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TOPIC:

PHARMACY: ETHICAL DRUG DISTRIBUTION AS PANACEA TO THE FAKE DRUG PANDEMIC

By
PROFESSOR NDU DAVID IFUDU

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By

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Mr. Vice-Chancellor Sir, permit me to start this inaugural lecture by giving honour and glory to Almighty God who made this day possible. This is in line with my family tradition of giving glory to God before any major event and this occasion deserves nothing less.

This presentation will be made in three parts with each part addressing a specific issue. Who is the pharmacist? The changing face of pharmacy education; my contributions as a scientist and technologist; and the fake drug pandemic in Nigeria and the possible impact of Ethical Drug Distribution.

There are several definitions of the pharmacist. I shall dwell on a few of them to synthesize the true pharmacist.

Pharmacy from the Greek work 'pharmakon' is the health profession that links the health sciences with the clinical sciences, and it is charged with ensuring the safe and effective use of medicines (1).

Pharmacists are health professionals who practice the art and science of pharmacy. In their traditional role, pharmacists typically take a request from a prescribing healthcare provider in the form of a medical prescription and compound and dispense the medication to the patient and counsel on them (1).

A pharmacist is a person qualified by a graduate degree in pharmacy to formulate, dispense and provide clinical information on drugs and medication to health care professionals and patients and holding a license in a particular jurisdiction to practice pharmacy (2).

Thus the pharmacist is an artist, scientist, a licensed health care provider and a technologist.

The changing trends in the education of the pharmacist or development of pharmacy education in Nigeria.

Pharmacy practice worldwide has undergone a paradigm shift from product emphasis to being patient care oriented. Demographic changes, disease patterns and the rapid advances

in science and technology have resulted in the use of more drugs and more expensive drug delivery systems. Such changes are challenging those who are responsible for educating the nation's future pharmacy practitioners.

THE PHARMACIST COUNCIL OF NIGERIA

This Council recommended preparing pharmacy students who will be more adaptable and better prepared to work in different environments and within interdisciplinary teams. The faculties of Pharmacy or Pharmacy educators are thus challenged to prepare graduates for practice in the changing drug delivery system by refocusing the curriculum towards such areas as proof –driven therapies,collaboration with patients and other health team members about drug therapy decisions, counseling patients about their drug therapies, monitoring patient responses to drug therapies, and educating the public about drug-related information.

REQUIRED CHANGES IN PHARMACY CURRICULUM

The required changes in pharmacy curriculum should:

(i) Initiate curricular reform that engenders competencies essential to pharmaceutical care (e.g. critical thinking, communication, ethical behaviour, teamwork, leadership, and caring);

(ii) Develop systems of peer review and evaluation that include documentation and review of care delivered, analysis of the outcomes of care, and efforts to ensure the continuing quality and effective coordination of care;

(iii) Develop and promote a medication use information system for application to the ambulatory care setting; and

(iv) Develop a sufficient number and variety of ambulatory clinical training models and sites to provide ample education opportunity for pharmacy and other health professional students in the delivery of pharmaceutical care. This is in line with the Pew Health Professions Commissions 1993 report (3).

TRADITIONAL PHARMACY EDUCATION

Traditionally, pharmacy education has focused on drug products, emphasizing chemistry, pharmaceutics and the control and regulation of drug product delivery systems. The dramatically changing health care delivery system and the increasingly prominent role of pharmaceutical agents in the diagnosis and treatment of disease is shifting this focus to a broader role for pharmacy practitioners. This broader role demands a set of generalist competencies to augment traditional discipline-specific competencies in order to assure that pharmacy practitioners are prepared to practice effectively in the changing environment.

PCN COMMITTEE TO IMPLEMENT CHANGE TO PHARM D

In 2001, the PCN set up a committee under the then chairman of the Board – Dr Fred Adenika of blessed memory to review the pharmacy curriculum.

This group re-examined the role of pharmaceutical education in relation to the dramatic changes occurring in health care system. The committee determined that the bachelor's degree in pharmacy would not longer meet the changing needs of the profession and the health care system. Instead, the committee recommended that the doctoral degree in pharmacy (Doctor of Pharmacy, or PharmD) should become the entry level credential for the profession. The program should be at least four academic years in length, with at least two years of pre-pharmacy coursework as a foundation for the upper level professional curriculum. Attendees believed that the new PharmD curriculum should emphasize skills such as patient assessment, drug therapy management, and problem-solving. The committee noted that pharmacists of the future would assume greater responsibility for the management of drug therapy in patients. To this end they identified four major areas of competence:

- Conceptual competence – Understanding the theoretical foundations of the profession,

- Technical competence – Ability to perform skills required in the profession
- Integrative competence – Ability to merge theory and skills in the practice setting, and
- Career marketability – Become marketable as a result of education and training.

The committee stressed that the ideal curriculum should focus on patient-centered, therapeutic knowledge. Less emphasis should be placed on the pharmacist controlling the supply of the drug product. Instead the pharmacist should coordinate the drug use process in collaboration with other health professionals.

NUC'S APPROVAL/ENDORSEMENT OF PHARM D PROGRAM

The PCN submitted the final work of the committee to NUC as a body involved also in the accreditation standards for pharmacy education. The need for the PharmD was re-emphasized.

NEED FOR PHARMD DEGREE

Pharmacy students will not be prepared to meet the demands of these new roles without more extensive and intensive education. In addition to requiring the PharmD degree as the entry-level credential for pharmacy practice, most pharmacy educators advocated that schools and colleges must reconceptualize and reconstruct their curricula so that graduates would be prepared to meet the complex challenges of providing pharmaceutical care. While pharmacy education programs have expanded the curriculum coverage of pharmacy-specific knowledge and skills, it is not clear to what extent they are also preparing their students with the broad competencies and skills needed for practice in an increasingly complex and shifting health care system and social environment (4).

Mr. Vice-Chancellor Sir, I will now go into certain aspects of my work in detail. My first challenge as a graduate student was the

stability of the compound, Baker's Antifol – (NSC 113, 423) 4 – (p-(4,6-Diamond – 1, 2 – Dihydro 2, 2 – Ethyl- S- Triazin – 1- yL) Hydrozinnamido) – O- Toluene sulfinyl fluoride, anti-cancer drug. This anticancer agent was obtained from the American National Cancer Institute Lots CC 44-87 – 1 and BR 27-79 – 1(5).

In studying the stability of Bakers Antifol – a pretty complex molecule – it became expedient to synthesize some of the sub-prototypes of the compound. This led us to the synthesis of p-hydroxycinamido. – o- methyl benzene sulfonyl fluoride,  and 2-methyl benzene sulfonyl fluoride according to a scheme reported by Baker and Lourens (5). I dare say that was not a piece cake as some of the critical steps were not described fully by Baker and Lourens (5). The studies on these sub-prototypes of Baker's Antifol was aimed at gaining insight into the stability problem of the compound. Besides we had only five grams of the parent compound with a zero possibility of obtaining more.

Since the major route of degradation of Baker's Antifol at high pH involved catalysis by hydroxide ion and since it is generally accepted that an anionic micelle would repulse attack of the hydroxide ion on its substrate,anionic micellar solutions were investigated as a means of stabilization of Baker's Antifol. Mr. Vice-Chancellor sir, it was quite exciting to observe that the half-life of Baker's Antifol was prolonged by such a large factor as 1400 times in the presence of 0.5% sodium dodecyl sulphate at 27°C.

This result dictated that experiments should be designed and completed to obtain more information about the possible mechanism of reaction and stabilization. The several studies that ensued showed that the substrate location in the polyoxyethylene linkages of the micelle rather than electrostatic factors was responsible for the degree of stabilization observed in 0.5% w/v sodium dodecyl sulphate solutions (5).

