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INAUGURAL LECTURE

"ROOTED IN NATURE, REFINED BY SCIENCE: A NEW HORIZON IN ADVANCED DRUG DELIVERY"

By

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My Lords, Spiritual and Temporal,
Distinguished Invited Guests,
Gentlemen of the Press,
Students of the Faculty of Pharmaceutical Sciences and other students here present,
Great Students of the University of Ilorin,
Distinguished Ladies and Gentlemen.

Preamble

All thanks to the Almighty Allaah for the opportunity He gave me to be here before you all today. With profound gratitude, I am honoured to present the 285th Inaugural Lecture of the University of Ilorin. The first lecture from the Faculty of Pharmaceutical Sciences titled *Pharmacokinetics: Essential Tool in Drug Therapy*, was delivered by the esteemed Professor Moji T. Bakare-Odunola on the 7th of November 2013. The second lecture, titled *Drug Formulation as Essential Construct for Safe Delivery*, was presented by Professor I.O. Aremu, on the 14th March, 2024. Today, it gives me great pleasure to deliver the third lecture, precisely from the Department of Pharmaceutics and Industrial Pharmacy on the titled, **Rooted in Nature, Refined by Science: A New Horizon in Advanced Drug**

Delivery. With this title, I plan to synthesize useful findings from more than a decade of research since my Ph.D. into a lecture that I hope will enlighten the listeners today on the vital role of Pharmacists in advancing healthcare for all. My winding sojourn to today began with my first undergraduate degree (B.Sc.) in Pharmacology from the University of Lagos. Driven by my passion for Pharmacy, I returned to study Pharmacy at the same University, where I obtained my second undergraduate degree (B.Pharm). After my one-year internship, I enrolled for the Master programme and obtained a M.Sc. degree in Pharmaceutics and Pharmaceutical Technology at UNILAG.

My Ph.D. journey began at the University of Lagos but later transitioned to De Montfort University in Leicester, UK, where I worked as a Technical Demonstrator and Part-Time Lecturer, in addition to my rigorous research. Inspired by my interest in impacting knowledge at this stage, and a commitment to contributing to Nigeria's educational sector, I was privileged to take up a lecturing position in this prestigious university, University of Ilorin, where I have served diligently since 2015. It would be impossible for me not to appreciate my wonderful family, friends, mentors and colleagues, too many to count, who have made this journey possible.

Mr. Vice-Chancellor, this lecture is an interwoven piece of my research and the process of pharmaceutical innovation in improving patient outcomes towards saving lives.

Introduction

The definition of a pharmacist encompasses the ability and responsibility of the professional to research, prepare, dispense and provide medications to patients whilst ensuring safe and effective use, playing an essential role in patient education and healthcare. More specifically, a Pharmaceutical Scientist specializes in the research and discovery of novel drugs and drug formulations for improved therapeutic outcomes. In this vast ocean of discipline, I have devoted myself to the development of pharmaceutical formulations and enhancing their delivery in enabling optimum activity of active drug ingredients.

Drug formulation, a critical component of pharmaceutical development, is the combination of an active ingredient (with predetermined activity in a particular disease) and other non-active ingredients (known as excipients) into a drug that meets acceptable standards of quality, safety and efficacy. It is important to know that formulation is not just a mere mixing of ingredients to give a final product, it entails careful consideration of the physical and chemical properties of all ingredients and the stepwise integration of each component to give a product that is not just safe and efficacious, but one that can also encourage the patient to maintain adherence.

A good formulation is just as important as a good active ingredient. The role of a formulation scientist goes a long way in making or breaking a drug product. As described earlier, an active pharmaceutical ingredient in a medicine, also known as an API, is the component that elicits the desired healing (or pharmacological) activity. It may just be a single ingredient, or a mixture of ingredients. In your typical paracetamol tablet, the paracetamol (or acetaminophen) itself is the single API, but in an antimalarial like Artemether/Lumefantrine, these two compounds constitute the APIs. However, it is not realistic to administer these APIs alone without supporting substances that preserve the structure and integrity of the dosage form and ensure appropriate delivery of the drug to intended body sites.

That leads us to some 'extra substances'-the excipients. Excipients do not directly affect disease progression or impact healing but enable the API to perform its function. For example, excipients known as binders enable the aggregation of powders to form the tablet structure we commonly see. On the other hand, excipients known as disintegrants enable these tablets to break quickly in the body system so that the active component is released to act. As such, during drug formulation, we determine if a drug is best administered as tablet, capsule, syrup, suspension, infusion, or any dosage form that would provide the patient with the most benefit.

Mr. Vice-Chancellor, perhaps it would be useful to use the simple analogy of jollof rice in explaining this concept. The rice itself is the API, but since it cannot be served bare, you add

condiments that make it palatable to the consumer, Nigerian or Ghanaian. These condiments are the excipients. The processes of boiling and frying that take place before the food is finally served correspond to the different stages of pharmaceutical formulation.

Away from food and back to drugs, we commonly see a classification that divides medicines as either natural or synthetic. Natural medicines are defined as therapeutic products obtained from various natural sources, including plants, animals and minerals that are useful for managing or treating illnesses. Vice-Chancellor Sir, permit me to clarify to the audience that all herbal remedies are natural drugs, but not all natural drugs are herbal remedies. Herbal remedies are plant-derived and only one of the various sources of natural medicines. On the other hand, synthetic medicines are artificially produced or modified from natural principles; they are also useful in treating or managing diseases.

While these definitions make it clear that a drug is either here or there, it is not always the case, and in many cases, a "synthetic" drug may still contain natural components in its excipients for formulation and improved delivery. The mention of "natural drug" or "traditional medicine" often evokes an imagery of *agbo* or concoctions in suspicious-looking dark-coloured preparations in transparent bottles. And when I say "synthetic", what may come to mind is the image of a well-labelled solid or liquid drug in a neatly arranged pharmacy. I want to begin by clearing away these prevalent assumptions and help to draw a bridge between the two stark classifications.

Clearing the Myths

"*Natural is dirty, synthetic is clean".* All drugs should be clean and prepared in an acceptable form that meets standards for quality and safety. The unclean conditions of sale of many natural products are only reflective of the gaps in regulation and control. An ideal natural medicine should appeal to users as much as synthetic medicine.

"*All natural drugs are safe"*. Nature is home to a diversity of plants that are both beneficial and harmful to humans

and animals. Our flora contains medicinal as well as poisonous compounds that improve and harm human health, respectively. We have a common quote in pharmacy that "all drugs are poisons". This goes to say that a natural product may be beneficial, but if used beyond the stipulated limit, it can also harm the patient. Also, a poorly prepared natural product may contain harmful toxins in addition to the beneficial plant extracts. Therefore, a natural product should be used with the same caution as a synthetic medicinal product.

"Natural drugs and synthetic medicines cannot co-exist". Far from reality, it is almost impossible for natural and synthetic medicines not to co-exist, but it is the degree of integration that may matter more to healthcare advancement and national empowerment. We have seen relevant examples of countries utilising both forms of medicine in mainstream practice. In China, we see the parallel use of traditional Chinese medicine and synthetic medicines as combination therapies, especially in multifactorial diseases. In India, the Ayurvedic system is well-established and widely utilised alongside modern allopathic medicine. Our motherland is not excluded, as more than 70% of the country's population use some form of traditional therapy in disease management. Indeed, the side-by-side adoption of natural and synthetic medicines is beneficial for national health. However, let us think of a deeper level of integration.

Vice-Chancellor Sir, can we go beyond the side-by-side implementation and move into a wholesome combination, where the natural product is indistinguishable from the synthetic product and rather constitutes a vital portion of it or an entirely new one? Certainly, we can, and here is where the lecture begins.

Inherent Gaps in Synthetic Medicines

Literature is replete with reports of formulation complexity in addressing inherent gaps of synthetic products. The determination of the activity of a compound is not enough to guarantee its use in patients. In some cases, this API may possess a bitter taste or poor solubility that creates a challenge in formulation. It is up to researchers in the pharmaceutical science

space to determine the most efficient formulation that ensures stability and appropriate delivery in human systems. This formed the basis of my Ph.D. thesis and the early years of my research experience. The solubility of drugs plays a key role in its pharmacokinetics, how the body affects the drug, and pharmacodynamics, how the drug affects the body (Rodriguez-Aller *et al.*, 2015). Poorly water-soluble drugs necessitate the development of special dosage forms to enhance their absorption, distribution and activity in the body (Pouton, 2006).

Mr. Vice-Chancellor, there are numerous poorly water-soluble drugs. Permit me to use Ibuprofen as a prototype drug onwards. Ibuprofen is a common Non-Steroidal Anti-Inflammatory Drug (NSAID) with analgesic, anti-inflammatory and antipyretic properties. It is frequently prescribed as a "pain-relief" in pharmacies across the country. Physically, it is a colourless powder with a molecular weight of 206 g/mol, crystalline, with melting and boiling points at 75–77 °C and 157 °C, respectively (Huttenrauch, 1983; Baum *et al*., 1985). What you may not know is that ibuprofen is practically insoluble in water (highly hydrophobic). It belongs to the Biopharmaceutical Classification System (BCS) Class II (high permeability and low solubility), which makes it difficult for it to be prepared as a solution.

