THE ROAD TO NANOMEDICINES

PROTOCOL

The Vice-Chancellor, Prof. Benjamin Chukwuma Ozumba
Deputy Vice-Chancellors
Principal Officers of the University
Chairman, Senate Ceremonials Committee
Distinguished Professors of our Great University
Eminent Past Inaugural Lecturers
Respected Academics
Other Staff of the University
Ministers of the Gospel
Distinguished and Highly Honoured Guests
Your Royal Highnesses
My Lords, Spiritual and Temporal
Great Lions and Lionesses
Ladies and Gentlemen

1. INTRODUCTION

It is with great pleasure and gratitude to Almighty God that I deliver today, Thursday, March 12, 2015, the ninety-first (91st) Inaugural Lecture of the University of Nigeria; the second from the Department of Pharmaceutics, and the fifth from the Faculty of Pharmaceutical Sciences. I will count today as one of my happiest days in life.

1.1 Inaugural Lecture

Inaugural Lecture is a lecture delivered by a newly appointed/promoted professor in a university to inform the university community and the public of all the activities he undertook to become a professor, current research activities

and future plans in his chosen field. It is a very significant occasion in the career of an academic staff in the university and is also a central part of university academic life.

For me Mr. Vice-Chancellor, Inaugural Lecture is an opportunity to share my achievements in research, innovation, engagement and teaching activities to members of the University community and the general public. I will also use this opportunity to thank our research team and the wider group of academics that I have collaborated with over the years and to celebrate our shared successes.

1.2 The Roots!

Amaechi was born on All Souls Day, November 2nd, 1970 as the 3rd child into the family of Late Chief and Mrs. Boniface Attama of Amadim Ohom-Orba in Udenu Local Government Area of Enugu State. He had his primary education at Ogene Premier School, Imilike-Enu at a tender age, which he sailed through with ease and regularly adorned with prizes. During his secondary school days at Boys' High School, Orba, he had great urge to study engineering because of his wonderful performance in the sciences. He had the opportunity of going through all the science textbooks in the school library, being the Library Prefect! As God would have it, he later found himself in the Faculty of Pharmaceutical Sciences, University of Nigeria, Nsukka where he studied Pharmacy and graduated with distinction in 1994.

Today's lecture entitled *"The Road to Nanomedicines"* was borne out of my vast and rich experience in research in novel drug delivery systems, which started in 1997 with my M.

Pharm. Dissertation. On my admission for M. Pharm. programme (and also my Ph.D), we decided and were determined to shift from the traditional research carried out in the Department at that time despite the shortcomings, knowing full well that if we took the right "road", we would reach the expected destination at least, in the long run.

> *A road leads someone from one place to another. It may start somewhere and terminate elsewhere, but can also continue. There may be diversions, junctions of different kinds, obstacles (e.g. roadblocks), etc. It may be one's ability to surmount the obstacles that will determine how fast he reaches his destination.*

2. THE LECTURE

Mr. Vice-Chancellor, Sir, in this inaugural lecture, I will discuss, in very concise detail, my work and research findings including my collaboration with scientists in pharmaceutical and allied sciences within and outside Nigeria. As I have supervised many postgraduate students in pharmaceutics, I will also showcase my contributions to research and development of pharmaceutics and drug delivery through supervision of higher degrees. My research works span through various aspects of pharmaceutical sciences, which are akin to someone on a journey from known to unknown, through a road familiar to the one unfamiliar. These include:

- Drug Discovery/Development and Solid State Pharmaceutics
- Drug Analysis and Quality Control
- Drug Formulation and Delivery.....Nanomedicines

2.1 Drug Discovery/Development and Solid State Pharmaceutics

Drug discovery/development is the process through which potential new medicines are identified and developed. Pharmaceutical development is one of the most challenging aspects of pharmaceutical and biopharmaceutical innovations. It involves navigating the complexities of pharmaceutical sciences and manufacturing, while achieving regulatory compliance (Fig. 1).

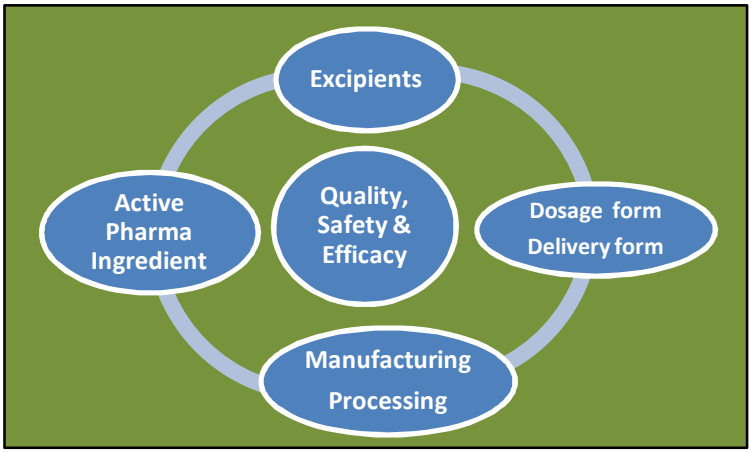


Fig. 1. Complexity of drug development

Modern drug discovery involves the identification of screening hits, medicinal chemistry and optimization of those hits to increase the affinity, selectivity (to reduce the potential of side effects), efficacy/potency, metabolic stability (to increase the half-life), and oral bioavailability. However, it should be noted that discovery of new drugs alone is not sufficient to ensure progress in therapy. Choosing the right excipients can make all

the difference in the efficient production of a robust drug delivery system.

Mr. Vice-Chancellor, Sir, having introduced drug discovery and development and some aspects of solid state pharmaceutics (excipients), I will now focus on my research in this area.

2.1.1 Drug Discovery/Development

One of our works on drug developments was on predicting intestinal permeability of drugs through Neural Network Analysis based on five molecular predictors. Most drugs from development 'factories' do not have adequate solubility and permeability for oral absorption. Maestro of MacroModel (Schrödinger Inc.) was used to build molecules of 74 drugs and properties like dipole moment, polarizability and atomic charges of each conformer studied using MOPAC2002. A Neural Network Model was generated with Alyuda Forecaster XL permitting to optimize the resulting Neural Network Model. From the model, the relative importance of each of the descriptors in determining the permeability was: Hydrogen: 48.369 %, Oxygen: 23.683%, dipole moment: 13.741 %, Nitrogen: 7.268 % and polarizability: 6.939 % (Mbonu *et al*., 2006).

Artemisinins, the main stay in the treatment of malaria today, are used in combinations with other antimalarials to forestall resistance as artemisinin-combination therapies (ACTs). Combination of an artemisinin-based compound and a medicinal herb extract could provide an indigenous alternative/herb-based ACTs. The *in vivo* schizontocidal activity of the crude aqueous extract (CAE) of *Azidirachta indica* (Dogonyaro) fresh leaves and artesunic acid was investigated.

Combination of the CAE and artesunic acid produced a significant reduction of parasitemia compared with artesunic acid alone. The CAE increased the activity of artesunic acid in terms of reduction in parasitemia, and increased survival time and cure rate by at least 40 %. Aqueous extract of mature fresh leaves of *Carica papaya* (Pawpaw) was also tested for antiplasmodial activity and was found to have a very good antiplasmodial activity (Anagu *et al*., 2014; Onaku *et al*., 2011).

The plant, *Millettia aboensis* Hook F. (Fabaceae) ('*Uturuekpa*'), is used in Nigerian folkloric medicine for the treatment of veneral diseases, acute malaria, ulcer and liver disorder. Our research team evaluated the hepatoprotective effect of aqueous and ethanol root extracts of *Millettia aboensis* in comparison with Liv-52®. The extracts produced good hepatoprotection as they decreased the activity of serum enzymes and bilirubin. The hepatoprotective effect was confirmed by histopathological examination of the liver (Attama *et al*., 2014).

Infections due to *Staphylococcus aureus* have been on the increase globally with serious implications for public health. Although *S. aureus* commonly resides in the nose of apparently healthy humans, it can also colonize such other areas as the intestine, vagina, groin and armpit. In developing countries and poor resource settings, due to lack of adequate facilities or cost, staphylococcal isolates may not be definitively identified to the species and strain level. The result is that other members of the genus *Staphylococcus* may be erroneously identified as *S. aureus* with obvious negative impact on chemotherapeutic outcome and antibiotic resistance. Thus, a cross-sectional

prospective study involving pregnant and non-pregnant women was done. The isolated organisms were identified using the Biomieriux API staph® testing system, which revealed a variety of staphylococcal species beside *S. aureus*. Antibiotic susceptibility test revealed that the prevalence of *S. aureus* infection was 6.9 % and 7.7 % in pregnant and non-pregnant women respectively. The *S. aureus* isolated was susceptible to levofloxacin, ceftriaxone, clindamicin and erythromycin, but resistant to ciprofloxacin and cefixime, a third generation oral cephalosporin. Other pathogenic non-aureus coagulase-negative staphylococci such as *S. xylosus* and *S. haemolyticus* were identified. This will ensure targeted prescribing by clinicians aimed at minimizing the development and spread of antimicrobial resistance, a global concern (Stanley *et al*., 2013). Some other published researches done in drug development are presented in Table 1.

2.1.2 Excipient Development/Solid State Pharmaceutics

Starch is a polymer of glucose which can be obtained from different sources, ranging from roots, stems, seeds and fruits of plants. It is a common source of food for man. Mr. Vice-Chancellor, Sir, we have worked on starches from different sources and have also added value to some of the starches by modification. The starches include those from yam, tacca, gladiolus, cassava, maize and avocado. We have also worked on gums (polysaccharides) from different tropical plants: okra, prosopis (‘Okpeye’), detarium (‘Ọhọ’), etc.

Table 1: Some researches in drug discovery/development

S/No.	Nature of investigation	Result	Reference
1.	*In vitro* interaction of amoxicillin and norfloxacin with lansoprazole against selected bacterial isolates	Lansoprazole increased the MIC of amoxicillin and norfloxacin against the test organisms.	Attama *et al.,* 2005.
2.	*In vitro* interaction of acyclovir with norfloxacin and pefloxacin against some clinical isolates of *Pseudomonas aeruginosa* and *Escherichia coli*.	Synergism observed at some ratios.	Onugwu *et al.*, 2009.
3.	Wound healing effect of gelatin and polyethyleneglycol (PEG) containing Cicatrin® powder	The combined agents had synergistic effect	Momoh *et al.* 2009.
4.	Effect of formulations of metformin and *Vernonia amygdalina* extract on haematological and liver indices of diabetic rats.	The liver enzymes showed no significant difference from that of the control and the LD_{50} was > 650 mg/kg.	Momoh *et al* 2011
5.	Thermodynamic parameters of the inclusion complexation of piroxicam and beta-	Interactions were exothermic and spontaneous; stable complexes formed.	Osadebe *et al.*, 2008.

	cyclodextrin.		
6.	Diclofenac β-cyclodextrin inclusion complexes in aqueous medium.	Increased aqueous solubility of diclofenac. Maximum stability of the complex was at pH value of 4.0.	Attama *et al*., 2004.
7.	Interaction of β-cyclodextrin with tetracycline.	Tetracycline forms a complex in a 1:1 stoichiometry with β-cyclodextrin.	Attama *et al*., 2002
8.	Effect of low doses of phenformin (50 mg/kg) administered intraperitoneally to rats	No serum perturbation observed.	Attama and Adikwu 2004.
9.	Modification of *D. reflexa* gum by ionotropic gelation	Stable hydrogels which showed differential pH sensitive swelling in aqueous media.	Builders *et al*., 2012.
10.	Evaluation of antifungal activities of the crude leaf extracts of *Mitracarpus vilosus*.	All the fractions and their combinations with standard drugs showed significant antifungal activities	Asogwa *et al.,* 2013
11.	Combined antimicrobial activity of *Albizia adianthifolia* root extract with two antifungal agents	Synergy was predominantly observed against *Candida spp.*	Ofokansi *et al*., 2013
12.	Molecular characterization and efficacy of antibiotic combinations	Plasmid curing showed resistance was both plasmid and chromosomally–mediated and could be reversed using combinations of	Ugwu *et al.*, 2013

		antibiotics of different mechanisms of action.	
13.	Comparison of susceptibility patterns of *Escherichia coli* isolated from urinary tract infections	*E. coli* accounted for 49.16 % of urine isolates with cotrimoxazole, chloramphenicol and amoxicillin having lowest susceptibility and ofloxacin and ciprofloxacin highest susceptibility.	Oreh and Attama, 2013

Dioscorea bulbifera (Fam. Dioscoreaceae) starch was found to contain high amylopectin content, which means that the starch could be employed in several food and pharmaceutical products as a thickening agent or stabilizer (Nnamani and Attama, 2003). Tacca starch extracted from the root tubers of *Tacca involucrata* plant ('Ogege ipachi' in Idoma) has oval granules with single, double or triple cleft helium. The starch gelatinizes at 52-65 ^{o}C, and has an amylose content of 36 %. Granule morphology (Fig. 2A) and swelling index showed that the starch would perform well as disintegrant or glidant in tablet formulation (Attama and Adikwu, 1999).

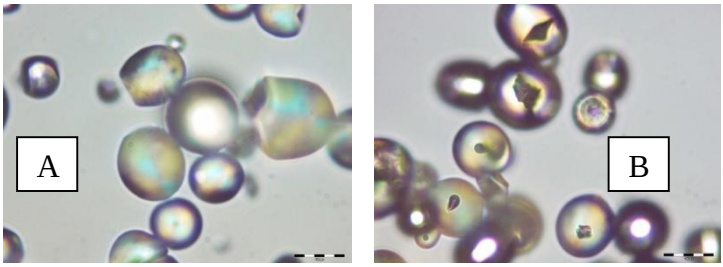


Fig. 2. Photomicrograph of tacca starch (A) and dextrinized tacca starch (B)

Purified tacca starch was converted to pyrodextrins (Fig. 2B) together with gladiolus starch (Fig. 3A) extracted from the corms

of *Gladiolus actinomorphanthus* plant ('Okledu' in Idoma) and the physicochemical properties studied to determine their applicability in tablet formulations. The pyrodextrins and some tablets produced conformed to pharmacopoeial standards and the pyrodextrins could be ideal tablet excipients with multifunctionality (Attama and Akpa, 2009; Attama and Adikwu, 2002). Furthermore, the compaction behaviour of the gladiolus starch derived pyrodextrins (Fig. 3B), and their cogranulates with polyvinyl pyrrolidone (PVP) was studied. The pyrodextrins alone had high elastic recoveries, while all the cogranulates showed predominantly plastic behaviour, which approximated that of Avicel® PH 101 and could serve as an alternative to Avicel® PH 101 in drug formulation by direct compression (Attama *et al*., 2009).

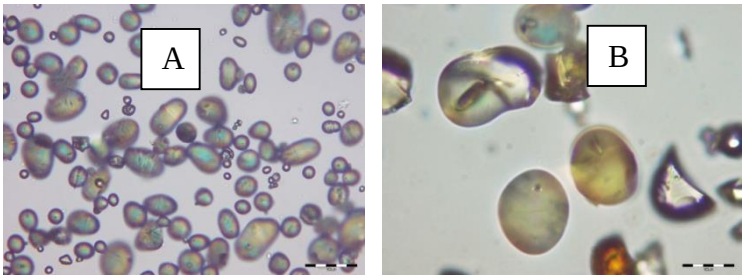


Fig. 3. Raw gladiolus starch (A) and pyrodextrin from gladiolus starch (B)

Cassava starch was modified by hypochlorite oxidation and some physicochemical properties of the oxidation products evaluated as directly compressible excipient in the formulation of ascorbic acid tablets (Attama *et al.*, 2007). The physicochemical properties were dependent on the oxidation time. Oxidized cassava starch tablets were better than those of unoxidised cassava starch. However, the compressibility of the oxidized cassava starch was lower than that of Avicel® PH 101. The effect of hypochlorite oxidation on the physicochemical properties of gladiolus starch

was also investigated, where oxidation resulted in whiter and finer starch of clearer dispersions, poor flow, distorted granular structure and decreased equilibrium moisture content (Attama *et al*., 2003).

Avocado starch was extracted from the kernels of the fruit of *Persea americana* Miller (Fam. Lauraceae), and its excipient properties evaluated as an alternative to maize starch. Granules prepared with avocado and maize starch pastes as binder were evaluated for their flowability, friability and compaction characteristics. Scanning electron microscopy (SEM) showed that avocado starch has two characteristic granule shapes; triangular and circular, both having approximately equal distribution (Fig. 4). The swelling, moisture uptake and paste clarity were generally lower than those of the maize starch. Avocado starch gel exhibited syneresis (weeping) after freeze–thaw that increased cumulatively with increase in the number of freeze–thaw cycles. The glass transition (T_g) and gelatinisation temperatures of avocado starch were higher than those of maize starch. Granules prepared with avocado starch pastes as binder showed superior compactibility and mechanical strength to those of maize starch, but with similar flow characteristics (Biulders *et al*., 2010).

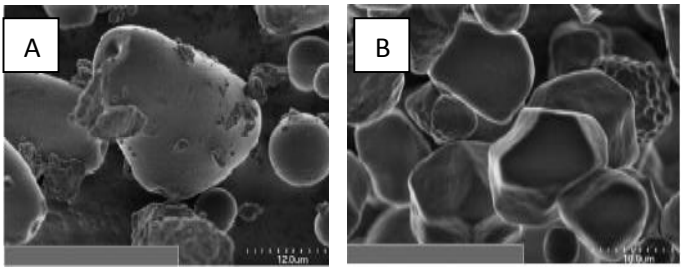


Fig. 4. SEM of (A) avocado starch and (B) maize starch

The determination of the T_g, thermogravimetric response and the amorphicity of some natural gums was done. These parameters are very important in pharmaceutical material science. Knowledge of the thermal and crystal properties will widen the horizon of usage of these excipients. *Irvingia gabonensis* gum (IG), *Mucuna flagillepes* gum (MG) and *Prosopis africana* gum (PG) possessed different T_g values (Fig. 5A) and thermal responses (Fig. 5B), which would affect their processability during pharmaceutical formulation (Attama and Akpa, 2008). Polymers are essential components of oral solid dosage forms and are used as binders, disintegrants or coatings. Given the increase in poorly water-soluble drugs, these natural polymers can be used to improve both drug dissolution and bioavailability of drugs by solid dispersion technique. Solid dispersions – incorporation of drug molecules at a molecularly dispersed state into an amorphous polymer – have shown superior bioavailability in comparison to other drug delivery systems. Their amorphous nature suggests these polysaccharides will perform well in solid dispersion drug delivery systems.

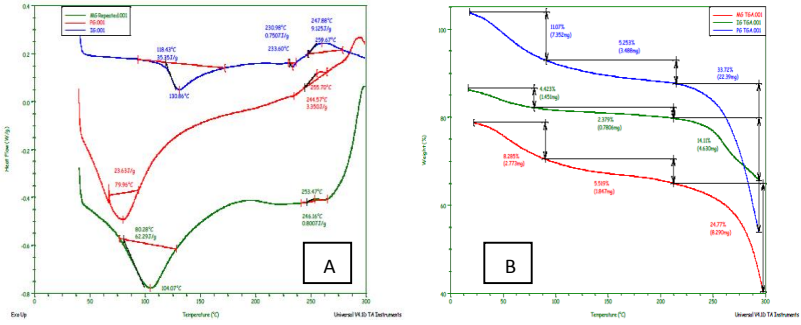


Fig. 5. DSC (A) and TGA (B) of the natural gums.

Engineering of new polymeric biomaterials could be employed to address some problems associated with delivery of some APIs and

biomolecules. To obtain new polymer biomaterials that will meet the carrier needs of challenging drug molecules, blending of polymers with desirable properties becomes imperative. We studied mixtures of polyethylene glycol (PEG) 4000 and snail mucin matrices using Fourier transform infared (FTIR) spectroscopy. The presence of different peaks in the FTIR spectrum of the PEGylated mucin matrices compared with that of non-PEGylated mucin indicated the formation of new polymers, which could be employed in drug delivery (Kenechukwu *et al.*, 2013). *Cola accuminata* gum was also modified through PEGylation process and evaluated for mucoadhesive sustained release diclofenac sodium matrix tablets. Differential scanning calorimetry (DSC), wide angle X-ray diffracftion (WAXD) and FTIR studies confirmed the PEGylation process, which substantially modified the physicochemical properties of the native gum, and influenced the rate of drug release from the matrix tablets tested (Bamigbola *et al*., 2013).

2.2 DRUG ANALYSIS AND QUALITY CONTROL

Mr. Vice-Chancellor, Sir, fake and counterfeit medicines have been a recurrent decimal in our country. The World Health Organization (WHO) defined counterfeit medicines as medicines that are deliberately and fraudulently mislabeled with respect to identity or source: their quality is unpredictable as they may contain wrong amount of active ingredients, wrong ingredients or no active ingredients. While the exact extent of the problem posed by faking and counterfeiting of medicines is still unknown, the prevalence of counterfeit medicines has increased tremendously.

Counterfeit medicines around the world (Sanofi Report):

- One in every 10 drugs sold around the world is fake, and this can reach 7 out of 10 in some countries.

- The number of identified cases of counterfeit drugs increased by 9 % between 2008 and 2010.

- In 2011, medicines ranked first among the list of counterfeit products kept by European customs (24 % of total), beating counterfeit cigarettes.

- The profits from counterfeit medicines are higher than the profits from drug trafficking (reaching U.S. $75 billion in 2010).

- For every U.S. $1,000 invested, a criminal can garner U.S. $20,000 profits from heroin and U.S. $400,000 from trafficking in counterfeit drugs.

The purpose of quality assurance in pharmaceuticals is to help ensure that each medicine reaching a patient is safe, effective, and of acceptable quality. Mr. Vice-Chancellor, Sir, there are quite a number of challenges to the development of novel, rapid, cheap, versatile and user-friendly analytical method for drugs and drug products in Nigeria. The major challenge is non-availability of analytical instruments like spectrophotometer, high performance liquid chromatography (HPLC), infra red spectroscopy, etc. Despite these challenges, we were able to develop a very rapid and precise analytical method for drugs of a unique class called charge transfer complexation as elaborated in our researches that follow:

2.2.1 Analytical Method - Charge Transfer Complexation

A charge-transfer complex or electron-donor-acceptor complex is an association of two or more molecules, or of different parts of one large molecule, in which a fraction of electronic charge is transferred between the molecular entities. The resulting electrostatic attraction provides a stabilizing force for the molecular complex. The source molecule from which the charge is transferred is called the electron donor and the receiving species is called the electron acceptor. Colour developed by charge transfer interactions between chloranilic acid or other π-acceptors and some drugs were used to assay some drugs with high precision and accuracy.