From further studies we are able to derive the equations

$$\frac{Q_T}{Q_w} = \frac{P\,d_w}{100 d_m}(\%_T - \%_{cmc}) + 1 \qquad \text{Eq. 1}$$

$$= 1 + P^1\%_m \qquad \text{Eq. 2}$$

Where the partition factor $P^1 = \frac{Pd_w}{100\,d_m}$

d_m = Density of micellar phase
d_w = Density of aqueous phase
$\%_m$ = Percentage of surfactant in form of micelle
$\%_T$ = Total apparent surfactant solubility in the system
Q_T = Total apparent substrate solubility in the micellar phase
Q_w = Apparent substrate solubility in the aqueous phase

The significance of equation 2 is the fact that the partition coefficient P^1 is independent of the micellar aggregation number and the molecular weight of the sufactant in contrast to earlier publication by Mukerjee and Mysels (6a) where P^1 is dependent on both factors which have variable literature values.

Applying this Partition concept the overall observed rate constant (k_{obs}) in aqueous micellar phase was obtained.

$$k_{obs} = \frac{k_w + k_m P^1 \%_m}{1 + P^1 \%_m} \qquad \text{Eq 3}$$

Where $\%m = (\%_T - \%_{cmc})$ ie the concentration of surfactant which is in form of micelles expressed as %w/w
$\%_T$ = total concentration of SAA expressed %w/w and
% cmc = conc. of SAA at the CMC expressed as %w/w

It is significant (Ifudu & Simonelli) (8) that the observed rate constant is a function of percentages rather than the effective molar weight and the aggregation number, N, of the SAA. Also equally important is the fact that the literature values of these parameter, normally used, were evaluated under different

experimental conditions and in surfactant systems subjected to varying degrees of purification and therefore their values may not be applicable to the experiments or the surfactants used in other laboratories. For the example the aggregation number sodium dodecyl sulphate in the literature ranged from 60 (6) to 100 (7). Our overall rate equation does not require that the shape of the micelle remains constant, since it is clearly a function of the total micelle volume and the micelle micro environment surrounding of substrate. (8).

We decided to further investigate the applicability of our partition model and equations in other reactions occurring in the presence of a different type of micellar environment. This involved a study of the effect of a cationic surfactant , Cetyl trimethyl ammonium bromide (CTAB) on the rate of alkaline hydrolysis of p-substituted benzene sulfonyl fluorides (9).

Our results showed that the alkaline hydrolysis of p-substituted benzenesulfonyl fluoride derivates in the presence of CTAB is not determined by the electron activity of the substituent groups, although it is possible that this could influence the magnitude of the observed effects. Inhibition of hydrolysis was observed for all derivatives as a function of CTAB concentration. We thus concluded that the inhibitory effect arises from a combination of submicellar substrate solubilization and interaction between the surfactant and sulfonyl fluoride derivatives. The kinetic partition coefficients were calculated from the reaction rate constant-surfactant concentration data by using rearranged forms of our Partition Model derived equation (6). Ordinarily the partition or distribution coefficient would be obtained from independent experiments such as equilibrium solubility and gel filtration studies. Mr. V.C Sir, a literature review clearly showed that the result of such experiments may not be applicable to kinetic systems and its use even for simple comparison may lead to erroneous conclusions, hence the import of our contribution.

NON-PARENTERAL DOSAGE FORMS

A dosage form is a drug delivery system designed to deliver the active ingredient to the body and upon administration should deliver the drug at a rate and amount that assures the desired pharmacological effects. Such dosage forms are manufactured under current good manufacturing procedures (cGMP), using adequate equipment and packaging to ensure product stability (10).

SOLID DOSAGE FORMS

- powders and granules
- tablets

Types:- lozenges, effervescent, chewable, Sublingual and Buccal, Molded and Multi layered tablets.

A multilayered tablet consists of several different granulations compressed one on top of the other to form a single tablet. They may also be bi-layer when incompatible drug substances are used e.g. charcoal and metronidazole (Iteun, Ifudu and Uboh 2009) (11).

- Capsules
  - hard gelation capsules (HGCs)
  - Soft gelation capsules (SGCs)

LIQUID DOSAGE FORMS

- **Solution**

Types : Draughts and Elixirs,Linctuses,Mouthwashes and Gargles, Nasal Drops, Ear drops, Enemas, Lotions, Liniments, Colloidons

Suspension: Focculated and deflocculated Emulsions

SEMISOLID DOSAGE FORMS

Ointments, creams and pastes intended for topical application

- To skin, and also used nasally, rectally and vaginally .

NEW DRUG DELIVERY TECHNOLOGIES

Newer technologies are emerging as we move into the new millennium. These technologies promise to have lots of benefits such as simplifying administration regimens, enhancing adherence, improving clinical benefits and reducing the overall healthcare costs. For instance, rapid-dissolving tablets are designed for patients who have difficulty in swallowing standard tablets/capsules such as paediatric and geriatric patients (12,13).

SUPPOSITORIES

Suppositories are solid dosage forms intended for insertion into body orifices where they melt, soften, or dissolve and exert localized or systemic effects. Suppositories are commonly employed rectally and vaginally, occasionally urethrally. The shape and size of a suppository must be such that it is capable of being easily inserted into the intended body orifice without causing undue distension, and, once inserted, it must be retained for the appropriate period of time. Rectal suppositories are generally inserted with the fingers, but certain virginal suppositories, particularly may require the use of a special insertion appliance (13).

The factors affecting the rectal absorption of a drug administered in the form of a suppository may be divided into two main groups: (1) physiologic factors and (2) physiochemical factors of the drug and the base.

Physiologic Factors

Among the physiologic factors affecting drug absorption from the rectum are the colonic contents, circulation route, and the pH and lack of buffering capacity of the rectal fluids. (13).

Physicochemical factors include such properties as the relative solubility of the drug in lipid and in water and the particle size of a dispersed drug. Physicochemical factors of the base include its ability to melt, soften, or dissolve at body temperature, its ability

to release the drug substance, and its hydrophilic or hydrophobic characteristics.

RESEARCH AREAS IN PHARMACEUTICS

The core research areas in the department of pharmaceutics include: formulation and evaluation of dosage forms, stability studies, pharmaco-kinetics among others.

General Considerations in Drug Product Formulation

Pharmaceutical formulations are usually complex systems consisting not only of the active drug substance(s) but also of a number of excipients in order to fulfill the goals of a dosage form. Excipients, the non-drug components of a formula, are critical to the design of the delivery system and play a major role in determining its quality and performance. Numerous factors such as cost, physicochemical properties, regulatory requirement, compatibility, functional reliability, and international acceptability determine their selection.

These basic studies which must be carried out on the active(s) and excipients comprise the pre-formulation work before actual product formulation begins.

ACTIVITIES OF PRE-FORMULATION WORK

OBJECTIVES OF PRE-FORMULATION

The objectives of pre-formulation studies is to collect information about the drug substance which will serve as a reference source against which detailed formulation design can be carried out. Preformation work on a new compound is usually initiated after the compound has shown sufficient activity, especially in animal models to merit further testing in man. The studies should focus essentially on those physicochemical properties of the drug substance and excipients that could affect drug performance and the development of an acceptable dosage form. A thorough understanding of these properties may ultimately provide the rationale for formulation design or support the need for molecular modifications (14).

The physicochemical and biopharmaceutical properties of the drug can have a tremendous impact on its bioavailability and, hence, on its efficacy and toxicity profiles. Thus, understanding these parameters is often tantamount to the selection and development of the optimum dosage form.

These properties of the drug include its:

- pH solubility profile and dissolution rate.
- Partition coefficient between lipoidal barriers and aqueous physiologic media.
- Stability and/or degradation rate in the physiologic fluids.
- Susceptibility to metabolic inactivation and
- Mechanism of transport through biologic membranes.

Once the physicochemical and biopharmaceutical properties of the drug are determined and the desired plasma concentration profile is defined, the pharmaceutical scientist can select and develop an efficacious dosage form by utilizing a formulation approach, a prodrug approach, a device approach, or an alternative administration route approach.

FORMULATION APPROACH

Use of formulation techniques can improve the bioavailability and/or minimize the toxicity and side effects of drugs. Factors to consider include those that impact on solubility and dissolution rates, chemical and enzymatic stability, and absorption capability.

Several parameters, including particle size, crystalline habit, and salt form, which can affect the solubility and dissolution rate of relatively insoluble compounds becomes significant when the drug is administered as a suspension or solid dosage form and the material is well dispersed within the GI tract.