Due to its high cohesive nature, it flows poorly and does not exhibit good compressibility, making it difficult to be compressed as tablets (Abioye, **Kola-Mustapha** *et al*., 2014). Typically, the granulation method is used in improving the **flowability** of powders, when preparing tablets. This method involves the aggregation of small particles into larger spherical masses where each original particle is still identifiable. This method minimises dustiness and material loss but does not solve the problems faced in manufacturing and those that emerge unpredictably in ibuprofen's product life cycle (Abioye & **Kola-Mustapha**, 2015). Some efforts to modify the behaviour of ibuprofen include the addition of plastically deforming excipients, which enables the formation of strong bonds necessary for tablet compression (Kachrimanis *et al*., 2003).

However, this is limited by dose heterogeneity and particle segregation.

To dissolve components, large amounts of organic solvents (hexane and heptane) are used in preparing commercial ibuprofen powder by crystallisation and subsequent drying of these harmful organic solvents. This lengthens the process and increases the costs of production. More so, the significant impact of organic solvents on the environment and the potential danger in residual solvents create a cause for concern in optimising the ibuprofen production process.

As a well-conceived response to these difficulties in utilising ibuprofen, Abioye, **Kola-Mustapha** and Ruparelia (2014) attempted to develop a polymer-drug conjugate to enhance its solubility property. Conjugate drugs are composed of an active therapeutic component (ibuprofen), which is covalently attached to a water-soluble polymer that helps to improve drug delivery and enhance the drug's physicochemical properties. Considered as new chemical entities, they do not merely envelop the drug but create a new drug structure with improved properties. Since the 90s, there have been some conjugates actively researched, but progress has been limited due to unspecific drug release based on wrong conjugate design.

Hence, it is not sufficient that the conjugate is formed, but it is paramount that it is properly designed to ensure the appropriate release of the drug *in vivo*. Ibuprofen is an amphiphile, which ionizes at high pH values to give species that interact with oppositely charged molecules, such as hydrophilic cationic polysaccharides, to produce drug-polymer conjugates. Eliminating the need for any organic solvent, we complexed ibuprofen melt solution and Diethylaminoethyl Dextran (Ddex) to prepare stable amorphous ibuprofen-polyelectrolyte crystal-granule conjugate (crystanules) using melt *in situ* granulation-crystallization with temperature quenching technique (Fig. 1). Results showed the presence of hydrogen bonding and electrostatic interactions between ibuprofen and Ddex, and further analysis suggested polymer-drug compatibility.

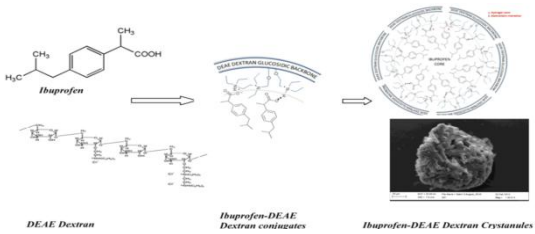

Fig. 1: Formation of Ibuprofen-DEAE Dextran conjugates/crystanules (Abioye, **Kola-Mustapha** & Ruparelia, 2014).

Furthermore, we sought to elucidate the impact of conjugation on pre-compression, solubility, dose distribution and release properties of ibuprofen (Abioye, **Kola-Mustapha** *et al*., 2014). We discovered that the initial step of melt-*in situ*-granulation-crystallization resulted in a lesser solubility compared with the uncomplexed ibuprofen, but the final conjugate crystanules demonstrated an increased solubility value. In the same manner, Ddex conjugation increased the *in vitro* ibuprofen release rate (Fig. 2). Artificial neural networks showed an excellent correlation between predicted and experimental data in solubility and dissolution. In addition, particle rearrangement was improved in the crystanules. Overall, Ddex conjugates of Ibuprofen exhibited a better pre-compression profile than pure ibuprofen.

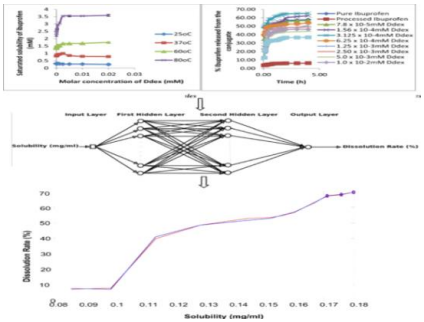

Fig. 2: Solubility, percentage release, and dissolution profile of ibuprofen-Ddex conjugate (Abioye, **Kola-Mustapha** *et al*., 2014).

Mr. Vice-Chancellor, what started with the problem of poor water solubility of ibuprofen led to the development of a polymer-drug conjugate specifically with cationic diethylaminoethyl dextran (Ddex). We did this without the need for toxic organic solvents commonly used in the mainstream production of pure ibuprofen. Furthermore, Abioye and **Kola-Mustapha** (2015) characterised the ibuprofen-Ddex conjugate granules via scanning electron microscopy (Fig.3), particle size analysis, Fourier-transform infrared spectroscopy (FT-IR), differential scanning calorimetry (DSC), and thermal gravimetry. Tests were carried out to determine granule flow rate, moisture content, pre-compression indices such as compressibility index and Hausner ratio, tablet characterisation after compression, and dissolution kinetics. Surface morphology characterisation results (Fig. 3) showed that the ibuprofen-Ddex conjugates exhibited plate-like agglomerates that were well-defined and non-symmetrical in shape, unlike pure ibuprofen with a regular surface. These traits aided the compressibility of the modified ibuprofen, increasing the propensity to consolidate in tabletting (Wong & Pilpel, 1990).

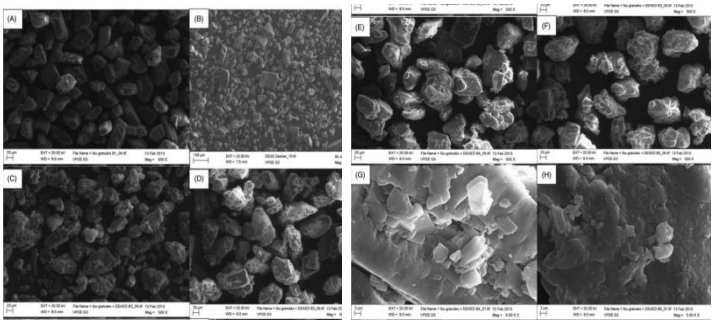

Fig. 3: Scanning electron micrographs showing the surface characteristics of (A) pure ibuprofen sodium crystals; (B) pure Ddex; and ibuprofen sodium–Ddex conjugate granules at weight ratios (C) 1:0.03125; (D) 1:0.0625; (E) 1:0.25; (F) 1:0.5 and plate-like surface characteristics (5000 magnification) at (G) low Ddex concentration and (H) high Ddex concentration, respectively (Abioye and **Kola-Mustapha,** 2015).

Taking a step further, our next objective was to optimise ibuprofen formulation via another approach distinct from the earlier described wet granulation method in ibuprofen-Ddex conjugates as presented in Table 1. Here, we developed ibuprofen-DEAE-Dextran nanoconjugates by surfactant solubilization.

Table 1: Physicochemical properties of Ibuprofen-DEAE-Dextran nanoconjugates (mean ± SD, n = 6)

Formulation	Conjugation Efficiency (%)	Conductivity (mS/cm)	Surface tension (N/m)	Viscosity (mPaS)	Absorbance/Transmittance	Particle size (nm)	Polydispersity Index	Zeta Potential (mV)
IbTw80-control	-	2.43±0.07	47.25±1.22	2.39±0.05	0.075±0.001	2872.12±128.9	0.67±0.08	-7.251±1.3
IbD1Tw80	90.26±0.95	3.16±0.02	38.30±1.00	3.04±0.01	0.056±0.002	122.17±4.65	0.37±0.02	3.45±0.2
IbD2Tw80	90.26±1.03	4.76±0.03	39.68±1.04	4.01±0.02	0.047±0.004	104.08±4.99	0.37±0.01	3.30±0.46
IbD3Tw80	89.05±0.91	6.25±0.04	37.78±1.09	5.09±0.02	0.033±0.003	19.92±1.59	0.32±0.04	1.84±0.12
IbD4Tw80	91.30±1.35	10.40±0.08	40.65±0.39	7.57±0.03	0.033±0.003	13.02±0.92	0.16±0.14	1.37±0.16
IbD5Tw80	96.34±1.46	12.78±0.04	39.58±0.81	11.83±0.16	0.030±0.003	13.02±1.19	0.15±0.14	1.02±0.21

With this, we observed that the nanoconjugate exhibited surface activity and high probability of reducing the surface free energy which could enable increased solubility. Additionally, we were able to achieve high loading capacity and reduced particle size of ibuprofen (**Kola-Mustapha** & Abioye, 2015). From this study, we were able to conclude that the ibuprofen-DEAE-Dextran nanoconjugate possessed preferred properties in drug release when compared with pure ibuprofen (Fig. 4).

