(xviii) For *euthanasia*

An euthanaticum is used for euthanasia and physician-assisted suicide. Euthanasia is not permitted by law in many countries, and consequently medicines will not be licensed for this use in those countries.

3.6 DRUG ADMINISTRATION

Administration refers to the delivery of a pharmaceutical drug to a patient. Drugs, both medicinal and recreational, can be administered in numerous ways including:

- Bolus. In this, they can be administered all at once as a bolus, at frequent intervals or continuously. Frequencies are often abbreviated from Latin, such as *every 8 hours* reading Q8H from *Quaque VIII Hora*.
- Inhaled, (breathed into the lungs), as an aerosol or dry powder. (This includes smoking a substance)
- Injected as a solution, suspension or emulsion either: intramuscularly (through the muscles), intravenously (through the veins), intraperitoneally (through the peritoneal cavity), intraosseously.

- Insufflation, or snorted into the nose.
- Orally, as a liquid or solid, that is, through the mouth and absorbed through the intestines.
- Rectally as a suppository, that is absorbed by the rectum or colon.
- Sublingually, diffusing into the blood through tissues under the tongue.
- Topically, usually as a cream or ointment. A drug administered in this manner may be given to act locally or systemically
- Vaginally as a suppository, primarily to treat vaginal infections.

3.7 ACTIVE INGREDIENTS DISCOVERY

Active ingredient refers to the component of a pharmaceutical formulation that is responsible for the main action of the drug product. It is to be distinguished from the excipients, which are those other components that contribute to the desirable quality of the drug product but are not directly involved in its therapeutic activity.

Drug development is the process by which a drug is created. Drugs can be extracted from natural products (pharmacognosy) or synthesized through chemical processes. The drug's active ingredient will be combined with a "vehicle" such as a capsule, cream, or liquid which will be administered through a particular route of administration.

Over the years, my research activities have focused essentially on the extensive search for pharmaceutical **active ingredients** as well as **drug excipients.** It has been said that

the secret of success is to love what you do and to do what you love. The subject of drug and excipient development is one I cherish dearly and have consistently worked on, with great passion. In searching for new drug entities, I have utilized two approaches viz: molecular modeling and search from indigenous plant sources.

3.7.1 Modeling using QSAR/QSPR for new drug discovery (Ibezim *et al*., 2009[a], Ibezim *et al*., 2009[b], Ibezim *et al*., 2009[c], Ibezim *et al*., 2009[d], Ibezim *et al*., 2009[e], Ibezim *et al*., 2010, Ibezim *et al*., 2011, Ibezim *et al*., 2012)

Molecular modeling encompasses all theoretical methods and computational techniques used to model or mimic the behaviour of molecules. The techniques are used in the fields of computational chemistry, computational biology and materials science for studying molecular systems ranging from small chemical systems to large biological molecules and material assemblies such as drugs. During a 3 months research visit to the Instituto de Investigationes Fisicoquimicas Teoricas Y applicadas (INIFTA) Argentina, I carried out elaborate modeling studies using computational techniques like quantitative structure/property – activity relationship (QSAR/QSPR) as tools to search for novel drug entities. Computer softwares like MATLAB, REKON, Dragon and Hyperchem were utilized in the studies. These studies subsequently led to the establishment of a quantitative structure – activity relationship (QSAR) for the development of new antimalarial aryl piperazines with activities against chloroquine resistant and sensitive strains of *Plasmodium falciparum.* This relationship helped to discover more than 22 potential aryl piperazines that would

be very useful in treating malaria caused by chloroquine-resistant strains of *P. falciparum.* Malaria is a vector-borne infectious disease caused by protozoan parasites. It is widespread in tropical and subtropical regions, including parts of the Americas, Asia, and Africa. Every year, there are approximately 350–500 million cases of malaria.

3.7.2 New drug discovery from plant sources (Ibezim *et al.,* 2011; Ibezim *et al*., 2006; Ibezim, *et al*., 2005; Ibezim, 2005; Ibezim and Esimone, 2006**)**

Plants constitute one of the greatest sources of new drugs for management of human diseases. All through the ages, man has relied extensively on herbal sources for his drug needs. My studies have led me to investigate a retinue of plant sources for possible therapeutic activities (Tables 1 and 2). A study, carried out in 2011 evaluated the *in vitro* antimicrobial properties of the methanol extract of *Garcinia kola* seed and its syrup formulation and compared the latter with commercial antibiotic syrups against *Escherichia coli* and *Staphylococcus aureus* by the standard agar diffusion method (Ibezim *et al*., 2011). The test micro-organisms were significantly susceptible ($p < 0.01$) to the extract (MIC = 3.50 ± 0.04 mg/ml for *Escherichia coli* and 5.05 ± 0.12 mg/ml for *Staphylococcus aureus*) and the syrup formulation (IZD = 12.00 ± 0.05 mm for *Escherichia coli* and 24.00 ± 0.19 mm for *Staphylococcus aureus*). The antibacterial activity of *Garcinia kola* syrup was greater than amoxicillin and metronidazole syrups but less than co-trimoxazole formulation against the test micro-organisms. The wound healing properties of herbal ointments formulated with *Ocimium gratissimum* (*Nchu anwu*) leaf

Table 1: Novel antimicrobials from plant sources

Plant source	Local name	Formulation/ Plant part	Discovered therapeutic use	Reference (s)
Garcinia kola	Bitter kola or *Aki ilu*	Syrup (Seed)	Antibiotic	Ibezim *et al*., 2011
Ocimum gratissimum	*Nchu anwu*	Herbal ointment (Leaf)	Antibacterial/ Wound healing	Ibezim, 2006
Napoleona imperialis	-	Herbal ointment (Leaf)	Antibacterial/ Wound healing	Ibezim *et al.,* 2005
Ocimum gratissimum + *Napoleona imperialis*	-	Herbal ointment (Leaves)	Synergistic antibacterial/ Wound healing	Ibezim, 2005
Dissotis theifolia	-	Cream (Leaf)	Antibacterial/ Wound healing	Odimegwu, Ibezim & Others, 2007; Odimegwu, Ibezim and Others, 2010
Dissotis theifolia	-	Ointment (Leaf)	Antibacterial/ Wound healing	Odimegwu, Ibezim & Others, 2008
Azadirachta indica	Dogwon yaro (Neem)	Leaf	Antimicrobial properties	Ngwu, Ibezim and Others, 2009
Parmelia perlata	Lichen	Whole plant	Antiviral agent	Esimone, Ibezim and Others, 2007
Denneti tripetala	*Mmimi*	Cream (Seed)	Preservative	Ibezim and Esimone, 2006

Table 2: Other novel drugs from plant and related sources

Source	Local name	Plant part	Discovered therapeutic use	Reference (s)
Euphorbia hirta	*Ogwu ugwo*	-	Reduced Platelet activity/Clotting time	Omeje, Amayo, Adikwu, Osadebe and Ibezim., 2007
Vernonia amygdalina	Bitter leaf or *Onugbu*	Leaf	Enhanced CD4+ count	Momoh, Adikwu, Ibezim and Others, 2009
Vernonia amygdalina + Metformin	Bitter leaf or *Onugbu*	Leaf	Enhanced Antidiabetic activity	Momoh, Adikwu, Ibezim and Others, 2009
Thermostable enzyme-producing Bacillus species	-	From animal dung	Important pharmaceutical enzyme	Ibezim *et al*., 2009
Dorstenia multiradiata	-	Leaf	Phytochemical characterization	Ibezim and Okunji, 1992

extract in different emulsifying ointment bases (anionic, cationic and non-ionic) have been evaluated *in vivo* using

the excision wound healing model on guinea pigs. In all cases, there was a progressive decrease in wound area with time, indicating an efficacy of the formulations in healing the induced wounds (Ibezim, 2006). The efficacy was superior to that of Cicatrin®, a standard wound healing powder, used for comparison. A similar study was carried out on another plant extract, *Napoleona imperialis* (Ibezim *et al*., 2005). A progressive decrease in wound area, with time, was also obtained, superior to those obtained with the standard wound healing agent. The two plant extracts were then admixed and their combined wound healing property assessed. The results showed a synergistic wound healing activity at the 50:50 ratio, superior to any of the plant extracts used alone and the standard antibiotic wound healing powder, Cicatrin® (Ibezim, 2005).