Polymorphism is the ability of a chemical species to crystallize in more than one distinct crystal habit. The pharmaceutical applications of polymorphism has been reviewed by several authors (15-17). The differences in dissolution rate and solubility that polymorphs can produce may have dramatic impact on

bioavailability when dissolution is the rate-limiting step in the absorption process.

Tawashii (18) investigated the GI absorption of two polymorphs of aspirin, the stable and metastable forms, forms 1 and II, respectively. He found that the metastable form produced a 70% higher total serum salicylate levels than the stable form I.

The selection of a salt form directly influences the physiochemical and biopharmaceutical properties of a compound. The impact of salt selection has been reviewed (19-21). Nelson (22) examined the dissolution of theophyline salts and commented on their impacts on oral administration. The dissolution rates of the theophyline salts proceeded independently of the pH of the medium but was governed by the diffusion layer pH. The choline and isopropanolamine salts dissolved three to four times faster than the ethylenediamine salt and produced higher and prolonged blood levels. Thus, the selection of the most appropriate salt form should be made early in the development process to optimize bioavailability.

The stability of a drug in the gut is influenced by both chemical and enzymatic factors. Protection from chemical degradation may be accomplished via coating techniques, and enzymatic protection may be achieved with enzymatic inhibitors (23).

Altering the availability for absorption permits tailoring of the concentration-time profile for a drug. In the case of theophyline dosage forms, the approach should be to slow the release rate so that undesirable spikes in the plasma levels are minimized. This effect can be accomplished with a sustained-release formulation.

In formulating a drug in a sustained release dosage form, the following must be taken into consideration :

(a) The effective drug plasma level .
(b) The rates of absorption and elimination of the compound.
(c) Site(s) of absorption.

Having established these parameters, calculating the release rate from the dosage form is a relatively simple matter as formulation techniques are readily available to produce the desired release rate.

PRODRUG APPROACH

An alternative to the formulation approach is the prodrug approach. A prodrug is defined as a drug that is prepared by chemically modifying a pharmacologically active species to form a new chemical entity that undergoes transformation to the active species within the body. The modification alters the physicochemical and biopharmaceutical properties of the drug in some beneficial manner.

The ideal prodrug should have the following characteristics:

- Possesses no pharmacologic activity
- Be eliminated more slowly than its rate of cleavage to the parent
- Be non-toxic
- Be inexpensive to prepare

Prodrugs can be used to increase or decrease the aqueous solubility, mask bitterness, increase lipophilicity, improve absorption, decrease local side effects, and alter membrane permeability of the parent molecule. For example, chloraphenicol has an aqueous solubility of 2.5 mg/ml, but chloramphenicol sodium succinate, a prodrug, has an aqueous solubility of 100 mg/ml (24,25).

PAEDIATRIC FORMULATION

These are formulations intended to be used for children from neonate to adolescent.

Paediatric formulations can be delivered by many routes such as oral, rectal, nasal, buccal/sublingual, topical/transdermal,

injectable, pulmonary,ocular, and ear drops (26). Conventionally paediatric formulations are actually referred to as oral paediatric formulation because it is this form of administration that has a clear distinction between how adults and children formulations are presented.

Types of Paediatric Oral Formulations

1. Syrups
2. Suspensions
3. Chewable tablets
4. Oral Dissolving Tablets (ODTS)

Pharmaceutical Challenges of Paediatric Formulations

The development of multiple dosage forms for different ages will rarely be a commercially viable venture and liquid formulations which will be given to a broad age group present particular pharmaceutical challenges (26). Some of the obvious challenges include taste, problems with paediatric oral liquid formulations, dose-estimation and toxicity.

Taste

The taste of a drug formulation is one of the most important parameters governing patient adherence (27). Most active pharmaceutical ingredients and in some cases excipients have bitter taste. Adults may think that the worse a medication tastes the better it works, children do not appear to support this belief (28). Taste is a strong factor in determining medication adherence and completion of drug therapy in children (32). Therefore, any pharmaceutical formulation with a pleasing taste would definitely be preferred over a competitor's product and would translate into better adherence and therapeutic value for the patient and more business and profits for the company (27). Taste masking of a bitter tasting drug is an important process in the formulation of oral pharmaceutical dosage forms especially for paediatric use. Taste masking is defined as the perceived reduction in undesirable taste that would otherwise exist (27).

governmental funding bodies, in that too little resources have been committed to developing effective and safe medicines for children, and in particular defining the right dose(s) for appropriate paediatric populations (31). The estimation of the doses of drugs for children is usually based on extrapolation from the data obtained from adult-based research which is not right. Before any medicine is authorized for use in adults, the product must have undergone clinical testing to ensure its safety, quality and efficacy but for children population this is not always carried out (32).

The vast majority of drugs which are used for paediatric population are actually developed for use in adult population and the reason being that:

- Ethical objection to conducting clinical trials in children.
- The resources that are required to discover and develop new drugs for use in paediatric population present poor return on investment.
- The uncertainty of types of clinical trial in children that will satisfy both regulatory authorities and prescribers as to the efficacy, safety and quality of new potential medicines (33).

Achieving an Ideal Paediatric Formulation (34)

An ideal formulation for children should have the following characteristics:

- Allow minimal dosage and frequency
- Have one dosage form or fit all or a full range
- Have minimal impact on lifestyle
- A minimum number of excipients
- Have convenient, easy, reliable administration
- Be easily produced, elegant, stable, cheap and commercially viable

Contributions in Dosage Form Formulation

To achieve the ideal paediatric formulation characteristics will require much efforts on the part of the research and development scientist, production pharmacists, manufacturer as well as incentives from the government and regulatory bodies.

PHARMACOKINETICS RESEARCH

Pharmacokinetics is the science that treats the rate of drug absorption, extent of absorption, rates of distribution among body compartments, rates of elimination and related phenomena. In these areas of research, Mr Vice-Chancellor Sir, we have made some significant contributions.

1. Nifedipine in Nigerians

Nifedipine is a calcium antagonist used in the management of hypertension and related disorders. Pharmacokinetics studies conducted thus far have shown that Nifedipine is rapidly and almost completely absorbed from the oral dosage form resulting in expected plasma concentration (35). To date reports on the pharmacokinetic studies among Nigerians are very scanty. In view of the possible pharmacokinetic differences in human races, metabolic and eating habits of the peoples of the world, we conducted a study to re-evaluate the bioavailability of Nifedipine in negroids especially Nigerians. The results of our findings was published in 1988 (36) . The study compared the bioavailability of the Adalat –a tablet - and another popular brand Nifecard,(a capsule) Results from our work demonstrated that the presence of food retards the rate of absorption of Nifedipine from the small intestine but does not influence the extent of absorption of the drug. This is a very important/relevant factor in monitoring the time of set of action of Nifedipine. In addition the pharmacokinetic parameters for both dosage forms – tablet and capsule – were similar. Based on these results we concluded that the two different formulations may be used interchangeably with insignificant alteration in net therapeutic response/outcome.

2. Fleroxacin vs Ciprofloxacin in the management of typhoid fever in Nigerian patients

The antibacterial efficacy of fleroxacin was compared with that of ciprofloxacin in 72 adult Nigerian patients with typhoid fever. The results demonstrated that while the clinical response rates with both drugs are comparable, fleroxacin exhibited a faster

bactetriological clearance rate. We therefore concluded that the 7 days' therapy with fleroxacin 400mg once daily was as effective as 14 days' therapy with ciprofloxacin 500mg given twice daily, in the management of typhoid fever in Nigerian patients. It was also observed that the quinolones possessed greater potential and benefits as first line therapy for the management of typhoid fever in this environment. The tolerability profile was good for both treatment regimens though adherence was higher in the once a day regimen with fleroxacin (37).

3. Bioavailability of Ciprofloxacin and Fleroxacin in Adult Nigerian male Volunteers

The main purposes of this study was to establish the absolute bioavailability profile of ciprofloxacin in Nigerian subjects and compare it with that of Fleroxacin in view of their different chemical structures and use in the management of typhoid fever. Nigerian male volunteers who complied with the inclusion criteria were involved in this study.