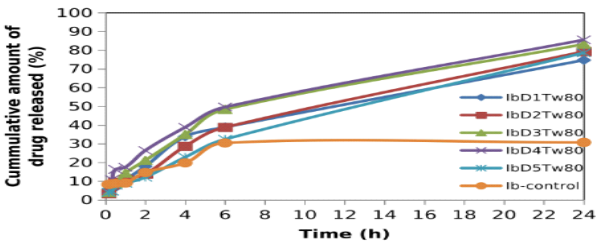

Fig. 4: Release profile of ibuprofen from DEAE-Dextran nanoconjugates. Each data point represents mean ± SD (n = 4) (**Kola-Mustapha** & Abioye, 2015).

Polymeric film coatings offer another option in drug development, especially in sustained drug release and masking unpleasant drug taste. Generally, they are used for enhancing the appearance of a product, protecting the API and modifying its release (Bruce *et al*., 2011; Pearnchob *et al*., 2003). Polymeric films can be prepared in organic or aqueous solvents, but the latter is preferred because it is safer, less expensive and environmentally friendly. The development of aqueous systems is however plagued with the challenge of coalescence between polymer and particle which affects the long-term release of the drug. **Kola-Mustapha** *et al*. (2016) sought to improve the integrity of aqueous polymeric films via the use of polyelectrolyte complex. This method entails the use of the drug as a functional crosslinking structure with other components in the system, thereby modifying its biopharmaceutical properties. We developed a formulation of Ddex-Ibuprofen-gellan ternary nanoconjugate as nanomatrix films for sustained ibuprofen delivery.

Gellan is a ***natural*** polysaccharide produced by *Pseudomonas elodeac* , which produces a negative charge in water. It is a suitable agent for film formation because it is biocompatible and produces films with net negative charges. Drug loaded aqueous nanomatrix film was developed by a controlled interaction between the positively charged protonated amino functional group of Ddex and the negatively charged carboxylate ions of ibuprofen, and *in situ* ionic crosslinking of gellan nanomatrix films (Hadgraft & Valenta, 2000). Results from this research effort showed that drug loading capacity and conjugation efficiency increased with increasing Ddex concentration. This increased loading capacity may be attributed to hydrophobic and ionic interactions between ibuprofen and constituent polymers. Morphological examination of the developed nanomatrix films showed that the surface of the plain gellan film was smooth, homogeneous and transparent- a good quality in improving appearance of the final drug product. On introduction of Ddex in conjugation, the surface began to exhibit opaque and rough features, and the opacity increased with additional Ddex. Some of the nanoconjugates also grouped

together to form fluffy aggregates (Fig. 5) which increased with additional levels of Ddex either due to the increase in adhesiveness or non-electrostatic interaction.

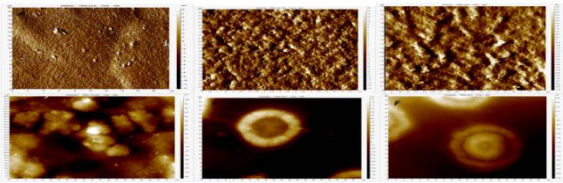

Fig. 5: Atomic Force Microscopic images of ibuprofen-loaded ternary nanomatrix films A. pure ibuprofen powder; B. surface of ibuprofen-loaded gellan film; C. cross section of ibuprofen-loaded gellan film; D. Ddex-ibu-gellan nanomatrix films E. at low and F. high concentrations of Ddex (**Kola-Mustapha** *et al*, 2016).

Results of *in vitro* drug release studies showed that ibuprofen-loaded gellan film had a higher drug release of 71.53 ± 2.05 % compared with 54.97 ± 1.24 % from pure ibuprofen. This increase in release may be attributed to the hydrophobic interactions between the drug and polymer which enhanced the wettability of ibuprofen. A similar experiment by Mallick *et al* (2008) also reported an increase in ibuprofen dissolution rate from 46 % to 77 % when mixed physically and 89 % by melt dispersion with silicon dioxide (Mallick *et al*., 2008; **Kola-Mustapha** *et al*., 2016). Summarily, we were able to develop optimized ibuprofen conjugate polymeric films with increased loading capacity and efficiency in dissolution.

While polymeric nanoconjugates are useful in enhancing the delivery of poorly soluble drugs, synergism with hydrotropic complexation resulted in a marked increase in drug release (**Kola-Mustapha** & Abioye, 2018). The synergism of polymer-drug self-assembly and hydrotropic complexation led us to develop a ternary ibuprofen-DEAE-Dextran-nicotinamide nanoconjugates. Analysis of this reformed ibuprofen showed that the size of the drug particles had significantly reduced, with low repulsion stabilisation. We obtained spherical surface morphologies and FTIR (Fig. 6) showed that amide functional

group was formed via hydrogen bonding, electrostatic, and hydrophobic interaction between ibuprofen and the polymer.

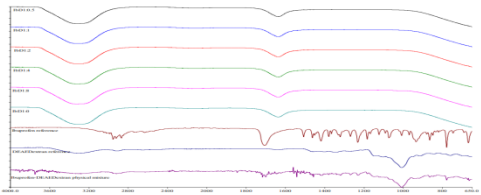

Fig. 6: The FTIR spectra of ibuprofen-DEAE-Dextran nicotinamide nanoconjugates, ibuprofen control, ibuprofen reference, DEAE-Dextran-reference and ibuprofen-DEAE-Dextran physical mixture (**Kola-Mustapha** & Abioye, 2018).

Vice-Chancellor, Sir, what if we could try a different polysaccharide?

Abioye, Armitage and **Kola-Mustapha** (2015) tested chitosan by developing an amorphous nanoparticle complex with ibuprofen. We confirmed intermolecular attraction by FTIR spectroscopy, and conductivity measurements. Results showed a significant affinity between chitosan and ibuprofen. Compared to pure ibuprofen, the formed nanoplexes exhibited fast and extended-release profiles, with the major means of drug release being diffusion, amidst the occurrence of anomalous transport and super case II transport.

Further to these, the natural excipient, gellan was also found to be useful in topical formulations to enhance the external delivery of poorly soluble molecules. **Kola-Mustapha** and Abioye (2016) formulated a hydrogel without the use of crosslinkers, based on the interaction between the gellan gum and oppositely charged DEAE-Dextran. This three-dimensional hydrophilic polymeric network (hydrogels) can absorb huge amounts of water or biological fluids, giving them the appearance of biological tissues (Peppas & Mikos, 2019). The homopolymers or copolymers that make up the polymeric networks are rendered insoluble by the presence of physical or chemical crosslinks. Chemical hydrogels are created through covalent crosslinking, which is irreversible. If a drug is added

before the crosslinking process, the crosslinker may compromise the integrity of the drug contained since crosslinking reagents, such as glutaraldehyde and epichlorohydrin, are hazardous in tiny amounts (Hennink & Nostrum, 2002). Therefore, we sought to develop and characterize a novel polyelectrolyte complex hydrogel from gellan gum and DEAE-Dextran with potential use in transdermal drug delivery (**Kola-Mustapha** & Abioye, 2016). Again, the complementary utilisation of synthetic and natural components in advancing drug delivery saves the day.

Piroxicam is another prominently prescribed NSAID with poor solubility properties in water. With this drug, Tella, Eliagwu, …, **Kola-Mustapha** *et al* (2020) tested another mechanism in optimizing delivery in the body using a novel class of viable hybrid materials called metal-organic frameworks (MOFs). They are made up of organic bridging ligands and metal connecting sites (Tella & Aaron, 2012). Due to their relatively labile metal-ligand bonds, MOFs have many desirable properties as drug carriers, such as large pore sizes and exceptionally high surface areas for drug encapsulation, intrinsic biodegradability, and versatile functionality for post-synthetic grafting of drug molecules (Huxford *et al*., 2010). Because the framework's functional groups and pore size may be tuned, MOFs can be thought of as good drug delivery systems (Huxford *et al*., 2010). In our study, Tella, Eliagwu, …, **Kola-Mustapha** *et al* (2020) piroxicam was successfully loaded on to Zinc and Copper Metal-Organic Frameworks. They were further tested for solubility, drug release, and dissolution properties (**Kola-Mustapha** *et al*, 2020). Results showed that Zn MOFs had the highest release for piroxicam.

Vice-Chancellor, Sir, synthetic drugs are inherently imperfect and may often require special formulation processes in optimising delivery. Some of these optimisation processes involve the use of natural products such as gellan and chitosan as seen with some of our work with ibuprofen. These drug delivery research efforts to advance the application of existing drug molecules is a continuous quest for me, the objective is to have some of the mentioned techniques integrated into the Nigerian local pharmaceutical scene in the nearest future.