The possible use of the volatile oil from *Denneti tripetala* (*Mmimi*) as a preservative in aqueous creams was studied *in vitro* (Ibezim and Esimone, 2006). The cream formulations showed good antimicrobial activities against the strains of organisms – *Staphylococcus aureus, Pseudomonas aeruginosa* and *Candida albicans,* though the standard preservative, chlorocresol, used for comparative studies showed a superior activity. Aqueous creams are prone to microbial contamination hence require preservatives to contain possible microbial attack.

Substances extracted from lichens have previously been reported to possess antimicrobial activities against various groups of bacteria, fungi and viruses. Due to the high abundance of *Parmelia perlata* in the Eastern parts of

Nigeria, we decided to explore its potential antiviral activity against some common animal and human viruses (Esimone, Ibezim and Others, 2007). The dried and powdered lichen was extracted with acetone, water and 4% (v/v) NaOH (to yield a crude polysaccharide fraction) using standard methods. The cytotoxicity of the extracts was investigated on HEP-2, Vero and L20 cell lines. The antiviral properties were determined against yellow fever, poliomyelitis and infectious bursal disease virus of chickens using the end-point cytopathic effect assay. The results showed that the crude polysaccharide fraction from *Parmelia perlata* possesses specific antiviral activity against yellow fever virus. It is postulated that a major mechanism of inhibition of yellow fever infection by the crude polysaccharide fraction of the lichen could be by attack on the viral envelope.

With my research team, I had formulated and evaluated an herbal ointment containing *Dissotis theifolia* stem extract for wound healing and antibacterial activities against clinical wound isolates of *Staphylococcus aureus* and *Pseudomonas aeruginosa* (Odimegwu, Ibezim and Others, 2008). The ointment batches containing different concentrations of the *D. theifolia* extract were applied topically to both infected and uninfected wounds inflicted on rats and the rate of wound closure assessed by wound area measurement. *In vitro*, the *D. theifolia* extract inhibited the growth of different clinical wound isolates of *S. aureus and P. aeruginosa* with MICs ranging from 3.0 mg/ml for 3 of the 5 clinical strains of *S. aureus* to 8.0 mg/ml for all the 3 clinical strains of *P. aeruginosa* tested. In the study of uninfected wounds, incorporation of *D. theifolia* extract (60,

90, and 120 mg/g) into the applied ointment enhanced the rate of wound closure and reduced the epithelialization period from 14.98 ± 0.46 days for the control group treated with blank ointment to 8.8 ± 0.2 days for the group treated with 120 mg/g of *D. theifolia* ointment.

There appear to be limited data on the temperature-induced chemical stability/instability profile of herbal medicines, which correspondingly impinges on their efficacy and safety. In view of this, we undertook a quality control monitoring of the content of active ingredient of pharmaceutical cream and ointment containing the methanol extract of the *Dissotis theifolia* stem extract exposed to variegated temperatures using a specific microbiological assay method (Ibezim *et al*., 2007; Odimegwu, Ibezim and Others, 2010). Results showed reduction of potency of the formulated extracts due to chemical degradation through the first order reaction pathway. The ointment formulation demonstrated a longer half-life and shelf-life being more stable than the cream.

The *in vitro* antimicrobial activity of crude water extract of *Azadirachta indica* (Neem or *Dogon yaro*) and its interaction with some standard antibiotics: doxycycline, gentamicin, streptomycin, erythromycin, ciprofloxacin, and norfloxacin have also been studied (Ngwu, Ibezim and Others, 2009). The *in vitro* activities and interactions were evaluated using a combination of agar diffusion and Checkerboard techniques against *Staphylococcus aureus* as test microorganism. The plant extract showed distinguishable antimicrobial activity. There were synergistic interactions between the crude extract (0.1

mg/ml or 0.25 mg/ml extract) and all the antibiotics used except tetracycline in the agar diffusion technique ($p< 0.05$). In the Checkerboard technique, fractional inhibitory concentration (FIC) indices reveal that the crude extract showed synergistic antimicrobial activity with tetracycline (1:9), streptomycin (1:9, 9:1), ciprofloxacin (2:8, 5:5) and norfloxacin (2:8, 6:4). There is therefore, a possible beneficial clinical application of the co-administration of doxycycline, gentamicin, streptomycin, erythromycin, ciprofloxacin or norfloxacin and the crude extract of *A. indica* in the treatment of infections caused by *S. aureus*. However, unguided concomitant usage may result in therapeutic failure.

Apart from antimicrobial agents, I have discovered some other therapeutic applications of some plants as presented in Table 2. *Euphobia hirta* has, for instance, been found to reduce platelet count, clotting time and bleeding time (Omeje, Ibezim and Others, 2007). *Euphorbia hirta* Linn (Fam: Euphorbiaceae), locally known as '*ogwu ugwo'* (eczema drug) in some Eastern parts of Nigeria is used locally to arrest bleeding in the event of an injury. The extracts (aqueous and methanolic) were administered orally to albino Wistar rats. Platelet count, bleeding and clotting times were determined before and at different time intervals after administration of the extracts. The aqueous extract at 60 min reduced bleeding time by 54% compared to 49.5% for methanolic extract. Similarly, 84.1% and 42.5% reductions in clotting time were achieved with aqueous and methanolic extracts respectively. Platelet count reductions with aqueous and methanolic extract were 19.2% and 36.1% respectively. There was significant ($p<0.05$) difference in

clotting time of the two extracts after 30 min of administration. There was however, no significant correlation between the dose and activities of the extracts. These findings validate the claim that *Euphorbia hirta* arrests bleeding and modulates haemostasis.

Vernonia amygdalina (Bitter leaf) is used folklorically in Nigeria as a tonic, and as a remedy in the treatment of constipation, fever, high blood pressure and many infectious diseases. We have carried out a study to show the effect of the leaf extract of this plant on the CD4+ cells count of diabetic rats (Momoh, Adikwu, Ibezim and Others, 2009). Three different concentrations were orally administered to the rats through the nasogastric route via a tube, once daily for 21 days. There was a significant increase in the CD4+ cell count compared to the control group ($p>0.5$). The increase was concentration dependent.

We also looked at the effect of metformin and *Vernonia amygdalina* - loaded PEGylated mucin formulation on haematological, kidney and liver indices of normal and diabetic rats (Momoh, Adikwu, Ibezim and Others, 2009). This study was carried out to assess the pharmacodynamic properties of metformin/*Vernonia amygdalina*-loaded Polyethylene glycol (PEG)-mucin matrices. The safety of the formulations on vital organs and haematological parameters was similarly assessed. Aqueous leaf extract of *Vernonia amygdalina* was obtained by cold maceration. The formulations restored the electrolyte (Na^+, K^+ and Cl^-) and urea imbalance associated with diabetic rats but did not lead to any significant changes ($p \leq 0.05$) in all the haematological parameters investigated. The formulations

substantially reduced blood glucose level in both alloxan-induced diabetic and non diabetic rats as compared to metformin or *V. amygdalina* extract used alone.

I have isolated and characterized a thermostable enzyme - producing bacteria from their natural environment – animal dung (Ibezim *et al*., 2009). The animal dungs were collected at temperatures of 40^{o}C and above, generally regarded as normal growing condition for thermophilic microorganisms. The samples were inoculated and incubated at three different temperatures of 50^{o}C, 60^{o}C and 80^{o}C. The isolates obtained were characterized to species level using standard biochemical methods. The result shows that horse dung had the heaviest growth of microorganisms at 60^{0}C involving *Bacillus species* that were further confirmed to be *Bacillus stearothermophilus* after characterization. It can be concluded that the dung could be employed as a source of *Bacillus stearothermophilus* used in the pharmaceutical and allied industries.