Generally the bioavailability of fleroxacin was higher than that of ciprofloxacin as has been previously established (38). The value of 37% obtained for ciprofloxacin in our study is considered quite low and calls for a positive reappraisal of the bioavailability of ciprofloxacin in black Africans. Also large within-group variability in absorption was observed for ciprofloxacin.

Fleroxacin, on the other hand, exhibited a different trend from that observed in the literature with respect to Cmax and AUC where the values observed in this study were 3-4 fold lower than expected following identical doses as reported by Cullman et al, (39) ; 2.2 – 3.0 mg/l compared to the 0.42 – 0.81 mg/l obtained in our study. The difference between the blood level profiles following oral and iv administrations was significant for only ciprofloxacin.

Table:1. Paired t-Test Parametric comparison of i.v. vs. Oral Profile for Ciprofloxacin and Fleroxacin

	Ciprofloxacin			Fleroxacin		
Parameter	Mean			Mean		
	i.v.	Oral	P	i.v.	Oral	P
a (h^{-1})	17.93	1.1	0.0096*	7.98	0.33	0.13
β (h^{-1})	0.12	0.09	0.34	0.054	0.059	0.6
K_{10}-HL(h)	0.78	3.64	0.0001**	4.25	7.92	0.007*
Alpha-HL(h)	0.17	1.3	0.001*	0.75	3.54	0.005*
Beta-HL(h)	7.52	15.14	0.026*	13.75	13.6	0.96
AUC (mg. h/1)	9.5	10.16	0.74	7.81	6.87	0.5
C_{max} (mg/l)	2.3	1.2	0.005*	0.81	0.42	0.007*
Volume (l/kg)	0.35	1.39	0.003**	2.85	5.8	0.2

*Significant, ** Highly significant.

The reasons for the differences in disposition profiles between our study population and those previously studied could not be immediately ascertained. However, a closer look at the absorption and elimination profile of both drugs gives some indications for speculation on the possible reasons for the observed differences. In our study the 'absorption rate constant' (K_a) for ciprofloxacin was 10-fold higher than that of fleroxacin thus explaining the differences in the values of (the maximum concentration) , C_{max} obtained following oral absorption. It has previously been postulated that ciprofloxacin is more lipophilic than fleroxacin (38,39). This may explain the significant differenes in the C_{max} value following i.v. administration, more so in view of the fact that the iso-electric point (IP) for Ciprofloxacin is at the physiological pH of 7.4. One would expect this property of ciprofloxacin (IP at pH 7.4) to greatly enhance its extent of distribution in comparison to fleroxacin. However our findings were contrary to this speculation. As discussed in an earlier publication, we are of the opinion that fleroxacin is more widely distributed than ciprofloxacin, at least in the population we studied.

One of the possible confounding variables between the population we studied and others is the possibility of traces of chloroquine (CQ) being present in the blood of our volunteers. There exists a potential for interaction since CQ is a 4-amino-quinoline, a group somewhat structurally related to the 4-quinolones. Chloroquine and other antimalarials are routinely taken then for malaria chemoprohylaxis and therapy in our environment. Chloroquine has a very long half-life and studies have shown that levels of CQ and its metabolites persist in plasma long after the last administration of the drug (Essien and Ifudu). There is thus an urgent need to study the possible interactions between the quinoline anti-malarials and the quinolones, particularly in a malaria endemic environment such as Nigeria since to date Nigerians still use chloroquine in the treatment of malaria.

We have been able to establish that there are significant differences in the disposition profile of Ciprofloxacin and Fleroxacin between our study population and those studied previously in the literature. We were also able to justify the need for more work to be done, in particular, focusing on the interaction potentials between the 4-amino quinolines and the 4-quinolones.

Development of local raw materials as excipents/additives for pharmaceutical dosage formulations

Mr. Vice-Chancellor Sir, in considering local raw materials for the pharmaceutical industry, one must pay attention to those materials which are needed for both the primary and secondary phases of production. With the diminishing returns from oil one must recognize that our natural products have a lot of potential for pharmaceutical raw materials. Pharmaceutical raw materials may be derived from any of the following main sources:

- Agro-based sources i.e. from plants and animals
- Mineral-based sources
- Petrochemical-based sources

In the course of our work, we have registered considerable successes in processing locally available materials as excipients for pharmaceutical dosage form formulation.

Liquid formulation-Emulsion

Cissus population Gum, Gull and Perr (Ampelidaceae)

Cissus populnea gum was obtained from the macerated stem of *Cissus populnea.* The description of the collection and purification to pharmaceutical grade was reported in our earlier publications (40,41). The gum was evaluated as a potential emulsifying agent for the preparation of the liquid oral dosage from – Emulsion (42). Populnea gum formed a primary emulsion at water: oil: gum ratio of 32:64:1 (0.78% w/v) due to its significant surface tension lowering effects . Stable arachis oil and liquid paraffin emulsions have been prepared with 0.78%, w/v populnea gum. At a gum concentration of 1.56%w/v with oil: water: gum ratio of 16:32:1 the new gum yielded more stable arachis oil and liquid paraffin emulsions than 6.25% w/v and 8.33% w/v acacia respectively. This new gum has obvious economic advantages in that the plant source is relatively more abundant, with less competitive nutritional values, cheap, readily available and can be easily cultivated on a large scale with little or no maintenance cost.

Evaluation of local kaolin powder as a lubricant in tableting

Sources: Kaolin deposits abound in the different part of Nigeria. Samples mined from Okitipupa was processed to pharmaceutical grade in our laboratory . The effectiveness of the locally sourced and processed kaolin powder as a lubricant in tableting was evaluated against standard lubricants, stearic acid and talc. They were used for comparison in the production of sulphadimidine tablets via wet granulation. Lubricants constitute a category of excipients that ensure that the tablets formed do not vary appreciably in weight, have pitted appearance and are released with ease from the die cavity . From these results the following conclusions were drawn: in terms of weight variation kaolin at

concentrations of 0.50% w/w and 1.00% w/w was superior to both talc (1.00% and 5.00% w/w) and stearic acid (0.25% w/w and 1.00% w/w) (43).

Although both concentrations of kaolin produced tablets that were softer than those produced with talc and stearic acid,in terms of disintegration time all concentrations of kaolin from 0.2% -1.00%w/w produced lower values than those produced with talc and stearic acid.

Our work showed that locally sourced and processed kaolin can be used as a lubricant in the formulation of tablet dosage forms at concentrations ranging from 0.20% w/w to 1.00% w/w, with 1.00%w/w being the optimum concentration. This adds to the long list of locally available pharmaceutical excipients yearning for investors to support their processing to pharmaceutical grade.

Novel suppository base – Mango seed oil

A variety of suppository bases have been used for the development of rectal drug formulations. Cocoa butter (theobroma oil) has been used as an official fatty base for over 200years but it is characterized by a number of serious disadvantages including polymorphism , rancidity, adherence to mould and low softening point . We processed milled mango seeds to produce mango seed oil. Percentage fat was determined to be in the range of 5.75% w/w to 8.36%w/w depending on the age of the dried seeds and method of extraction. (44)

The melting range, displacement value and softening point of both test (mango seed fat) and reference (cocoa butter) bases were similar. Besides the physicochemical characteristics, we compared *in-vitro* drug release from rectal formulations of mango seed oil suppositories to that of the official theobroma oil suppositories in order to determine the suitability of the test base for rectal dosage form development in Nigeria.

Mr. Vice-Chancellor Sir, we have thus identified another natural fat – mango seed fat as possessing good physico-chemical characteristics that recommend it for rectal suppository development suitable for use in tropical climate. Mango seed fat is more resistant to auto-oxidation, suffers no polymorphic changes and appears to possess better organoleptic properties than cocoa butter, the only official natural fatty base for extemporaneous preparation of suppository products. The drug release profile of this test base has been shown not to be as good as that of cocoa butter. However the modification of drug release characteristics by the use of certain additives such as surfactants could be considered in the formulation development of mango seed fat suppository products. As additional advantage of mango seed fat is the application of waste re-cycling technology in the processing since the base is derived essentially from waste materials. Thus the use of mango seed oil for drug dosage form manufacture, would be environment friendly.