Usefulness of Natural Products

Mr. Vice-Chancellor, nature has blessed humans with a countless number of plants with effective phytochemicals for managing various illnesses. Sometimes, one single plant may even be useful in two or more diseases; the bark may be used for disease A, the leaves for disease B, and the root for disease C. In parallel with working on synthetic medicines, I have also peered into the bioactivity of natural plants and their potential benefits for patients.

In Nigeria, there is an increasing interest in natural medicines, especially herbal formulations across all age groups. Ghazali, Bello and **Kola-Mustapha**, (2019) carried out a study to determine the use of herbs among outpatients at the University of Ilorin Teaching Hospital, and we realised that all patients knew about herbal medicines; 67.8% used them, and 25% were currently taking herbs. Over half did not follow specific dosing, many combined herbs with additives or synthetic drugs. About 67% reported illness resolution, 13% no effect, and 20% temporary relief. This study highlights widespread herbal medicine use, often alongside conventional treatments, underscoring the need for standardised dosing, safety evaluation, and integration strategies in Nigerian healthcare.

Kola-Mustapha *et al* (2023) carried out a study in Kwara State among traditional medicine practitioners to obtain a list of herbal therapies used in managing sickle cell disease in the state. Working with 37 traditional medicine practitioners as study participants, we gathered the following list of plants (Table 2) identified as sickle cell disease therapies. This highlights how nature's vast local botanical resources can be identified and channeled to address sickle cell disease, which remains a significant public health challenge in Nigeria.

Table 2: Plants identified for use in sickle cell disease therapies

Local name	Botanical name	Common names	Family name	Voucher Numbers from Authentication
Mafowokanomomi	*Alstonia boonei*	Starbur, Bristly starbur	Asteraceae	UILH/005/1153/2022
Emi isu	*Bryophyllum prinatum*	Goat weed	Asteraceae	UILH/021/140/2022
Alubosa elewe	*Allium ascalonicum Linn.*	Wild onion	Amaryllidaceae	UILH/011/1335/2022
Ahun	*Alstonia boonei*	Stoolwood, Pattern wood	Apocynaceae	UILH/006/1035/2022
Abamoda	*Bryophyllum prinatum*	Air plant, Life plant	Crassulaceae	UILH/019/909/2022
Pawpaw	*Carica papaya*	Pawpaw	Caricaceae	UILH/001/945/2022
Ewe rere abo	*Cassia occidentalis*	Coffee senna, Antbush	Fabaceae	UILH/015/885/2022
Ogede odo	*Crinum jargos*	Crinum Lily	Amaryllidaceae	UILH/003/1022/2022
Egun eja (plant)	*Diospyros monbuttensis*	Yoruba ebony	Ebenaceae	UILH/009/013/886/2022
Abiwere	*Eragrostis tremula*	Japanese lovegrass	Poaceae	UILH/027/104/2022
Igi obo	*Erythrophleum guineense*	Ordeal tree, Sasswood tree	Fabaceae	
Oro adete	*Euphorbia poissoni Pax.*	Spurge	Euphorbiaceae	
Ipin	*Ficus exasperate*	Sandpaper tree, White fig tree	Moraceae	UILH/017/1296/2022
Owu akese	*Gossypium barbadense*	West Indian Cotton	Malvaceae	UILH/012/977/2022
Lapalapa	*Jatropha curcas Linn.*	Physic nut	Euphorbiaceae	UILH/020/978/2022
Odundun	*Kalanchoe crenata*	Never die	Crassulaceae	
Yewuru	*Luffa cylindrical*	Sponge gourd, Dishwash gourd	Cucurbitaceae	UILH/013/523/2022
Ege	*Manihot esculenta*	Manoc, Bitter cassava, Tapioca	Euphorbiaceae	UILH/018/1094/2022
Ogede	*Musa paradisiaca*	Banana	Musaceae	UILH/002/138/2022
Egbesi	*Nauclea Africana / Nauclea latifolia*	Nauclea African peach	Rubiaceae	UILH/016/1412/2022
Efinrin	*Ocimum basilicum*	Scent leaf, Balsam basil	Lamiaceae	UILH/004/1354/2022
Idi ipete	*Securidaca longepedunculata*	Violet tree	Polygalacea	UILH/008/192/2022
Tomati	*Solanum lycopersicum*	Love apple, Tomato	Solanaceae	UILH/010/1350/2022
Ewuro	*Vernonia amygdalina*	Bitter leaf	Asteraceae	UILH/007/1023/2022
Eru alamo	*Xylopia aethiopica*	African pepper, Guinea pepper	Annonaceae	UILH/014/1089/2022

The following herbals were studied by our team:

Hibiscus sabdariffa

Native to Asia and tropical Africa, *H. sabdariffa L.* belongs to the Malvacea family. It is named Roselle and famously known in our language as Zobo. Commonly served as a drink, *H. sabdariffa* is a nutraceutical with reported antioxidant, anti-hypertensive and hypocholesteromic activity (Onyenekwe *et al*., 1999; Hirunpanich *et al*., 2006; Inuwa *et al*., 2012). Phytochemical analysis of the aqueous extract of this plant showed the presence of phenols, saponins, tannins, glycosides, flavonoids and alkaloids. Evaluation of antioxidant and anti-inflammatory activity showed that *H. sabdariffa* had higher DPPH antioxidant activity than ascorbic acid, the standard. In our study, red blood cell membrane stabilisation assay and proteinase inhibition assay were utilised, *H. sabdariffa* extract exhibited a very significantly high protection (61.1 %) of the red blood cell and high proteinase inhibitory activity (Kambizi, Bakare-Odunola, …, **Kola-Mustapha**, *et al*., 2017). When tested for toxicity, the aqueous extract of *H. sabdariffa* calyces, there were no signs of acute toxicity at a single dose of 300 mg/kg, sub-acute toxicity results showed that there was a significant increase in total protein concentration. When administered for 90 days, a dose-dependent increase in urea concentration was observed (Njinga, **Kola-Mustapha,** *et al*., 2020).

Moringa oleifera

Belonging to the family Moringaceae, Moringa is a multipurpose medicinal plant with reported activities as an antifungal, anti-tumour, anti-ulcer, stimulant, anti-inflammatory and more. All parts of the plants are used in traditional medicine with different parts containing different phytochemical composition (Siddhuraju & Becker, 2003; Anwar *et al*., 2006). *M. oleifera* is also reported to contain tannins, glycosides, flavonoids, alkaloids, phenols and saponins. Kambizi, Bakare-Odunola, …, **Kola-Mustapha**, *et al*. (2017) analysis showed that *M. oleifera* leaf extract had 55.91 % hydrogen peroxide scavenging potential and a 29.35 % proteinase inhibitory activity.

Ocimum gratissimum

Part of the Lamiaceae family, *O. gratissimum* is a perennial shrub native to tropical Africa, Asia, and South America (Gupta *et al.*, 2011). The ethanolic extract of its leaves have been used traditionally in managing several ailments such as wound, skin, and urinary tract infections. Commonly known as African basil, clove basil, or wild basil and 'efirin', it is a spice used in cooking in various countries. Traditionally, it is reportedly used for the treatment of conjunctivitis, bronchitis, and as an anti-diarrhoea agent (Nweze & Eze, 2009). Phytochemical analysis of this plant showed the presence of fats and oil, sugars, terpenes, cyanogenetic glycosides, saponins, alkaloids and steroidal aglycone. *O. gratissimum* plant extract was also found to inhibit the growth of strains of *S. aureus*, *P. aeruginosa*, *P. mirabilis*, and *C. albicans* at a minimum concentration of 50 mg/mL of plant extract (Nweze & Eze, 2009). In our study, the leaf aqueous extract of *O. gratissimum* contained flavonoids as the highest constituent and phenols as the least. Kambizi, Bakare-Odunola, …, **Kola-Mustapha**..., (2017) also recorded a 69.34 % DPPH antioxidant activity and a 22.57 % proteinase inhibitory activity.

Telfairia occidentalis

Part of the Cucurbitaceae family, *T. occidentalis* is indigenous to the southern part of Nigeria, where it is commonly

used in cooking. Popularly known as 'ugwu', it is a common vegetable whose leaves have been traditionally used in anaemia, diabetes, and fatigue treatment. Oxidative stress, which is typically brought on by free radicals like superoxide anions, hydrogen peroxide, hydroxyl radicals, and nitric oxide, is the cause of many human diseases. These free radicals cause damage to macromolecules like proteins, lipids, and DNA through their reactions (Potterat, 1997). *T. occidentalis* has been reported for its antioxidant activity and can thus play a beneficial role in diseases that exhibit this characteristic cellular damage (Eseyin & Rathore, 2014). Researchers have also documented its antihyperglycemic activity (Aderibigbe *et al*., 1997; Eseyin *et al*. 2010). Kambizi, Bakare-Odunola, …., **Kola-Mustapha**, *et al*., (2017), *T. occidentalis* exhibited 71.66 % DPPH antioxidant activity and 57.85 % hydrogen peroxide scavenging potential, greater than *M. oleifera, O. gratissimum* and *H. sabdariffa*.