A phytochemical study has been carried out on the acetone leaf extract of *Dorstenia multiradiata* (Family: Moraceae), a plant extensively employed in traditional medicine for treating various skin diseases and wound healing. Phytochemicals like flavonoids, sterols/triterpenes, glycosides and resins were found present in the extract. Flavonoids and sterols/triterpenes constituted the major components. Column chromatography was used to separate the constituents while thin layer chromatography, chromogenic reactions and spectral analysis were employed to characterize them. The characterization led to the

identification of ß – sitosterol and an aurone (a flavonoid) (Ibezim and Okunji, 1992).

My research team is currently trying to produce some penicillins from available local sources. Reasonable quantities of the drug have been produced and are currently undergoing some extensive standardization studies.

3.8 DRUG EXCIPIENTS DISCOVERY

Apart from pharmaceutical active ingredients, I have been involved, albeit, extensively, in the search for effective and readily available as well as affordable pharmaceutical excipients which would greatly improve our national reserves in view of the huge amount expended in importing the currently used ones. An **excipient** is generally a pharmacologically inactive substance used as a carrier for the active ingredients of a medication A lot of these excipients have been standardized while others are still heavily groaning under the weight of constant neglect and presumption. Some of the excipients, so far discovered through our search are presented in Tables 3 and 4.

A comparative stability study has been carried out on Chalk suspensions prepared with the gum obtained from *Colocasia esculenta* (Cocoyam) (Ibezim and Onuegbu, 1992). The gum was extracted from the peeled, sliced, dried and milled cocoyam corm and cormel by maceration in distilled water for 24 h. The gum was employed as a suspending agent in the preparation of Chalk suspension. It was discovered that cocoyam gum possessed

Table 3: Plant gums/Latex as novel drug excipients

Source	Local name	Plant part	Discovered use	Reference (s)
Colocasia esculenta	Cocoyam	Gum	Suspending agent	Ibezim and Onuegbu, 1992
Anacardium occidentale	Cashew	Latex	Suspending agent	Ibezim *et al*., 2000
Colocasia esculenta	Cocoyam	Gum	Emulsifying agent	Ibezim, 1992;Ibezim , 1994
Colocasia esculenta + *Abelmoschus esculenta*	Cocoyam + Okro	Gum + Mucilage	Emulsifying agent	Ibezim and Okorie, 2004
Colocasia esculenta + Acacia	Cocoyam (*Ede*)	Gum	Emulsifying agent	Ibezim *et al*., 2010[c]
Afzelia africana	*Akparata*	Seed gum	Binder	Ibezim *et al*., 2006
Afzelia africana + Tragacanth	*Akparata*	Seed gum	Binder	Ibezim and Okorie, 2004
Landolphia dulcis		Latex	Binder/ Microencapsulating agent	Ibezim, Adikwu and Esimone, 1997
SCMC+ Carbopol	-	-	Bioadhesive agent	Ibezim *et al*., 2000
SCMC+Acacia +Veegum	-	-	Bioadhesive agent	Ibezim and Ofoefule, 2006
Prosopis africana	*Okoho*	Gum	Standard-ization	Ibezim *et al*., 2003

good suspending properties though not as good as that produced by compound tragacanth, a standard

pharmaceutical suspending agent. Another study on cocoyam gum looked at its use as an emulsifying agent in the formulation of paraffin oil and arachis oil emulsions (Ibezim, 1992; Ibezim, 1994). Emulsions are important pharmaceutical formulations used to deliver drugs to the body system. They are made up of oil and aqueous phases which are brought into intimate contact by the aid of an emulsifying agent. In this study, cocoyam gum was employed at a 6% w/w concentration. Emulsion properties studied included creaming rate, cracking rate, rheology, globule size distribution, pH, and organoleptic behaviours. Results obtained showed that the gum produced emulsions with good stability properties comparable to those exhibited by acacia, a standard emulsifying agent (Fig. 1).

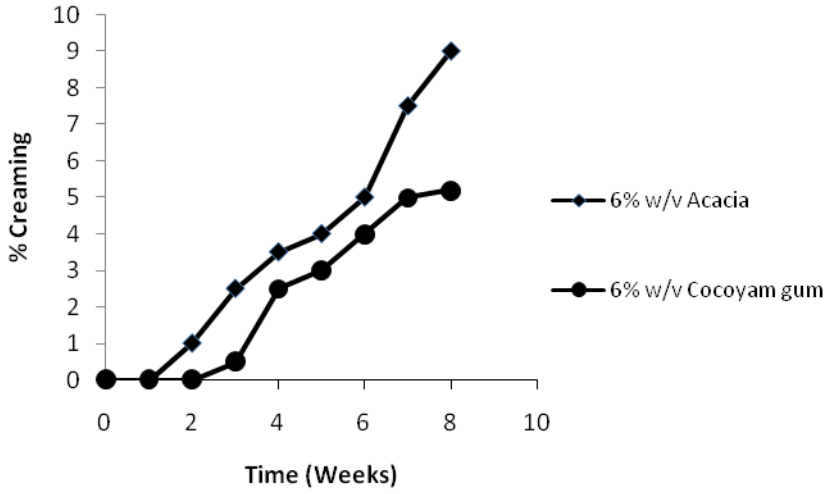


Fig. 1: Creaming patterns of paraffin oil emulsions prepared with acacia and cocoyam gum

Admixtures of excipients are sometimes known to yield more superior products than any of the components used singly. So, an attempt was made to study the emulsifying properties of cocoyam gum and okro (*Abelmoschus esculenta*) gum used in a binary combination (Ibezim and Okorie, 2004). The gums were extracted by precipitation using acetone and used as emulsifying agent to formulate various batches of arachis oil emulsion at various combination ratios. The combination led to the production of emulsions with superior stability characteristics to those of cocoyam gum alone, but comparable to the properties of the okro gum. A related study examined the emulsifying properties of cocoyam gum admixed with acacia at different ratios with the intention of improving the emulsifying properties of the gums (Ibezim *et al*., 2010). Results obtained from the above study showed that the emulsions prepared with a combination of various proportions of acacia and *Colocasia esculenta* gums were more stable when compared to similar preparations containing either *Colocasia esculenta* or acacia gums alone. Thus, a combination of acacia gum with C*olocasia esculenta* gum could serve as useful emulgent in arachis oil emulsions.

Polymerized latex of *Landolphia dulcis* has been used as wall material for microencapsulation of sodium salicylate by non-solvent method of coacervation (Ibezim *et al*., 1997). Sodium salicylate granules prepared with sodium carboxymethyl cellulose as binder were used as control. Results of the drug release profile from the microcapsules in HCl showed a prolonged release of the drug if compared to

that of the unencapsulated drug (Fig. 2). The drug release rate decreased as the latex : drug ratio increased. The drug release was faster in distilled water than HCl and obeyed both the Higuchi matrix release model and the first order model but mainly by the former.

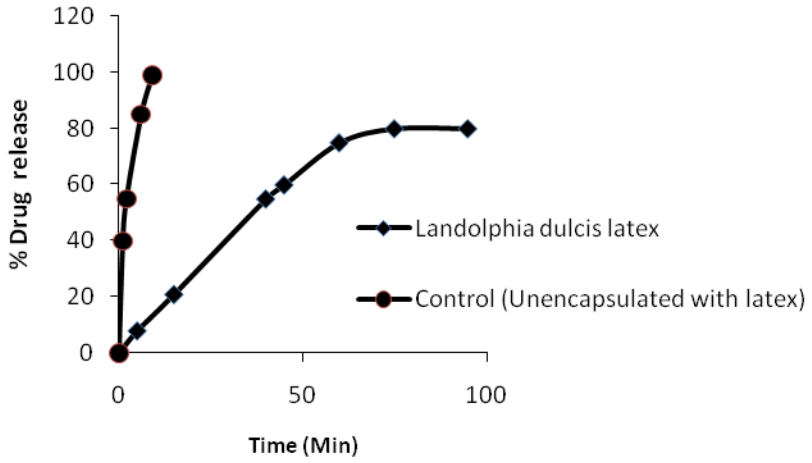


Fig. 2: Release profile in 0.1 N HCl, of sodium salicylate microcapsules prepared with *Landolphia dulcis* latex

The exudates from the stem bark of *Anacardium occidentale* (Cashew) has been studied for its possible suspending properties (Ibezim *et al.,* 2000). Chalk suspensions were prepared with different concentrations (2.5 – 20.0 %w/v) of the gum, stored for 56 days and various stability indices such as sedimentation ratio, rate of redispersibility, rheological changes and pH variations studied. The effects of preservatives, electrolytes and pH on the stability of the

suspensions were also evaluated. Veegum® was used as a standard for comparison. Cashew gum was found to possess good suspending properties though the suspending profile of Veegum®, a standard, currently marketed agent, seemed to be superior. In view of the rising costs of acacia and Veegum® and their fluctuating availability, cashew gum can be exploited for use as suspending agent in pharmaceutical suspensions.