We developed a spectrophotometric method based on charge transfer complexation for the assay of haloperidol in pure form and in dosage form. Chloranilic acid formed a complex of 1:2 stoichiometry with haloperidol (haloperidol: chloranilic acid), with a maximum absorption band at 576 nm. The complex obeyed Beer's law. The method was successfully used to analyse commercially available haloperidol tablets without interference from the excipients, with good precision and reproducibility compared with the official assay method (non-aqueous titration) described for haloperidol in the British Pharmacopoeia (Attama *et al*., 2003). The thermodynamic parameters (stability constant, molar absorptivity, free energy change, enthalpy and entropy) of the charge transfer complex between chloranilic acid and haloperidol were also studied. The complex was found to be very stable at room temperature (Attama *et al*., 2004). The method was successfully validated for the analysis of commercially available haloperidol tablets.

Charge transfer interaction involving chloranilic acid was similarly used to analyse or detect the following drugs with accuracy and precision: cephalexin, proguanil, halofantrine, mefloquine, diethylcarbamazine, moclobemide and promethazine hydrochloride (Attama *et al*., 2006; Adikwu *et al*., 2001, 2000, 1999, 1998).

In a related study, spectrophotometric method was used to assay lamivudine in pure form and in dosage form, but this time, chloranilic acid and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), acted as □-acceptors (Madu *et al*., 2011). Chloranilic acid and DDQ were found to form charge-transfer complexes of 1:1 stoichiometry with lamivudine of maximum absorption bands at 521 and 530 nm respectively. The complexes obeyed Beer's law at a concentration range of 0.04 - 0.28 mg/ml. The thermodynamic parameters obtained for the complexes were such that analysis of lamivudine in dosage forms was effectively done with precision and accuracy.

2.2.2 Quality Control

Mr. Vice-Chancellor, Sir, it is also very necessary to monitor the quality of pharmaceutical products on the market to assess compliance with Good Manufacturing Practice (GMP) and regulatory authorities' guidelines. In this regard, several studies were carried out.

The *in vitro* dissolution profiles of four commercial brands of aspirin tablets (one soluble brand and three plain brands of aspirin) were assessed and various dissolution parameters obtained. The results indicated that the soluble aspirin brand exhibited faster dissolution compared with the non-soluble brands (Bamigbola *et al*., 2009). Level C *in vitro – in vivo* correlation was performed for the four brands of aspirin tablets using urinary excretion profiles from eight human volunteers.

Significant rank order correlations were observed between all the *in vitro* dissolution parameters and all the *in vivo* bioavailability parameters (Bamigbola *et al*., 2011). With proper standardization of methods of assessment, *in vitro* dissolution parameters can be used to predict *in vivo* bioavailability of aspirin tablets.

Also, pharmaceutical equivalence studies on ten different brands of commercially available samples of metronidazole tablets from different manufacturers were carried out (Ibezim *et al.*, 2008). Results obtained showed that there were wide variations in the various tablet parameters among the different brands, with some of the brands having acceptable tablet characteristics while others did not. Result of this study is significant in therapy where drugs are expected to not only conform to their label claims, but also have satisfactory bioavailability and show bioequivalency to make substitution practicable.

The compatibility of four brands of gentamicin sulphate injection with five parenteral drugs - dexamethasone, diazepam, hyoscine butylbromide, furosemide and promethazine was also studied (Ibezim and Attama, 1998). Results showed that gentamicin sulphate is compatible with dexamethasone, hyoscine butylbromide and promethazine but not with furosemide and diazepam. Admixtures should however be made with caution because an admixture may not be efficacious even in the absence of any visible incompatibility. Recently, a study was carried out to assess the microbial quality of some injections and infusions used in hospitals in Nigeria. The study involved 19 injections and infusion. Their microbial quality - sterility and pyrogenicity - were critically assessed. Ten out of the 19 were found to be sterile, while only one infusion was found to be unsterile and failed to conform to standards for parenteral administration. The other eight conformed to specification. The organisms identified were

Bacillus cereus, *Lactobacillus spp*., *Micrococcus luteus*. All the injections and infusions were pyrogen-free (Ude and Attama 2014).

2.3 DRUG FORMULATION AND DELIVERY

Development of suitable drug formulations and delivery systems remains a major challenge in the full drug product development and industrialization process. A drug delivery system (DDS) is defined as a formulation or a device that enables the introduction of a therapeutic substance in the body and improves its efficacy and safety by controlling the rate, time, and place of release of drugs in the body. DDS is an interface between the patient and the drug (Jain, 2008). Since it is known that development of new drugs alone is not enough to ensure progress in therapy, old drugs could be formulated using novel drug delivery strategies for enhanced performance. We recently developed solid dispersion dosage form of glimepiride, a hypoglycaemic drug using SoluPlus® (Achuam *et al.*, 2014).

Mr. Vice-Chancellor, Sir, many existing drugs as well as those coming out of discovery are poorly soluble, and they need special efforts and techniques to be formulated into dosage forms. The quest for the development of ideal drug delivery systems for these drugs led our group to venture into novel drug delivery systems. An important strategic focus of our Drug Delivery and Nanomedicine Research Group is development of state-of-the-art drug formulations and delivery systems for pharmaceutical and medical applications.

2.3.1 Conventional Formulations/Drug Delivery Systems

Conventional drug formulations include dosage forms such as tablets, capsules, granules, emulsions, suspensions, etc. A tablet is a dosage form that comprises a mixture of active substance(s)

and excipient(s), usually in powder form, pressed or compacted into a solid. Tablets are the most popular dosage form in use today as they are simple and convenient. Manufacturing processes and techniques can provide tablets of special properties, for example, sustained release, delayed release or fast dissolving or immediate release tablets. Faster disintegration and dissolution are necessary in immediate release tablets. Researches to achieve faster dissolution or to deliberately slow drug release and dissolution of drugs from tablets were carried out in addition to other conventional dosage forms such as suspension, ointments, suppositories, gels, patches, etc (Table 2).

In one of our researches, two pH sensitive polymers (Eudragit® L30 D55 and L100) were used as coating materials respectively, for promethazine hydrochloride and chloroquine phosphate granules formulated with sodium carboxymethylcellulose (SCMC) and Carbopol 940 (Attama and Ezeamama, 2005). Result obtained showed that the coated and uncoated granules could be used to tune the release of the drugs to favour release of promethazine before chloroquine phosphate to counteract the itching side effect of chloroquine phosphate that lowers compliance in chloroquine phosphate therapy.

Table 2: Some studies on conventional formulations/drug delivery systems

S/No.	Nature of investigation	Result	Reference
1.	Suspending properties of *Detarium microcarpum* (Fam. Caesalpinaceae) gum and in combination with Veegum	Good for short-term/extemporaneous use	Attama *et al*., 1999

2.	Emulsifying characteristics of cassava and maize starches, and acacia and tragacanth gums in paraffin oil emulsions	Cassava starch and acacia gum exhibited superior properties compared with maize starch and tragacanth gum	Ibezim and Attama, 1998
3.	Mixture of *Detarium microcarpum* gum and Veegum as binder in sodium salicylate tablets	The 1:1 ratio at 5 % w/w concentration performed well as a binder	Attama *et al.,* 1999
4.	Effect of directly compressible excipients -Avicel, Dipac, Ditab and Emdex on stability of ascorbic acid tablets	Moisture and temperature affected the stability. Tablets had very short shelf lives	Ofoefule *et al.*, 1999
5.	Effect of direct compressible excipients – Avicel®, Dipac®, and Emdex®, on stability of pyridoxine hydrochloride tablets	Moisture and high temperature affected stability. Tablets had very short shelf lives	Ofoefule *et al.*, 1998
6.	Use of cellulosic material from *Prosopis africana* as disintegrant in sodium salicylate tablets	Tablets with higher mean disintegration times compared with alginic acid obtained	Attama and Adikwu, 1998
7.	Aloe gum from the mucilage of *Aloe barbadensis* leaves as binder in metronidazole tablets	Increase in gum concentration increased the hardness and disintegration time, and slowed drug release	Nduka *et al.* 2012

8.	*Prosopis africana* gum use in the formulation of gels containing salicylic acid	Release and permeation of the drug from the gel were low	Adikwu and Attama 2000.
9.	Release and permeation properties of gels formulated with mucuna gum	Release and permeation were higher in mucuna gum gel than from tragacanth gel	Attama and Adikwu 1997
10.	Effects of trona and some properties of sodium salicylate tablets	Dissolution time decreased with increase in trona concentration	Attama and Adikwu, 1999
11.	Dissolution of hydrophobic drugs from tablets containing sodium sesquicarbonate (trona)	Dissolution rate increased with increase in trona concentration	Attama and Adikwu, 2000
12.	Analgesic effect of diclofenac potassium entrapped in snail mucin-Eudragit® L30 D-55 PEC	The analgesic effect was improved and prolonged	Attama, 2007
13.	Mosquito repellent activity of herbal ointments	Very good mosquito repellent activity was obtained	Esimone *et al.*, 2011
14.	Characterization and controlled release of gentamicin from novel hydrogels	Hydrogels showed good encapsulation, stability and spreadability, and higher percentage drug release than commercially available gentamicin ointment	Nnamani *et al.*, 2013
15.	Bioactivity of	The formulations	Nnamani

	gentamicin contained in novel transdermal drug delivery system	showed higher zones of inhibition compared with a commercial gentamicin sulphate cream	*et al.*, 2013
16.	Release and permeation properties of gels formulated with mucuna gum	High concentration of the gums slowed release and permeation rates and release were higher in alkaline medium than in acidic medium.	Attama and Adikwu, 1997

Mr. Vice-Chancellor, Sir, excipients used in DDS can enhance drug bioavailability and may allow controlled release and tissue targeting of the API. Polyelectrolyte complexes (PECs) represent an interesting class of macromolecular assemblies stabilized by a cooperative system of inter-macromolecular forces. These products of electrostatic interaction between oppositely charged polyelectrolytes are of considerable interest because of their potential applications as drug carriers and surface modifying agents. In a study, the *in vitro* and *in vivo* properties of PECs formulated with Eudragit® L30 D-55 and gelatin by non-stoichiometric method were determined (Attama, 2007). WAXD and small angle X-ray diffraction (SAXD) studies indicated formation of strong PECs between gelatin and Eudragit® L30 D-55 (Fig. 6). The PECs prolonged the antinociceptive effects of piroxicam in experimental rats. Non-stoichiometric interactions of gelatin (type A) and Eudragit L30 D-55 could yield matrices with adequate characteristics for the formulation of sustained release delivery system of piroxicam.

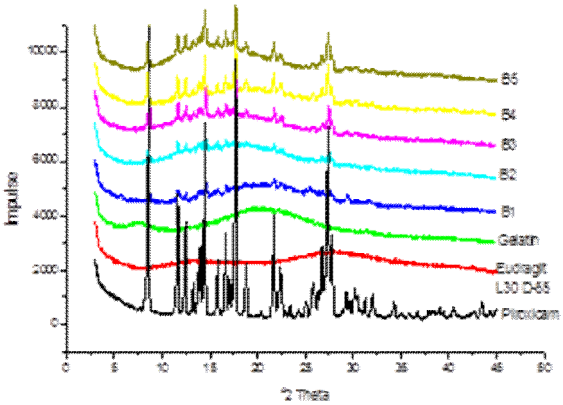


Fig. 6. Diffractograms (WAXD) of the PECs and the starting materials (B1 to B5 represent 0:1, 1:1, 2:1, 1:2, and 1:0 ratios of Eudragit L30 D-55 and gelatin (type A), respectively).

Ionic liquids are a novel class of green solvents used in chemistry and pharmacy. In another study, ionic-liquid soluble PECs were developed from mixtures of Eudragit® E PO and Eudragit® L 100-55 and evaluated for use in orodispersible dosage forms of ibuprofen, aspirin, stavudine and artesunate (Akpa *et al*., 2013). PECs generated by solution blending approach were confirmed by FTIR spectroscopy (Fig. 7A) and transmittance measurement. SEM of the PECs (Fig. 7B) showed that they were discrete with some degree of asperity. WAXD indicated that the PECs were largely amorphous. The tablets and films formulated performed well as orodisperible dosage forms with very short dispersion times.

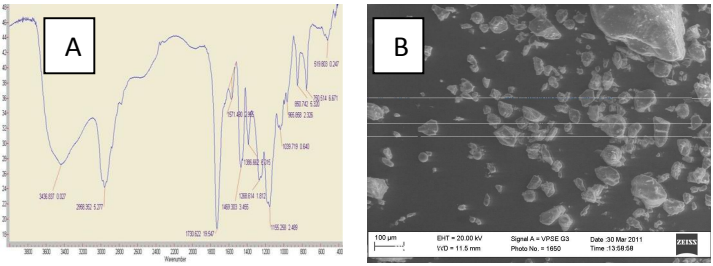


Fig. 7. FTIR (A) and SEM (B) of the PECs

Suppositories are solid dosage forms loaded with drug(s) and intended to be inserted into body cavities. There are different types of suppositories- rectal, vaginal, nasal, ear and urethral suppositories. The use of blends of palm kernel oil (PKO) and goat fat (GF) as suppository bases was studied using salicylic acid as the model drug. Suppositories containing different ratios of PKO and GF were prepared by pour moulding and assessed and found useful in the formulation of medicated suppositories. However, while the 3:2 blend may be suitable for temperate regions, 1:2 and 1:3 blends of PKO and GF were found to be suitable for suppository formulations in the tropics because of their different melting points so that liquefaction *in vitro* during storage would not occur (Attama *et al*., 2000). Similar studies were carried out using cow fat and PKO (Attama *et al*., 2001; Attama, 2008). In our dispensing laboratory, these suppository bases have replaced the very expensive theobroma oil in our routine undergraduate practical exercises and postgraduate researches. Some other researches in this area are presented in Table 2.

2.3.2 Bioadhesion/Mucoadhesion

Bioadhesion is the state in which two materials, at least one of which is biological in nature, are held together for extended period of time by interfacial forces. In the pharmaceutical sciences, when the adhesive attachment involves mucus or a mucous membrane, the phenomenon is referred to as

mucoadhesion or buccoadhesion, when it occurs in the buccal cavity.

Mr. Vice-Chancellor, Sir, in the course of our research in bioadhesion, which started during my Masters Degree programme, we adopted and modified some equations for evaluation of the bioadhesive strengths of tablets, suppositories, granules, microparticles, etc. Also, the instrument normally used for the determination of surface tension of liquids called Lecomte du Nuoy tensiometer (Fig. 8A) was adapted for determination of bioadhesive strengths of materials. Similarly, Fig. 8B was the set-up used for the determination of bioadhesive strengths of polymers by detachment of coated glass bead.

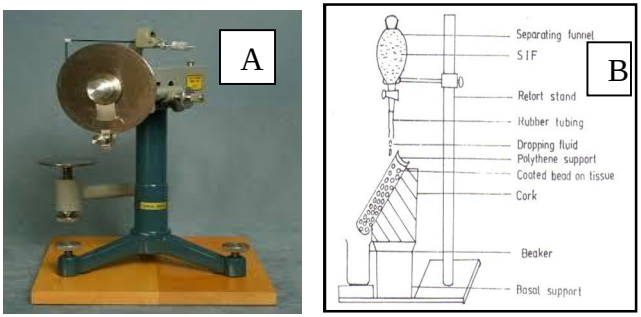


Fig. 8. Apparatus for determination of bioadhesive strength: A): Lecomte du Nuoy tensiometer B): Using coated glass beads/granules

The buccoadhesive and *in vitro* release properties of patches formulated with ethylcellulose (EC) and hydroxypropyl methylcellulose (HPMC) interpolymer complexes of different ratios were studied (Attama *et al*., 2008). The adapted Lecomte Du Nouy tensiometer was used to assess the buccoadhesion of the patches on freshly excised buccal mucosa of a pig. All the patches had uniform diameters. The area swelling ratio (ASR) indicated that the patches did not swell up to two times their

initial areas, with the batch containing 3:2 ratio of EC and HPMC possessing the highest ASR. This patch could be used as an alternative delivery system of hydrochlorothiazide.

Another study was designed to enhance the eradication of *Enterobacteriaceae* by delivering ciprofloxacin through Carbopol 941 and exogenous mucin mucoadhesive microparticles formulated to adhere strongly to the intestinal mucosa and thereby extending the residence time of the antibiotic in the small intestine where enteric infections manifest (Attama and Onuigbo, 2008). The swelling and mucoadhesion of the microparticles to the everted tissue were higher in SIF (pH 7.4) than in SGF (pH 1.2). Clinical isolates of *S*almonellae and *E. coli* were susceptible to the mucoadhesive microparticles containing ciprofloxacin.

Carbopol 940 and theobroma oil were used to formulate melt extrusion bioadhesive tablets of diclofenac. Different batches of the tablets were formulated using different quantities of Carbopol 940 granules containing diclofenac and theobroma oil in a plastic mould by pour moulding (Attama and Nnamani, 2005). The bioadhesion of the tablets were measured by determining the bioadhesive strength generated when the tablet interacted with the mucus on everted hog jejunum on a tensiometer. The tablets conformed to pharmacopoeia specifications, had low liquefaction times and were highly bioadhesive and also sustained the release of diclofenac.

In situ gelling mucoadhesive rectal suppositories of metronidazole were formulated with different quantities of Carbopol ETD 2020 and theobroma oil (Attama *et al*., 2004). The *in vivo* release of metronidazole from the suppositories was studied in rabbits. The plasma concentration time plots indicated that absorption of metronidazole from the mucoadhesive suppositories actually

occurred in the rectum and that sustained effect was achieved. Carbopol ETD 2020 could be successfully used to modify the pharmacokinetics of metronidazole in rectal suppositories. This mucoadhesive granules exposed by melted suppository would adhere *in recto* and prevent drug absorption into the superior rectal vein. Other studies on bioadhesive/mucoadhesive delivery systems are presented in Table 3.

Table 3: Studies on bioadhesive/mucoadhesive delivery systems

S/No.	Nature of investigation	Result	Reference
1.	Diclofenac sodium-containing mucoadhesive tablets prepared with Carbopol 675 and PVP	Tablets formulated with 1:1 physical mixture had the highest mucoadhesive strength with low swelling and release properties	Attama *et al.,* 2007
2.	*Prosopis africana* gum for bioadhesive delivery of theophylline	Prosopis gum could be used to deliver theophylline in a bioadhesive dosage form	Attama *et al.,* 2000
3.	Mixtures of tacca starch, Carbopols 940 and 941; and SCMC for bioadhesive delivery of hydrochlorothiazide	Tacca starch showed poor bioadhesion at low concentration, but admixtures showed improved bioadhesion	Attama and Adikwu 1999
4.	Effect of pH and ionic strength on the bioadhesive properties of	Increase in both ionic strength and pH favoured bioadhesion	Attama *et al.*, 2005

	prosopis gum		
5.	Bioadhesive properties of snail mucin and its admixtures with Carbopol Ultrez-10	Snail mucin had high bioadhesive strength, which was maximal when SGF was used as the washing fluid	Adikwu *et al.,* 2005
6.	Physically cross-linked polyacrylic acid (Carbopol 941) in the formulation of buccoadhesive film of nifedipine	Cross-linking affected the film. Polymer:sucrose ratio of 1:8 showed the highest mechanical strength and least buccoadhesiveness	Attama, 2004
7.	Diclofenac sodium bioadhesive tablets prepared with PVP and SCMC	Prolonged drug release achieved	Attama *et al.,* 2003.
8.	Pharmacodynamics of metformin in a mucoadhesive delivery system of detarium gum	Gum compacts alone showed blood glucose lowering capacity. The combinations showed marked antidiabetic effect	Adikwu *et al.,* 2004.
9.	Bioadhesive delivery of diclofenac sodium via non-disintegrating tablets	Release of diclofenac sodium was prolonged compared with the commercial sample	Attama *et al.,* 2003.
10.	Mechanism of diclofenac sodium release from non-disintegrating bioadhesive tablets	The mechanism of release of diclofenac sodium followed different release models	Attama and Nnamani, 2004

11.	*Mucuna flagillepes* (mucuna) gum for bioadhesive delivery of theophylline	Mucuna gum performed well as biaodhesive motif for theophylline	Attama *et al.,* 2003.
12.	Carbopol 940 and theobroma oil based melt extrusion bioadhesive tablets of diclofenac	Tablets were highly bioadhesive with low liquefaction times	Attama and Nnamani, 2005..
13.	Effect of prosopis gum on the entero-insular axis.	Prosopis gum was found to help in serum glucose lowering capacity of metformin.	Adikwu *et al.,* 2006.
14.	Bioadhesive rectal suppository containing metronidazole	High bioavailability and increased circulation time of metronidazole were observed	Attama *et al.,* 2004.
15.	Mucoadhesive tablets of indomethacin using Carbopol 941 and *Abelmuschus esculentus* gum.	Tablets formulated with 1:1 ratio had the highest bioadhesive strength and prolonged the release of indomethacin	Attama *et al.,* 2003
16.	Bioadhesive delivery of metronidazole using polymer binary mixtures	Carbopol 940 and 941 (1:1) had the best performance	Ibezim *et al.,* 2000
17.	Physico-chemical properties of a new polysaccharide gum from *Prosopis*	The best temperature for coacervation was 40 ^{o}C at pH 3 and at pH of 3.5 and 4, it was	Attama and Adikwu, 2002.

	africana	42 ^{o}C. Increase in pH led to decrease in the coacervate volume.	

2.3.3 Microcarrier Drug Delivery Systems

Particulate drug carrier systems include microparticles, nanoparticles, nanocrystals, self-assembly systems, etc. Microparticle technology offers several advantages for improving the entrapment efficiency of lipophilic API or for providing controlled release system. Microparticles are particles between 1 and 1000 µm, i.e. all particles within the micrometer range. Microparticles are made from natural, semisynthetic and synthetic polymers like proteins (albumin, gelatin), starch, ethyl cellulose, waxes and lipids, etc.

Microparticles could be administered orally, topically, parenterally or by the nasal route. Microparticles have some disadvantages as drug carrier systems. Some of these are: clearance and uptake from circulation by the reticuloendothelial cells, burst effect (i.e. premature drug release), target site inconsistencies and poor entrapment of drugs (low payload capability). To overcome these disadvantages is the main objective of our microparticle research group.