Integration in Drug Development and Formulation

Mr. Vice-Chancellor, I began this lecture with an illustration of an imagery that is prevalent in our minds when we talk about natural medicines used side-by-side with synthetic medicines. This common imagery sometimes limits the use of natural medicines even when they are efficacious for an ailment. I envision a future where synthetic and natural medicines are indistinguishable from each other, both appealing to the user, with efficacy and safety for use in patients. Such a future would entail the formulation of natural products as finished pharmaceutical products where herbal constituents are prepared in synthetic dosage forms such as emulgels, capsules and tablets. just as it is done in advanced parts of the world. In the most recent part of my research career, I have focused on expanding novel technologies in synthetic formulations to optimise natural medicines with proven efficacy.

Herbal Gels

Entandrophragma utile is a flowering plant commonly known as 'Igi jebo' in Yoruba. It is a part of the Meliaceae family and is widely prevalent in West Africa, including Nigeria. It has traditionally been used in various conditions such as sickle

cell illness, gastrointestinal ulcers, and ocular irritation (Jain *et al*., 2019; John & Onabanjo, 1990). Phytochemical analysis highlights the presence of tannins, saponins, flavonoids and phenols (Usman *et al*., 2018) in this plant. Despite reported activity, there is a paucity of data on the scientific study of its pharmacological benefits. In addition to testing its anti-inflammatory activity, we also sought to develop an emulgel of this plant as a topical dosage form for the management of inflammatory conditions. Using the carrageenan-induced rat paw model, we tested the anti-inflammatory property of *E. utile* and observed that a 100 mg/kg dose of the plant extract produced a 43.62 % inhibition of inflammation, while a higher dose of 200 mg/kg had a lesser inhibition of 15.96 %. The emulgel formulated from this plant had satisfactory physical properties with a minty odour characteristic of the extract. Spreadability results were satisfactory, with a small amount of shear. The emulgels had good extrudability, and when tested on a chronic inflammation animal model (Fig. 7), treatment resulted in a dose-dependent effect. The emulgels were comparable with the standard diclofenac emulgel in efficacy. This experiment provided a useful rationale for the integration of natural medicines in synthetic formulation methods (**Kola-Mustapha** *et al*., 2023).

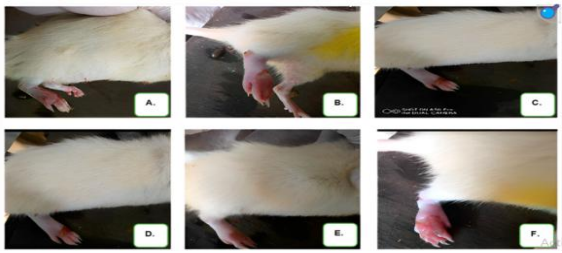

Fig. 7: Image showing the effect of the treatments (with the formulated herbal emulgel) on CFA-induced inflammation in the rats; A. EUE1, B. EUE2, C. EUE3, D. EUE4, E. EUE5, (F)-DIC]. - EUE: *E. utile* DIC: Diclofenac

Nevertheless, essential oils are aromatic compounds obtained from various parts of plants and are usually very

volatile. *Melaleuca alternifolia* and *Cymbopogon flexuosus* are common essential oils with proven activity against various microorganisms. *Melaleuca alternifolia* (tea tree) oil is obtained from the leaves of the plant by steam and vacuum distillation processes. Major components in tea tree oil include: Terpinen-4-ol, Viridiflorol, Limonene, Sabinene, Ledene, Globulol, δ-Cadinene, Aromadendrene, p-Cymene, 1, 8-Cineole, Terpinolene, α-Terpineol, α-Pinene, α-Terpinene, and γ-Terpinene (Lam *et al*., 2020). Tea tree oil has shown multiple activities as a biocidal agent, an anti-inflammatory agent or an antitumoral agent (Swords & Hunter, 1978). *Cymbopogon flexuosus,* also known as lemongrass, produces an essential oil with citral as the main bioactive component. Its activity is reported across various microbes' species. For example, Silva *et al.* showed that lemongrass essential oil is effective in inhibiting Candida species (Silva *et al*., 2008). Other studies have also shown the activity of lemongrass essential oil against bacteria such as *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, and more (Zouhir *et al*., 2016; Naik *et al.*, 2010).

In our study, we sought to combine both essential oils in developing a synergistic formulation for the treatment of vulvovaginal candidiasis (**Kola-Mustapha** *et al*., 2023). Candidiasis is a prevalent opportunistic infection that affects immunocompromised persons as well as fully healthy persons. Vulvovaginal candidiasis is characterised by vagina inflammation due to the Candida fungi. It is quite prevalent, affecting about 70 % of women at least once in their reproductive years. Preliminary results of the antifungal activity of these essential oils show efficacy with minimum inhibitory concentrations ranging from 50 to 100 µL/mL for *M. alternifolia* oil and 25 to 100 µL/mL for *C. flexuosus* essential oil. When combined to form an emulgel preparation, we observed a synergistic effect, resulting in better activity against the implicated fungi. When applied against *C. albicans* in this study, the emulgel diffused to release the essential oil components (Fig. 8). The formulation was also stable and showed satisfactory characteristics for vagina use (**Kola-Mustapha**, *et al*., 2023).

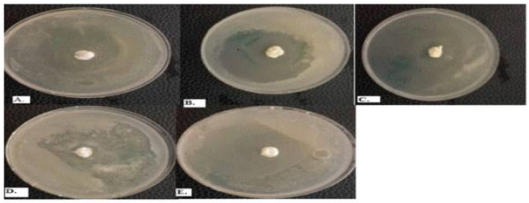

Fig. 8: Antifungal activity of emulgel formulations as presented by zones of inhibition A. *Melaleuca alternifolia* emulgel; B. *Cymbopogon flexuosus* emulgel; C. combination of *Melaleuca alternifolia* and *Cymbopogon flexuosus* emulgel; D. 1% clotrimazole emulgel (positive control); E. emulgel only in DMSO (negative control) (**Kola-Mustapha**, Aliu *et al*., 2023).

In another research, **Kola-Mustapha**, Abdulrahman and Ishola (2023) sought to develop *Arctium lappa* root extract-based emulgels for the potential management of chronic inflammatory disorders. *A. lappa* is utilized in multiple continents for the treatment of chronic inflammatory conditions. It is reported to be beneficial in managing pain from rheumatoid arthritis (Zarei *et al*., 2017), but it is linked to unfavourable side effects after oral use. **Kola-Mustapha**, Abdulrahman and Ishola (2023) developed an emulgel system with the ethanol extracts of the roots of *Arctium lappa* using liquid paraffin for the oil phase and purified water for the aqueous phase (Table 3). Characterization results showed that the herbal emulgels had glossy appearance, cream colour and would be easy to apply to the skin. The extract was quite compatible with the emulgel, and there was no separation of constituents. When tested for activity, the herbal emulgel produced significant results in anti-inflammatory activity. We also achieved good spreading coefficient and desirable viscosity for this dosage form (**Kola-Mustapha** *et al*., 2023).

Table 3: Composition of emulgels from ethanol extract of *Arctium lappa* root

	Emulgels (%w/w)			
Ingredients	F1	F2	F3	F4
A. lappa extract	0.00	0.50	1.00	1.5
Carbopol 940	1.00	1.00	1.00	1.00
Liquid paraffin	7.50	7.50	7.50	7.50
Span 20	1.00	1.00	1.00	1.00
Tween 20	0.50	0.50	0.50	0.50
Propylene glycol	5.00	5.00	5.00	5.00
Ethanol	2.50	2.50	2.50	2.50
Ethyl paraben	0.01	0.01	0.01	0.01
Methyl paraben	0.03	0.03	0.03	0.03
Glutaraldehyde	0.50	0.50	0.50	0.50
Clove oil	–	–	–	10.00
Mentha oil	–	6.00	–	–
Purified water	q.s	q.s	q.s	q.s

Mr. Vice-Chancellor, there is a high prevalence of rheumatoid arthritis in our society, especially among the elderly, and we must consider natural remedies in pain and inflammation management. This motivated my colleagues and I to consider more plants (with verifiable potentials) for formulation into an emulgel for easy use and application by patients.

Terminalia macroptera is a plant specie from the Combretaceae family. It is known in Hausa as 'kwandari' and is easily found in Nigeria, Ghana, Senegal, the Benin Republic, and Burkina Faso (Ibrahim, 2005). Various parts of the plant have been reportedly used for treating ailments such as hepatitis and ringworm. It has also been tested to possess antimicrobial activity (Silva *et al*., 1997; Usman *et al*., 2017). Walking you through the research process, we started with plant collection with authentication by the Herbarium Unit of University of Ilorin's Department of Plant Biology.