Admixtures containing Carbopols 940, 941 and sodium carboxymethyl cellulose were assessed for bioadhesive delivery of metronidazole (Ibezim *et al*., 2000). The bioadhsevie properties of the admixtures were estimated by using the adhesion of polymer - coated beads on a biological tissue and the modified Lecomte Du Nouy tensiometer. The rheological behaviours of the polymers and their admixtures were studied as well. The bioadhesive, swelling and release characteristics of tablet compacts formulated with the polymers and their admixtures, which contained metronidazole were also studied and the results obtained indicated that although all single polymers and their admixtures had high bioadhesive potentials, Carbopol 940 and 941 admixtures (2:1) showed the best performance while SCMC/Carbopol 940 admixture (2:1) exhibited the least bioadhesive strength.

During a three month research visit to Instituto de Macromolecula Eloisa Mano Rio de Janeiro Brazil, I undertook a spectral characterization and visco-elastic study on the gum extracted from the seeds of *Prosopis africana* (*Okoho*) with a view the aim of characterizing it for potential use as pharmaceutical excipient. The gum was

extracted by maceration, followed by precipitation. The galactose:mannose ratio was determined by ^{13}CNMR spectroscopy. The ash content, moisture content, solubility, pH, dry weight and intrinsic visco-elastic properties were determined by standard methods. The extraction yielded 22% w/w of a yellowish brown gum with an ash value of 0.47%, moisture content of 10.2%, pH of 6.5, and intrinsic viscosities of 13.2 and 12.0. The ^{13}CNMR spectroscopy revealed a galactose – mannose ratio of 1.17 (Ibezim *et al.*, 2003).

A study was carried out to determine the suitability of the hydrocolloids, sodium carboxymethyl cellulose (SCMC), Veegum®, acacia and their combinations as bioadhesive matrices for the delivery of metronidazole (Ibezim & Ofoefule, 2006). Aqueous dispersions containing 8% w/v of the hydrocolloids and their combinations were prepared and their bioadhesive properties evaluated using detachments of coated glass beads and tablet compacts from isolated biological tissue, as well as the adhesive force between the aqueous dispersion and I-mucin measured with a tensiometer adapted to measure adhesive force. The viscosity of the polymer-polymer admixture and the swelling capacity of the tablet compacts were determined as well as the dissolution profile of the compacts. Results obtained showed that the hydrocolloids and their admixtures possessed bioadhesive properties. On the basis of bead detachment, SCMC had the highest bioadhesive strength while acacia had the least. SCMC also exhibited the highest strength on the basis of tensiometry while the dispersion containing 2:3:3 ratio of Veegum, SCMC and acacia had the least.

At the Central Drug Research Institute, Lucknow, India, I worked extensively on the seed gum from an indigenous plant, *Afzelia africana* (*Akparata*). I looked at the physicochemical properties as well the application of the seed gum as binder in the formulation of tablets. The following physicochemical properties of the gum, extracted by cold maceration in distilled water, were evaluated by standard methods: presence of starch, saponin, tannin, reducing sugar, glycosides, alkaloids, oils, flavonoids, oils and steroidal aglycones, solubility profiles, rheology and densities. Differential calorimetry, NMR spectroscopy and mass spectroscopy were carried out on the gum. The yellowish-brown translucent gum, with angular and irregular shaped particles contained saponins, glycosides, reducing sugars, proteins and steroidal aglycone (Ibezim *et al*., 2006). It swells in water and is soluble in 1% sodium hydroxide. A 2 % solution has a viscosity of 143 cP and an acidic pH of 4.58. Other physicochemical properties were similar to those of acacia, a standard binder for tablets. The DSC shows that the gum absorb heat at 140-150 ^{O}C while the NMR spectra show the product to be a polysaccharide possibly with CH_7O-R units at the region 3.369. The Electrospray MS shows the presence of negative M-HT groups of disaccharides, trisaccharides, tetrasaccharides and pentasaccharides. The presence of C, N and H in the gum were 0.00, 48.09 and 1.11 respectively. The overall properties of tablets formed with *A. africana* compared well with those formed with acacia.

In another study, I combined *Afzelia africana* seed gum with

Table 4: Starches as novel drug excipients

Source	Local name	Plant part	Discovered use	Reference (s)
Mannihot esculenta + *Zea mays*	Cassava + Maize	Starch	Binder	Ibezim and Ugwu, 2003
Zingiber officinale	Ginger	Starch	Binder	Ibezim and Omeje, 2008[b]
Mannihot esculenta starch, *Zea mays* starch, Acacia, Tragacanth	Cassava, Maize, Acacia, tragacanth	Starches /Gums	Emulsifying agent	Ibezim and Attama (1998)
Mannihot esculenta starch+Veegum	Cassava	Starch	Suspending agent	Ibezim, 2006
Dioscorea dumetorium	Three leaved yam (*Ona*)	Starch	Disintegrant	Ibezim, 1994; Ibezim and Omeje, 2008
Zea mays	Corn	Starch (Modified by cross-linking)	Standardization	Ibezim *et al*., 2006; Ibezim and Andrade, 2006[a]; Ibezim and Andrade, 2006[b]; Ibezim, Cristina and Andrade, 2007

compound tragacanth and looked at the binding properties of the combination in sodium salicylate tablet formulations (Ibezim *et al.,* 2004). Different combination ratios of the gums were assessed at 2-3% w/w concentrations of binders. Formulations containing the gums used alone as binders were also prepared for comparative purposes. Results obtained showed that of all the formulations, the batch containing a binary mixture of *Afzelia africana* seed gum/Tragacanth at 2% w/w concentration possessed the most superior binding properties, suggesting a potential use of the binary mixture as a superior alternative, to any of the binders used alone, in tablet formulation.

Apart from the gums, I have carried my exploration for pharmaceutical excipients to the world of starches. In 2003, I examined a combination of cassava and maize starches as potential binders for paracetamol tablet formulation (Ibezim and Ugwu, 2003). Varying ratios of the two hydrocolloids were employed in preparing batches of 500 mg paracetamol tablets. The properties of the tablets were studied such as hardness, weight uniformity, friability, content uniformity, disintegration time and dissolution profile. The various combinations produced tablets of acceptable properties, but the tablet produced with a maize/cassava starch ratio of 1:3 yielded tablets of such hardness and release characteristics that makes it a possible candidate for sustained release drug delivery. I also comparatively studied the emulsifying properties of the following plant hydrocolloids: cassava starch, maize starch, tragacanth and acacia in paraffin oil emulsion (Ibezim and Attama, 1998). The prepared emulsions were evaluated for stability parameters. The results showed that cassava starch and acacia exhibited

superior properties as emulsifying agents to those of maize starch and tragacanth.