CONTRIBUTIONS TO DOSAGE FORM FORMULATION

Chloroquine Suppository

The physiochemical characteristics of chloroquine phosphate suppositories in four different bases were evaluated by Ifudu and Odimgbe (45). We also studied the influence of the different bases and different drug concentrations on the in-vitro release of the drug. The bases studied were Theobroma oil (Displacement value 1.47 ± 0.25) and three macrogal mixtures composed of various combinations of Macrogols 400, 1000, 1500, 4000, 6000 (displacement values 1.22 ± 0.14, 1.24 ±0.19, 1.19 ± 0.2 respectively). At 37°C Theobroma oil suppositories melted at a much greater rate than the macrogal-based (water soluble) preparations. At low concentrations of chloroquine phosphate (5% or less) drug release (*in- vitro)* for the macrogol based (water soluble) suppositories was higher than from the theobroma oil (water insoluble) base. However this pattern was reversed when the drug concentration was increased to 10% w/w (45).

We also undertook a further study to investigate the rectal absorption of chloroquine phosphate from the bases examined in our initial study to identify any correlation between *in- vitro* and *in- vivo* results.

We also studied the influence of different drug concentrations on the *in-vitro* release of the drug. Theobroma oil melted at body temperature, releasing the drug with rapid partitioning into the rectal fluid. Dissolution of the vehicle in the rectal fluid appeared to be rate limiting step of absorption from macrogol formulations. Ten hours after administration there was no significant difference in the cumulative amounts of drugs and its metabolite excreted from the different bases.

Higher drug concentrations were released from the theobroma oil base and one of the macrogol mixtures. These two bases were used in a study comparing oral and rectal administration of Chloroquine phosphate. The results clearly indicated that the two routes compared favourably in terms of peak time of onset of action and total amount of drug absorbed. Good correlation was obtained between *in-vivo* and *in-vitro* results. Furthermore rectal administration reduced the type and number of side-effects and produced a more steady urinary excretion profile compared with the oral route.

Mr. Vice-Chancellor Sir, with all sense of humility, I make bold to state that these research findings have become the gold standard in suppository formulation and correlation studies. It was quoted and described extensively in the British Pharmaceutical Codex (47a) an authoritative reference text in pharmacy education worldwide.

FORMULATION OF FIXED-DOSE PAEDIATRIC COMBINATION OF ARTESUNATE AND AMODIAQUINE HYDROCHLORIDE

Combination therapies are becoming important options for the treatment of malaria due to the resistance of malaria parasites to the older and affordable antimalarial drugs such as chloroquine and sulphadoxine-pyrimethamine. Since the introduction of artemisinin combination therapy (ACT), it has been recognized that Artemisinins are thermolabile, chemically reactive and therefore might be prone to degradation in the presence of other drugs and also during manufacturing processes. It was therefore advised that the use of a dual combination in which formulations of each drug are made in such a manner that prevents direct interactions or are individually packaged for separate administration must be considered. We therefore developed prototype, stable formulations combining Artesunate (ART) and Amodiaquine hydrochloride (AMQ).

Our results indicated that the degradation of artesunate in the presence of high temperature and high relative humidity is an inherent property of artesunate. The formulation excipients as well as the method of formulation did not enhance the degradation. This is particularly important because mannitol which constitutes 43.0 % w/w of the formulation is an osmotic agent. Mr. Vice-Chancellor Sir, we produced a fixed-dose formulation of ART and AMQ by first preparing individual granules of each drug and mixing these granules. This provides a flexible option for adjusting the dose for different age ranges within the paediatric population. Humidity was recognized as the primary factor leading to the chemical instability of artesunate. These formulations must however be protected from extremes of relative humidity and temperature using suitable packaging materials (47).

CO-FORMULATION OF METRONIDAZOLE AND ACTIVATED CHARCOAL AS A BI-LAYERED TABLET – A NOVEL APPROACH IN THE TREATMENT OF DIARRHEA CAUSED BY *ESCHERICHIA COLI* 0157:H7 IN AN *IN-VITRO* PHARMCODYNAMIC MODEL.

Existing medications used to treat mild to moderate diarrhoeal episodes include Adsorbents, Anti inefectives and Drugs affecting intestinal motility. These do not include a single formulation with absorbent and anti-infective properties. It was for this reason that we undertook the present study.

We evaluated the efficacy of the combination of Metronidazole and Activated charcoal in the lysis of *Escherichia coli* 0157: H7 *in -vitro*. The results of this study established that activated charcoal adsorb micro organisms in the gastro intestinal tract (GIT) on contract thus reducing the microbial load in the GIT and that Metronidazole will synergistically act with activated charcoal on the residual microbial load to bring about a faster remission of the diarrhoeal episode.

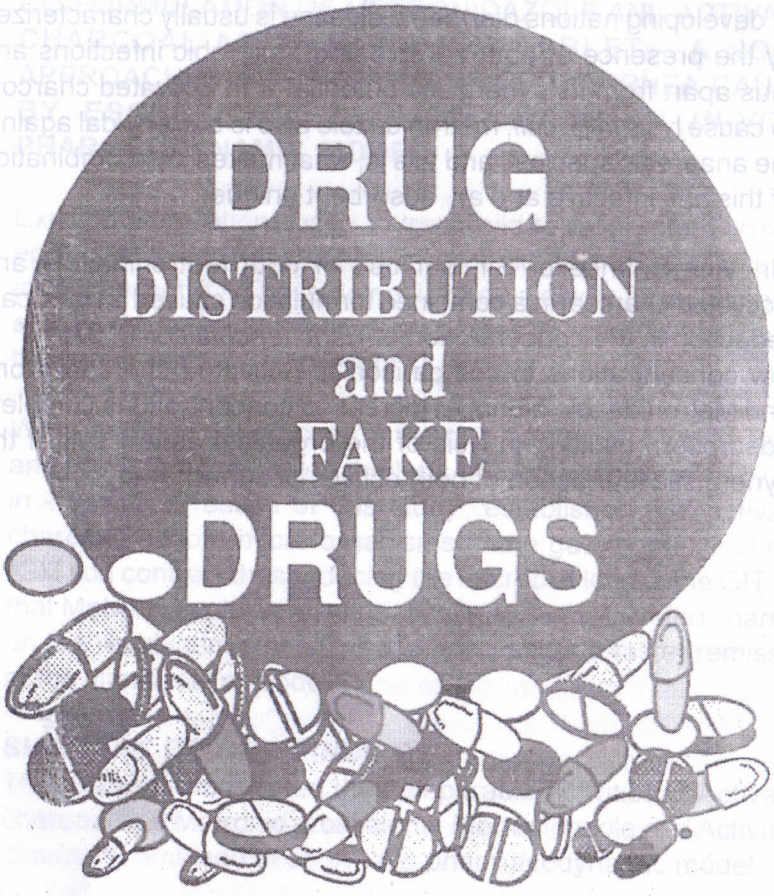
SUMMARY OF OUR FINDINGS

This study demonstrated the comparable activities of Activated charcoal and Metronidazole alone, Metronidazole and Activated charcoal combined in an *in-vitro* pharmacodynamic model.

Our results show that Activated charcoal accounted for the adsorption and possible lysis of *E. Coli* 0 157: H7 adsorbed unto to the numerous interstices of the activated charcoal. Since it's a micro organism, adsorption has a 'spreading effect' on the surface of the organism. This 'spread' causes some stress on the cell wall/membrane of the organisms, and it's at these points of stress that the adsorbed and/or free anti-infective i.e. metronidazole gains access, readily being taken up into the cytoplasm of the organism thus resulting in lysis of the organism.

In developing nations diarrhoeal disease is usually characterized by the presence of both aerobic and anaerobic infections and thus apart from its synergistic potential with activated charcoal to cause lysis in *E. coli*, metronidazole also is bactericidal against the anaerobic species , and this is, what makes our combination of this anti infective and an adsorbent unique.