Mr. Vice-Chancellor, Sir, the choice of excipients remains a critical factor in pharmaceutical formulations. Microparticles could be developed to serve as excipients or to deliver API. Microcrystalline cellulose (MCC)–maize starch (Mst) composites were prepared by compatibilized reactive polymer blending at controlled temperature conditions for use as multifunctional excipients with direct compression and enhanced disintegration abilities using aspirin and paracetamol as model drugs (Builders *et al.*, 2010). SEM showed that the microparticles had a marked

degree of asperity (Fig. 9). The hardness of aspirin tablets was enhanced by incorporating the microparticles, but was reduced by Mst. While the tablets prepared with MCC–Mst and Mst disintegrated within 7 min, aspirin compacts devoid of any excipient and those prepared with MCC did not disintegrate even after 2 h. Paracetamol compacts prepared with MCC and MCC–Mst showed similar compact hardness and loading properties as aspirin compacts. The loading capacity of the different samples of the composite decreased with increase in the freeze–thaw cycles.

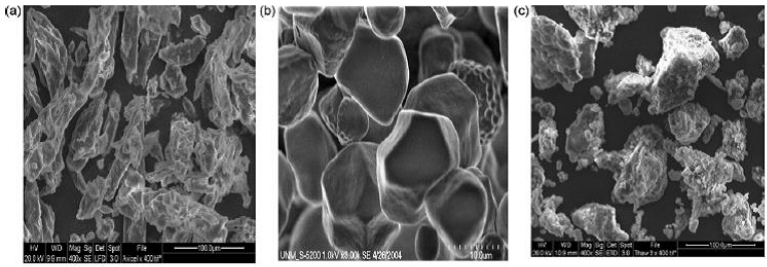
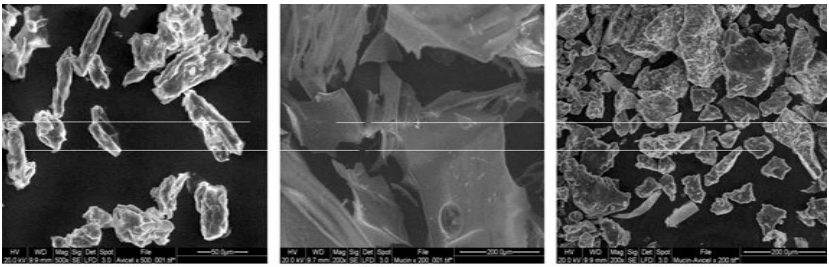


Fig. 9. SEM micrograph of (a) MCC, (b) Mst and (c) MCC–Mst.

Mucinated-cellulose polymer hybrid was generated by mixing equal concentrations of colloidal dispersions of porcine mucin (Mc) and MCC (Builders *et al.*, 2009). The polymer hybrid was converted to microparticles (Mc-MCC) and recovered by precipitation at controlled temperature and pH conditions using acetone. Some physicochemical, functional and thermal properties of the Mc-MCC were determined and compared with those of Mc and MCC. The hybrid microparticles had swelling and moisture sorption profiles that were different from those of Mc and MCC in buffer solutions with different pH values and relative humidity. SEM showed that the microparticles generated from the polymer hybrids were similar to those of MCC, but with some larger and denser particles (Fig. 10). The FTIR spectrum of the hybrid polymer was different from those of Mc and MCC. The

presence of new peaks in the FTIR spectrum confirmed the formation of a new polymer with synergistic physicochemical and functional properties.



a MCC b MC c Mc-MCC

Fig. 10. SEM micrographs of MCC, Mc and Mc-MCC.

Effective oral delivery system of insulin remains a challenge to pharmaceutical scientists. Insulin-loaded microparticles (enclosed in capsules) for oral delivery were prepared with mucinated sodium alginate using a novel method based on polymer coacervation and diffusion filling (Builders *et al*., 2008). The various insulin-loaded microparticles exhibited lag time during *in vitro* insulin release. The time taken to reach maximum insulin release from the various formulations varied with the mucin–sodium alginate ratio. The blood glucose reduction effect produced by orally administered insulin-loaded microparticles prepared with 3:1 ratio of sodium alginate and mucin after 5 h was equal to that produced by the subcutaneously administered insulin solution, an indication that it was effective for the delivery of insulin.

Mucuna gum microspheres were formulated under different conditions of polymer concentration and crosslinking time at constant speed (Attama and Nwabunze, 2007). The formulated microspheres were thereafter loaded with glibenclamide by the remote loading process and evaluated. *In vitro* release was

studied in SIF, pH 7.4. All the microspheres showed good swelling characteristics in distilled water. Microspheres produced with 5 %*m*/*V* mucuna gum with a crosslinking time of 5 h had the optimum prolonged release pattern. Microspheres produced using 10 %*m*/*V* mucuna gum with a crosslinking time of 1 h had the highest delayed release of the incorporated drug, whereas those without crosslinking had the fastest release. Formulation of glibenclamide-loaded mucuna gum microspheres would provide a reliable means of delivering glibenclamide by the oral route.

2.3.4 Microstructured Lipid Carriers

Mr. Vice-Chancellor Sir, microstructured lipid carriers are specialized form of microcarriers that contain lipids and modified lipids as the drug carrying matrix material. The aim of structuring is to reduce the crystallinity of the lipid matrix so as to promote drug encapsulation and retention, irrespective of the crystal behaviour or thermal history of the lipid(s). These structured lipid carriers were used to formulate different forms of lipid microparticles such as microspheres, solid lipid microparticles (SLM), lipospheres, solidified reverse micellar lipid microparticles, etc. In some instances, a patient may be advised to take some medicines with fatty meal, e.g. halofantrine, griseofulvin. The idea is that the absorption of these drugs would be increased because of the presence of fat, which shifts the absorption mechanism of the API and prevents it from experiencing first pass metabolism in the liver. Different drugs such as antimalarials, analgesics, antitubercular drugs, antibiotics, antacids, antifungal drugs, phytopharmaceuticals, HIV drugs, antidiabetic drugs, etc. were formulated for oral, topical, and parenteral delivery. Permit me, Mr. Vice-Chancellor, to elaborate on very few of these research works because of space constraint.

Artemisinins and their derivatives are considered the mainstay for the treatment of *Plasmodium falciparum* malaria due to their high potency and rapid action. However, they have short half life, low solubility, and poor oral bioavailability; hence the need to formulate novel dosage forms of these drugs. A research to improve the solubility, bioavailability and therapeutic efficacy of artemether using homolipid-based microparticles was carried out. Solid lipid microparticles (SLM) were formulated, characterized, filled into capsules and compressed into tablets and drug release studied (Agubata *et al*., 2015). *In vivo* anti-plasmodial activity of artemether SLMs was evaluated in mice. Increase in % plasmodial growth inhibition and reduced parasitemia were observed in mice treated with the SLM dispersions compared with the controls. SLMs prepared with composite mixtures of a homolipid and phospholipid improved the solubility, dissolution, permeability, bioavailability and anti-malarial efficacy of artemether.

One of our researches reported artesunate-loaded SLMs based on structured lipid matrices consisting of soybean oil and dika wax prepared by melt-homogenization (Chinaeke *et al*., 2014). *In vivo* antimalarial studies were performed using a modified Peter's 4-day suppressive protocol using mice infected with *Plasmodium berghei*. Thermograms of the lipid matrices showed modifications in the microstructure of dika wax as a result of inclusion of soybean oil. SAXD and WAXD diffractograms showed non-lamellar and moderately crystalline lipid matrices. The SLMs had marked reduction in parasitaemia compared with reference commercial tablet (Fig. 11), with bioavailability enhancement factor of 2.108. Level A correlation between the *in vitro* dissolution and the *in vivo* absorption showed a linear correlation ($r^2 > 0.9$), meaning that *in vitro* properties could be used to predict *in vivo* properties of the formulation with very high accuracy.

In a related work, the *in vitro* and *in vivo* properties of artesunate-loaded SLMs based on phospholipid-modified dika wax matrices were studied (Chinaeke *et al.*, 2014). The SLMs exhibited high EE% and had good sustained release properties. *In vivo* studies showed that the SLMs also had marked reduction in parasitaemia level compared with reference tablet and could be used orally for the treatment of malaria. SLMs with better properties were obtained from structuring the lipid matrix with a phospholipid. We also adapted a novel method of preparation of SLMs termed spray congealing (Agbo *et al.*, 2013) different from melt-emulsification, and successfully used it to formulate artemether-lumefantrine-loaded SLMs.

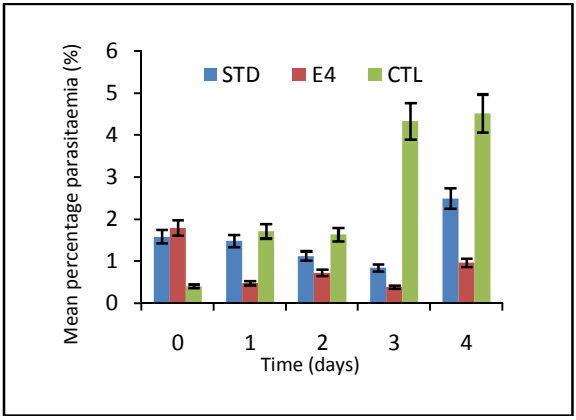


Fig. 11. Percent parasitaemia of mouse treated with artesunate-loaded SLMs. Artesunate tablets (STD), SLM formulation (E4), Normal saline (CTL).

Ceftriaxone sodium lipospheres dispersions were prepared and evaluated for oral administration (Attama *et al.*, 2009). Bioassay was performed using *E. coli* as the model organism in addition to *in vitro* permeation studies. The particles having high EE% were

spherical and within micrometer range with minimal growth after 1 month. The bioactivity and permeation coefficients were inversely related to PEG 4000 concentration. The result of this study gave insight that the issue of ceftriaxone stability in oral formulation could be adequately addressed by careful selection of lipid based excipients.

Halofantrine-loaded SLMs were formulated and *in vitro* and *in vivo* studies carried out (Ogbonna *et al*., 2014). The SLM showed prolonged pH-dependent release profile with high percentage reduction in parasitemia compared with Halfan® (Fig. 12). Histological studies revealed that the SLM formulations had no harmful effects on the kidney and liver.

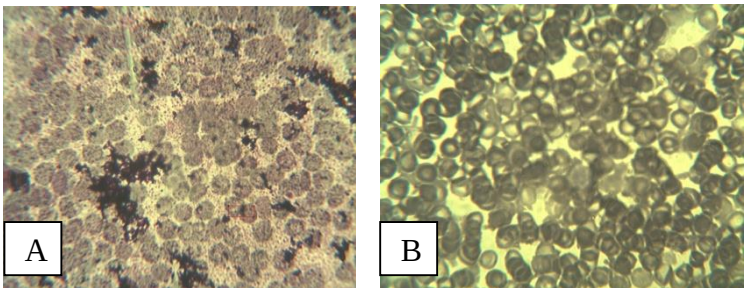


Fig. 12. Micrographs of mice red blood cells infected with malaria parasite (A); after treatment with the formulation (B).

Lipospheres of benzyl penicillin were formulated using combinations of shea butter, surfactant (Span 80) and goat fat by thin film hydration technique (Esimone *et al*., 2012). Particle size increased with an increase in drug loading. The test micro-organisms showed high sensitivity to two optimized batches in marked contrast to the unencapsulated benzyl penicillin, especially against the multiple-antibiotic resistant strains of *S. typhi, P. vulgaris* and *P. aeruginosa* used in the study. Thus the lipospheres improved the antimicrobial activity of benzyl

penicillin against the microorganisms. The pure drug resistant microbe species all showed sensitivity to the two best formulations. Lipospheres encapsulating ethanol extract of *Garcinia kola* Heckel and methanol extract of *Anogeissus leiocarpus* were also formulated and evaluated (Aguwamba and Attama, 2011; Okoro and Attama, 2014). Good results were obtained from the antibacterial and antidiabetic studies respectively.

Mr. Vice-Chancellor, Sir, gentamicin is an aminoglycoside antibiotic that has no oral delivery system available because of lack of permeability among other factors. Our research group has conducted a lot of researches on development of novel oral and other delivery systems of gentamicin. Different approaches were used among which was solidified reverse micellar solutions (SRMS). SRMS-based SLMs technology is a new formulation field with advantages over other micro carrier systems with high potentials for sustained drug release and gastro-protection for drugs prone to ulceration. It is based on inversion of reverse micelles to normal micelles during formulation or in use (Fig. 13).

The *in vitro* properties of gentamicin encapsulated in SRMS-based SLMs were evaluated. SRMS matrices formulated with Phospholipon® 90G and Softisan® 154 at different ratios were used to prepare gentamicin-loaded SLM dispersions by melt homogenization, followed by lyophilization (Umeyor *et al.*, 2011). The SRMS possessed imperfect matrices that promoted drug encapsulation, thus yielding high EE% and loading capacity. Sensitivity studies showed good susceptibility of microorganisms to the SLMs compared with pure gentamicin. It is thus possible to encapsulate gentamicin in SRMS-based SLMs without loss of antibacterial activity, and this would likely offer a reliable oral delivery system for gentamicin.

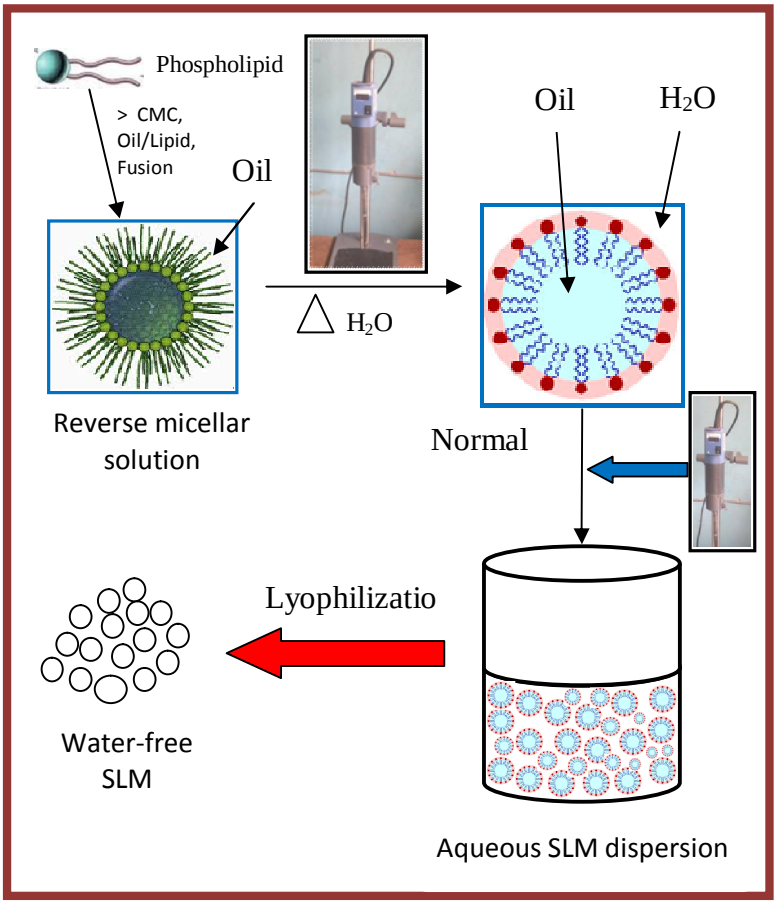


Fig. 13. Transformation of reverse micelles in aqueous medium for drug encapsulation and sustained release (Attama® 2015)

As an extension of the research on gentamicin, novel PEGylated SRMS-based SLMs of gentamicin were formulated and their physicochemical and pharmacokinetic properties determined (Kenechukwu *et al*., 2014). The SLMs showed sustained drug permeation and exhibited time-dependent and capacity-limited bioactivity. *In vivo* pharmacokinetic studies showed an $AUC_{(0\text{-}24\ h)}$

of 1507 mg/h/ml for the optimized formulation, while that of gentamicin solution was 678 mg/h/ml (Fig. 14), equivalent to a 2.2-fold increase in the systemic bioavailability. PEGylated SRMS-based SLMs prepared with lipid from *Irvingia gabonensis* could prove to be a reliable oral delivery system for gentamicin.

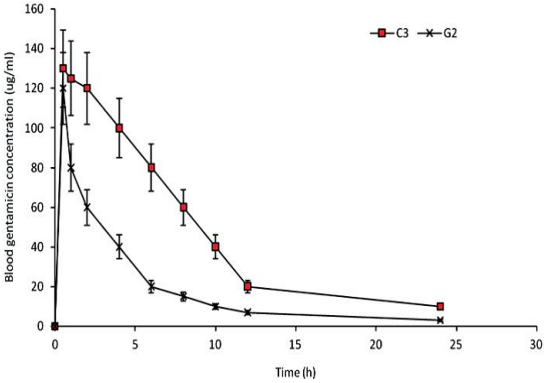


Fig. 14. Cp of gentamicin over 24-h in rats administered with oral optimized gentamicin-loaded PEGylated SLM (C3) and gentamicin pure sample (G2) at a dose of 5 mg.kg^{-1} (n = 5).

Phospholipid-modified SLMs encapsulating gentamicin were produced and loaded into hydrogels of Poloxamer 407 and polyacrylic acids (Carbopols 971P and 974P) (Nnamani *et al*., 2013). The SLMs-loaded hydrogels (microgels) were evaluated for viscosity, spreadability, pH, drug content, and *in vitro* antimicrobial activity against *Klebsiella spp*., *E. coli*, *B. subtilis*, *S. aureus*, and *Ps. aeruginosa*. Poloxamer 407 microgels possessed the most desirable properties in terms of fast antibacterial activity on all tested microorganisms (Fig. 15), *in vitro* diffusion-dependent permeation through rat abdominal skin, spreadability, pH, and viscosity, superior to polyacrylic acids microgels.

Indomethacin tablets based on SRMS consisting of mixtures of phospholipid and triglyceride (Softisan® 154) were formulated

using a validated plastic mould, and were also evaluated (Chime *et al*., 2014). The tablets exhibited good sustained-release properties and can be further developed to achieve once daily administration for improved patient adherence to therapy.

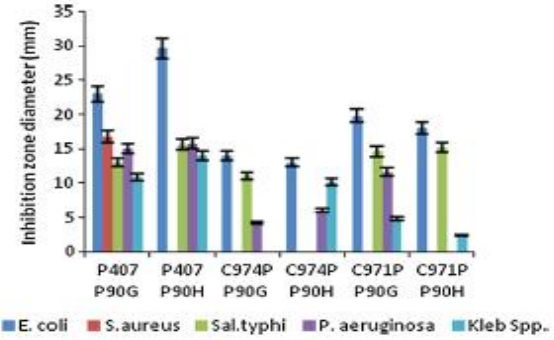


Fig. 15. *In vitro* release study as a function of inhibition zone diameter (IZD).

The anti-inflammatory, antinociceptive and ulcerogenic properties of the indomethacin tablets (75 mg) based on SRMS were also evaluated (Chime *et al*., 2013). Results showed that the tablets had good anti-inflammatory properties and also inhibited the ulcerogenicity of indomethacin by 70 to 80 %. Therefore, indomethacin tablets based on SRMS could be used for improved oral bioavailability of indomethacin and to enhance patient's compliance due to inhibition of gastric irritation effect of this drug.

2.3.5 Microemulsions

Microemulsions are isotropic, thermodynamically stable systems consisiting of either oil dispersed in water (o/w) or water dispersed in oil (w/o) with globule size within micrometer range. Microemulsions enhance the bioavailability of API via topical, oral and systemic routes. A new development in this field is the emergence of self-emulsifying drug delivery system (SEDDS).

SEDDS consists of a mixture of pharmaceutically acceptable surfactant/cosurfactant, oil and drug that emulsify on simple agitation when in contact with aqueous system. Depending on the degree of agitation and concentration and nature of the surfactant system, SEDDS can emulsify to microemulsion or nanoemsulsion. Mr. Vice-Chancellor, Sir, many researches were also conducted in this area as elaborated hereunder.

Novel lipid based drug delivery systems (LBDDS) of tioconazole (a potent antifungal agent), composed of oil, surfactants and co-surfactants were formulated and their physicochemical and pharmacokinetic parameters determined (Attama *et al*., 2011). The oil, surfactant and co-surfactant used were soya bean oil, Cremophor® S9 and Brij® 35, respectively. The *in vitro* permeation of the tioconazole-loaded LBDDS was evaluated and permeation coefficients were between 1.204×10^{-3} cm/sec and 2.178×10^{-3} cm/sec. Microbiological test revealed increased antifungal activity (≈ 1.4 times) against clinically isolated *Candida albicans* as compared with tioconazole solution. Pharmacokinetic studies also showed an AUC_{0-12} of 2930 µg/h/ml for the optimized LBDDS formulation, while that of oral suspension was 1171 µg/h/ml with C_{max} of 797 µg/ml and 355 µg/ml respectively, translating to a 2.5-fold increase in systemic bioavailability.

The effect of oil, surfactant and co-surfactant concentrations on the phase behaviour, physicochemical properties and artemether release from SEDDS was investigated using Precirol® (oil), Labrasol® (surfactant) and Transcutol by water titration method (Agubata *et al*., 2014). Pseudoternary phase diagram (Fig. 16) was developed for the combinations to determine the combination that would give high quality and stable microemusions. Combinations of oil, surfactant and co-surfactants at varied ratios produced SEDDS with different emulsification, drug release and

dispersion qualities. Table 4 contains other researches done on microcarrier drug delivery systems.

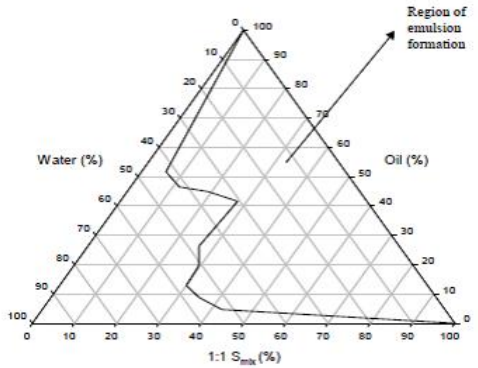


Fig. 16. Ternary phase diagram of the Smix (surfactant-co-surfactant mixture) at 1:1 ratio showing the region of emulsion formation.

2.3.6 Nano Drug Delivery Systems

2.3.6.1 Nanotechnology

Nanotechnology is the design, characterization, production and application of structures, devices and systems by controlling shape and size at the nanoscale (Nano Werk, 2014). The term broadly refers to such fields as biology, physics or chemistry, any scientific field, or a combination thereof that deals with the deliberate and controlled manufacturing of nanostructures. Today, most definitions revolve around the study and control of phenomena and materials at length scales below 100 nm.