In another visit to IMA, Rio de Janeiro, Brazil, in 2006, I undertook an extensive work aimed at modifying maize starch, for superior pharmaceutical usage as compared to the native starch. Starch modification is usually undertaken to improve its mechanical properties and expand their usefulness. Cross-linking with sodium trimetaphosphate (STMP) was carried out by reactive processing and involved treating the native starch with varying concentrations of sodium trimetaphosphate in the presence of sodium hydroxide and 25% moisture content in an internal mixer (Ibezim *et al*., 2006; Ibezim, Cristina and Andrade, 2007). Processing was carried out at a constant rotors speed of 40 rpm for 15 min, at temperatures varying within a limited range. After processing, the samples were compression – moulded conditioned at 28^{O}C and 68% relative humidity for 20 days, and submitted to tensile tests. The effects of the independent variables, concentration of STMP expressed as phosphorous content, and temperature on specific mechanical energy and mechanical properties of the cross linked starch materials were analyzed by the response surface methodology. The native starch was additionally cross-linked by pregelatinization at 90^{O}C for 45 min. The resulting slurry was treated subsequently with varying amounts of STMP and sodium sulfate at pH 11. Spectral (^{13}CNMR, Infra red) and thermogravimetric analysis (TGA) (Ibezim and Andrade, 2006[a]) as well as flow behaviours and goniometry (Ibezim and Andrade, 2006[b]) of the cross linked and native starches were carried out using relevant standard techniques. The ^{13}CNMR spectroscopy showed that cross

linking resulted to a reduction in the chemical shifts of the starch. Cross linking introduced more peaks in the IR spectra due to the incorporated phosphoryl groups. The results of the TGA showed that cross linking reduced the total organic matter present, while increasing the peak degradation temperatures and total inorganic matters. The result of the flow and goniometric studies showed that cross linking reduced the swelling volume and paste clarity as well as the effect of sucrose on the swelling of the starch. It also increased the contact angles formed by the starch implying that cross linking reduced the hydrophilicity of the native starch.

A study has been carried out on the combined suspending behavior of cassava starch and Veegum® (Ibezim, 2006). The study which followed standard procedures showed that the combination yielded suspensions with superior suspending properties to those exhibited by suspensions formed by each of the agents used alone implying that the two plant hydrocolloids can be used in combination as an efficient suspending agent.

We have equally tried to look at the usefulness of the starch obtained from the tuber of *Dioscorea dumetorium* (Three leaved yam). The starch was obtained by cold maceration of the peeled, sliced and milled tuber in distilled water after which the slurry obtained was dried and passed through a suitable sieve. They were used at varying concentrations to formulate granules and tablets of chloroquine phosphate and the granule as well as tablet properties studied. The results obtained showed that the produced granules and tablets possessed good granule and tablet properties comparable

Table 5a: Drug excipients from other sources

Source	Local name	Plant part	Discovered use	Reference (s)
Eudragits, Ethyl cellulose, Carbopol 941	-	-	Sustained release agents	Ofoefule, Orisakwe and Ibezim, 1997
Colocynthis vulgaris	Melon seed (*Egusi*)	Seed cake	Binder	Ibezim and Ofoefule, 2007
Colocynthis vulgaris	Melon	Seed oil	Vehicle for methyl salicylate liniment	Ibezim and Chukwu, 1990
Colocynthis vulgaris	Melon	Seed oil	Vehicle for salicylic acid lotion	Ibezim and Chukwu, 1991
Goat fat	-	Fat	Suppository base	Ibezim *et al*., 2010
Goat fat	-	Fat	Lipid base for medicated creams	Ezeabasili, Ibezim and Others, 2010[a]; Ezeabasili, Ibezim and Others, 2010[b]; Ezeabasili, Ibezim and Others, 2010[c]
Goat fat	-	Fat	Lipid base for medicated ointments	Ezeabasili, Adikwu, Ibezim and Others, 2010[d]
PEGylated mucin	-	-	Bioadhesive	Momoh, Adikwu, Ibezim and Others, 2009; Momoh, Adikwu and Ibezim, 2010[a]; Momoh, Ibezim and Others, 2010[b]
Solid – lipid matrices	-	-	Matrix for oral drug delivery	Nnamani, Ibezim and Others, 2010

to those produced by another standard disintegrant, maize starch, and can be employed as a disintegrant in the formulation of chloroquine phosphate granules or tablets (Ibezim, 1994; Ibezim and Omeje, 2008[a]).

A similar study looked at the possibility of utilizing the starch obtained from the rhizome of ginger (*Zingiber officinale*) (Roscoe; Zingiberaceae) as a binder in tablet formulation (Ibezim and Omeje, 2008[b]). The rhizomes of ginger have been reported to contain up to 56.0% starch. The starch was extracted from the fresh rhizomes, evaluated for relevant properties and used as a binder in acetaminophen tablets at concentrations of 2.0 - 8.0% w/w. The tablets were evaluated for hardness, friability, weight uniformity, disintegration and dissolution profiles. Acetaminophen tablets containing gelatin as standard binder were produced and assessed comparatively. Results obtained indicate that ginger starch performed as good as gelatin as a binder in acetaminophen tablet formulation.

My search for pharmaceutical excipients has continued beyond gums and starches. My team had in 1997 formulated nifedipine with three different polymeric materials namely: Eudragit L100 and RS, ethyl cellulose and Carbopol 941, in order to ascertain if they possess sustained release potentials (Ofoefule, Orisakwe and Ibezim, 1997). The polymers were employed at 20% w/w concentrations and the different release kinetics of the tablets determined. Sustained release products were subsequently obtained and the release kinetics

Table 5b: Drug excipients from other sources *ctd*

Source	Local name	Plant part	Discovered use	Reference (s)
Native clay+Bentonite +Tragacanth + acacia	*Nzu*	-	Suspending agent	Ibezim *et al*., 2010[a]
P90Gylated tallow fat-based solid lipid micro-particles	-	-	Matrix for piroxicam	Nnamani, Ibezim and Others, 2010[a]; Nnamani, Ibezim and Others, 2010[b]
Heterolipid microcarriers	-	-	Microparticles for delivery of cimetidine	Nnamani, Ibezim and Others, 2010[c]
Ionically cross linked chitosan/ tripolyphosphate microparticles	-	-	Microparticles for delivery of pyrimethamine	Ibezim *et al*., 2010[b]
Surface modified solid lipid micro-particles based on homolipids and Softisan® 142	-	-	Characterized	Nnamani, Ibezim and Others, 2010[d]

were found to fit into Hixson Crowell cube root and Higuchi diffusion models. Release of nifedipine occurred by both infiltration of dissolution medium and dissolution after release of drug particles following erosion of the matrix tablets. Rate of infiltration of dissolution medium and erosion of tablet matrix was highest in the formulation with Eudragit L-100 and least in that produced with ethyl cellulose.

The entire seed cake of melon (*Colocynthis vulgaris*) has been evaluated as possible binder in tablet formulation (Ibezim and Ofoefule, 2007). The melon seed was dehauled, defatted, dried and employed directly as a binder in the formulation of tablets. Studying the properties of the prepared tablets and comparing with standard binders showed that the melon seed cake possessed good binding properties, hence could be further processed to act as suitable binder in pharmaceutical tablet formulation. In a similar vein, the oil extracted from melon seed has been evaluated and found suitable as vehicle for the formulation of methyl salicylate liniment (Ibezim and Chukwu, 1990) and salicylic acid lotion (Ibezim and Chukwu, 1991). The formulations compared well with those formulated with standard vehicles (Figs. 3 and 4).

We have evaluated goat fat as a possible vehicle for some semi-solid pharmaceutical preparations. It has for instance been used to formulate suppositories as a base (Ibezim *et al*., 2010). It has equally been used as a medicated cream base (Ezeabasili, Ibezim and Others, 2010[a]; Ezeabasili, Ibezim and Others, 2010[b]; Ezeabasili, Ibezim and Others, 2010[c]) and as a medicated ointment base (Ezeabasili, Adikwu,

Ibezim and Others, 2010[d]). In each of these cases, goat fat produced high quality semi-solid dosage forms that were comparable to those produced by standard vehicles.