Mr. Vice-Chancellor Sir, our use of both Metronidazole and Activated charcoal in a combined formulation caused a significant reduction in the concentration of *Eshcherichia coli* 0157: H7 at low concentrations in comparison to Activated charcoal alone and Metronidazole alone. At increased concentrations complete adsorption resulting in lysis of the organism as a result of the synergistic interaction of both actives occurred.



INTRODUCTION

Up till now, the situation regarding the proliferation of fake medical products is worrisome. Most Nigerians are confused and skeptical about the quality, safety and efficacy of drugs available in our various drug outlets. The present economic situation has put the price of quality pharmaceuticals out of the reach of the common man who is now only able to afford some of the basic essentials of life, food and shelter.

The laboratory at the School of Pharmacy, College of Medicine, University of Lagos now Faculty of Pharmacy University of Lagos examined occasional samples of suspected medicaments over the past several years. The samples have generally been brought in by drug manufacturers/importers who have noticed very similar packs to their own on sale. A few suspected drugs were given to us for analysis by doctors who had noticed lack of the expected clinical response.

The situation then may have been aggravated by the import licence era when importation of pharmaceuticals was undertaken by all and sundry for purely economic reasons. In addition, products of unacceptable quality were manufactured locally in clandestine factories by unscrupulous persons in obscure corners of the country. Such unacceptable products are generally grouped together under the term "fake drugs".

WHAT ARE "FAKE" DRUGS ?

The term "fake" is used for anything which is not what it purports to be. It therefore embraces such terminologies as "spurious", "misbranded" and "adulterated" whose definitions are embodied in most drug legislations.

1. The term "fake" when applied to a medication can have a number of meanings. In the mildest sense, it is simply a carefully made copy of a successful commercial product with the same effective ingredients and a similar or identical packing. From a medical point of view, such preparations offer no immediate problems provided that the quality can be maintained. However, the frequent controls of the reputable manufacturers are not likely to be performed. There are additional factors to be considered such as profits no longer going to further research; ensuring a regular supply of the drug; and monitoring of side-effect(s). Another factor is the lack of control in the supply of such preparations on to the market. These are also referred to as CLONES.

According to the WHO definition, what makes a drug/medicine counterfeit is the deliberate or intentional nature of the mislabeling of a product with the intention to deceive the consumer.

However, the National Agency for Food and Drug Administration and Control (NAFDAC) of Nigeria, (49) has identified various forms of fake/counterfeit drugs and other unwholesome regulated products, which include:

a) Drugs with active ingredient(s) different from what is stated on the package e.g. paracetamol tablets packaged and labeled as "Fansidar", a Sulphadoxine/pyrimethamine combination.

b) Expired or about to expire drugs.

c) Herbal preparations that are toxic or harmful or ineffective or mixed with orthodox medicine.

d) Drugs without the full name and address of the manufacturer.

"A genuine drug manufacturer will never hide his/her address. It is only cloners, fakers and counterfeiters that hide their addresses so that they cannot be traced".

- Drugs not certified and registered by NAFDAC.
- Drugs labeled "for export only" (for whatever reason). This is to discourage importation of drugs from countries with discriminatory regulation for drugs meant for export as against those for internal use.

CONTRIBUTIONS IN AREA FAKE DRUG RESEARCH

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In order to obtain factual information on the extent of faking of drugs, we undertook a study of pharmaceuticals purchased in the open markets of selected Nigerian cities in the second half of

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1988. It was felt that in these parallel markets the problems of fake drugs would be most apparent and also potentially the most serious as the vendors lack the training of pharmacists. Cities were chosen to represent the main ethnic and geographic areas of the country. In one area –Onitsha – it was possible to include some vendors who operate on intercity bus services.

Cities Sampled

The cities chosen were: Lagos (Church Street, etc.), Ibadan (Dugbe, etc.), Kaduna (Kabala, Kazua, Magni Central Markets, etc.) and Onitsha (Head Bridge, Inter- city Bus Depot). Street markets and vendors in these 4 Nigerian cities were randomly selected and a sample of every type of different preparation on sale was purchased.

Chemical analysis of most of the products purchased was made. The overall results were combined in a global judgment. For preparations where the expected components were present in quantities complying with compendia specifications (about 90%-120% of expected) the judgment was taken as "normal". With 25%-89% of the expected component this was judged as "substandard". Less than 25% (including none at all) was judged as in "worthless", while the presence of the wrong or contaminated ingredients or an abnormally high dose was judged as "dangerous".

A total of 491 out of 555 samples (90%) could be identified as to the expected nature of the medicament being sold. The remaining 10% were mostly herbal preparations about which inadequate information was available.

How did the various expectations match up with the reality?

Based on the qualitative and quantitative laboratory findings, a global judgment was made on each sample assayed. Whether the product was Dangerous, Normal or Sub-standard was based on the recommendations of the British Pharmacoepoeia.

The type of judgement varied for different types of medicament. This is broken down in Table 2 for the most frequent drug groups found. Half the antipsychotics were abnormal while most of the hematinics and benzodiazepines were normal. The other drug groups fell between these two extremes. For example, 60% of the antibiotics were normal but 7% contained, in some cases, dangerous quantities of the drug or in other cases something else altogether.

Table 2: Judgment of quality of different drug groups

Drug Group	Total	Normal	S/Standard	Worthless	Dangerous
Antibiot	83	50	16	11	6
Antimalar	19	10	5	3	1
Antipsych	24	12	11	1	
Benzodiaz	13	10	2	1	
Hematinics	23	17	5	1	
Multiv./Vit	52	39	12	1	
Purgatives	8	7	1		
Other	264	186	55	10	13
Total	486	331	107	28	20

As a specific example where quality is important and expected, we have chosen chloramphenicol capsules. These were common among the street market samples purchased although they were at the time of the study rather difficult to obtain through normal channels in Nigeria. Table 3 shows a representative sample of the capsules studied. One (from PLIVA, a Yugoslavian company of high reputation) was normal, the others contained little or none at all of the active ingredient.

Table 3: Random sample of Chloramphenicol capsules

Manufacturer-Country Caps. Expected Class.	Weight (mg)	Source (Nigeria)	%	
Unknown- Nigeria	268.7	Ibadan	19.3	(W/D)
Pliva-Nigeria	346.5	Ibadan	99.3	(Normal)
Unknown – Nigeria	248.9	Ibadan	0	(W/D)
Unknown – W. Germany	378.8	Ibadan	17.0	(W/D)
Unknown- Nigeria	376.7	Kaduna	10.6	(W/D)
Unknown – Unknown	347.9	Kaduna	62	(S/S)
Unknown- Nigeria	267.5	Ibadan		

W/D = Worthless/Dangerous . S/S =Sub-standard

From this study, it was evident that a significant percentage of drugs on sale in Nigerian market places can be classified as substandard or worse. The clinical implications vary according to the pharmacological group of the drugs. Thus a worthless antibiotic formulation poses a more serious clinical problem than a worthless multivitamin preparation. Similarly, an excess of drugs such as vitamins is less serious than an excess of a potentially toxic substance such as aspirin. The final judgment on the quality of different pharmacological drug groups showed that was 60% of the antibiotics were normal, 7% contained actually dangerous quantities of drug or something else while about 33% were either sub-standard or worthless (50).See table 4.