Table 4: Other studies on microcarrier drug delivery systems

S/No.	Nature of investigation	Result	Reference
1.	Exogenous mucin combination with Carbopol 941 in	4:1 ratio showed highest mucoadhesion, drug entrapment efficiency	Attama and Onuigbo,

	mucoadhesive microparticles containing cotrimoxazole	and fluid sorption, 1:1 ratio showed highest sustained release potential	2007
2.	SLMs formulated with Softisan® 142 containing glibenclamide	The blood glucose–lowering effect of the SLMs was higher than that of a commercial sample of glibenclamide at equivalent doses	Nnamani *et al.,* 2010
3.	SRMS-based SLMs containing Phospholipon® 90G and Softisan® 154 for intramuscular administration of gentamicin	The release of gentamicin in phosphate buffer varied widely with the lipid content	Umeyor *et al.*, 2012
4.	SRMS-based SLMs using homolipid from *Capra hircus* for the delivery of gentamicin	SLMs showed a biphasic pattern of drug release and exhibited time-dependent and capacity-limited bioactivity	Kenechukwu *et al.*, 2014
5.	Excipient potentials of two natural lipids from *Irvingia wombolu* and *Moringa oleifera* in rifampicin-loaded lipospheres	Lipospheres had significantly higher *in vivo* absorption than the pure rifampicin sample	Onyishi *et al.*, 2014
6.	Water free SRMS SLMs based on Phospholipon® 90H and Softisan® 154	Particle size ranged from 2.19 ± 0.05 µm to 20.77 ± 0.03 µm with high EE % (> 96 %). Loading capacity increased with increase in drug loading	Chime *et al.*, 2012
7.	Characterization of	Structured goat fat	Nnamani

	three different lipid matrices as potential delivery systems for poorly water soluble drugs	matrices favoured drug loading more than tallow fat and Softisan® 142	*et al.*, 2010
8.	Development of topical microemulsion for miconazole nitrate	Stable microemulsion with good *ex vivo* permeation obtained	Ofokansi *et al.*, 2012
9.	Prepared and characterization of ibuprofen-loaded SLMs	Release varied widely with the lipid contents. Anti-inflammatory activity was observed with GIT protection compared with conventional tablet	Momoh *et al.*, 2012
10.	Development of oral delivery forms of diclofenac sodium - based on SRMS SLMs	Sustained release and good anti-inflammatory activity observed with lower GI toxicity in terms of ulcer protection	Momoh *et al.*, 2014
11.	Development of oral SLMs loaded with piroxicam with improved solubility	SLMs displayed significant anti-inflammatory activity quite comparable to Feldene®	Nnamani *et al.*, 2010
12.	SLMs formulation with P90G- modified tallow and goat fats for oral cimetidine	SLMs with 2:1 lipid matrix exhibited higher ulcer inhibition (81.20 %) than CEMTAB® (72.50 %)	Nnamani *et al.*, 2010
13.	Formulation and evaluation of self-emulsifying tablets containing diclofenac	The batches with higher Tween 65:goat fat content had better release rates	Attama *et al.*, 2003
14.	SMEDDS containing piroxicam, chlorpheniramine	Drug release was affected by the particle size of the SMEDDS.	Attama and Nkemnel

	maleate and metronidazole	Piroxicam release was highest in SIF compared with other drugs	e, 2005.
15.	SMEDDS of naproxen containing arachis oil and Tween 81	Arachis oil and Tween 81 formed good SMEDDS, which increased the *in vitro* dissolution of naproxen	Attama and Enete, 2004
16.	Pharmacodynamics of piroxicam from self-emulsifying lipospheres	Lipospheres produced with Tween 65 and homolipid (4:11) performed better than other batches of lipospheres	Attama and Mpamau go, 2006
17.	Piroxicam-loaded lipospheres formulated with a mixture of wax from *Irvingia gabonensis* and Phospholipon® 90G	Lipospheres with 1:1 lipid matrix containing 0.25 % piroxicam had the highest EE of 84 %. Increase in dika wax increased release with zero ulcer index	Brown *et al.,* 2013
18.	Indomethacin–loaded SLMs formulated with 10 %w/w of lipid matrix (Phospholipon® 90G and *Irvingia gabonesis* fat*)*	High EE (94 %) with good anti-inflammatory properties, and inhibition of the ulcerogenicity of indomethacin	Chime *et al.,* 2014
19.	Indomethacin SRMS SLMs formulated using Phospholipon® 90H and Softisan® 154.	EE > 93 %; release profile of 82 - 99 % after 13 h with good anti-inflammatory and ulcer protection	Chime *et al.*, 2012
20.	*In vitro* and *in vivo* properties of indomethacin-loaded	EE: 46 % to 72 % with sodium chloride enhancing EE. Maximum	Obitte *et al.*, 2012

	SLMs	drug released within 80 min and high ulcer protection achieved	
21.	Sustained release microspheres containing amodiaquine prepared by emulsion solvent evaporation using Eudragit® RS PO	EE ranged from 25.08 % to 57.33 %. *In vitro* release profile of amodiaquine showed controlled and prolonged release over 12 h	Uzor *et al.*, 2011
22.	Stavudine-loaded microspheres based on admixtures of Eudragit® RL100 and RS100	Slow and first order release of stavudine from microspheres in pH 1.2 (SGF)	Attama *et al.*, 2011
23.	*In vitro* properties of surface-modified lipid microspheres contining halofantrine	Sustained and controlled release of halofantrine was achieved compared with tablet dosage form	Attama and Igbonek wu, 2011
24.	Surface modified SLM based on homolipids and Softisan® 142:	Stable microparticles within the lower micrometer range produced	Nnamani *et al.*, 2010.

Nanoparticles (Fig. 17) used as drug delivery vehicles (Nanopharmaceuticals or nanomedicines) are generally within sizes up to 300 nm or even more depending on the route of administration. They consist of different biodegradable or biocompatible materials such as natural, semi-synthetic or synthetic polymers, lipids, or metals, or combinations of these materials. The bulk properties of materials often change dramatically when reduced to nanoscale dimensions, e.g. surface area.

Nanotechnology has some resemblance with spiritual matters: You are always expected to believe what you cannot see!

"Like the Ethiopian eunuch who read the book of Isaiah without understanding it (Acts 8:31), many who read scripts on nanotechnology and nanomedicines may not understand unless someone guides them"

"It was only after the resurrection that the disciples aided by power of the Holy Spirit understood the Christ who attained glory through His suffering and bore witness to him" (The Holy Bible).

It is expected that after this lecture, you will understand the concept of nanomedicines and so begin to advocate and bear witness to the fact that we should go 'nano' to achieve a lot in healthcare.

Nanoscience

Nanoscience is the study of phenomena and manipulation of material at the nanoscale. This is, in essence, an extension of existing sciences into the nanoscale.

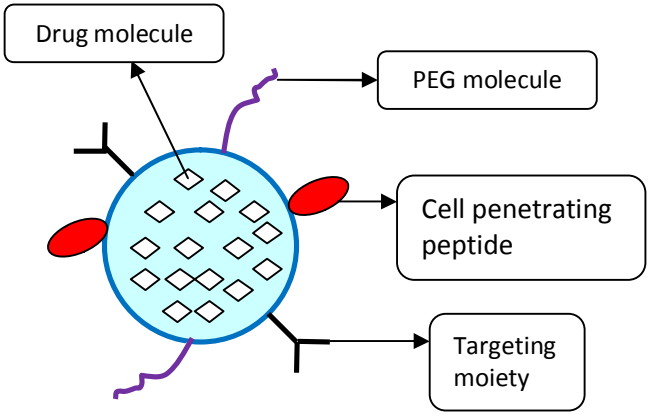


Fig. 17. A typical functionalized nanoparticle

Surface area

This is a very important property of nanomaterials. When compared to the same mass of material in bulk form, nanoscale materials have a relatively larger surface area. This can make materials more chemically reactive and affect their strength or electrical properties. In drug delivery, surface area affects drug loading (pay load capacity), diffusion and transport across membranes.

2.3.6.2 Nanomanufacturing

Nanomanufacturing requires a lot of skill and expertise to obtain good, quality particles of well-controlled size and shape. There are different ways of manipulating materials to obtain nanoparticles. The two most common ones are top-down and bottom-up methods (Fig. 18). After manufacturing, characterization follows to make sure the particles produced are within the desired nanometer range.

Top-down

Top-down approach involves particle size reduction/milling.

Bottom-up

Bottm-up technologies involve building nanoscale materials from atoms, molecules or solutions. There are two variants: self assembly and molecular assembly.

Whatever method adopted depends on the availability of materials, equipment and targeted application, but the ultimate issue is to arrive at the desired nanomaterial since “All roads lead to Rome.”

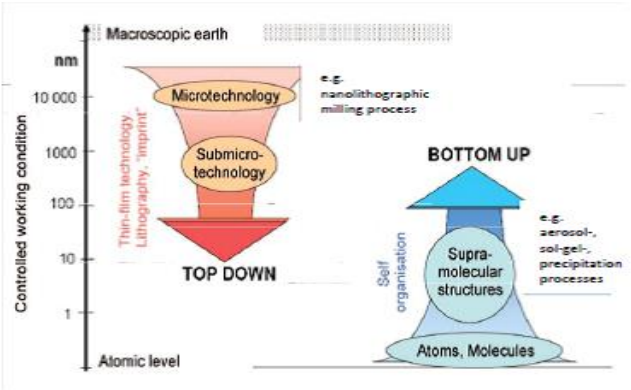


Fig. 18: Methods of nanoparticle production: top-down and bottom-up approaches (Adated from Raab *et al.,* 2011 with modification).

2.3.6.3 Nanomedicines

What is Medicine/a Medicine?

Medicine is the science of healing, the practice of the diagnosis, treatment and prevention of diseases, and the promotion of health…….to practise medicine!

A medicine, on the other hand, is a substance which is used in the treatment of illness or injury, or to maintain health and well-being, e.g. cough medicine, pain medicine, etc. Medicines come in

many forms, such as tablets, liquids, inhalers, drops, patches, creams, lotions, pessaries, suppositories and injections. Some are taken by mouth, while others are applied or injected to parts of the body.

What is Nanomedicine/a Nanomedicine?

Nanomedicine is defined differently by different scholars, but one very simple definition is that nanomedicine is the use of nano-scale science and technology for the benefit of the patient.

The field of 'Nanomedicine' is the science and technology of diagnosing, treating and preventing diseases and traumatic injury, of relieving pain, and of preserving and improving human health, using molecular tools and molecular knowledge of the human body. Nanomedicine, therefore, is not practising medicine at a nanoscale! Nanomedicines, on the other hand, refer to dosage forms of drugs in nanoform. They may also be called nanopharmaceuticals or nano drug delivery systems. For the field of nanomedicine to make any impact in healthcare, nanomedicines are paramount.

'Nano' in Medicine

The fundamental building blocks of life - DNA, proteins, lipids - are nano-sized systems. At the molecular level, a lot of biology happens at the nanometer scale. DNA (diameter ≈ 2 nm) and proteins (typically ≈ 3 - tens of nm) (Fig. 19) are effectively complex nanomachines, and their function, movements, mechanics and interactions with each other in health and disease can be studied and targeted, with nanotechnology tools. This convergence of nanotechnology and biology has led to the emergence of nanomedicine (Contera, 2014). Current research focuses on areas such as new targeted drug delivery systems.

Nanomedicine and nanomedicines offer hope for treating several diseases like cancer.

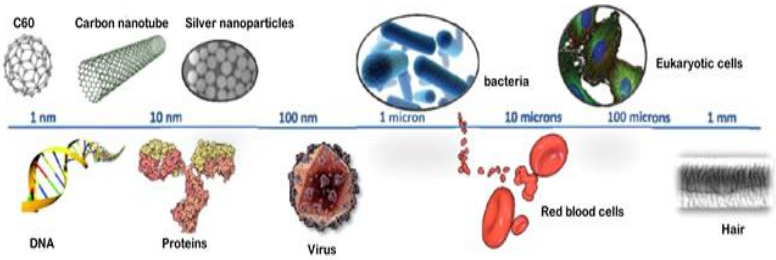


Fig. 19. Size comparison: nanoparticles and biological systems (Source: Contera S., http://www.azonano.com/article.aspx?ArticleID=3012 Accessed December 29, 2014)

From the foregoing, I would like to affirm that we need 'nano' for medicines because of the following:

Life is "Nano"

The basic unit of all living organisms, the cell, is made up of numerous smaller structures known as organelles consisting of biomolecules that interact with one another, bringing together mechanical and biochemical functions at the nano-scale level. The molecular "nano-machines" thus form the foundations of all living organisms.

Diseases are often "Nano"

Diseases are often 'nano', but most of the methods and medicines used in medicine today are not. Many disease processes begin in specific cell types with a dysfunction at the level of the cell organelles and the cellular biological "Nano-machines". Today's medicines are too crude for the diseased cell, or the medicines used "flood" the body in a very non-specific way

and also trigger side effects in organs that are not even involved in the disease process. It would also make sense to treat the disease processes occurring at the nano level in individual cells and organs by using nanomedicines that can specifically target these cells and organs.

Limited Efficacy of Medicines Today

Today's medicines have achieved a lot, but have not been able to eradicate the current principal medical problems: HIV-AIDS, malaria, tuberculosis, ebola virus disease (EVD), etc. Cancers are more responsive to treatment than they used to be, but often at the cost of severe side effects. New tools for these therapeutic areas would, therefore, be highly welcomed - **Nanomedicines?**

2.3.6.4 Position of Nanomedicines within the Healthcare Portfolio

Nanomedicine is expected to contribute significantly to the overall healthcare portfolio. In Europe, the highest causes of mortality are cardiovascular diseases and cancer, and demographic changes are producing an ageing population leading to new healthcare challenges. There is rising prevalence in diseases of the central nervous system, such as senile dementia, Alzheimer's disease, Parkinson's disease, and diseases associated with ageing, for example arthritis and ocular diseases. Whilst much progress was made in the 20th century in respect of the therapies for infectious diseases, emergence of resistance, HIV/AIDS and other new infectious diseases, for example, SARS, EVD, present new challenges.

In Nigeria and Africa in general, the reverse is the case: huge population of under 30, rising cases of HIV/AIDS, menace of malaria, tuberculosis, and sexually transmitted infections, etc. abound.

Currently, nanomedicines remain in the realm of future medicines in Nigeria and almost Africa as a whole. Therapies which are available to patients are for the treatment of cancer, a few infectious diseases, multiple sclerosis, arthritis and age-related degeneration, and not for diseases afflicting mostly Africa poverty-related diseases.

Advantages of Nanomedicines over Conventional Medicines

There are a number of drawbacks in the conventional delivery of some drugs such as their limited solubility, poor distribution within the body, lack of target selectivity, unfavourable pharmacokinetics and unwanted effects on adjoining tissues. Some of the areas that nanomedicines have made impact include:

- improvement of the solubility and bioavailability of hydrophobic drugs;
- improvement of the circulatory life-time of drugs, e.g. of protein-based and other hydrophilic drugs;
- lowering of doses of drugs as highly targeted drugs would reduce systemic toxicity;
- targeting of individual pathogens or biomolecules; and
- development of API tunable delivery systems.

The major advantages of nanomedicines over conventional medicines could be summarized in Fig. 20.

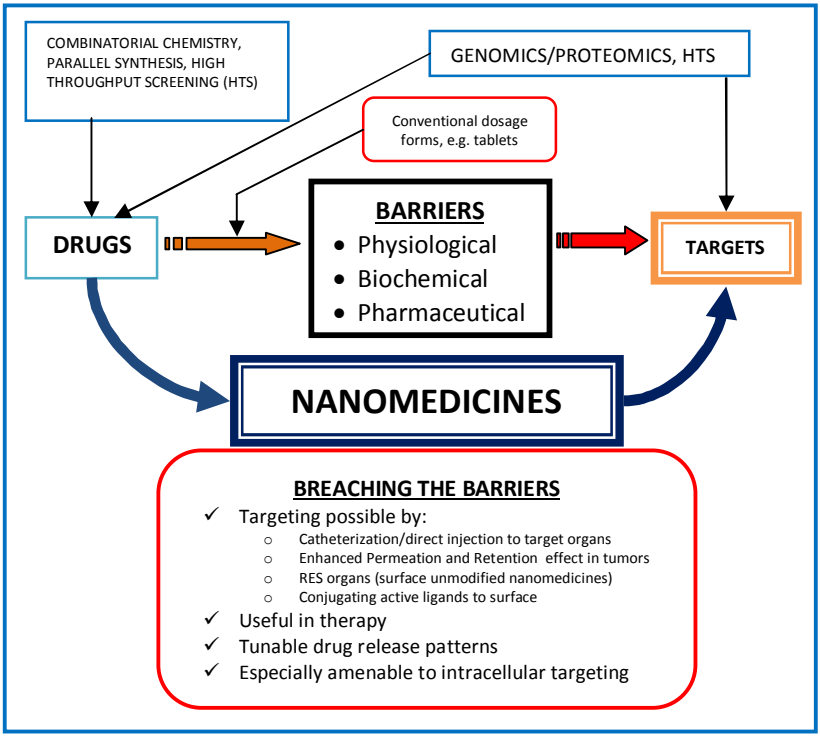


Fig. 20. Breaching the barriers to conventional medicines with nanomedicines (Recreated with modification from: Vasir *et al*., 2005)

2.3.6.5 Nanomedicines and Infectious Diseases

Infectious diseases are disorders caused by organisms such as bacteria, viruses, fungi or parasites (pathogenic organisms). Many organisms live in and on our bodies. They are normally harmless or even helpful, but some organisms under certain conditions may cause disease. Pathogenic bacteria can be grouped into three categories on the basis of their invasive properties for eukaryotic cells:

- ***Extracellular bacteria***, e.g. *Bacillus anthracis,* Enterotoxigenic *E. coli, Haemophilus influenza, Mycoplasma spp., Pseudomonas aeruginosa,*

Staphylococcus aureus, Streptococcus pyogenes, V. cholera.

- ***Facultative intracellular bacteria***, e.g. *Legionella pneumophila, R. rickettsii, Salmonella* and *Mycobacterium spp.,* invasive *Escherichia coli, Listeria monocytogenes, Neisseria spp., Shigella spp.* Salmonella and mycobacterium are very resistant to intracellular killing by phagocytic cells.
- **Obligate intracellular bacteria**, e.g. Chlamydia, *Coxiella burnettii* and *Rickettsia spp.*

Viruses depend on the host cells that they infect to reproduce. When found outside of host cells, viruses exist as a protein coat or capsid, sometimes enclosed within a membrane. The capsid encloses either DNA or RNA which codes for the virus elements. While in this form outside the cell, the virus is metabolically inert.

Anti-infectives and intracellular organisms

Treatment of infections caused by intracellular organisms (e.g. bacteria and viruses, including malaria parasites) remains both a medical and economic challenge. Pathogens thriving or maintaining themselves in cells, or simply taking transient refuge therein, are indeed shielded from many of the humoral and cellular means of defence (Fig. 21) and are more or less protected against many antibiotics because of their intracellular locations. This explains why intracellular organisms are not only harmful to the host cells, but may also constitute a reservoir for recurrence and reinfection. Since antibiotics poorly act on intracellular bacteria, resistant mutants may also develop (Table 5). Benefits accruable from nanomedicines in this regard are based on the ability of nanomedicines to breach barriers (Fig. 20) and traffic cells easily reaching their targets.

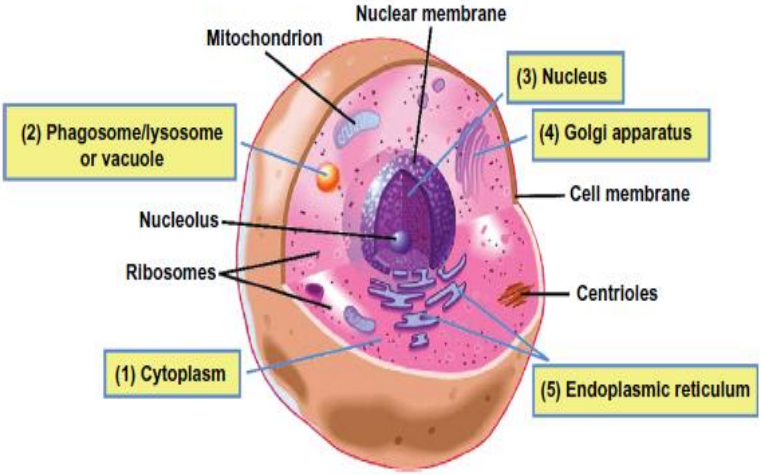


Fig. 21. Potential locations of intracellular pathogens (1): Cytosol (*Francisella tularensis*, *Listeria monocytogenes*, Shigella). (2): Phagosome/lysosome or vacuole (*M. tuberculosis*, *Brucella spp.*, Salmonella, Legionella). (3): Nucleus (HSV, HIV). (4): Golgi apparatus (Chlamydia). (5): Endoplasmic reticulum (HCV, Brucella, *Toxoplasma gondii*, *Legionella pneumophilia*). (Source: Armstead and Li, 2011).

Table 5. Influx, accumulation levels (at equilibrium), efflux, and predominant subcellular localization of the main antibiotics (grouped by pharmacochemical classes) (Carryn et al., 2003)

Pharmaco-chemical class	Antibiotic	Influx[a]	Efflux[b]	Accumulation level (at equilibrium)[b]	Predominant subcellular localization
Beta-lactams	All	Fast	Variable	< 1	Cytosol
Macrolides	Erythromycin	fast	Fast	4 - 10	2/3 lysosomes; 1/3 cytosol
	Clarithromycin	Fast	Fast	10 -20	
	Roxithromycin	Fast	Fast	10 -20	
	Azithromycin	Fast	Slow to very slow	40 - 300	
	Telithromycin	Fast	Fast to slow	15 - 50	
Fluoroquinolones	All	Fast to very fast	Very fast	4 – 10	Cytosol
Aminoglycosides	All	Very slow	Very slow	2 -4 (after several days)	Lysosomes
Lincosamines	Clindamycin	Fast	Fast	5 - 20	Unknown
	Lincomycin	Fast	Fast	1 - 4	Unknown
Tetracyclines	All (?)	Fast	?	1 - 4	Unknown

Ansamycins (Rifamycins)	Rifampicin	Fast	?	2 - 10	Unknown
	Rifapentin	Fast	?	60 – 80	
Glycopeptides	Vancomycin	Slow	?	8 (after 24 h)	Lysosomes (in kidney)
	Teicoplanin	Fast	?	60	Unknown
	Oritavancin	Slow	Slow	150 – 300 (after 24h)	Probably lysosomes
Oxazolidinones	Linezolid	Fast	Fast	≈ 1	Unknown

[a]very fast: less than 3 min to equilibrium; fast: 3 to 15 min to equilibrium; slow: 15 min to 3 h to equilibrium; very slow: more than 3 h to equilibrium.
[b]C_c/C_e: accumulation factor (ratio between the cellular concentration and the extracellular concentration)

Cellular Uptake and Disposition of Antibiotics (Cellular Pharmacokinetics)

Diseases such as typhoid fever, tuberculosis, hepatitis, and HIV/AIDS are caused by intracellular pathogens. Conventional treatments for these diseases typically consist of long-term therapy with a combination of drugs, which may lead to side effects and contribute to low patient compliance. The pathogens reside within intracellular compartments of the cell, which provide additional barriers to effective treatment. Therefore, there is need for improved and more effective therapies for such intracellular diseases. Therapeutic drugs targeting the intracellular pathogens should overcome the cell membrane barriers, release and retain the drug intracellularly at the therapeutic level for a desired time period.