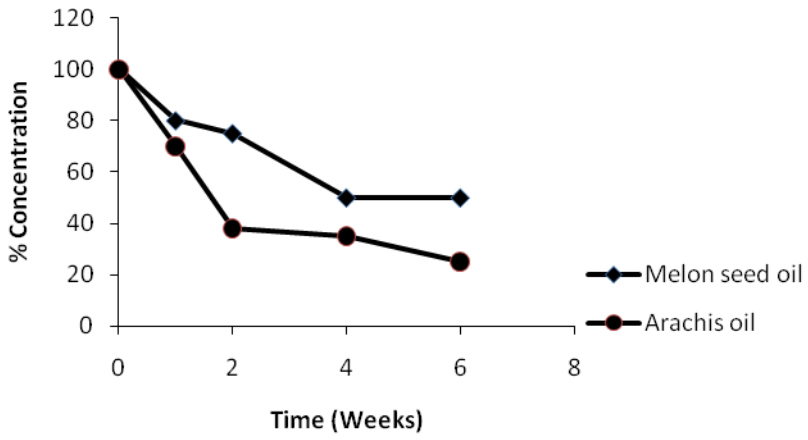


Fig. 3: Degradation of methyl salicylate in liniments formulated with melon seed oil and arachis oil as vehicles

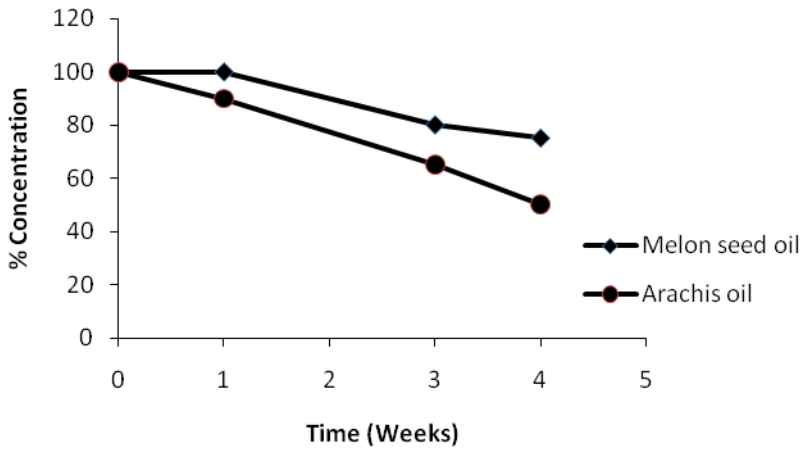


Fig. 4: Degradation of salicylic acid in lotions formulated with melon seed oil and arachis oil as vehicles

Mucin treated with polyethylene glycol (PEGylated mucin) has been studied as possible bioadhesive agent in the formulation of bioadhesive dosage forms (Momoh, Adikwu, Ibezim and Others, 2009; Momoh, Ibezim and Others, 2010[a]; Momoh, Ibezim and Others, 2010[b]). The PEGylated mucin samples proved to be good bioadhesive agents upon assessment using standard techniques.

We have tried to formulate solid lipid matrices and studied their potential for oral delivery of some drugs. A matrix system containing a combination of polyethylene glycol 90 and tallow fat, giving P90Gylated tallow fat-based solid lipid system has been developed for the delivery of

piroxicam, a known analgesic, antipyretic and anti-inflammatory agent (Nnamani, Ibezim and Others, 2010[a]; Nnamani, Ibezim and Others, 2010[b]). We introduced heterolipids to the system and were able to produce heterocarriers that successfully delivered cimetidine (Nnamani, Ibezim and Others, 2010[c]). An attempt was also made to surface - modify solid lipid microparticles based on homolipids and Softisan® 142 with a view to producing microparticles that could serve as potential carriers for some orally administered dosage forms (Nnamani, Ibezim and Others, 2010[d]).

Native clay (*Nzu*) has been admixed with bentonite, tragacanth and acacia and evaluated for possible use as a suspending agent. The combination yielded suspensions that were elegant, with good stability properties that compared favorably with those of suspensions produced by standard suspending agents (Ibezim *et al*., 2010[a]).

During my third and final visit to IMA Brazil, I cross linked chitosan with tripolyphosphate and studied its utility in the delivery of the antimalarial drug, pyrimethamine. The cross linked product had excellent stability behaviours and showed good promise as a possible microparticulate carrier for the successful delivery of pyrimethamine to the system (Ibezim *et al*., 2010[b]).

3.9 DRUG INTERACTIONS (DRUG/DRUG, FOOD/DRUG, DRUG/EXCIPIENT INTERACTIONS)

I have further stretched my drug research tentacles to the all-important area of drug interactions – with other drugs, coadministered food materials or other coadministered agents. Such interactions have tendency to affect significantly, the therapeutic efficacy of the drugs in question. They can reduce or totally cancel the activity of a given drug and can lead to adverse reactions, side effects or even death. However, some interactions can also be beneficial resulting to an improved therapeutic activity or a reduction of known side effect of the drug.

In one of such studies, gentamicin sulphate as an injection was found to be compatible with commonly coadministered parenterals – dexamethasone, diazepam, hyoscine butylbromide, furosemide and promethazone, implying that the drug can safely be used when the patient is on the parenterals (Ibezim and Attama, 1997) – Table 6a.

The interaction between salicylic acid and nystatin, two commonly used antifungal agents has been studied (Ibezim *et al*., 2003). It was discovered that an antagonistic interaction occurred between the two drugs as reduced antifungal activity against clinical isolates of *Candida albicans* was observed with the drug combination, suggesting that the two drugs should not be used concurrently for the treatment of candidiasis.

Caffeine, a central nervous system stimulant has been found to potentiate the activities of two fluoroquinolones –

ciprofloxacin and levofloxacin against *Escherichia coli* (Ibezim *et al*., 2004). A synergistic interaction has similarly been found between ampicillin trihydrate and cloxacillin, two commonly used antibacterial agents, against infections by ampicillin – resistant *Salmonella typhi* and *Staphylococcus aureus* (Ibezim *et al*., 2006).

A study on the effect of preservative combinations (methyl paraben, propyl paraben, EDTA, sodium benzoate) on the stability of some commercial herbal formulations has shown that they greatly improved the microbial stability of the preparations (Ibezim *et al*., 2003). The greatest stability was recorded with the combination of methyl paraben and propyl paraben. The least effective was the combination of EDTA and sodium benzoate.

Synergistic interactions have also been observed between Penicillin G, an antibiotic and tea extract on one hand (Esimone, Ibezim and Others, 2006) and some fluoroquinolones (ciprofloxacin, perfloxacin, levofloxacin) with *Kola nitida* extract on the other hand (Ibezim *et al*., 2006). However, ethylene diamine tetra-acetic acid (EDTA), a known preservative, has been shown to greatly inhibit the activity of ciprofloxacin against *Salmonella paratyphi* and *Shigella sonnei* (Ibezim and Omeje, 2006; Ibezim *et al*., 2011), calling for caution in the concomitant use of the two groups.

Some interactions have been observed between certain drugs and commonly concomitantly ingested food items or drug

Table 6a: Some studied drug-drug interactions

Drug/Agent	**Interaction with**	***In vitro* or *in vivo***	**Nature of interaction**	**Reference (s)**
Nystatin	Salicylic acid	*In vitro*	Antagonism	Ibezim *et al*., 2003
Ciprofloxacin	Ethylene diamine tetra-acetic acid (EDTA)	*In vitro*	Antagonism	Ibezim and Omeje, 2006; Ibezim *et al*., 2011
Caffeine	Fluoroquinolones	*In vitro*	Synergism	Ibezim *et al*., 2004
Ampicillin	Cotrimoxazole	*In vitro*	Synergism	Ibezim *et al*., 2006
Penicillin G	Tea extract	*In vitro*	Synergism	Esimone, Ibezim and Others, 2006
Fluoroquinolones	*Kola nitida* extract	*In vitro*	Synergism	Ibezim *et al*., 2006
Gentamycin	Parenteral drugs	*In vitro*	Compatible	Ibezim and Attama, 1997
Herbal formulations	Preservatives	*In vitro*	Enhanced stability	Ibezim *et al*., 2003

excipients (Table 6b). For instance, an adsorptive antagonistic interaction has been observed between two common antiamoebic drugs – chloroquine or metronidazole and some known drug excipients - magnesium trisilicate, maize starch, *Tacca involucrata* starch (Ofokansi, Ibezim and Others, 2004).