Kola-Mustapha *et al*. (2023) extracted the stem bark with ethanol and characterised it for physical properties such as pH, odour and colour. We carried out phytochemical analysis to determine its composition, using both qualitative tests to determine presence and quantitative tests to determine composition. We then conducted an assay of the anti-inflammatory activity of the extract before proceeding to emulgel preparation. We tested the formulated emulgels for physical characteristics (Table 4) such as organoleptic properties, extrudability, spreadability, pH, viscosity, swelling index, and skin irritation test. This was followed by testing the formulated emulgel to see if it was as

effective as the raw extract and to what extent. Results showed that the emulgel had comparable activity with the standard drug, diclofenac, and the product showed potential in the treatment of rheumatic arthritis (**Kola-Mustapha** *et al*., 2023).

Table 4: Physical characterization of emulgels

Emulgels	Appearance	Colour	Odour	Ease of application	Ease of removal	Homogeneity
TME1	Glossy, less viscous	White	Characteristic odour	Very easily applied	Very easily removed	Homogeneous
TME2	Glossy, viscous	Cream	Characteristic with bark odour	Very easily applied	Very easily removed	Homogeneous
TME3	Glossy, viscous	Light brown	Characteristic with bark odour	Very easily applied	Very easily removed	Homogeneous
TME4	Glossy, viscous	Caramel brown	Characteristic with bark odour	Very easily applied	Very easily removed	Homogeneous
TME5	Glossy, viscous	Brown	Characteristic with bark odour	Very easily applied	Very easily removed	Homogeneous
TME6	Glossy, viscous	Cream	Bark with aromatic odour	Very easily applied	Easily removed	Homogeneous
TME7	Glossy, viscous	Dark brown	Bark with aromatic odour	Very easily applied	Easily removed	Homogeneous
TME8	Glossy, viscous	Cream	Bark with minty odour	Very easily applied	Easily removed	Homogeneous
TME9	Glossy, viscous	Reddish brown	Bark with minty odour	Very easily applied	Easily removed	Homogeneous
TME10	Glossy, viscous	Cream	Bark with minty and aromatic odour	Very easily applied	Easily removed	Homogeneous
TME11	Glossy, viscous	Reddish brown	Bark with minty and aromatic odour	Very easily applied	Easily removed	Homogeneous

Mr. Vice-Chancellor, pain is a global phenomenon. From headaches to the bone strains, the extent of discomfort suffered in pain demands the production of better analgesic formulations. Based on this reality, we developed another plant-based dosage form for its analgesic and anti-inflammatory properties (**Kola-Mustapha**, *et al*, 2020). *Chasmanthera dependens* and *Chenopodium ambrosioides* are plants reported to be useful in treating pain and have been used by traditional bone setters (Ehiabhi, 2012). Leveraging on these prospects, an efficacious herbal gel was developed with desirable physical and pharmacological (Fig. 9) features. The gels were easy to apply and easy to remove with a characteristic minty smell.

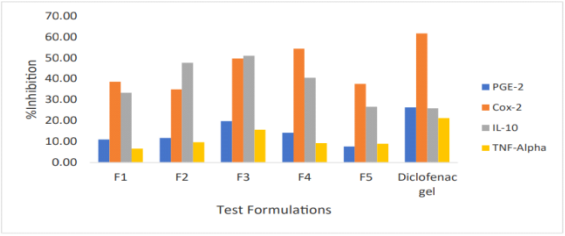

Fig. 9: Percentage inhibition of herbal formulations and diclofenac gel against pain biomarkers.

Kola-Mustapha and Khalid-Salako (2021) developed another emulgel for the management of rheumatoid arthritis using *Cola millenii* ('obi Edun' in Yoruba or 'uto' in Igbo) stem bark ethanol extract. The formulated emulgel (Table 5) exhibited a dose-dependent activity comparable to standard diclofenac emulgel with good pH and extrudability values, and a notable ease of spread.

Table 5: Formulation of emulgel from ethanol extract of *Cola millenii* stem bark

Ingredient	Emulgel Formulations (%$^{w}/_{w}$)			
	E0	E1	E2	E3
Cola millenii extract	0.00	0.50	1.00	1.50
Ethanol	2.50	2.50	2.50	2.50
Span 20	1.00	1.00	1.00	1.00
Tween 20	0.50	0.50	0.50	0.50
Methyl paraben	0.03	0.03	0.03	0.03
Propylene glycol	5.00	5.00	5.00	5.00
Light liquid paraffin	7.50	7.50	7.50	7.50
Mint oil	5.00	5.00	5.00	5.00
Carbopol 940	1.00	1.00	1.00	1.00
Purified water	100.00	100.00	100.00	100.00

If all these plants are not familiar, then you should know *Zingiber officinale* Rosc., also known as ginger, and *Ocimum basilicum* L., also known as Basil. With the essential oils of these two plants, we developed an oral gel for the management of oral candidiasis. Oral candidiasis is a fungal infection that occurs in about 5-7 % of infants and 20 % of persons with cancer (Lalla & Dongari-Bagtzoglou, 2013). Many antifungal oral preparations in the market have some drawbacks, such as antimicrobial resistance. As a result, new and effective preparations for the disease are necessary to improve patient outcomes. Ginger and basil are common plants accessible to many with little cost compared to synthetic medicines. Therefore, we decided to test and see if they could provide some benefits in helping patients with oral candidiasis. On testing against *Candida albicans*, **Kola-Mustapha**, *et al*. (2020) observed that the diameter of the zone of inhibition ranged from 23.00 ± 1.70 to 32.00 ± 1.67 mm for *Z. officinale* and 22.00 ± 1.57 to 26.00 ± 2.08 mm for *O. basilicum.* When combined, the

highest activity was seen at a ratio of 25:75 for ginger and basil essential oils. After formulation, the emanating herbal gel was effective in inhibiting the growth of *Candida* and has been recommended for extensive tests and subsequent clinical trials.

Herbal Creams

Creams are one of many types of topical semi-solid formulations. Consisting of two phases, the aqueous phase and the oily phase; creams may contain the active ingredient dispersed in any of the phases. *Ceiba petandra* is a popular plant in Nigeria known as the Kapok tree in English, Akpu-ota in Igbo, Vamber in Tiv, Riimaayee in Hausa, and Ogungun, Araba in Yoruba. Traditionally, it is used in diabetes treatment, as a laxative and even in oedema. In many African countries, its bark and stem are used for relieving asthma, diarrhoea and wash sores (Burkill, 2000). *Lannea kerstingii* (Anacardiceae family), locally known as 'tudi' in Hausa, is used traditionally in curing haemorrhoids and externally for ulcers and sores. Combining both extracts, Aremu, **Kola-Mustapha** and Ayotunde (2017) developed a cream using aqueous cream base and evaluated its properties and efficacy. Results showed that the product was also stable at 25 and 40 ˚C for concentrations at 0.4 %w/w for *L. kerstingii* and 0.8 %w/w for *C. petandra*.

Herbal Suspensions

Mr. Vice-Chancellor, our natural flora remains an endless source of medicines in managing our ailments. Diarrhoea is a leading cause of death among children and adults in Nigeria. Defined as "the passage of three or more loose or liquid stools per day or more frequent passage than is normal for the individual", it can occur as a symptom of another disease or may sometimes present in individuals without any underlying condition. **Kola-Mustapha** *et al* (2019) identified a plant with reported activity in managing diarrhoea, *Parquetina nigrescens* (Pn), a plant native to various parts of Africa and traditionally used to treat diarrhoea. It is often prepared as a decoction or infusion and drunk directly. We aimed to develop a standardised

oral suspension for the consumption of this medicinal plant to aid dosing and guarantee safety after use. A ‘super suspension’ (with minimal tendency for sedimentation due to structured internal layers) was prepared with synthetic and naturally sourced excipients. The pharmacological action of the suspension in stool control in test animals is presented in Table 6.

Table 6: Pharmacological activities of the suspensions of methanol extract of *Parquetina nigrescens*

Test animals	Group I (suspension 5 mg/kg)	Group II (suspension 200 mg/kg)	Group III (positive control)	Group IV (negative control)
Rat 1	2 loose stools	1 loose stool	3 loose stools	4 loose stools
Rat 2	3 loose stools	2 loose stools	3 loose stools	4 loose stools
Rat 3	2 loose stools	1 loose stool	4 loose stools	4 loose stools

Herbal Suppositories

Vice-Chancellor Sir, you would be pleased to know that herbal products can be formulated into other dosage forms as well, depending on the intended means of administration. One example is suppositories. Suppositories are external formulations designed to deliver one or more actives into local or systemic circulation through the rectum (rectal suppository) or vagina (vaginal suppository) by melting or dissolving (Lam *et al*., 2020). *Nigella sativa*, also known as black cumin, belongs to the Ranunculaceae family and is shown to have beneficial properties in treating cough, fever, influenza, etc. Some studies also support its use as an antimicrobial (Khan *et al*., 2003). **Kola-Mustapha** *et al*. (2021) extracted black seed oil, characterised and determined its antifungal activity. We proceeded to formulation by the fusion method using cocoa butter and shea butter (both containing 5% beeswax) as the suppository bases. Thereafter, we evaluated the formed suppository (Fig.10) and determined its final antifungal activity.