Some antibiotic drugs like aminoglycosides and ß-lactams have limited cellular penetration, whereas others such as

fluoroquinolones or macrolides have the ability to penetrate host cells, but are poorly retained and therefore inefficient (Briones *et al*., 2008).

2.3.6.6 Nanomedicines as Sustainable Medicines

One of the characteristics of nanomedicine is the highly targeted use of very small quantities of substance for therapy; in experimental studies, for example, certain therapeutic effects have been achieved using quantities of substance hundred times lower than conventional medicines. The characteristics offer huge potential for sustainable medicine. Reduction in dose is also envisaged in addition to dosage regimen modification.

2.3.6.7 My Nanomedicines Research

Mr. Vice-Chancellor, Sir, you will notice that I have dwelt so much on lipid drug delivery systems. That is true because there is increasing interest in lipid-based drug delivery systems due to factors such as better characterization of lipidic excipients and formulation versatility, and the choice of different drug delivery systems. It is also important to know the thermal characteristics, crystal habit, texture and appearance of a new lipid matrix when determining its suitability for use in pharmaceutical formulation. My research into nanomedicines started with the study of the lipid matrices that we intended to use to formulate nanomedicines. In line with this research, we embarked on the characterization of mixtures involving beeswax, theobroma oil and goat fat, and their phospholipid-modified variants, which we termed structured lipid matrices for nano drug delivery applications (Attama *et al*., 2006, 2007). These studies were begun during my post-doctoral stay at Institut für Pharmazeutische Technologie, Technische Universität Carolo-Wilhelmina zu Braunschweig, Germany, where I have visited several times for more nano research in addition to other

collaborative researches. Binary mixtures of lipids with fatty acids that differ by two or more carbon atoms often show incongruent melting behaviour and partial solid solutions, due to distortion in crystal arrangement (Fig. 22). Perfect solid solutions form when lipids with similar fatty acids are involved with a resultant increase in crystallinity. The lipids used in this study contain fatty acids of different chain lengths and their mixtures had low degree of crystallinity.

Binary lipid matrices containing a novel homolipid from *Capra hircus* (goat fat) and theobroma oil were formulated by fusion and characterized by DSC, SAXD and WAXD. The internal structures of some of the lipid matrices were also studied by freeze-fracture transmission electron microscopy (TEM). DSC results obtained indicated that stable goat fat melts completely with two detectable melting peaks at 33.0 ± 0.2 and 49.9 ± 0.1 ^{o}C, and total enthalpy of 99.9 ± 2.5 mJ/mg. New interferences were detected for the mixtures in WAXD mostly between $2\theta = 17.5^{o}$ and $2\theta = 27.5^{o}$ (Fig. 22). Other crystal studies revealed that lipid matrix containing 50 %w/w goat fat in theobroma oil showed unique crystallization kinetics necessary for nanoparticle formulation.

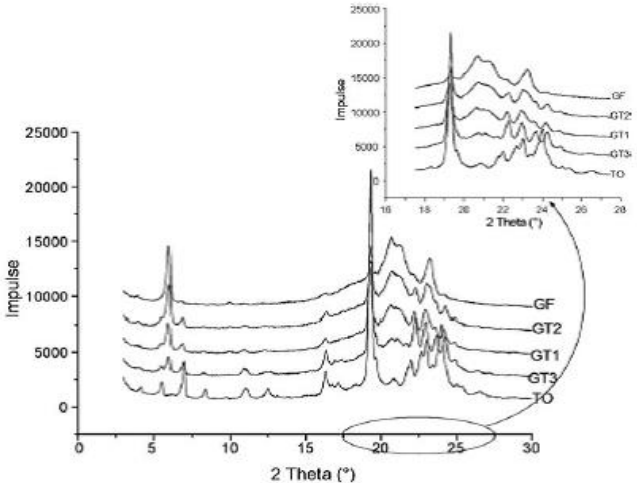


Fig. 22. WAXD diffractograms of the lipid matrices showing the region of mixed crystals and mixtures of crystals

In a related study, lipid matrices containing various proportions of beeswax and goat fat were prepared by fusion, and fully characterized. Analysis of thermal data from DSC indicated that the physically structured lipid matrices revealed varied melting peaks between those of the pure lipids. Kinetics of crystallization of the molten lipid matrices were studied in an isothermal heat conduction microcalorimeter (IMC), otherwise called the Pharmaceutics 'Black Box'. Results of kinetic studies (Figs. 23) confirmed that mixtures of these lipids produced matrices composed of mixtures of crystals alongside mixed crystals (Fig. 22) with imperfections necessary for increased drug loading and retention capacities.

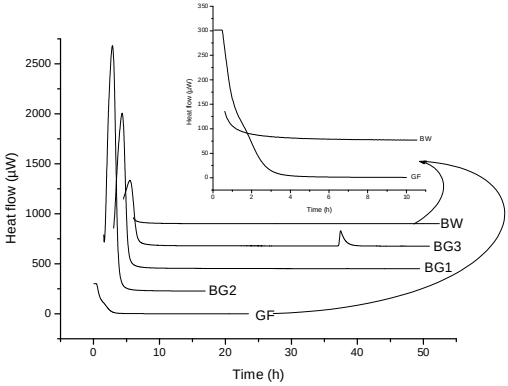


Fig. 23. Crystallization exotherms of the lipid matrices: BW (beeswax), GF (goat fat), BG3 (75 %w/w beeswax), BG1 (50 %w/w beeswax) and BG2 (25 %w/w beeswax). Inset shows the magnified crystallization exotherms of BW and GF.

Surface-modified lipid nanocontainers were formulated with a homolipid from *Capra hircus* (goat fat) templated with a heterolipid (Phospholipon® 90G) by melt-emulsification with high pressure homogenisation using polysorbate 80 as the mobile surfactant and characterized (Attama and Müller-Goymann, 2007). DSC results revealed minor increase in crystallinity of the lipid matrix after one month (Fig. 24). The size of the particles remained within the lower nanometer range after one month. WAXD results showed low crystalline matrices and particles, while DSC only showed a very low endothermic process after one month of storage at 20 ^{o}C. TEM micrograph of the lipid matrices revealed lamellar sheets for Phospholipon® 90G and layered triglyceride structures for the homolipid and Phospholipon® 90G-templated homolipid; that of SLN revealed anisometric structures (Fig. 25). The implication of this finding is that the lipid nanocontainers would not experience modification to highly ordered particles over time and this would be favourable for any

incorporated drug as drug expulsion, due to increase in crystallinity, would not occur.

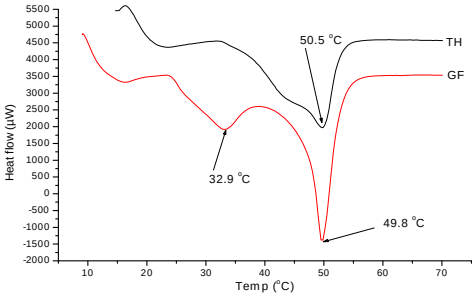
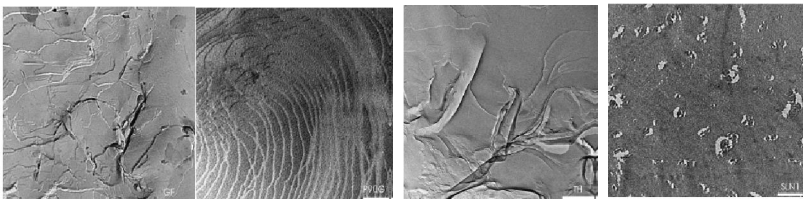


Fig. 24. DSC traces obtained for the lipid matrices after one month: Goat fat (Homolipid) (GF), templated homolipid (TH).



(1) (2) (3) (4)

Fig. 25. FFTEM micrographs: homolipid (GF) (1), Phospholipon 90G® (P90G) (2), templated homolipid (TH) (3), SLN containing 1.0% (w/w) ploysorbate 80 (SLN1) (4). Bars represent 500, 200, 100 and 100 nm, respectively

The influence of a heterolipid (Phospholipon® 90G), which directly modifies the surface of solid lipid nanoparticles (SLN), and goat fat on the crystallinity of beeswax matrix and the SLN prepared therefrom was studied (Attama and Müller-Goymann, 2008). Results showed that the lipid matrices containing P90G had some amorphous portions (Fig. 26). Most SLN formulated possessed low z-average diameters and polydispersity indices and crystallized into stable modification within 48 h of preparation. The overall result indicated that P90G and goat fat reduced the

crystallinity of beeswax matrix and SLN. There was no increase in crystallinity of SLN on storage. Modification of beeswax with P90G or goat fat offers a way of improving the SLN formulated with beeswax in terms of reduction of its crystallinity responsible for its low-drug incorporation efficiency.

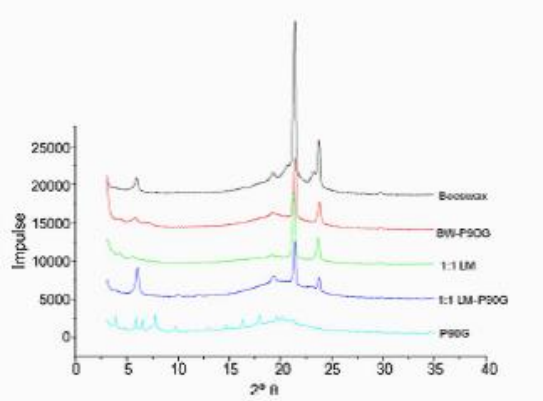


Fig. 26. WAXD of lipid matrices: Beeswax containing 30%w/w P90G (BWP90G), 1:1 mixture of beeswax and goat fat (1:1 LM), lipid matrix containing 1:1 mixture of beeswax and goat fat and 30 %w/w P90G (1:1 LM-P90G).

Solid lipid nanodispersions were prepared with a 1:1 mixture of theobroma oil and goat fat as the main lipid matrix (Attama *et al*., 2007). WAXD studies (Fig. 27) and DSC revealed low crystalline SLN after 3 months. *In situ* crystallization studies in IMC revealed delayed crystallization of the SLN with 1.0 % w/w polysorbate 80. The lipid mixtures produced nanodispersions with lower crystallinity and higher particle sizes compared with those prepared with theobroma oil alone with or without P90G, and would lead to higher drug incorporation efficiency when used in formulation of API. Mixtures of theobroma oil and goat fat would be suitable for the preparation of nanostructured lipid carriers but theobroma oil containing phospholipid is good for ocular or parenteral drug delivery system considering the low particle size,

particle size stability. Lipid nanodispersions prepared with the lipid admixture, which had higher increase in particle size on storage would be suitable for preparation of topical and transdermal products.

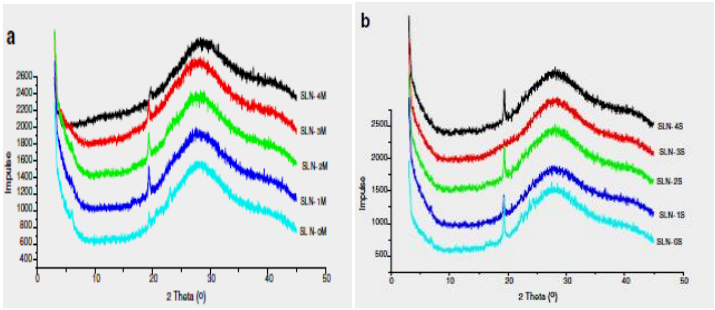


Fig. 27. WAXD diffractograms of the SLN after 3 months. (a) SLN-0M to 3M (mixed lipid matrix) and (b) SLN-0S to 3S (single lipid matrix).

Mr. Vice-Chancellor, Sir, delivery of drugs to the tear film is routinely done with eye drops, which are well accepted and for most patients easy to use. However, attainment of an optimal drug concentration at the site of action is a major problem. Poor bioavailability of drugs from ocular dosage form (≈ < 5 %) is mainly due to the pre-corneal loss factors which include tear dynamics, non-productive absorption, transient residence time in the cul-de-sac, and relative impermeability of the corneal epithelial membrane. Development of an alternative to solution-type eye drop that would provide sustained delivery of a drug is a major challenge. SLN formulations are adhesive, and could prolong the residence time of the dosage form in the eye and increase bioavailability.

In one of our researches, SLNs were prepared with a combination of homolipid from goat (goat fat) and phospholipid, and evaluated for diclofenac sodium delivery to the eye using bio-

engineered human cornea (Attama *et al*., 2008). The encapsulation efficiency was high with sustained *in vitro* release. High permeation of the drug through the bio-engineered cornea was achieved (Fig. 28). This showed that permeation of diclofenac sodium through the cornea construct was improved and sustained by formulation as SLN modified with phospholipid.

Surface-modified SLN sustained delivery systems of timolol hydrogen maleate, a prototype ocular drug, were formulated and evaluated using human cornea construct produced from immortalized human corneal endothelial cells (HENC), stromal fibroblasts and epithelial cells CEPI 17 CL 4 (Attama *et al*., 2009). Drug transport studies through the bioengineered cornea were carried out and drug concentration analyzed by HPLC. Results showed that surface-modified SLN were very small (< 47.2 ± 0.3 nm) with low polydispersity indices (Fig. 29A) and sustained *in vitro* release and permeation compared with unmodified lipid nanoparticles, whose particles were greater than 160 nm (Fig. 29B). Surface-modified SLN could provide an efficient way of improving retention and ocular bioavailability of timolol hydrogen maleate.

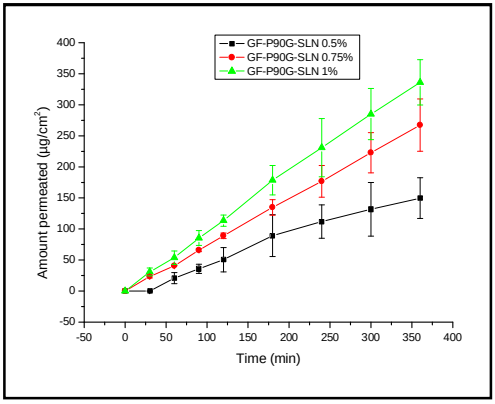
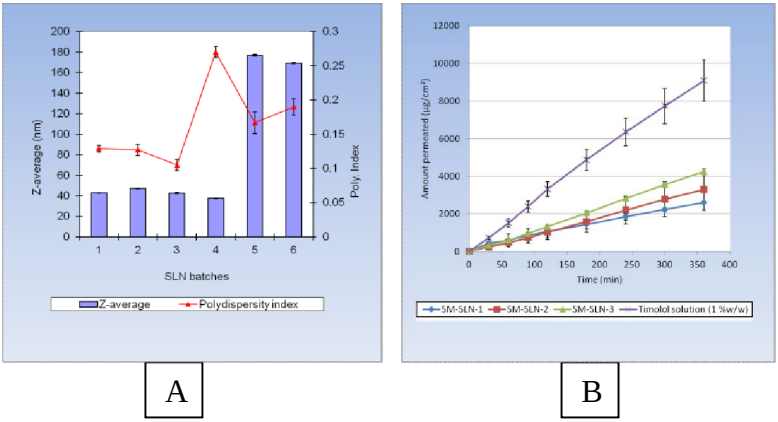


Fig. 28. Permeation profile of the diclofenac-loaded SLN prepared with phospholipid (mean ± S.D., *n* = 3).



A B

Fig. 29. (A) Particle size distribution of the SLN after 1 week of preparation (*n* = 3). (B) Permeation of timolol hydrogen maleate through the bioengineered cornea (*n* = 3).

In another study, the permeation of three model drugs (diclofenac sodium, timolol hydrogen maleate and hydrocortisone) from SLN was assessed using artificial skin construct (ASC) bio-engineered from human dermal fibroblast

(HDF) and human adult keratinocytes, low calcium condition, elevated temperature (HaCaT) cell line (Attama *et al*., 2008). DSC and WAXD results showed low crystalline nanoparticles. Particle size analysis indicated very low growth in particle size with time and high zeta potentials. Encapsulation efficiencies of the SLN batches were high and permeation of the drugs through the ASC was sustained (Fig. 30).

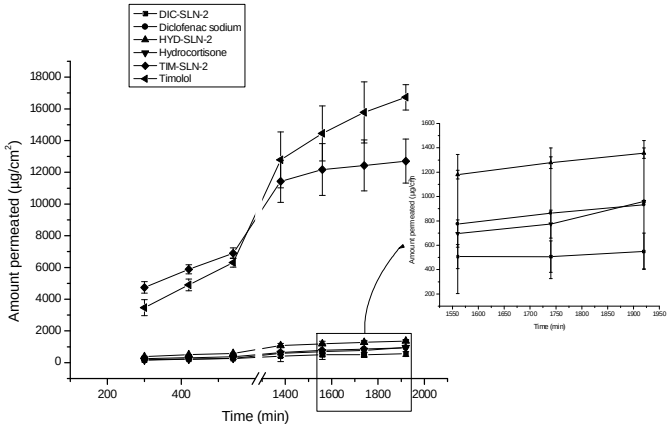
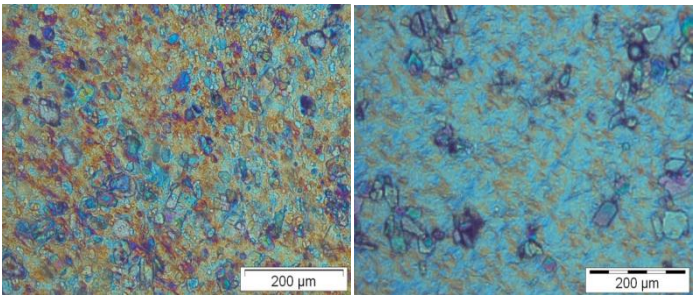


Fig. 30. Permeation profiles of the free drugs and the SLN through ASC (n = 3). DIC-SLN-2, TIM-SLN-2 and HYD-SLN-2 contain 1.0 %w/w each of diclofenac sodium, timolol hydrogen maleate and hydrocortisone, respectively.

Mr. Vice-Chancellor, Sir, you will agree with me from the foregoing that the use of mixed lipids, with low crystallinity termed structured lipids and surface modification with phospholipid in addition, led to high drug encapsulation efficiency and sustained release of the incorporated drugs of different lipophilicities. Permeation of the model drugs from these mixed lipid core SLN through artificial skin construct indicated that these SLNs could prove to be good, prolonged drug delivery vehicles for

ocular or topically active drugs. For topical delivery, this SLN could be applied to the skin as such, or incorporated into creams, gels or hydrogels before application. However, it should be noted that the permeation properties would be modified when incorporated into a different dosage form.

In a very recent study, SLN were formulated with a specially designed nanoparticle production equipment called microPart® and encapsulating the antimalarial drugs- artemether and lumefantrine. Particle size and size distribution of the nanomedicines were determined by PCS. The molecular environment of the lipid particles was studied by fluorimetric spectrophotometry. Interaction of the nanoparticles with cells was studied. Result of this study revealed that the drug and the lipid matrix were compatible, but different crystal properties were noted for artemether and lumefantrine (Fig. 31), which affected their solubilities in the lipid matrix.

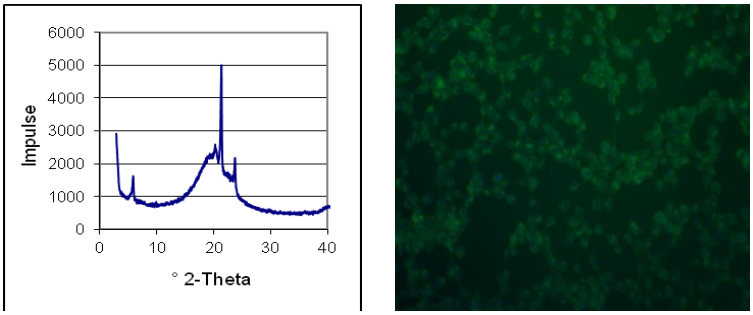


(A) (B)

Fig. 31. Crystal characteristics of the drug/lipid matrix mixtures at 20 %w/w at 30 ^{o}C. (A): Artemether (B) Lumefantrine

Particle size and size distribution of the SLN determined by PCS indicated that the particles were within the range of 150 nm - 600 nm, with varied polydispersity indices. The particle size and size distribution were affected by the drug crystal characteristics and

drug loading. Light microscopic studies indicated the presence of micrometer particles at increased drug loading. WAXD (Fig. 32A) and DSC results indicated the presence of particles of solid nature.



(A) (B)

Fig. 32. (A): Representative diffractogram of mixture of artemether and lumefantrine (1% of 1:1 ratio) in lipid marix. (B) Fluorescent image of the nanoparticles in the presence of cells (MHEC5-T).

Results of interaction of the nanoparticles with cells indicated ability of the coumarin 6-labeled SLN to enter cells as shown in Fig. 32B. CLSM studies also proved the presence of the labelled SLN in cells (Figs. 33).