Table 4: Summary of judgment of quality

Drug Group	Normal (%)	S-Standard /Worthless (%)	Dangerous (%)
Antibiotics	60	33	7
Antimalarials	53	42	5
Antipsychotics	50	50	0
Benzodiazepines	77	23	0
Hematinics	74	26	0
Multivitamins	75	25	0
Purgatives	85	12	3

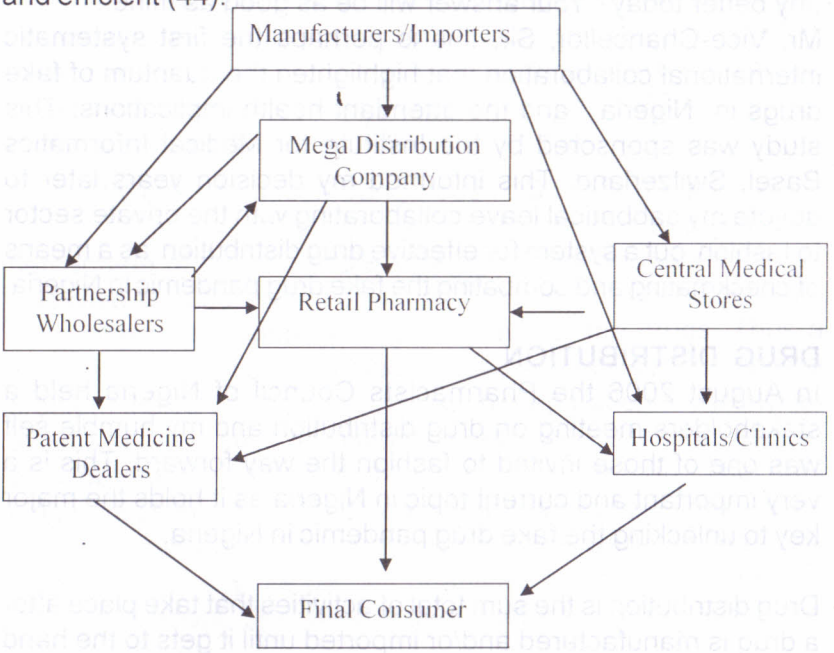
From these results, one can assert very strongly that the drug situation in Nigeria calls for immediate, firm and decisive actions in order to arrest the life-threatening spread of fake drugs. The menace of fake drugs is worse than AIDS and demands urgent national action, not rhetoric. This was in 1988 but are we really any better today? Your answer will be as good as mine !
Mr. Vice-Chancellor, Sir, this is perhaps the first systematic international collaboration that highlighted the quantum of fake drugs in Nigeria and the attendant health implications. This study was sponsored by the Institute for Medical Informatics Basel, Switzerland. This informed my decision years later to devote my sabbatical leave collaborating with the private sector to fashion out a system for effective drug distribution as a means of checkmating and combating the fake drug pandemic in Nigeria.

DRUG DISTRIBUTION

In August 2006 the Pharmacists Council of Nigeria held a stakeholders meeting on drug distribution and my humble self was one of those invited to fashion the way forward. This is a very important and current topic in Nigeria as it holds the major key to unlocking the fake drug pandemic in Nigeria.

Drug distribution is the sum total of activities that take place after a drug is manufactured and/or imported until it gets to the hand of the patient/consumer of that drug. Today, drug distribution in Nigeria is chaotic with manufacturers and importers supplying to all levels in the chain; medical and sales representatives competing with distributors and wholesalers; parallel importation and dumping; non-pharmacists mainly in control of distribution channels and Patent Proprietary Medicine Vendors Licence (PPMVL) holders operating beyond legal limits as well as failure of government purchases to follow due process and price abuses and margin manipulations. Also, an often ignored dimension in the chaotic drug distribution networks is the role played by hospitals and clinics which carry very substantial quantities of drugs albeit unlawfully, since most of these hospitals never employ pharmacists to oversee the use, sales, and dispensing

of these drugs in consonance with the Statutes of the Pharmacy and Poisson Act Cap 535 Laws of the Federal Republic of Nigeria, 1990 and Act 91 of 1992. It should be noted however, that an effective drug distribution would survive only if we have good Government Policies and relevant regulatory bodies are effective and efficient (44).



Scheme of the Present Chaotic Drug Distribution in Nigeria

Drug distribution scenario in Nigeria used to be a sane and ordered experience. In the 70's and early 80's the industry was disciplined in its distribution patterns. Drug manufacturers had a well defined system with price variations to different levels of clients (distributors, wholesaler, hospitals, and community pharmacies) in order to enable each level sell at a competitive price to the level below. Manufacturers had accredited distributors. Foreign companies engaged in the manufacture and/or distribution of pharmaceutical products, not having physical

presence in Nigeria, carried out their business through accredited agents in the country. These agents had their major buyers and distributors through which the products were religiously distributed (44).

THE PRESENT DISTRIBUTION CHANNELS IN NIGERIA SHOWN IN THE SCHEME IS AT BEST DISODERLY AND CHAOTIC.

Mr. Vice-Chancellor Sir,

The obvious question is: How did we get into this Mess?

Various factors undermined the pharmaceutical industry. One was the inadequate number of qualified pharmacists in the country at the time. Secondly, there was absence of political insight and will to empower enforcing agents to ensure that the law was abided by. Thirdly, the insistence by the Buhari regime that at least 40 percent local content must be present in local manufactures led to the systematic withdrawal of multinational companies. The consequence of this was that people began to cut corners in various ways. All sorts of brands came up both from unscrupulous importers and local manufacturers. In addition, the import license era of the 1980s exposed distribution/ wholesale of drugs to non professionals who are politically connected but whose main motive was to make profit. This group eventually got swallowed by traders who could mobilize huge sums of money and they hijacked the distribution aspect of drugs in Nigeria. This group had no regard for ethics and so engaged in the importation of fake and counterfeit products. Above all, professional members of drug distribution network were not as financially strong and could not compete with these traders or business men who had hijacked the business.

Fourthly, our porous borders still allow the importation of all sorts of drugs into the country since there are ready illegal markers for sale of such products. Fifth, regulatory bodies have not demonstrated enough political will to dismantle illegal outlets as provided by law in Decree 25 of 1999 section 2.

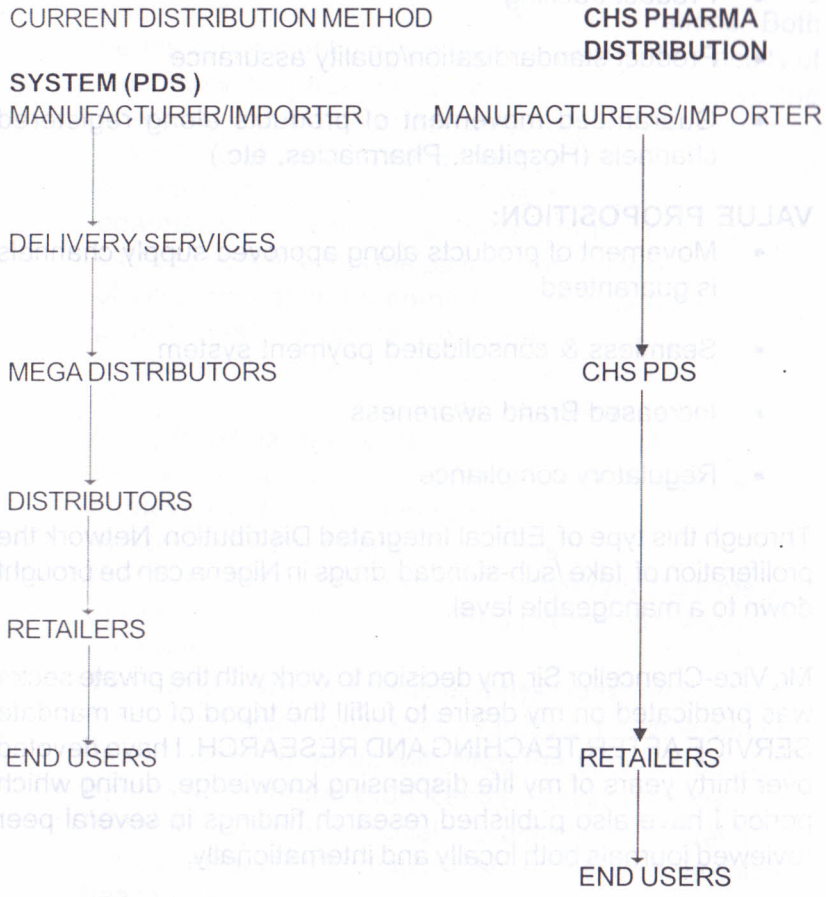
The big question now is: What is the way forward? The Cardinal Health services proposition COULD COME to our rescue!