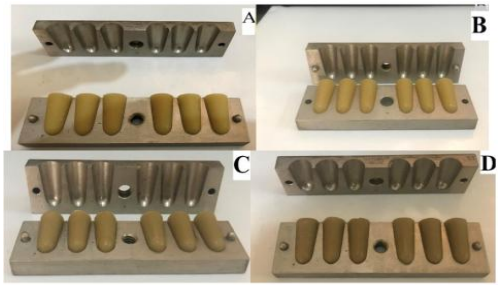

Fig. 10: Appearance of *N. sativa* vaginal suppositories: A. F1 (Suppository base- Cocoa butter, Natural product- Commercial oil), B. F2 (Suppository base- Shea butter, Natural product- Commercial oil), C. F3 (Suppository base- Cocoa butter, Natural product- Methanol extract), D. F4 (Suppository base- Shea butter, Natural product- Methanol extract) (**Kola-Mustapha**, Bamigboye *et al*., 2021).

Novel Drug Delivery

Central to the theme of natural and synthetic medicine integration is the design and development of novel drug delivery systems that enable the co-utilisation of both medicines either for synergistic impact or for supporting the activity and appeal of either, to the consumer. Evident in this lecture is the recurrent thread of nanomedicine, whether it is the mention of nanoconjugate or the mention of nanomatrix films. The terminology defines itself, because nanomedicine entails the use of nano-sized (10^{-9}) materials or the formulation of nanoscale products. Its relevance stems from the significant differences in the properties of materials at the nanoscale compared to normal scales. In other words, the properties of a material change when its size is reduced to the nano level. As a result, it is important to re-characterize such material at this level to ascertain behaviour and performance in absorption, distribution, metabolism, excretion and toxicity. Since the poor solubility of drugs is a common concern in drug development, nanomedicine offers a great benefit in solving this problem through nanoconjugates. An amorphous polymer-drug nanoconjugate is a hybrid of an active drug physically or chemically linked to a polymer from which it can be cleaved for release in the biological system (Abioye, Chi, **Kola-Mustapha** *et al*. 2016). This dosage form enhances the

solubility and bioavailability of poorly soluble drugs and can also contribute to reducing dosing and undesired side effects (Caron *et al*., 2011). Nanoconjugates have been successful in reaching the market since the 1990s and can be developed through different methods. Despite the level of progress in research seen so far (Fig. 11), there is still room for the use of this drug delivery system across various ailments.

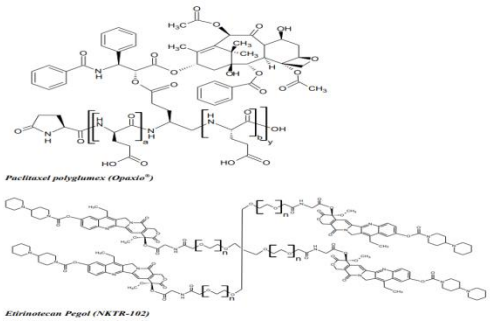

Fig. 11: Chemical structure of A. PGA-paclitaxel conjugate (Opaxio®) and B. PEG-Irinotecan conjugate (Etirinotecan pegol®)

The model for the rational design of polymer-drug nanoconjugates consists of five components, including a polymer carrier (natural or synthetic), a bioactive molecule (preferably low-weight and hydrophobic), a targeting group, a solubilizing group, and a bio responsive spacer. Ideally, the polymer should be biocompatible and biodegradable for easy excretion. The selection of a polymer and conjugation technique plays critical roles in the successful design of nanoconjugates (Abioye, Chi, **Kola-Mustapha** *et al*., 2016).

Another nano approach of interest is the use of nanocellulose and hydrophilic metal oxide composites. Cellulose is abundant in plants and can form strong hydrogen bonds with water, which makes it insoluble in water. Nanocellulose is obtained from cellulose by various methods such as mechanical disintegration, chemical treatment, or hydrolysis (Panateiscu *et al*., 2016; Nechyporchuk *et al*., 2016). Micro fibrillated, nano fibrillated cellulose or cellulose nanofibrils are obtained by

mechanical treatment, while cellulose nanocrystals or 'nano whiskers' can be obtained by acid hydrolysis. Metallic nanoparticles are a class of nanoparticles that can also form conjugates with polymers and exhibit some biological activity. Metal oxide nanocarriers can encapsulate therapeutic substances and help improve drug delivery. The hybridization of cellulose nanofibers together with metal oxide nanoparticles generates materials with improved properties. Olatunji, Saliu, **Kola-Mustapha** *et al*. (2017) studied the delivery of tramadol hydrochloride by regenerated cellulose nanofiber-TiO_2-ZnO composites. The regenerated cellulose/metal oxide hybrid allows for the extension of the application of cellulose polymer for enhanced antibacterial properties, biological activity, photocatalysis and drug release (Wang *et al*., 2014). Combined with tramadol, we aimed to develop a swellable hydrogel matrix for the sustained release of the active to enhance compliance and reduce habit-forming. Drug release kinetic studies showed that the composite with the least portion of ZnO and TiO_2 had the highest release percentage of tramadol. As their amount increased, the drug release slowed down and was sustained.

Nanodrug delivery is important for its ability to enhance the delivery of drugs to specific sites in the body. Conventional medications are often limited in their ability to cross the blood-brain barrier, and this is, in most cases, beneficial to prevent side effects on the brain. However, in the treatment of brain conditions, the drugs must be able to get to the brain. Hence, there is a need for nanodrug delivery systems that can bypass the brain's barriers in the treatment of diseases such as Parkinson's, Alzheimer's and others (**Kola-Mustapha**, Adedeji *et al*., 2023).

Nanotechnology has also been shown to be useful in enhancing the viability of *Lactobacillus* spp., a common probiotic for vaginal candidiasis (Ilomuanya, Ogundemuren, … **Kola-Mustapha** *et al*., 2024). Via the electrospun nanofiber-based delivery system, we were able to develop *Lactobacillus*-loaded nanofibers that did not cause any irritation to animal subjects and preserved the viability of the bacteria.

Computational Drug Analysis

Vice-Chancellor, Sir, the world is digital, and research processes are quickly evolving with novel computational tools that improve output and offer useful insights. In the past decades, it was impossible to know if a drug would work for a particular disease without testing it on an animal model. Nowadays, there are software that can predict the activity of a compound *in vivo* and its supposed safety and toxicity effects, and you can do all of this from the comfort of your office without entering the laboratory. However, additional laboratory tests are useful to validate computational results and enhance research robustness.

A **naturally occurring** phenolic chemical, eugenol is well known for its varied biological activity and pharmacological characteristics. Numerous plants contain it in large quantities, and one of its main natural sources is cinnamon oil. Because of its analgesic, anti-inflammatory, antioxidant, and antibacterial qualities, eugenol has long been used extensively in traditional medicine. Its wide range of biological activities has attracted a lot of interest in biomedical research, especially when it comes to creating new therapeutic agents to treat infectious disorders (Nagappan *et al*., 2019; Batool *et al*., 2019).

DNA gyrase is an important enzyme in bacterial DNA multiplication and is, thus, a target for antibacterial treatment. Given their proven antibacterial action against a variety of bacterial infections, including both gram-positive and gram-negative bacteria, eugenol and its derivatives have attracted a lot of attention in this regard (Nazzaro *et al*., 2013). However, compared to well-known antibacterial drugs, eugenol's comparatively low binding affinity to DNA gyrase limits its therapeutic efficiency (Zhang *et al*., 2018).

Computational drug analysis leverages digital tools to predict a compound's activity, safety, and toxicity without immediate laboratory testing, enhancing research efficiency. Using this approach, Elsewedy, Alshehri, **Kola-Mustapha** *et al*., (2024) designed structural derivatives of eugenol, a natural phenolic from cinnamon oil, with improved antibacterial activity against DNA gyrase, a key bacterial enzyme. Molecular docking and dynamics simulations identified Compound 24 as a

promising candidate with electrostatic binding interactions with GLU50 and alkyl interactions with VAL167, VAL43 and ILE78 (Fig. 12). This study highlights the value of computational methods in drug design and the potential to develop novel therapeutics from natural compounds.