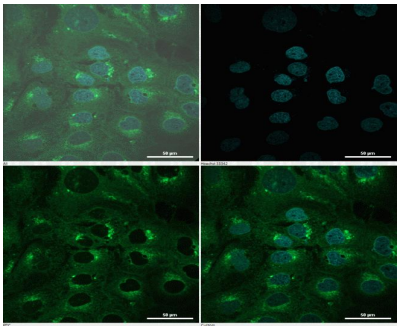


Fig. 33. CLSM image of the nanoparticles in the presence of Caco-2 cells

Vesicular Systems

Vesicular systems for drug delivery are highly ordered assemblies consisting of one or more bilayers formed as a result of self-assembling of the component materials. They include such systems as liposomes, cubosomes, hexosomes, bilosomes, ethosomes, sphingosomes, niosomes, transfersomes, aquasomes, etc, that are amenable for oral, topical or parenteral delivery. The self-assembled nature of these systems implies that these systems are in a tension-less state. Vesicular drug delivery systems are important in drug delivery because of their ability to encapsulate different API including proteins and peptides. They have been investigated as novel delivery systems for vaccines and antigens. Mr. Vice-Chancellor, Sir, we formulated bilosomes, ethosomes and liposomes containing bioactives for human use. Liposomes and niosomes containing vaccines and antigens for use in poultry management were also formulated and evaluated with good results. This area is referred to as Veterinary Pharmaceutics.

Bilosome drug delivery system for insulin was studied. Two bilosomal preparations were formulated using a lipid extract from soya beans seed, palmitic acid and cholesterol (BI), and palmitic acid and cholesterol (BII) (Ayogu *et al*., 2009). Each of the preparations contained sodium deoxycholate and soluble insulin. BI was given orally only, while BII was administered subcutaneously, intraperitoneally and orally to different groups of streptozotocin-induced diabetic male rats. The results of the studies showed that oral administration of the formulations produced blood glucose reduction, which could mimick endogenous release of insulin with prolonged activity, although less compared with parenteral administration.

Ethosomal and liposomal vesicular formulations containing griseofulvin, piroxicam, metronidazole and *Bridelia feruginea*

extract, were separately prepared by the solvent evaporation method. Spherically-shaped ethosome vesicles of nano-size ranges, which maintained morphological integrity (stability) for 60 days and up to 275 days after preparation (Fig. 34) were produced (Mbah *et al*., 2014). The DSC thermograms showed reversible perturbation of the skin lipids as the mechanism of permeation of the ethosomes. All the formulations showed potentials for controlled transdermal delivery. The amount of drug permeated per unit area generally increased with increase in ethanol concentration within the range tested. Metronidazole ethosome gel showed potential for sustained vaginal delivery.

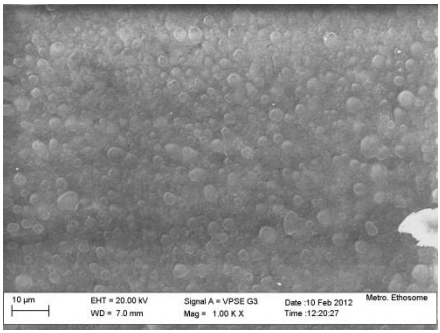


Fig. 34. SEM micrograph of ethosome vesicles of metronidazole after 60 days of preparation.

Stearylamine-based cationic liposomes containing amoxicillin were prepared by lipid film hydration technique and characterized (Onuigbo *et al*., 2011). Susceptibility of clinical isolates of *S. aureus* to amoxicillin encapsulated in the cationic liposome was compared with 1,2-dioleoyl-3-trimethylammonium propane–based cationic liposome and the marketed amoxicillin tablets. Particle size distribution had a peak at 94 nm, zeta potential was 34 mV and polydispersity was greater than 0.3. The

clinical isolate of *S. aureus* was most susceptible to stearylamine cationic liposome (Fig. 35).

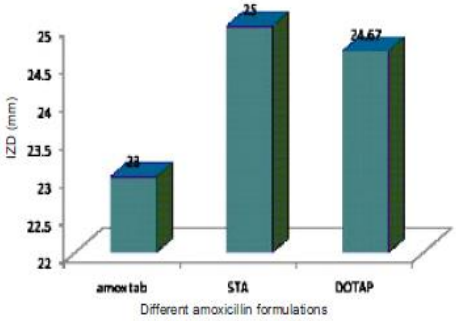
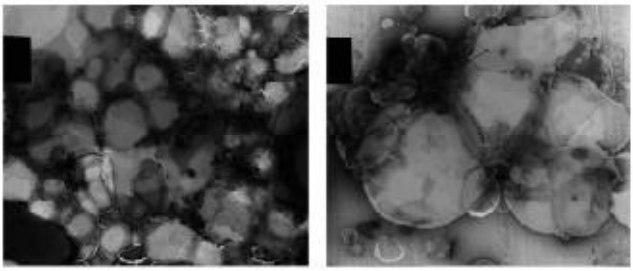


Fig. 35. Susceptibility of *S. aureus* to the different amoxicillin liposomes: STA-stearylamine DOTAP- 1, 2-dioleoyl-3-trimethylammonium propane

The enhancement of immune response of birds to Newcastle disease (ND) vaccine encapsulated in 1,2-dioleoyl-3-trimethylammonium propane (DOTAP)-based liposomes was evaluated (Onuigbo *et al*., 2012). The liposomal ND vaccine vesicles were spherical with mean particle size below 100 nm (Fig. 36) and zeta potential of 24 mV. Both the liposomal ND vaccine and live La Sota® vaccine groups were vaccinated orally and the birds challenged with oral administration of virulent Herts 33 strain at 9 weeks of age. After the boost vaccination, the chickens vaccinated with the liposomal ND vaccine had a higher mean antibody titre, indicating that encapsulating ND vaccine in DOTAP-based liposome induced significantly higher immunity than the live La Sota® vaccine.



X3400 x10500

Fig. 36. TEM images of the liposome-encapsulated ND vaccine.

Salmonella gallinarum is a non-motile host-specific bacterium in domestic poultry that causes fowl typhoid, especially in domestic poultry. A study was performed to compare the antibody titre of commercial subcutaneous Fowl typhoid® vaccine with its oral liposomal formulation (Onuigbo *et al*., 2013). It was found that there was no significant difference in the mean antibody titre of the birds by either the subcutaneous or oral vaccination of Fowl typhoid® vaccine, but the liposomal formulation is favoured because oral delivery route is more convenient.

Span 20-based niosome was prepared by lipid film hydration technique and loaded with Newcastle disease (ND) vaccine (Okore *et al*., 2011). Adjuvanticity was assessed using haemagglutination inhibition test. The vesicles of Span 20-based niosomes were distinct, near spherical, large and unilamellar with sizes < 1000 nm. Haemagglutination inhibition test showed a 71 % increase in immune response over that of the marketed La Sota® vaccine, which had a 60 % increase.

4. CONCLUSIONS

With the availability of nanotechnology tools, there are possibilities for design of novel nanomedicines with real potential to provide improved diagnostics and treatments for debilitating and life-threatening diseases. Inasmuch as we have arrived at nanomedicines, we should not forget the 'road' to nanomedicines in a hurry. The conventional drug formulations and delivery systems that dotted the road to nanomedicines are still very relevant today. We should be interested in the conversion of the already existing drugs to nanomedicines to derive maximum benefit nanomedicines offer while not losing the benefits we have been enjoying with 'macromedicines'.

Nanomedicines in the long run are expected to contribute significantly to the overall healthcare portfolio. They would provide medicines with: high stability (i.e., long shelf life); high pay load capacity (i.e., many drug molecules can be incorporated in the particle matrix); feasibility of incorporation of both hydrophilic and hydrophobic substances; feasibility of variable routes of administration; feasibility of targeting the diseased cell, tissue or organ; and feasibility of reduction of dose and side effects, etc. However, there are challenges. Nanomedicines must be cost-effective, amenable to reproducible manufacture and validated characterization, given the complexity of many technologies involved. There is the need to demonstrate that targeted nanomedicines can actually reach the diseased cells of a patient at therapeutic concentrations to mediate therapeutic benefit. Successful exploitation of nanomedicines will in the future rely on interdisciplinary collaboration of different scientists to guide improved design of practical-to-use nanomedicines.

RECOMMENDATIONS

Mr. Vice-Chancellor, Sir, based on my experience in drug analysis and quality control, pharmaceutical microbiology, solid state pharmaceutics, drug formulation and delivery for humans and animals, including the challenges our very young and vibrant research team has encountered over the years, permit me to offer some recommendations. I believe that if properly implemented, our country, Nigeria, will benefit maximally.

1. The Drug Pilot Production Unit in the University of Nigeria, Nsukka should be revitalized for research and training. This will also serve as a source of revenue for the University.

2. There is need for the government to provide adequate funds to support research in universities for the development of drug analysis and quality control methods for use in checking the menace of fake and counterfeit drugs in the country.

3. There is need for the government to set up a tax mechanism dedicated to support professional training in Nigerian universities. In this way, the gap between the industry and the academia may be bridged. This is because, if pharmaceutical companies know that they are being taxed for training and research in pharmacy schools in Nigeria, they will partner with these faculties of pharmacy to develop their drugs and drug products, rather than outsourcing all their product development research needs.

4. There should be support for the establishment of nanomedicine research centres in universities in Nigeria and interdisciplinary training in nanomedicine.

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I start by acknowledging the Lord God Almighty, the Creator of the Heavens and the Earth for His abundant grace upon my life. It has not been by power nor by might but only by His grace. He has always shown me in all aspects of my life that He has the final say no matter the situation. Despite the vicissitudes of life, His grace has enabled me to record the modest achievements that span the various vistas of my life, which I share with you today.

My precious family: I first want to thank my wife, Uchenna Perpetua, for her unconditional love, encouragement and support all these years; my children - the five 'Chiiis'- Chidera, Chidinma, Chifulumnanya, Chizitalu and Chibuenyim. I got re-engineerd each time one 'Chi' was born! They were very supportive throughout the preparation of this lecture.

My parents, the vessels that God used to bring me into this world: Chief Boniface Attama of blessed memory (my father), the great teacher and disciplinarian, Mrs. Veronica Attama (my mother), who constantly provides for all; my brothers and sisters: Leonard, Clifford of blessed memory, Chinasa, Emeka, Eberechukwu, Kenechukwu and Chiayanam. I appreciate you all for your support and encouragement.

I warmly thank my maternal uncles and their families - Mr. Sylvanus Onah and Ichie Eziokwu bu Ndu, Cyprian O. Onah. They took up the challenge when there was darkness and made me see the light at the end of the turnel, and my in-laws: Mr. and Mrs. Hyacinth Eze for giving me their daughter in marriage when I was yet at a 'crossroads'.

I deeply appreciate the Vice-Chancellor, Professor Benjamin Chukwuma Ozumba, an Associate of Pharmacy, for purposeful,

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My foundation (primary) school teachers at Ogene Premier School, Imilike-Enu: Chief Gabriel Onah, the late father of the Catholic Bishop of Nsukka Dioscese and my late father's compatriot; Mr. Cosmas Agbo, etc. I fondly remember those days they made me sit in front of the class to see the board very well. I thank you all.

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also mentoring. As you mentor, also impart the 'right spirit'! This is the principle of Prof. Adikwu. Prof. Sir, allow me to continue drinking from the fountain of your wisdom! Others are Prof. E. C. Ibezim, Dean of Faculty; Prof. Ken Ofokansi, my current HOD; Prof. V. C. Okore, former Dean; Mr. Dave Okechukwu, Drs. Nnamani, Onuigbo, Akpa, Momoh and Pharms. Kenechukwu, Ogbonna, Reginald-Opara (Nee Achuam) and Onugwu; my close friend and associate, Prof. C. O. Esimone, the current DVC (Academic) of NAU, Awka who was part of us here. I thank all the non-academic staff of the Department for their support.

Prof. S. I. Ofoefule was my boss - I was his Associate Dean during his Deanship. He is a knowledgeable, seasoned and accommodating administrator, whom I will continue to draw from his wealth of experience and well of wisdom. Other professors of the Faculty have been so nice and cooperative. I appreciate you all! I deeply appreciate the friendship of **ALL** academic staff and non-academic staff of other Departments who for want of space were not listed here. Our Drug Delivery and Nanomedicines Research Group, I thank you all for keeping the flag of research flying.

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REFERENCES

Adikwu M.U., **Attama A.A.** Okorie O. (2006). Effect of mucoadhesive delivery of metformin on the entero-insular axis. **J. Drug Deliv. Sci. Technol**. 16(2) 157-159.

Adikwu M.U., Builders P.F., Ofokansi K.C., **Attama A.A.** (2001). Studies of the complexation of chloranilic acid with proguanil. **Boll. Chim. Farm.** 140(3) 172-174.

Adikwu M.U., Esimone C.O., **Attama A.A.,** Builders P.F. (2000). Detection of halofantrine, mefloquine and proguanil by charge transfer complexation on thin layer plates. **Boll. Chim. Farm.** 139(1) 46-48.

Adikwu M.U., Nnamani P.O., **Attama A.A.** (2005). Evaluation of snail mucin for the bioadhesive delivery of chlorpropamide. **Bioresearch** 5, 75-85.

Adikwu M.U., Ofokansi K.C., **Attama A.A.** (1998). Thermodynamic studies of the charge transfer interactions of chloranilic acid with moclobemide and promethazine hydrochloride. **Biol. Pharm. Bull.** 21(2) 1243-1246.

Adikwu M.U., Ofokansi K.C., **Attama A.A**. (1999). Spectrophotometric and thermodynamic studies of the charge transfer interaction between diethylcarbamazine citrate and chloranilic acid. **Chem. Pharm. Bull.** 47(4) 463-466.

Adikwu M.U., Okorie O., **Attama A.A.** (2004). Pharmacodynamics of metformin in detarium gum mucoadhesive formulations. **J. Pharm. Res.** 3(3) 54-56.

Adikwu M.U., Uzuegbu D.B. and **Attama A.A.** (2008). Physiology of microorganisms In: V.C. Okore, A.A. Attama (Eds.). **Laboratory Techniques in Pharmaceutical Microbiology**, 1st edn., Jolyn Pub., Nsukka Nigeria.

Agbo C.P., **Attama A.A.** (2013). *In vivo* fate of synthetic biomaterial-based nanoparticles for drug delivery. In: J. N. Govil (Ed.). **Nanotechnology Vol.11: Biomaterials**. Studium Press, pp. 181-211.

Agboke A.A., **Attama A.A.,** Okoye C. and Jackson C. (2014). Evaluation of effectiveness of various combinations of penicillin groups commonly used in Nigeria clinics on selected microorganisms**. Inno. J. Med. Health Sci.** 4(2) 93– 98.

Agboke A.A., Ekwere E., **Attama A.A.** (2014). *In vitro* evaluation of the antimicrobial potentials of the leaves extracts of *Distemonanthus benthamianus* (Baill) and its interaction with amoxycillin**. Curr. Trends Tech. Sci.** 3(3) 159-164.

Agboke A.A., Opurum C.C., **Attama A.A.,** Ugwu C.C., Momoh A.A. (2011). Evaluation of the anti-microbial activities of crude extract of *Cryptolepis sanguinolenta* leaf and its interaction with some antibiotics. **Prime Research on Medicine (PROM)** 1(8) 233-238.

Agubata C.O., Nzekwe I. T., **Attama A. A.,** Müller-Goymann C.C., Onunkwo G.C. (2015). Formulation, characterization and anti-malarial activity of homolipid-based artemether microparticles. **Int. J. Pharm.** 478, 202–222.

Agubata C.O., Nzekwe I.T., Obitte N.C., Ugwu C.E., **Attama A.A.**, Onunkwo G.C. (2014). Effect of oil, surfactant and co-surfactant concentrations on the phase behavior, physicochemical properties and drug release from self-emulsifying drug delivery systems. **J. Drug Discov. Develop. Deliv.** 1(1) 1-7.

Anagu O.L., **Attama A.A.**, Okore V.C., Gugu H.T., Ngene A.A., Esimone C.O. (2014). *Azadirachta indica* extract-artesunic acid combination produces increased cure rate of *Plasmodium berghei*-infected mice. **Pharm. Biol.** 52(7) 883-889.

Armstead A. L. and Li B. (2011). Nanomedicine as an emerging approach against intracellular pathogens. International Journal of Nanomedicine 6, 3281–3293.

Asogwa S.I., Mbah C.C., **Attama A.A.**, Okore V.C. (2013). Evaluation of antifungal activities of the crude leaf extracts of *Mitracarpus vilosus.* **Afr. J. Pharm. Res. Dev.** 5(1) 30-35.

Attama A.A and Ibezim E.C. (2011). In: **Laboratory Techniques in Physical Pharmaceutics**, Praise House Pub., Enugu, Nigeria.

Attama A.A. (2004). Use of physically crosslinked polyacrylic acid in the formulation of buccoadhesive nifedipine hydrogel films. **J. Pharm. Allied Sci.** 2 (1) 161-168.

Attama A.A. (2007). Analgesic effect of diclofenac potassium entrapped in snail mucin-Eudragit L30 D-55 polyelectrolyte complexes. **J. Pharm. Res**. 6(2) 75-81.

Attama A.A. (2007). Polyelectrolyte complexes of Eudragit L30 D-55 and gelatin: Antinociceptive activity of entrapped piroxicam. **Drug Deliv**. 14(3) 155-162.

Attama A.A. (2011). Herbal drug formulation and delivery using nanotechnology. In: C. O. Okoli (Ed.). **Contemporary Issues in Ethnopharmacology**, Research Signpost, Kerala, India, pp. 9-21.

Attama A.A. (2011). SLN, NLC, LDC: State of the art in drug and active delivery. **Recent Patents on Drug Delivery & Formulation** 5(3) 178-187.

Attama A.A. Akpa P.A., Onugwu L.E., Igwilo G. (2008) Novel buccoadhesive delivery system of hydrochlorothiazide formulated with ethyl cellulose-hydroxypropyl methylcellulose interpolymer complex. **Sci. Res. Essays** 3(6) 343-347.

Attama A.A. and Adikwu M.U. (2008). Natural Products in Wound Healing. In: P.A. Akah (Ed.). **Ethnopharmacology**, Research Signpost, India, pp. 87-100.

Attama A.A. and Builders P.F. (2009) Particulate Drug Delivery: Recent Applications of Natural Biopolymers. In: M.U. Adikwu, C.O. Esimone (Eds.). **Biopolymers in Drug Delivery: Recent Advances and Challenges**. Bentham Science Publishers, UAE, eISBN: 978-1-60805-078-9**,** pp. 63 – 94.

Attama A.A. and Esimone C.O. (2008). Introducing polymers. In: A.A. Attama, C.O. Esimone (Eds.). **Polymers and Polymer Applications**, Jolyn Pub., Nsukka, Nigeria, pp. 1-15.

Attama A.A. and Esimone C.O. (2009). In: **Polymers and Polymer Applications**, Jolyn Pub., Nsukka, Nigeria.

Attama A.A., Nnamani P.O. (2004). Mechanism of diclofenac sodium release from non-disintegrating bioadhesive tablets. **J. Pharm. Allied Sci.** 2(2) 202-208.

Attama A.A., Nnamani P.O. (2005). Melt Extrusion bioadhesive drug delivery: A case of diclofenac contained in Carbopol 940 matrices. **Indian J. Pharm. Sci.** 67(1) 66-69.

Attama A.A., Adikwu M.U. (1997). Release and permeation properties of jellies formulated with mucuna gum. **Plant Prod. Res. Journal.** 2(1) 25-31.

Attama A.A., Adikwu M.U. (1998). Evaluation of a cellulosic material from *Prosopis africana* pods as a disintegrant in sodium salicylate tablets. **Boll. Chim. Farm.** 137(4) 97-102.

Attama A.A., Adikwu M.U. (1999). Bioadhesive delivery of hydrochlorothiazide using tacca starch/SCMC and Carbopols 940 and 941 admixtures. **Boll. Chim. Farm.** 138(7) 329-336.

Attama A.A., Adikwu M.U. (1999). Effects of trona on the properties of tablets formulated with three disintegrants. **J. Pharm. Res. Dev.** 4(2) 79-84.

Attama A.A., Adikwu M.U. (1999). The physicochemical properties of starch derived from *Tacca involucrata* plant. **J. Natural Prod. Med.** 2 70-72.

Attama A.A., Adikwu M.U. (2000). Dissolution of hydrophobic drugs from tablets containing trace amounts of trona as dissolution enhancer. **J. Pharm. Res. Dev.** 5(1) 61-66.

Attama A.A., Adikwu M.U. (2002). Physicochemical properties of a new polysaccharide gum from *Prosopis africana*: Prosopis gum–alginic acid complex coacervate system. **Plant Prod. Res. Journal.** 7 (2) 43-50.

Attama A.A., Adikwu M.U. (2002). Studies on modified gladiolus starch. **The Nig. J. Pharm.** 33 35-42.

Attama A.A., Adikwu M.U. (2004). Glucose lowering effects of parenteral doses of phenformin of expected low serum perturbations. **African J. Pharm. Res. Dev.** 1, 7-10.

Attama A.A., Adikwu M.U. (2004). Melt extrusion bioadhesive delivery of diclofenac sodium granules using theobroma oil. **Boll. Chim. Farmac.** 143 (4) 174-177.

Attama A.A., Adikwu M.U. Okpi O. (2004). Bioavailability of metronidazole from *in situ* gelling mucoadhesive suppositories formulated with Carbopol ETD 2020. **J. Biol. Res. Biotechnol.** 2(1) 75-81.

Attama A.A., Adikwu M.U., Amorha C.J. (2003). Release of indomethacin from bioadhesive tablets containing Carbopol 941 modified with *Abelmoschus esculentus* (Okra) gum. **Boll. Chim. Farm.** 142(7) 298-302.

Attama A.A., Adikwu M.U., Muko K.N. (2000). Evaluation of *Prosopis africana* gum in the formulation of gels. **Boll. Chim. Farm.** 139(4) 173-176.

Attama A.A., Adikwu M.U., Ngini O.V. (2001). *In vitro* release of metronidazole from suppositories formulated with blends of cow fat and palm kernel oil. **J. Univ. Sci. Tech.** 21, 62-66.

Attama A.A., Adikwu M.U., Nnamani P.O. (2003). Delivery of diclofenac sodium via non-disintegrating bioadhesive tablets of paraffin wax. **STP Pharma Sci.** 13 (2) 147-150.

Attama A.A., Adikwu M.U., Okoli N.D. (2003). Studies on bioadhesive granules II. Granules formulated with *Mucuna flagillepes* (mucuna) gum. **STP Pharma Sci.** 13 (3) 177-181.

Attama A.A., Adikwu M.U., Okoli N.D.(2000). Studies on bioadhesive granules I: Granules formulated with *Prosopis africana* (Prosopis) gum. **Chem. Pharm. Bull.** 48(5) 734-737.

Attama A.A., Akpa P.A. (2008). Determination of amorphicity and glass transition (T_g) of some natural polymers. **J. Drug Deliv. Sci. Technol.** 18(3) 219-220.