Similarly, *in vitro* adsorptive interactions of the antagonistic type have been observed with the following drugs and food items: sodium salicylate and mashed groundnut seeds (Ibezim and Omeje, 2006); tetracycline and palm oil (Ibezim, 1994); tetracycline and mashed groundnut seeds (Ibezim and Udeala, 1992); tetracycline and mashed coconut (Ibezim, 2004); tetracycline and margarine (Ibezim and Udeala, 2003). An *in vivo* study carried out on healthy human volunteers has confirmed an interaction between tetracycline and margarine (Ibezim, 1997).

In vitro antagonistic adsorptive interactions have also been identified between ciprofloxacin and talc/activated charcoal (Ibezim *et al.*, 1999); ciprofloxacin and *Garcinia kola* (Ibezim *et al*., 2001); ampicillin and plantain or fermented oil bean seed (Ibezim & Udeala, 2001); and between ceftriaxone and *Garcinia kola* seed extract (Esimone, Ibezim and Others, 2003). These notable interactions, generally antagonistic in nature, call for great caution in the intake of the implicated food items by patients on therapy with the stated drugs as they are likely going to interfere with the expected drug efficacy. The same caution is imperative in the use of the implicated excipients in the formulation of the stated drugs.

Table 6b: Some observed drug-food/drug-excipient interactions

Drug/ Agent	**Interaction with**	***In vitro* or *in vivo***	**Nature of interaction**	**Reference (s)**
Metronidazole/Chloroquine	Magnesium trisilicate, maize starch, *Tacca involucrata* starch	*In vitro*	Antagonism (Adsorption)	Ofokansi, Ibezim and Others, 2004
Sodium salicylate	Mashed groundnut seeds	*In vitro*	Antagonism (Adsorption)	Ibezim and Omeje, 2006
Tetracycline	Mashed groundnut seeds	*In vitro*	Antagonism	Ibezim and Udeala, 1992
Tetracycline	Palm oil	*In vitro*	Antagonism	Ibezim, 1994
Tetracycline	Mashed coconut	*In vitro*	Antagonism	Ibezim, 2004
Tetracycline	Margarine	*In vitro*	Antagonism	Ibezim and Udeala, 2003
Tetracycline	Margarine	*In vivo*	Antagonism	Ibezim, 1997
Ciprofloxacin	Talc and Activated charcoal	*In vitro*	Antagonism (Adsorption)	Ibezim *et al*., 1999
Ciprofloxacin	*Garcinia kola*	*In vitro*	Antagonism (Adsorption)	Ibezim *et al.,* 2001
Ampicillin	Plantain & Oil bean seed	*In vitro*	Antagonism	Ibezim and Udeala, 2001
Ceftriaxone	*Garcinia kola* seed extract	*In vitro*	Antagonism (Adsorption)	Esimone, Ibezim and Others, 2003

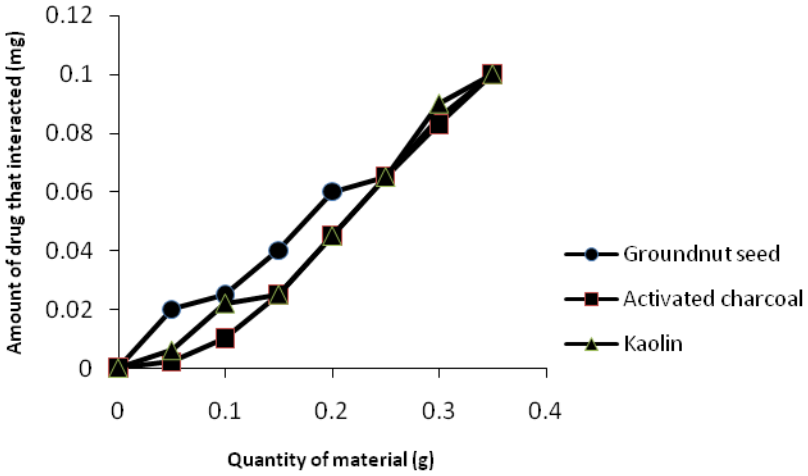


Fig. 5: Amount of sodium salicylate that interacted with different types of adsorbents

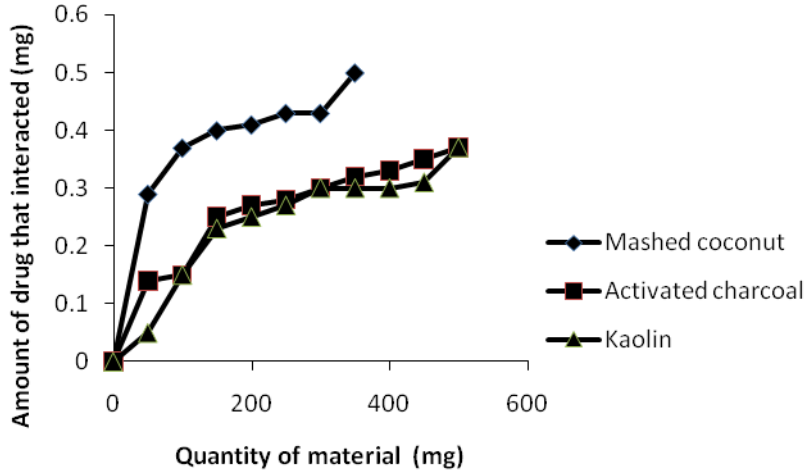


Fig. 6: Amount of tetracycline that interacted with different materials

3.10 DRUG QUALITY ASSESSMENT

My research also extended to the wide field of quality assessment of formulated and commercially available drugs. It is stating the obvious that many of the drug products available in the drug market today, are anything but wholesome. A lot of fakings, adulterations and the like are widespread, calling for urgent assessment of the qualities of commercial drugs available for the drug consumers. We have tried to assess the quality of some of these drugs and our findings are articulated in Table 7.

An attempt was made to assess the microbial quality of some commercially available syrups and suspensions in Nigerian market. Ten different samples each of syrups and suspensions were studied and our findings reveal that one syrup sample and nine of the suspensions had contaminations that exceeded the permissible level for syrups and suspensions (Ibezim *et al*., 2002). The contaminant organisms included *E. coli, Pseudomonas aeruginosa, Staphylococcus aureus, Bacillus subtilis,* and fungi. In a related study, the stability properties of some commercially available chloroquine phosphate syrups were studied (Ibezim and Nwachukwu, 2004). Whereas the products exhibited acceptable physicochemical properties like organoleptic properties, absence of particulate matter, pH, rheology, specific gravity and content of active ingredient, two of the samples studied had microbial contamination. A third study examined the microbial purity of some commonly marketed antidiarrhoeal preparations. All the samples were however found to possess acceptable microbial quality (Ibezim and Okoye, 2006).