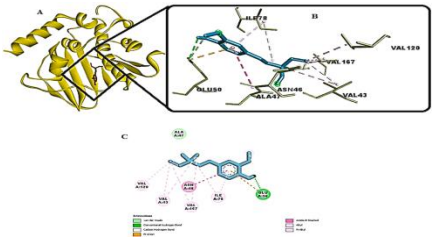

Fig. 12: (a) Compound 24 within the binding pocket of DNA gyrase (5MMN) (b) 2D and (c) 3D chemical interactions of compound 24 within the druggable pocket of DNA gyrase (5MMN) (Elsewedy, Alshehri, **Kola-Mustapha** *et al*., 2024).

In another study, **Kola-Mustapha** (2023) employed similar tools in the *de novo* design of pimarane diterpenoid compounds as potential therapies for the treatment of Acne Vulgaris. Acne Vulgaris is a highly prevalent multifactorial skin disorder that affects adolescents and adults and can impact psychological well-being. Central to its pathology is the role of *Cutibacterium acnes*, a gram-positive bacterium. To eliminate these bacteria, we can target its 30S ribosomal subunit, which is an integral component of its ribosome necessary for protein synthesis. By specifically targeting this region, bacterial growth and suppress skin inflammation can be reduced (Wilson, 2014). Pimarane compounds are a class of diterpenoids found in fungi and plants that have been reported for benefits in various conditions, including bacterial infections. By modifying the structure of pimarane compounds, a new compound was designed with better affinity for the drug target than sarecycline, the standard. This study showed that computational drug design and discovery offer a useful way to validate the activity of natural and nature-derived compounds and optimise the associated drug development process.

Research trail

Since my Ph.D. thesis to date, I have taken on a research path that has remained steadfast to the goal of improving treatment ***options*** for people, yet open to novel trends in pharmaceutical research. No single medicine is ultimately perfect and there is always room for improvement. The advent of novel trends should support the pharmaceutical researcher's objective in continuously refining the drug development process for topmost production efficiency and optimum patient outcomes. The domain of pharmaceutics stands at the juncture of production and clinical practice. On one hand, it bears the responsibility of designing the production process to ensure that drugs are safe, stable and of highest quality throughout the manufacturing process.

It also ensures that drugs produced do not harm the environment and are cost-effective to the patient. On the other hand, it bears the ultimate responsibility of defining the medication experience for the patient. The look of the drug, the smell of the drug, the palatability of the drug and eventual activity of the drug are hung on a well-designed pharmaceutical formulation process. It is important for the researcher to always ask a question on how a finished drug product can be re-finished with better qualities. When I chose to work on the 'simple' ibuprofen drug for my PhD thesis, I attempted to answer this same question.

In answering this question, we became aware of inherent deficiencies in a synthetic-medicine-only healthcare system and the crucial need for alternative approaches. We improved Ibuprofen molecules with some polymers, with **origin rooted** in nature. The interpretation here is that even an already commercialised synthetic molecule like Ibuprofen can still be further enhanced with refined naturally derived conjugates.

Further, the necessitated turn to elucidating the activity of natural products was borne out of the need to fully understand limitations in its uptake as well and how both can be integrated to achieve the critical need of healthcare advancement. A significant proportion of our research, in recent years have been about enhancing the presentation and application of natural

products, from essential oil-based gels to an array of formulations where the primary ingredients have been plant compounds; this fits directly into the **scientific refinement** bracket, to standardise their delivery.

Contributions to the University

In my elevation to this position, I consider service in mentorship and student development as my greatest contribution to the university. My love for academia is motivated by the desire to not only train students intellectually, but also morally and other facets of extracurricular development. I have served in various capacities as a teacher, researcher, and collaborator on various projects. My service to the academic, non-academic and global research community at large is not exempt from this. From initially starting out with teaching courses on Pharmaceutics to undergraduate students to now supervising postgraduate students, this maxim is clear: "*To whom much is given, much is expected*". Some of the positions I have served are:

- Member, University Senate, University of Ilorin (2024 to date)
- Member, University Senate, University of Ilorin (2021 - 2022)
- Member, Examination Committee (2015 – 2019)
- Member, University Research Committee (2015 – 2017)
- Member, Faculty Board of Examiners Committee (2016 – 2019)
- Member, Curriculum Committee (2016 - 2019)
- Member, Postgraduate School Committee (2021)
- Member, Fund Raising Local Organizing Committee for Nigerian Association of Academic Pharmacists (NAPA) Conference UNILORIN, August 2023
- Member, NAPA Abstract Screening Committee for 21st NAPA Conference, University of Ilorin, 2023

- Member (Pharmaceutics Group) for NUC (CCMAS) Textbook Project for the Nigerian Pharmacy Students (2023)
- Resource Person, Pharmacists Council of Nigeria Mandatory Continuing Professional Development (PCN-MPCD) January 2023
- Ag. Head of Department of Pharmaceutics and Industrial Pharmacy (2019, 2021 – 2022).
- Faculty of Pharmaceutical Sciences Admissions Clearing Officer (2021)
- Department of Pharmaceutics and Industrial Pharmacy Postgraduate Coordinator (2021)
- Member, Pharmaceutical Society of Nigeria (PSN) Kwara State Education Committee (2020 to date)
- Internal Examiner & Resource Person, 2021 Foreign-Trained Pharmacy Graduates Licensure Examination by Pharmacists Council of Nigeria (PCN) at UNILORIN
- Council Member (Medical Science Representative), Science Association of Nigeria (SAN) (2018 to date)
- Member, AAPS Abstract Screening Committee for PharmSci 360 Conference USA (2018 to date)
- Rapporteur, United Nations 75 Dialogue (UN75) on behalf of Centre for International Education, University of Ilorin (2020)
- Secretary Pharmacists Council of Nigeria- Mandatory Continuing Professional Development (PCN-MCPD) Organizing Committee (2017)
- Coordinator, Department of Pharmaceutical Microbiology and Biotechnology (2016 – 2017)
- Research Manager, Faculty of Pharmaceutical Sciences (2015 – 2017)
- Examination Officer, Department of Pharmaceutics and Industrial Pharmacy (2015 – 2019; 2020-2022)

Conclusion

Mr. Vice-Chancellor, as I stand before you today, I am in awe of my growth and the development of the academic community at this prestigious University. In about a decade of service to this institution, I have risen through the ranks to become a Professor of Pharmaceutics and Industrial Pharmacy. Being the first female Professor from my department, it gladdens me to inspire young women in the sciences.

For emphasis, Natural and synthetic medicines are complementary; they have always been. By reformulating natural medicines in 'synthetically appearing' formulations such as emulgels and suppositories, we redefine the user perception of traditional medicine and enhance its use in the population. By improving synthetic medicines with naturally occurring excipients, we strengthen its effects and alleviate drawbacks in its production and use. By combining both for activity, we achieve a synergism in benefit that exceeds the sum of its parts.

Lastly, the achievement of these can only be possible with the embrace of novel trends and developments in pharmaceutical formulation and development. Computational drug analysis with bioinformatics tools is here to stay and is now a gold-standard in many countries. In the end, the goal is to use what we have (synthetic medicines) in conjunction with what we have been given (natural medicines) to produce what we direly need (healthcare advancement). Our research niche is being achieved with materials that are either primarily or secondarily derived/rooted in nature, refining them with the aid of pharmaceutical technologies (including bioinformatics) and making them better drugs and excipients for advanced drug delivery.

Recommendations

Mr. Vice-Chancellor, ladies and gentlemen, here are my recommendations based on this lecture:

1. **One-in-one and not side-by-side**: The goal of integration is not to place natural and synthetic medicines side by side in a pharmacy, but that they are co-developed until one is indistinguishable from the

other. Indigenous pharmaceutical formulation practices should aspire to equal standards of quality, appeal and activity for natural and synthetic medicines and continuously attempt the co-formulation of both for the better health of Nigerian patients.

2. **No medicine is perfect**: To the audience, every drug is a poison and should be used with caution, whether natural or synthetic. To my fellow scientists, let us bring to the fore prevalent issues in medicinal development and use in patients. Scientists should continuously strive to identify active plant components, determine safety and standardized dose, and further improve drug formulations for industrial efficiency and patient benefit.

3. **More than this**: There is more to pharmaceutics than mortar and pestle. The modern world introduces students to cutting-edge technologies for formulation development, setting the pace in the next wave of industrial revolution. From computational hardware and software for predicting drug activity to the use of artificial intelligence in optimising the drug development pathway, there is a critical gap in the Nigerian healthcare system. Public and private partnerships are encouraged to accelerate access to these technologies in pharmaceutical training.

4. **Using what we have**: It is not enough to test these formulations in the laboratory; it is more important that we commercialize for use. 'Bridging town and gown' is a common term to describe research translation to societal use. However, I believe that we can achieve even more significant breakthroughs where there is no longer a need for a bridge between the laboratory and industry. It would be of great benefit to the University to consider the development of in-house production capacity for the commercialization of novel medicinal formulations. I am sure that the Nigerian populace is hungry for 'made-in-Nigeria' and will not hesitate in patronage of the university's products.

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