Attama A.A., Akpa P.A. (2009). The physicochemical properties of pyrodextrins derived from *Tacca involucrata* starch. **J. Pharm. Allied Sci.** 6(2) 737 - 750.

Attama A.A., Akpa P.A., Nwokeabia C.W. (2007). Mucoadhesive sustained delivery of diclofenac sodium using Carbopol 675 and PVP admixtures as mucoadhesive motif. **J. Pharm. Allied Scs.** 4(1) 374-380.

Attama A.A., Ayogu I.J., Kenechukwu F.C., Ogbonna J.D.N., Okore V.C. (2012) A New Lipid Based Drug Delivery System (LBDDS) for Oral Delivery of Tioconazole. **Int. J. Drug Deliv.** 3 (2011) 743-753.

Attama A.A., Bamigbola A.E. Okorie O. (2009). Plasto-elastic behaviour of gladiolus starch derived pyrodextrin (GSDD)-PVP cogranulates during compaction. **J. Pharm. Allied Sci.** 6(1) 657 - 662.

Attama A.A., Charles L. (2013). Nanotechnology in drug delivery. In: Ziknam (Ed.). **Handbook of Functional Nanomaterials**. Vol. 2, Nova Science Pub., Inc.

Attama A.A., Charles L., Onuigbo E.B. (2012) Nanotechnology for ocular and otic drug delivery and targeting. In: J. L. Arias (Ed.) **Nanotechnology and Drug Delivery**. Science Publishers, New Hampshire, USA. http://www.scipub.net.

Attama A.A., Chuku A.I., Muko K.N., Adikwu M.U. (1997). Effects of Veegum on the suspending properties of mucuna gum. **Boll. Chim. Farm.** 136(7) 548-553.

Attama A.A., Enete I.E. (2004) *In vitro* availability of naproxen from liquid self-emulsifying systems. **Discovery & Innovations** 16 (1&2) 22-25.

Attama A.A., Esimone C.O., Adikwu M.U. (1999). Binary combination detarium gum and Veegum as a binder in sodium salicylate tablets. **Boll. Chim. Farm.** 133(5) 199-202.

Attama A.A., Esimone C.O., Adikwu M.U. (1999). Sedimentation studies on chalk suspensions containing blends of Veegum and detarium gum as suspending agents. **Boll. Chim. Farm.** 138(10) 521-525.

Attama A.A., Ezeabasili S.I., Adikwu M.U. (2000). *In vitro* release of salicylic acid from suppositories formulated with blends of goat fat and palm kernel oil. **J. Pharm. Res. Dev.** 5(1) 17-22.

Attama A.A., Ezeamama U.F. (2005). Systematic delivery of chloroquine and promethazine using pH-sensitive polymers. **Drug Deliv.** 12 (2) 103-107.

Attama A.A., Igbonekwu C.N. (2011). *In vitro* properties of surface-modified solid lipid microspheres containing an antimalarial drug: halofantrine**. Asian Pacific J. Trop. Med.** 4(4) 253-258.

Attama A.A., Mbah C.C., Adikwu M.U. (2007). Use of trona as a permeation enhancer for ointments prepared with beeswax extracted from native honeycombs. **J. Pharm. Allied Scs.** 4(2) 467-480.

Attama A.A., Momoh M.A., Builders PF. (2012) Lipid nanoparticulate drug delivery systems: A revolution in dosage form design and development.

In: A.D. Sezer (Ed**.). Recent Advances in Novel Drug Carrier Systems**. Croatia: InTech, pp. 107-140.

Attama A.A., Momoh M.A., Ugwu A.A. (2011). Formulation and evaluation of stavudine-loaded microsphere using ammino methacrylate polymers. **J. Pharm. Res.** 4(10) 3492-3495.

Attama A.A., Mpamaugo V.E. (2006). Pharmacodynamics of piroxicam from self-emulsifying lipospheres formulated with homolipids extracted from *Capra hircus*. **Drug Deliv.** 13(2) 133-137.

Attama A.A., Müller-Goymann C.C. (2006). A critical study of novel physically structured lipid matrices composed of a homolipid from *Capra hircus* and theobroma oil**. Int. J. Pharm.** 322, 67-78.

Attama A.A., Müller-Goymann C.C. (2007). Investigation of surface-modified solid lipid nanocontainers formulated with a heterolipid-templated homolipid. **Int. J. Pharm.** 334, 179-189.

Attama A.A., Müller-Goymann C.C. (2008). Effect of beeswax modification on the lipid matrix and solid lipid nanoparticle crystallinity. **Colloids and Surfaces A: Physicochemical and Engineering Aspects.** 315, 189-195.

Attama A.A., Ndibe O.N., Nnamani P.O. (2004). Studies on diclofenac-β-cyclodextrin inclusion complexes. **J. Pharm. Res.** 3, 47-49.

Attama A.A., Nkemnele M.O. (2005). *In vitro* evaluation of drug release from self micro-emulsifying drug delivery systems using a novel biodegradable homolipid from *Capra hircus*. **Int. J. Pharm.** 304, 4-10.

Attama A.A., Nnamani P.O. (2003). Characterization of *Dioscorea bulbifera* starch. **J. Pharm. Allied Sci.** 1(2) 93-97.

Attama A.A., Nnamani P.O., Adikwu M.U. (2003). Diclofenac release from bioadhesive hydrophilic matrix tablets formulated with polyvinylpyrrolidone–sodium carboxymethylcellulose copolymer. **J. Pharm. Allied Sci.** 1 (1) 1-7.

Attama A.A., Nnamani P.O., Adikwu M.U., Akidi F.O. (2003). Spectrophotometric determination of haloperidol by charge transfer interaction with chloranilic acid. **STP Pharma Sci.** 13(6) 419-421.

Attama A.A., Nnamani P.O., Adikwu M.U., Akidi F.O. (2004). Thermodynamic consideration of the charge transfer interaction of the donor:acceptor type between chloranilic acid and haloperidol. **Chem. Pharm. Bull.** 52 (3) 303-306.

Attama A.A., Nnamani P.O., Agbo A.N. (2006). Development of alternative assay technique for cephalexin by charge transfer interaction of the donor:acceptor type with chloranilic acid. **The Chinese/Taiwanese Pharmaceut. Journal** 58(1) 11-18.

Attama A.A., Nnamani P.O., Akpa P.A., Nwachukwu C., Eze C.R. (2007). Properties of ascorbic acid tablets prepared with hypochlorite oxidized cassava starch. **J. Adv. Med. Pharm. Sci.** 1(3) 52-57.

Attama A.A., Nnamani P.O., Mbonu I.K., Adikwu M.U. (2003). The effect of hypochlorite oxidation on the physicochemical properties of gladiolus starch. **J. Pharm. Allied Sci.** 1 (1) 28-35.

Attama A.A., Nnamani P.O., Nwafor C.N. (2005). *In vitro* study of the interaction between amoxicillin and norfloxacin with lansoprazole. **Bioresearch** 3, 52-55.

Attama A.A., Nnamani P.O., Okorie O. (2005). Effect of pH and ionic strength on the bioadhesive properties of *Prosopis africana* gum. **J. Pharm. Bioresources** 2(2) 141-145.

Attama A.A., Nnamani P.O., Ugwoke C. (2002). Studies on beta cyclodextrin-tetracycline inclusion complexes. **Plant Prod. Res. Journal**. 7 (2) 85-88.

Attama A.A., Nwabunze O.J. (2007). Mucuna gum microspheres for the oral delivery of glibenclamide: *In vitro* evaluation. **Acta Pharmaceutica** 57, 161-171.

Attama A.A., Nzekwe I.T., Adikwu M.U., Onugu O., Nnamani P.O. (2003). Use of solid self-emulsifying systems in the delivery of diclofenac sodium. **Int. J. Pharm.** 262 (1,2) 23-28.

Attama A.A., Obi J., Ugochukwu O.N., Onuigbo B.E. (2010). Evaluation of the cytoprotective effects of the formulation variables of snail mucin and cimetidine in rats. **J. Pharm. Res.** 9(1) 31-34.

Attama A.A., Ofokansi K.C., Kenechukwu F.C., Ugwueze M.E. (2014). Hepatoprotective activity of aqueous and ethanol root extracts of *Millettia aboensis* on carbon tetrachloride-induced hepatotoxicity in experimental rats. **Indian J. Novel Drug Deliv**. 6(2) 132-141.

Attama A.A., Okafor C.E., Builders P.F., Okorie O. (2009). Formulation and *in vitro* evaluation of a PEGylated microscopic lipospheres delivery system for ceftriaxone sodium. **Drug Deliv.** 16(8) 448–457.

Attama A.A., Okorogu O.J. Onuigbo E.B. (2009). Evaluation of the *in vitro* combined antimicrobial activities of *Garcinia kola* Heckel and honey. **Bio-Research** 7(2) 525 – 528.

Attama A.A., Onuigbo E.B. (2007). Properties of cotrimoxazole microparticles prepared with Carbopol 941 and exogenous mucin. **Sci. Res. Essays** 2(10) 421-425.

Attama A.A., Onuigbo E.B. (2008). Preparation of stabilized mucoadhesive microparticles containing ciprofloxacin for eradication of *enterobacteriaceae*. **J. Pharm. Res.** 7(1) 32-35.

Attama A.A., Reichl S., Müller-Goymann C.C. (2008). Diclofenac sodium delivery to the eye: *In vitro* evaluation of novel solid lipid nanoparticle formulation using human cornea construct. **Int. J. Pharm.** 355, 307-313.

Attama A.A., Reichl S., Müller-Goymann C.C. (2009) Sustained release and permeation of timolol from surface modified solid lipid nanoparticles through bio-engineered human cornea. **Curr. Eye Res.** 34(8) 698-705.

Attama A.A., Schicke B.C., Müller-Goymann C.C. (2006). Further characterization of theobroma oil-beeswax admixtures as lipid matrices for improved drug delivery systems. **Eur. J. Pharm. Biopharm.** 64, 294-306.

Attama A.A., Schicke B.C., Müller-Goymann C.C. (2007). Novel physically structured lipid matrices of beeswax and a homolipid from *Capra hircus* (goat fat): A physicochemical characterization. **J. Drug Deliv. Sci. Technol**. 17(2) 103-112.

Attama A.A., Schicke B.C., Paepenmüller T., Müller-Goymann C.C. (2007). Solid lipid nanodispersions containing mixed lipid core and a polar heterolipid: Characterization. **Eur. J. Pharm. Biopharm**. 67, 48-57.

Attama A.A., Uzochukwu I.C. and Onunkwo G.C. (2009). An Overview of Synthetic Biopolymers in Drug Delivery. In: M.U. Adikwu, C.O. Esimone (Eds.) **Biopolymers in Drug Delivery: Recent Advances and Challenges**. Bentham Science Publishers, UAE, eISBN: 978-1-60805-078-9**,** pp. 122 - 130.

Attama A.A., Uzor P.F., Nnadi C.O., Okafor C.G. (2011). Evaluation of the wound healing activity of gel formulation of leaf extract of *Aspila africana* Fam. Compositae. **J. Chem. Pharm. Res. (India)** 3(3) 718-724.

Attama A.A., Weber C., Müller-Goymann C.C. (2008). Assessment of drug permeation from SLN formulated with a novel structured lipid matrix through artificial skin construct bio-engineered from HDF and HaCaT cell lines. **J. Drug Deliv. Sci. Technol.** 18(3) 181-188.

Ayogu I.J., Ogbonna O., Ayolugbe C.I., **Attama A.A.** (2009) Evaluation of the pharmacodynamic activity of insulin from bilosomal formulation. **Curr. Drug Del.** 6(4) 415 – 418.

Bamigbola E.A., Ibrahim M.A., **Attama A.A.** (2009). Comparative in vitro dissolution assessment of soluble and plain brands of aspirin tablets marketed in Nigeria. **Sci. Res. and Essays.** 4(11) 1412-1414.

Bamigbola E.A., Ibrahim M.A., **Attama A.A.**, Arute J.E. (2009). Comparative bioequivalence assessment of aspirin tablets marketed in Nigeria. **Int. J. Health Res.** 2(4) 375-379.

Bamigbola E.A., Ibrahim M.A., **Attama A.A.**, Uzondu A.L. (2011). *In vitro-in vivo* correlation of four commercial brands of aspirin tablets marketed in Nigeria. **Afr. J Pharm. Pharmacol.**, 5(14) 1648-1654.

Briones E., Colino C.I., Lanao J.M. (2008). Delivery systems to increase the selectivity of antibiotics in phagocytic cells. J. Control. Rel. 125, 210–227.

Brown S.A., Chime S.A., **Attama A.A.**, Agu C.I., Onunkwo G.C. (2013). Piroxicam-loaded dika wax lipospheres: *in vitro* and *in vivo* characterisation. **Trop. J. Pharm. Res**. 12(1) 33-38.

Builders F.P., Chukwu C., Obidike I., Builders I.M., **Attama A.A.**, Adikwu M.U. (2009) A novel xyloglucan gum from seeds of *Afzelia africana* Se. Pers.: Some functional and phtysicochemical properties. **Int. J. Green Pharm.** April – June, 112 – 118.

Builders F.P., Kunle O.O., Okpaku C.L., Builders I.M., **Attama A.A.**, Adikwu M.U. (2008). Preparation and evaluation of mucinated sodium alginate microparticles for oral delivery of insulin. **Eur. J. Pharm. Biopharm.** 70, 777-783.

Builders P.F., Agbo M.B., Adelakun T., Okpako L.C., **Attama A.A.** (2010). Novel multifunctional pharmaceutical excipients derived from microcrystalline cellulose-starch microparticulate composites prepared by compatibilized reactive polymer blending. **Int. J. Pharm.** 388, 159-167.

Builders P.F., **Attama A.A.** (2011). Functional Properties of Biopolymers for Drug Delivery Applications. In: B. M. Johnson, Z. E. Berkel (Eds). **Biodegradable Materials**, Nova Science Pub., Inc., ISBN: 978-1-61122-804-5.

Builders P.F., Ibekwe N., Okpako L.C., **Attama A.A.**, Kunle O.O. (2009) Preparation and characterization of mucinated cellulose microparticles for therapeutic and drug delivery purposes. **Eur. J. Pharm. Biopharm.** 72(1) 34-41.

Builders P.F., Mbah C.C., **Attama A.A.** (2012). Intrinsic and functional properties of a gelling gum from *Dioclea reflexa*: A potential pharmaceutical excipient. **British J. Pharm. Res.** 2(1) 50-68.

Builders P.F., Nnurum A., Mbah C.C., **Attama A.A.**, Manek R. (2010). The physicochemical and binder properties of starch from *Persea americana* Miller (Lauraceae)**. Starch - Stärke** 62(6) **309-320.**

Builders P.F., Nnurum A., Mgbokwere C.R., **Attama A.A.** (2009). Effect of pH of dispersion on some physicochemical properties of regenerated cashew gum. **J. Phytomed. Ther.** 13, 7 -15.

Carryn S., Chanteux H., Seral C., Mingeot-Leclercq M-P., Van-Bambeke F., Tulkens P. M. (2003). Intracellular pharmacodynamics of antibiotics. Infect Dis. Clin. North Amer. 17, 615–634.

Charles L., **Attama A.A.** (2011). Current state of nanoemulsions in drug delivery. **J Biomat. Nanobiotech.** (**JBNB**), 2 626-639.

Charles L., **Attama A.A.** (2013). Image-guided Assessment of Nano Drug Delivery Systems. In: **Nanotechnology Vol.12: Bioimaging**, J. N. Govil (Ed.), Studium Press, pp. 211-221.

Chime S.A., **Attama A.A.**, Builders P.F., Onunkwo G.C. (2013). Sustained-release diclofenac potassium-loaded solid lipid microparticle based on solidified reverse micellar solution: in vitro and in vivo evaluation. **J. Microencap.** 30(4) 335-345.

Chime S.A., **Attama A.A.**, Kenechukwu F.C., Umeyor C.E., Onunkwo G.C. (2013). Formulation, *in vitro* and *in vivo* characterization of diclofenac potassium sustained release tablets based on solidified reverse micellar solution (SRMS). **British J. Pharm. Res.** 3(1) 90-107.

Chime S.A., **Attama A.A.**, Obitte N.C., Kenechukwu F.C., Agubata C.O., Ezekwe C.C. (2012). *In vitro* and *in vivo* characterisation of indomethacin–loaded dika fat-based solid lipid microparticles. **Int. J. Pharm. Rev. Res.** 16(2) 10-16.

Chime S.A., **Attama A.A.**, Onunkwo G.C. (2012) Sustained release indomethacin-loaded solid lipid microparticles, based on solidified reverse micellar solution (SRMS): *In vitro* and *in vivo* evaluation **J. Drug Deliv. Sci. Tech.** 22(6) 485-492.

Chime S.A., Kenechukwu F.C., **Attama A.A.** (2014). Nanoemulsions- Advances in Formulation, Characterization and Applications in Drug Delivery. In: A.D. Sezer (Ed.). **Application of Nanotechnology in Drug Delivery**. Rijeka Croatia: InTech; 77-126.

Chime S.A., Kenechukwu F.C., Onunkwo G.C., **Attama A.A.**, Ogbonna J.D.N. (2012) Recent advances in lipospheres drug delivery system. **J. Pharm. Res.** 5(3) 1743-1748.

Chime S.A., Momoh M.A., Onyishi V.I., Abonyi A.C., Onunkwo G.C., **Attama A.A.** (2014). Evaluation of properties of *Garcinia kola* (Heckel) seed extract in lipospheres based on fat from *Capra hircus*: An antimicrobial study. **J. Curr. Pharma Res.** 4 (4) 1274-1280.

Chime S.A., Onyishi I.V., **Attama A.A.** (2014). Evaluation of excipient potentials of *Irvingia wombolu* fats and moringa oil in rifampicin-loaded lipospheres: *In vitro-in vivo* characterisation**. J. Drug Deliv. Sci. Tech.** 24 (4) 404-412.

Chime S.A., Onyishi I.V., **Attama A.A.**, Onunkwo G.C. (2013). Preliminary investigation of the properties of diclofenac potassium in SRMS-based tablets. **Afr. J. Pharm. Res. Dev.** 5(1) 17-24.

Chime S.A., Onyishi I.V., **Attama A.A.**, Onunkwo G.C., Ajaraonye M.C. (2013) Lipospheres: A potential delivery system of herbal extract for the treatment of diabetes mellitus. **Am. J. Pharm. Tech Res**. 3(4) 480-491.

Chime S.A., Onyishi I.V., Momoh M.A., **Attama A.A**. (2013) Anti-inflammatory, antinociceptive and ulcerogenic properties of indomethacin tablets based on solidified reverse micellar solution (SRMS). **Afr. J. Pharm. Pharmacol.** 7(43) 2813-2822.

Chime S.A., Onyishi I.V., Onunkwo G.C., **Attama A.A.** (2014). Solidified reverse micellar solution (SRMS)-based indomethacin sustained-release tablets: Formulation and *in vitro* evaluation. **Trop. J. Pharm. Res.** 13(2) 211-216.

Chime S.A., Onyishi I.V., Ugwoke P.U., **Attama A.A.** (2014). Evaluation of the properties of *Gongronema latifolium* in Phospholipon 90H based solid lipid microparticles (SLMs): An antidiabetic study. **J Dietary Suppl**. 11(1) 7-18.

Chinaeke E.E., Chime S.A., Kenechukwu F.C., **Attama A.A.**, Müller-Goymann C.C., Okore V.C. (2014). Formulation of novel artesunate-loaded lipid microparticle (SLMs) based on dika wax matrices: *in vitro* and *in vivo* evaluation**. J. Drug Deliv. Sci. Tech**. 24(1) 69-77.

Chinaeke E.E., Chime S.A., Ogbonna J.D.N., **Attama A.A.**, Müller-Goymann C.C., Okore V.C. (2014). Evaluation of dika wax-soybean oil-based artesunate-loaded lipospheres: *in vitro-in vivo* correlation studies. **J. Microencapsul.** 31(8) 796-804.

Chinaeke E.E., Chime S.A., Onyishi V.I., **Attama A.A.**, Okore V.C. (2014). Formulation development and evaluation of the anti-malaria properties of sustained release artesunate-loaded solid lipid microparticles based on phytolipids. **Drug Deliv. Early Online:** 1–14.

CLINAM 5/12, European Foundation for Clinical Nanomedicine, Basel, 2012.

Dibua Uju M.E., Kalu A., **Attama A.A.**, Esimone C.O., Eyo J.E. (2013)**.** *In vivo* and *in vitro* evaluation of the inhibitory effect of some medicinal plant extracts on haemozoin concentration. **Anim. Res. Int.** 10(2) 1699-1712.

Duncan R. and Richardson S.C.W. (2012). Endocytosis and intracellular trafficking as gateways for nanomedicine delivery: Opportunities and challenges. Mol. Pharmaceutics 9, 2380−2402.

Esimone C.O., **Attama A.A.**, Ngwu G., Iloabanafo C.A., Momoh M.A., Onaku L.O. (2011). Mosquito repellent activity of herbal ointments formulated with *Occimum gratissimum oil*. **J Pharm. Res.** 4(10) 3442-3444.

Esimone C.O., **Attama A.A.**, Osonwa U.E., Nwakile C.D., Onochie F.T.O. (2012) Formulation and evaluation of goat fat and shea butter based lipospheres of benzyl penicillin. **Int. J. Pharm. Sci. Res**., 3(4) 1022-1027.

Ezeabasili S.I., Ibezim E.C., Adikwu M.U., **Attama A.A.** and Ugoeze K.C. (2009). Studies of some animal fats as lipid bases in the formulation of some medicated semi – solid dosage forms iv: release of hydrocortisone acetate from creams. **Int. Conf. Polymer Dev. Applic.** 1, 132-138.

Ezeabasili S.I., Ibezim E.C., Adikwu M.U., **Attama A.A.** and Ugoeze K.C. (2009). Studies of some animal fats as lipid bases in the formulation of some medicated semi-solid dosage forms v: rheological and stability studies of hydrocortisone acetate creams. **Int. Conf. Polymer Dev. Applic.** 1, 151-159.

Ezeabasili S.I., Ibezim E.C., Adikwu M.U., **Attama A.A.,** Ugoeze K.C. (2009) Studies of some animal fats as lipid bases in the formulation of some medicated semi – solid dosage forms I: physicochemical properties**. Int. Conf. Polymer Dev. Applic**. 1, 87-91.