Table 7: Quality assessments on some marketed drugs and drug related products

Drug/Material	Quality assessed	Finding	Reference (s)
Commercial syrups/suspensions	Microbial	Conta-minated	Ibezim *et al*., 2002
Commercial herbal formulations	Microbial	Gross contaminati on	Oleghe, Ibezim and Others, 2007[a]; Oleghe, Ibezim and Others, 2007[b]
Locally chewed clay (*Nzu*)	Microbial	Conta-minated	Ibezim and Momoh, 2009
Pure Water samples	Microbial	Trace contamination	Ibezim *et al*., 2010
Soy bean milk products	Microbial	Trace contamination	Ibezim *et al*., 2011
Chloroquine syrups	Physicochemical / Microbial	Few were substandard	Ibezim and Nwachukwu, 2004
Commercial fruit juice	Microbial	Few samples were unsafe	Ibezim and Jackson, 2010
Ofloxacin and Laevofloxacin	Physicochemical properties	Few were unwholesome	Oyim, Ibezim and Others, 2009
Commercial antidiarrhoeal suspensions	Microbial	Stable	Ibezim and Okoye, 2006
Commercial toothpastes	Microbial	Stable	Ibezim *et al*., 2007[a]
Hydrocortisone injections	Storage properties	Stable	Ibezim, 2005
Disinfectants	Kinetic degradation properties	Effective	Iroha, Ibezim and Others, 2005; Ibezim and Okoye, 2007
Metronidazole tablets	Bioequivalence	Bioequival ent	Ibezim *et al*., 2007[b]

A study carried out in 2007 evaluated the bioequivalence of some commercially obtainable metronidazole tablets. The samples were found to be bioequivalent attesting to their good quality (Ibezim *et al*., 2007). A related study carried out to assess the microbial standard of two commonly marketed antibiotic tablet formulations – ofloxacin and levofloxacin, identified a few unwholesome brands (Oyim, Ibezim and Others, 2009). The stability behavior of commercial samples of hydrocortisone injection has also been studied (Ibezim, 2005). The samples were subjected to varying amounts of some environmental factors like light, heat and moisture and their properties evaluated at regular time intervals. The hydrocortisone injection samples were found to degrade extensively when the environmental factors were elevated up to some levels, calling for precaution and selectivity in the storage of the drug.

The degradation/stability profiles of some commercially available disinfectant formulations have been studied (Iroha, Ibezim and Others, 2005; Ibezim and Okoye, 2007). Using the killing rate constant as a pharmacodynamic index, the activities of seven different commercial disinfectants marketed in Nigeria against single and mixed bacterial populations isolated from an indigenous hospital environment were evaluated. The disinfectants were generally active against the strains of microorganisms studied. The mixed populations appeared more susceptible to the disinfectants than the single population. *Staphylococcus aureus* turned out the most susceptible of all the organisms tested.

We have gone ahead to investigate the microbial quality of some indigenous herbal formulations marketed in Nigeria (Oleghe, Ibezim and Others, 2007[a]; Oleghe, Ibezim and Others, 2007[b]). Our findings indicate gross microbial contamination of majority of the samples studied.

The microbial purity of some other non-drug but widely consumed related items has also been evaluated *in vitro.* There have for instance, been studies on commercial toothpastes (Ibezim *et al*., 2007), fruit juice (Ibezim and Jackson, 2010) native clay - *Nzu* (Ibezim and Momoh, 2009), pure water samples (Ibezim *et al*., 2010) and soybean milk products (Ibezim *et al*., 2011). Results obtained showed that, whereas the locally chewed clay had heavy contamination, the fruit juice samples, pure water samples and soybean milk products had trace contaminations. The toothpaste samples were on the other hand microbiologically pure.

3.11 CONCLUSION

Drugs form one of the most useful products mankind has ever developed. Its usage dates back to antiquity. Over the years there have been progressive improvements in the volume and quality of drug products available for human consumption. The study of drugs is both exciting and challenging because it deals with a practical aspect of human existence – his health. My research over these twenty-three years stint with this great university has centred on these wonders called drugs. I have extensively looked at the issue of developing new drugs and drug raw materials/excipients from our vast natural environment and

resources, with very promising results. I have also worked concertedly on drug interactions – with other drugs, food items and excipients, with emphasis on their effects on drug efficacy and therapeutic output. My research has also made in-road into the all-important area of drug quality assurance in view of the current spate of drug adulteration and unwholesomeness plaguing our society presently.

4.0 MY DREAMS

I dream of a University of Nigeria, where true love, warm fellowship, complete dedication, sincere commitment and genuine brotherhood reign supreme; a united community where witch-hunting, victimization, injustice, unbridled gossip and backbiting are strange.

I dream of a time when all the research findings, lying dusty and rusty in Nigerian university libraries shall be translated into viable, high quality, cheap and affordable drug products of industrial, economic and commercial relevance. I dream of a time when our indigenous pharmaceutical firms will, re-direct their gaze and focus to the avalanche of qualitative research findings in our pharmacy schools for alternative sources of their drugs and drug excipients.

I dream of a future Nigeria, where industrial giants, as is the pattern in committed developing economies like Brazil, China and India, will endow resources and sponsor projects in our pharmacy schools to put flesh to the myriad of veritable research endeavours in our faculties of pharmacy, which are at best, dry bones, for now.

I dream of a future, when our up-coming drug researchers would not have to wait endlessly for the results of their analysis to be returned from USA, Canada, Germany or even Ghana, but would just quietly walk into the comfort of their own well-equipped faculty laboratories and have their work done militarily with dispatch.

I dream of a Nigeria with a very functional herbal medicinal policy that will help to conserve the abundant natural resources of biodiversity that exists in the country through its sustainable utilization; that will preserve, through documentation, existing indigenous knowledge and technology used in traditional medicine; that will ensure that existing expertise and activities in the relevant Government Ministries are harnessed and coordinated to avoid unnecessary duplication of efforts and wastage of funds; that will guarantee intellectual property and patent rights of individuals and institutions involved in research and development of new medicines from traditional medicines.

Oh! I dream of a Nigeria, where the government of the day, will cease from paying ignoble, rhetorical lip service but begin to radically mobilize our drug research institutes to be more responsive to our pharmaceutical resource needs.

I believe, with sincerity and commitment, we can realize these dreams. Do you believe?

5.0 ACKNOWLEDGMENTS

There is no duty as urgent as that of returning thanks. My utmost appreciation first of all, goes to the Almighty God, the creator of the universe, who has shown me so much

mercy and favour that I cannot just fathom. It has indeed been a sweet experience, walking and working closely with Him.

I cannot fail to express my indebtedness to my one and only pretty jewel of inestimable value – my heartthrob, my beautiful darling wife, Nnenna Ekpereka. She has been so outstanding in her support, loyalty, care and commitment. She is such an invaluable treasure, a dependable asset, the joy of the home and a strong pillar. Honey, I love you, dearly.

I will not be able to thank enough, my sweet and wonderful kids – Favour Izuchukwu, Precious Ugochinyere, Gift Chinazaekpere, Ozioma Blessed and Ngozi Pearl. You have added a lot of sunshine and glow to my life and have brought immeasurable pleasantness to our home.

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GUIDING PRINCIPLES

- **T**o have something to offer, you must suffer for something
- **T**here is more to life than just existing. Survivors exist, overcomers live. But it takes courage to go beyond survival and into life.
- **T**here is no casual work, men only choose to be casual in their approach
- **T**o be somebody, you must be somewhere
- **T**he most important single ingredient in the formula of success is knowing how to get along with people
- **P**eople always move toward someone who increases them and away from anyone who decreases them
- **T**o get outside of your comfort zone, start with those in your comfort zone. Every friend you have, has a friend you don't have
- **I**ts okay to let those you lead outshine, for if they shine brightly enough, they reflect positively on you
- **K**eep your head and your heart going in the right direction, and you will not have to worry about your feet
- **Y**our existence is evidence that this generation needs something that your life contains
- **G**oals create priorities, determine decisions, dictate companions and predict choices
- **Y**ou are here to be yourself and to express yourself fully; if you fail to deploy yourself, you will soon be employed by others
- **F**ear God and keep His commandments! That is the whole duty of man
- **W**hatever your circumstances at birth, whatever your childhood story, whatever your life in the intervening years, all that matters now is that God has a purpose for you even before you got here
- **Y**ou are not a misfit. You are not a mistake. You are important to God and when you understand His purpose for you, your life will truly have meaning
- **T**rying to do something about something you can't do anything about, is frustrating
- **T**he good we do is never lost. Each kindly act takes root, and every bit of love we sow in time will bear rich fruit. It takes only a moment to be kind, but the result can last forever.
- **H**e who is not thankful for what he's got isn't likely going to be thankful for what he's going to get
- **W**hile one person hesitates because he feels inferior, the other is busy making mistakes and becoming superior.

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