Ezeabasili S.I., Ibezim E.C., Adikwu M.U., **Attama A.A.**, Ugoeze K.C. (2009). Studies of some animal fats as lipid bases in the formulation of some medicated semi – solid dosage forms II: release of salicylic acid from ointments. **Int. Conf. Polymer Dev. Applic**. 1, 103-110.

Ezeabasili S.I., Ibezim E.C., Adikwu M.U., **Attama A.A.,** Ugoeze K.C. (2009). Studies of some animal fats as lipid bases in the formulation of some medicated semi – solid dosage forms iii: rheological and stability studies of salicylic acid ointments. **Int. Conf. Polymer Dev. Applic.**, 1, 119-125.

Haywood A. and Glass B. D. (2011). Pharmaceutical excipients – where do we begin? Aust. Prescr. 34: 112–114.

http://en.wikipedia.org/wiki/Drug_discovery. Accessed on October 10, 2014.

Ibezim E. C. and **Attama A. A.** (2004). Advanced physical pharmaceutics. In: **Techniques in Pharmaceutics and Pharmaceutical Microbiology**, El Demak Pub., Enugu, Nigeria.

Ibezim E. C., Adikwu M. U., Okore V. C., **Attama A. A.**, Esimone C. O., Uzuegbu D. B. and Ofokansi K. C. (2001). In: **Techniques in Pharmaceutics**, El Demak Pub., Enugu, Nigeria.

Ibezim E.C., **Attama A.A**. (1997). Compatibility studies on some commercially available gentamicin sulphate injections with commonly co-administered parenterals. **Afr. J. Health Sci.** 4 1-5.

Ibezim E.C., **Attama A.A**. (1998). A comparative study of the emulsifying characteristics of some oil-in-water emulgents in paraffin oil emulsions. **Plant Prod. Res. Journal**. 3 8-14.

Ibezim E.C., **Attama A.A.**, Dimgba I.C., Ofoefule S.I. (2000). Use of Carbopols-sodium carboxymethylcellulose admixtures in the formulation of bioadhesive metronidazole tablets. **Acta Pharmaceutica** 2 121-130.

Ibezim E.C., **Attama A.A.**, Obitte N.C., Onyishi V.I., Brown S.A. (2008). *In vitro* prediction of *in vivo* bioavailability and bioequivalence of brands of metronidazole tablets in Eastern Nigerian drug market. **Sci. Res. Essays** 3 (10) 552-558.

Ibezim E.C., Osonwa U.E., **Attama A.A.** and Ugwu N.C. (2009). Preliminary investigation into the use of goat fat as a base in metronidazole and chloroquine suppositories. **Int. Conf. Polymer Dev. Applic.**1, 224-229.

Jain K. K. (2008). Drug Delivery Systems – An Overview. In: Drug Delivery Systems, K. K. Jain (Ed.), Humana Press, NJ, USA, pp. 1-50.

Kenechukwu F.C., Ibezim E.C., **Attama A.A.**, Momoh M.A., Ogbonna J.D.N., Nnamani P.O., Chime S.A., Umeyor C.E., Uronnachi E.M. (2013). Preliminary spectroscopic characterization of PEGylated mucin, a novel polymeric drug delivery system. **Afr. J. Biotech.** 12(47) 6661-6671.

Kenechukwu F.C., Momoh M.A., Nnamani P.O., **Attama A.A.** (2014). Solid lipid micro-dispersions (SLMs) based on PEGylated solidified reverse micellar solutions (SRMS): a novel carrier system for gentamicin. **Drug Deliv. Early Online**: 1–13.

Kenechukwu F.C., Momoh M.A., Nnamani P.O., Ogbonna J.D.N., Umeyor C. E., **Attama A.A.** (2014). Improved bioactivity of gentamicin from novel solid lipid microparticles based on beeswax. **Nig. J. Pharm. Res.** 10(1) 35-45.

Kenechukwu F.C., Umeyor C.E., Momoh M.A., Ogbonna J.D.N., Chime S.A., Nnamani P.O., **Attama A.A.** (2014). Evaluation of gentamicin-entrapped solid lipid microparticles formulated with a biodegradable homolipid from *Capra hircus*. **Trop. J. Pharm. Res.** 13(8) 1199-1205.

Madu K.C., Ukoha P.O., **Attama A.A.** (2011). Spectrophotometric determination of lamivudine using chloranilic acid and 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). **Amer. J. Anal. Chem**. 2, 849-856.

Mbah C.C., Builders P.F., **Attama A.A.** (2014). Nanovesicular carriers as alternative delivery systems: Ethosomes in focus. **Expert Opinion on Drug Delivery** 11(1) 31-43.

Mbah C.C., Builders P.F., Nzekwe I.T., Kunle O., Adikwu M.U., **Attama A.A.** (2014). Formulation and *in vitro* evaluation of pH-responsive ethosomes for vaginal delivery of metronidazole. **J. Drug Del. Sci. Tech**. 24 (6) 565-571.

Momoh M.A., Adikwu M.U., **Attama A.A.** (2009). Evaluation of wound healing effect of gelatin and polyethyleneglycol (PEG) containing Cicatrin® powder. **Arch. Pharm. Sci. Res.** 1(1) 54 - 57.

Momoh M.A., Adikwu M.U., Ibezim C.E., Ofokansi K.C., **Attama A.A.** (2010). Thermal characterisation of PEGylated-mucin. **Asian Pacific J. Trop. Med.** 3(6) 412-420.

Momoh M.A., Adikwu M.U., Ibezim E.C., **Attama A.A.** (2011). Effect of metformin and *Vernonia amygdalina* leaf extract loaded PEGylated mucin formulation on haematological, kidney and liver indices of healthy and diabetic rats. **J. Pharm. Res.** 4(10) 3455-3459.

Momoh M.A., Akpa P.A., **Attama A.A.** (2012). Phospholipon 90G based SLMs loaded with ibuprofen: An oral antiinflammatory and gastrointestinal sparing evaluation in Rats. **Pakistan J. Zool**., 44(6) 1657-1664.

Momoh M.A., **Attama A.A.**, Kunle O.O. (2014). Formulation *in vitro* and *in vivo* evaluation of SRMS-based heterolipid-templated homolipid delivery system for diclofenac sodium. **Drug Deliv. Early Online:** 1–9.

Momoh M.A., **Attama A.A.**, Okonta J.M., Ezugwuorie O.J. (2009). Evaluation of the impact of adherence counselling among clients on anti-retroviral therapy in an approved missionary hospital in Eastern Nigeria. **Arch. Pharm. Sci. Res.** 1(1) 62 - 65.

Momoh M.A., Kenechukwu F.C., Adedokun M.O., Odo C.E., **Attama A.A.** (2014). Pharmacodynamics of diclofenac from novel Eudragit entrapped microspheres. **Drug Deliv.** 21(3) 193-203.

Momoh, M.A., Adikwu, M.U., Nwachi, U.E., **Attama A.A.,** Gugu T. **(2010).** In-vitro evaluation of bioadhesive and release properties of thiamine hydrochloride formulation from Gelatin, Gellan and their admixture. **Bio-Research** 7 (1) 460 – 463.

Nano Werk, 2014. http://www.nanowerk.com/nanotechnology/ten_things_you_should know_about_nanotechnology.php. Accessed on January 7, 2015.

Nduka S.O., Okorie O., **Attama A.A.**, Ugwu M.C. (2012). Evaluation of aloe vera gum as a binder in metronidazole based tablets. **J. Pharm. Res.** 5(9) 4906-4909.

Nnamani P.O., Adikwu M.U., **Attama A.A.**, Eze O.C. (2010). Polyelectrolyte complexes of *Irvingia gabonensis* gum and gelatin: performance of suspended chalk particles. **J. Pharm. Res. India**. 9(3) 117-121.

Nnamani P.O., Adikwu M.U., **Attama A.A.**, Ibezim E.C. (2010). SRMS142 based solid lipid microparticles: application in oral delivery of glibenclamide to diabetic rats. **Eur. J. Pharm. Biopharm.** 76(1) 68 - 74.

Nnamani P.O., Akpa P.A., Ogbonna J.D.N., **Attama A.A.** (2011). Aggregation behavior of surface active agents. In: A.A. Attama, E.C. Ibezim (Eds.). **Laboratory Techniques in Physical Pharmaceutics**. 1st Edn. Praise House Publishers, Enugu, Nigeria, pp. 27 – 30.

Nnamani P.O., **Attama A.A.**, Kenechukwu F.C., Ibezim E.C., Adikwu M.U. (2013). Pharmacodynamics of piroxicam from novel solid lipid microparticles formulated with homolipids from *Bos indicus*. **Curr. Drug Del. 10, 645-655.**

Nnamani P.O., Ibezim E.C., **Attama A.A.**, Adikwu M.U. (2010). New approach to solid lipid microparticles using biocompatible homolipids-templated heterolipid microcarriers for cimetidine delivery. **Nigerian J. Pharm. Res.** 8(1) 92 – 111.

Nnamani P.O., Ibezim E.C., **Attama A.A.**, Adikwu M.U. (2010). Piroxicam-loaded pegylated tallow fat-based solid lipid microparticles: characterization and *in vivo* evaluation. **Nigerian J. Pharm. Res.** 8(1) 19 – 35.

Nnamani P.O., Ibezim E.C., **Attama A.A.**, Adikwu M.U. (2010). Surface-modified solid lipid microparticles based on homolipids and Softisan® 142: Preliminary characterization. **Asian Pacific J. Trop. Med.** 3(3) 205 – 210.

Nnamani P.O., Kenechukwu F.C., Anugwolu C.L., Agubata C.O., **Attama A.A.** (2013). Characterization and controlled release of gentamicin from novel hydrogels based on Poloxamer 407 and polyacrylic acids. **Afr. J. Pharm. Pharmacol.** 7(36) 2540-2552.

Nnamani P.O., Kenechukwu F.C., Anugwolu C.L., **Attama A.A.** (2014). Evaluation of hydrogels based on Poloxamer 407 and polyacrylic acids for enhanced topical activity of gentamicin against susceptible infections. **Trop. J. Pharm. Res**. 13 (9) 1385-1391.

Nnamani P.O., Kenechukwu F.C., Dibua E.U., Ogbonna C.C., Momoh M.A., Ogbonna J.D.N., Okechukwu D.C., Olisemeke A.U., **Attama A.A.** (2013). Bioactivity of gentamicin contained in novel transdermal drug delivery systems (TDDS) formulated with biodegradable polyesters. **Afr. J. Pharm. Pharmacol**. 7(28) 1987-1993.

Nnamani P.O., Kenechukwu F.C., Dibua E.U., Ogbonna C.C., Momoh M.A., Olisemeke A.U., Agubata C.O., **Attama A.A.** (2013). Formulation, characterization and *ex-vivo* permeation studies on gentamicin-loaded transdermal patches based on PURASORB® polymers. **Sci. Res. Essays** 8(22) 973-982.

Nnamani P.O., Kenechukwu, F.C., Dibua E.U., Ogbonna C.C., Monemeh, U.L., **Attama A.A.** (2013). Transdermal microgels of gentamicin. **Eur. J. Pharm. Biopharm.** 84 345–354.

Nnamani P.O., Ogbonna C.C., Dibua E.U., Ezedigboh N.N., **Attama A.A**. (2012). Sustained circulation time of glibenclamide from PEGylated solid lipid microparticles. **Int. J. Novel Drug Deliv. Tech.** 2(2) 283-290.

Nwodo N.J., Okonta J.M., Ezugwu C.O., **Attama A.A.** (2009) Anti-ulcer potential of phylum mollusca (Tropical snail) slime. **Asian Pacific J. Trop. Med.** 2(3) 23 – 28.

Obitte N.C., Chime S.A., **Attama A.A.**, Odo J.I., Brown S.A. (2013). Evaluation of the pharmacodynamic properties of indomethacin-loaded lipospheres. **Int. Res. J. Pharmacy Pharm.** 3(5) 77-84.

Obitte N.C., Chime S.A., Magaret A.A., **Attama A.A.**, Onyishi I.V., Brown S.A. (2012). Some *in vitro* and pharmacodynamic evaluation of indomethacin solid lipid microparticles. **Afr J. Pharm. Pharmacol.** 6(30) 2309-2317.

Obonga W., Omeje E.O., Nnadi C.O., Osadebe P.O., **Attama A.A.,** Onunkwo G.C. (2014). Some physical properties of novel marijuana suppositories formulated with theobroma oil. **Afr. J. Pharm. Pharmacol.** 8(44) 1127-1131.

Ofoefule S.I. and **Attama A.A.** (2009) Biopolymer Blends: Applications, Limitations and Future Prospects. In: M.U. Adikwu, C.O. Esimone (Eds.). **Biopolymers in Drug Delivery: Recent Advances and Challenges**. Bentham Science Publishers, UAE, eISBN: 978-1-60805-078-9**,** pp. 198 - 223.

Ofoefule S.I., Chukwube V.O., **Attama A.A** (1999). Effects of direct compression excipients on the stability of ascorbic acid (Vitamin C) tablets. **Boll. Chim. Farm.** 138(8) 418-421.

Ofoefule S.I., Uzuegbunam E.C., **Attama A.A**. (1998). Effects of some direct compression excipients on the stability of pyridoxine hydrochloride tablets. **Boll. Chim. Farm.** 137(9) 685-689.

Ofokansi K.C., Kenechukwu F.C., Ezugwu R.O., Reginald-Opara J., **Attama A.A.** (2014). Design and characterization of solid dispersions based on Peg 8000 for the delivery of trandolapril, a poorly water-soluble ACE inhibitor. **Nig. J. Pharm. Res.** 10(1) 1-18.

Ogbonna J., Emeje M., Momoh M., **Attama A.A.**, Ofoefule S. (2011). The dual role of carboxymethylated starch in monolithic polymeric matrices of ciprofloxacin. **Int. J. Pharm. Pharmaceut. Sci.** 3(4) 419 – 423.

Ogbonna J.D.N, Kenechukwu F.C., **Attama A.A.**, Chime S.A. (2012) Different approaches to formulation of herbal extracts/phytopharmaceuticals/bioactive phytoconstituents. **Int. J. Pharm. Rev. Res.** 16(1), 1-8.

Ogbonna J.D.N., Inya-Agha S.I., Kenechukwu F.C., Momoh M.A., Chime S.A., **Attama A.A.** (2013) Evaluation of six herbal plants used in the treatment

of malaria in south-eastern Nigeria: A review. **Int. J. Pharm. Res. Biosci.** 2(1) 148-167.

Ogbonna J.D.N., Kenechukwu F.C., Chime S.A., **Attama A.A.** (2015). Cellulose-Based Biopolymers: Formulation and Delivery Applications. In: Munmaya Mishra (Ed.). **Encyclopedia of Biomedical Polymers and Polymeric Biomaterials**, Taylor and Francis Group, New York, NY, USA.

Ogbonna J.D.N., Kenechukwu F.C., Nwobi C.S., Chibueze O.S., **Attama A.A.** (2014). Formulation, *in vitro* and *in vivo* evaluation of halofantrine-loaded solid lipid microparticles. **Pharm. Dev. Technol**. **Early Online:** 1–8.

Ogbonna J.D.N., Nnamani P.O., Okore V.C., **Attama A.A.** (2011) Phase rule. In: A.A. Attama, E.C. Ibezim (Eds.). **Laboratory Techniques in Physical Pharmaceutics**. Praise Printers, Enugu Nigeria, pp. 10 – 13.

Okore V.C. and **Attama A.A.** (2008). In: **Laboratory Techniques in Pharmaceutical Microbioology**, Jolyn Pub., Nsukka, Nigeria.

Okore V.C., Ibezim E.C., Adikwu M.U., **Attama A.A.** and Ofokansi K.C. (2004). Basic dispensing procedures. In: **Techniques in Pharmaceutics and Pharmaceutical Microbiology**, El Demak Pub., Enugu, Nigeria.

Okoro U., Ogbonna J.D.N., **Attama A.A.** (2014). Nanoparticles for Dermal and Transdermal Drug Delivery. In: A.D. Sezer (Ed.), **Application of Nanotechnology in Drug Delivery**. Rijeka Croatia: InTech; pp. 193-235.

Onaku L.O., **Attama A.A.**, Okore V.C., Tijani A.Y., Ngene A.A., Esimone C.O. (2011). Antagonistic antimalarial properties of pawpaw leaf aqueous extract in combination with artesunic acid in *Plasmodium berghei*-infected mice. **J. Vector Borne Dis.** 48 96–100.

Onugwu L.E., Akpa P.A., **Attama A.A.** (2009). A study of the interaction between acyclovir and some fluoroquinolones by the Checkerboard technique. **J. Pharm. Allied Sci.** 6(2) 761 - 765.

Onuigbo E.B., **Attama A.A.**, Esimone C.O., Ofokansi K.C., Okore V.C. (2011). Formulation and evaluation of niosomes. **Indian J. Pharm. Sci.** 3, 337-342.

Onuigbo E.B., Esimone C.O., Onwuka C.O., Okore V.C., **Attama A.A.** (**2009).** Preliminary studies on the functional properties of amoxicillin in a cationic liposome. **Int. Conf. Polymer Dev. Applic.** 1, 126-131.

Onuigbo E.B., Gyang D.M., **Attama A.A.** (2013). Preliminary evaluation of the immunoenhancement potential of fowl typhoid vaccine formulated as an oral cationic liposome. **Afr. J. Pharm. Pharmacol.** 7(32) 2291-2294.

Onuigbo E.B., Ogbonna J.D.N., **Attama A.A.** (2011). Antibiotic assay. In: V.C. Okore, K.C. Ofokansi (Eds.). **Laboratory Techniques in Pharmaceutical Microbiology**, 1st Edn., Praise House Publishers, Enugu, Nigeria, pp. 10 – 14.

Onuigbo E.B., Okore V.C., Ngene A.A., Esimone C.O., **Attama A.A.** (2011). Preliminary studies of a stearylamine-based cationic liposome. **J. Pharm. Res. India** 10(1) 25-29.

Onuigbo E.B., Okore V.C., Ofokansi K.C., Okoye J.O.A., Nworu C.S., Esimone C.O., **Attama A.A.** (2012) Preliminary evaluation of the immunoenhancement potential of Newcastle disease vaccine formulated as a cationic liposome. **Avian Pathology.** 41(4) 355-360.

Oreh N.C., **Attama A.A.** (2013). Comparison of susceptibility patterns of *Escherichia coli* isolated from urinary tract infections in two health institutions in South-South Nigeria to commonly used antimicrobials. **Afr. J. Micro. Res.** 7(24) 3066-3070.

Osadebe P.O., Onugwu L.E., **Attama A.A.** (2008). Energetics of interaction between piroxicam and beta-cyclodextrin in inclusion complexes. **Sci. Res. Essays**. 3(3) 086-093.

Raab C., Simkó M., Fiedeler U., Nentwich M., Gazsó A. (2011). Production of nanoparticles and nanomaterials. Nano Trust Dossier, No. 006, epub.oeaw.ac.at/ita/nanotrust-dossiers/dossier006en.pdf.

Sanofi Report: Sanofi Fights against Counterfeit Medicines. http://www.sanofi.com. Accessed on June 7, 2014.

Ugwu M.C., Ikegbunam M.N., Nduka S.O., **Attama A.A.**, Ibezim E.C. and Esimone C.O. (2013). Molecular characterization and efficacy of antibiotic combinations on multiple antibiotic-resistant *Staphylococcus aureus* isolated from nostrils of healthy human volunteers. **J. Pharm. Sci. Res.** 5(1) 26 – 32.

Umeyor C.E., Kenechukwu F.C., Ogbonna J.D.N., Builders P.F., **Attama A.A.. (2011).** Preliminary studies on the functional properties of gentamicin in SRMS-based solid lipid microparticles. **Int. J. Novel Drug Deliv. Technol.** 1(2) 130-142.

Umeyor C.E., Kenechukwu F.C., Ogbonna J.D.N., Chime S.A., **Attama A.A.** (2012). Preparation of novel solid lipid microparticles loaded with gentamicin and its evaluation *in vitro* and *in vivo*. **J. Microencapsul**. 29(3) 296–307.

Umeyor E.C., Kenechukwu F.C., Ogbonna J.D., Chime S.A., **Attama A.A**. (2012). Investigation of solidified reverse micellar systems as novel carriers for oral delivery of gentamicin. **J. Pharm. Res.** 5(9) 4914-4920.

Uronnachi E.M., Ogbonna J.D.N., Kenechukwu F.C., **Attama A.A.**, Chime S.A. (2012) Properties of zidovudine loaded solidified reverse micellar microparticles prepared by melt dispersion. **J. Pharm. Res.** 5(5) 2870-2874.

Uronnachi E.M., Ogbonna J.D.N., Kenechukwu F.C., **Attama A.A.**, Okore VC., Chime S.A. (2014). Formulation and release characteristics of zidovudine-loaded solidified lipid microparticles. **Trop. J. Pharm. Res.** 13(2) 199-204.

Uronnachi E.M., Ogbonna J.D.N., Kenechukwu F.C., **Attama A.A.**, Okore V.C. (2013). Formulation and *in vitro/in vivo* evaluation of zidovudine contained in solidified reverse micellar delivery system in immune compromised rats. **J. Appl. Pharm. Sci.** 3(2) 031-035.

Uronnachi E.M., Ogbonna J.D.N., Kenechukwu F.C., Chime S.A., **Attama A.A.**, Okore V.C. (2014). Formulation and release characteristics of zidovudine-loaded solidified lipid microparticles. **Trop. J. Pharm. Res.** 13(2) 199-204.

Uzor P.F., Agbo I.U., Omeje E.O., David E.K., **Attama A.A.,** Adikwu M.U. (2009). Molecular weight determination of some natural gums by dilute solution viscometry. **Int. Conf. Polymer Dev. Applic.** 1,168-176.

Uzor P.F., Nnadi C.O., **Attama A.A.**, Ezeuchu J.O., Oli A.N. (2011). Design and *in vitro* evaluation of sustained release amodiaquine-loaded Eudragit microspheres. **Int. J. Novel Drug Del. Technol.** 1(3) 176-180.

Uzor P.F., Ofokansi K.C., **Attama A.A.** (2013). Phytochemical study and evaluation of the combined antimicrobial activity of *Albizia adianthifolia* root with two antifungal agents against clinical Candida species. **World Res. J. Antimicr. Agents.** 2(1) 034-038.

Vasir J. K., Reddy M. K. and Labhasetwar V. D. (2005). Nanosystems in drug targeting: Opportunities and challenges. Current Nanoscience 1, 47-64.

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