Mr. Vice-Chancellor Sir, it is on record that in the academic 2005/2006, I was granted sabbatical leave to serve Director of Research to Cardinal Health Services Ltd. (CHS **). Cardinal Healthcare's primary mission is to deploy appropriate infrastructure, technology and logistics to ensure that high quality drug products are delivered wholesomely from source to final destination by well trained and responsible team (45).**

THE ROLE OF CHS

- Products distribution nationwide
- Product warehousing
- Inventory management solutions
- Reverse distribution
- Regulatory compliance

DISTRIBUTION SYSTEMS



REVERSE DISTRIBUTION

Product Recalls/Expired drug products

- CHS acts as product recall managers
- Coordinates pick down of products from retail pharmacies/hospitals
- Arranges for product destruction and proper credit.

REGULATORY COMPLIANCE

- Product tracking
- Product standardization/quality assurance
- Guaranteed movement of products along registered channels (Hospitals, Pharmacies, etc.)

VALUE PROPOSITION:

- Movement of products along approved supply channels is guaranteed
- Seamless & consolidated payment system
- Increased Brand awareness
- Regulatory compliance

Through this type of Ethical Integrated Distribution Network the proliferation of fake /sub-standad drugs in Nigeria can be brought down to a manageable level.

Mr. Vice-Chancellor Sir, my decision to work with the private sector was predicated on my desire to fulfill the tripod of our mandate SERVICE AFTER TEACHING AND RESEARCH. I have devoted over thirty years of my life dispensing knowledge, during which period I have also published research findings in several peer reviewed journals both locally and internationally.

RECOMMENDATIONS

Recommendation for improved pharmacy health education and delivery

1) Joint Faculty Positions.
   Joint faculty position will help the faculty and students stay current in their teachings and learning of real-world pharmacy and help the institutional partners assist their patients by having an expert pharmacist at hand. The teaching and specialist hospitals in the country need

clinical pharmacists to work with their residency and intership programme while the Faculties of Pharmacy need additional sites for our students rotations. Both needs will be met by a joint appointment in the Faculty of Pharmacy and the outside hospital. This will give the pharmacist students enhanced access and experience of working at the hospital without diminishing the role of the medics. Students can see teamwork between pharmacists and other specialists in the hospital. The ultimate beneficiary is the patient who will receive the best of care from all the members of the health care team-pharmacist, doctors, nurses, etc each group complementing the role of others and transcending the bridge between academia and the real-world setting.

2) **Drug information centre**: This is an invaluable asset as part of a Faculty of Pharmacy. **The centre will achieve the following major goals**:

a) Service health care professionals

b) Provide experiential training for pharmacy students and

c) Conduct a post-graduate drug information residency program.

The health care professional (physicians, pharmacists, nurses and veterinarians) in a variety of practice settings and the general public will utilize the services provided by the drug information centre. Access to the drug Information Centre is crucial to practitioners in rural areas without adequate information resources to provide optimal healthcare.

During the experiential training students should become competent in data retrieval, literature evaluation and written and communication skills. They would respond to enquiries from health care professionals and general public regarding contemporary therapeutic regimens in human and animals.

3 **Creation of centre for integrative therapies in pharmaceutical care .**

It is common knowledge that as many as two thirds of our population use conventional and herbal remedies at the same time. Basic questions seeking urgent answers include:

1) Do the herbal remedies enhance or eliminate the benefits of orthodox medicines?
2) What, if any adverse reactions could occur from such combinations?

The use of these combinations should be of great concern to all health care professionals with special emphasis for the pharmacists, the experts on drug utilization.

It is not a secret that a large amount of our scarce foreign exchange is expended in the importation of a wide range of herbal supplements.

This centre will provide a much-needed service on herbal-supplement standards for Nigerians. All herbal supplements are not created equal? Products such as St. John's Wort, a herbal remedy taken for depression, for example vary considerably with regard to their active ingredients and therefore their therapeutic benefits. Consumers need the vital information to determine the proper dosage and for comparison shopping. This is a potential public safety issue based on the large proliferation of different herbal products readily available in our various major towns and villages. The resolution of these issues will put our faculties of Pharmacy on the map, globally and attract substantial foreign grant and collaboration.

To curb the menace and proliferation of fake/substandard drugs in Nigeria a number of urgent actions still needs to be taken:

1) Establishment of independent quality control laboratories in each geo-political zone. The volume of work handled by the few laboratories owned by NAFDAC can be overwhelming. One Faculty of Pharmacy in each of the six geopolitical zones should be fully equipped and certified to handle the analysis of pharmaceuticals and participate fully in post-marketing surveillance in their respective geopolitical zones

2) The drug regulatory agencies specifically PCN and NAFDAC should develop and engage a systematic programme to enforce all drug laws particularly the dismantling of all illegal drug outlets, since no model of distribution can make a difference as long as these illegal drug outlets exist.

3) Pharmaceutical society of Nigeria cooperative societies/ private sector collaboration.

The various PSN state cooperative societies can team up and form a mega group. This group can then attract the money 'bags' in Nigeria and together approach foreign investors for funding to set up a world class distribution System comparable to the Distribution systems in America. This is big business that requires enormous finance.

It is by setting up of such a mega distribution network(s) patronized by manufacturers and importers that the open markets and other illegal drug outlets can be starved of drugs and consequently undergo natural death and "embalming".

ACKNOWLEDGMENTS

Again, I thank God, the Almighty for His continued blessings, guidance and protection against all evil forces including kidnappers, both physical and spiritual.

I wish to acknowledge the contributions of some individuals to my development and sustained growth in life.

I thank my parents, late Mr. Joseph Oguejifor Ifudu and late Madam Elizabeth Akuchukwu Ifudu, who personally took the responsibility of walking me to school in those formative days for as long as it was necessary. Without my late mother's insistence I never would have gone to school much less end up as a professor at the University of Lagos. May their departed gentle souls continue to reside in the bosom of God Almighty. Sisters Pati, Eugenia and Julie I love you all.

To my great brother, Ozo Engr. F. C. Ifudu alias Agunecheibe, who successfully took over the mantle of family leadership after the demise of our father, May God Almighty continue to guide and protect you now and forever, Amen. My sister, Chief (Mrs.)Christy Nkem Okoye, former Executive Director First Bank of Nigeria Plc, what could I have done without your financial support and advice? May God Almighty reward you a billion-fold. Mr. Peter Eloka Okocha my friend and brother God bless you for your contributions to the welfare of my family.

I thank my teachers and mentors too many to mention. At the elementary school I have Mr. Chukwu Ikeme, Mr. Patrick Ogbodu, Sir Patrick Anigbo and Mr. Philip Amadi, all of blessed memory.

At the secondary school my thanks go to the following great people. Rev. Father P. Butler who believed in me and ensured that I obtained a government scholarship for my secondary school education, Mr. D. Eche my English and Latin teacher, you made the difference . Rev. Fr. Nicholas Tagbo – my principal at Christ the King College, Onitsha and a very kind disciplinarian, I salute you.

At the University Ife, (Undergraduate), I met many great teachers, notably Dr. J. D. Kulkani, Prof .E. A. Ogunlana and Prof. A. A. Olaniyi. Jointly they showed me the beauty in academics. I shall not leave the Nigeria terrain without recognizing and appreciating Prof. H. Oluwasanmi, then Vice-Chancellor at University of Ife for his love and kindness in rehabitating all the returnee students after the Biafran war. He created the enabling environment for me to emerge as the best overall student in the graduating class of 1972. This feat eventually earned me the African American Graduate Fellowship (AFGRAD) to study in the US. I shall forever remain grateful.

While in the US, I met many great scientists across board – physical and pharmaceutical sciences. Worthy of special mention is Prof Anthony Patrick Simonelli known by all his graduate students as, Tony. He is an epitome of humility, a supervisor, a mentor and the chairman at my wedding reception held on,21st August 1976.

I want to appreciate all the Vice- Chancellors of this great citadel of learning – UNILAG – for their love and support in giving me the opportunity to become a Professor at University of Lagos , the university of first choice and the nation's pride. Of special mention is Prof Tolu Odugbemi who as provost of College of Medicine showed the true meaning of leadership by example and Prof. Oye Ibidapo-Obe who was the Director of UNILAG Consult when I joined the university in 1984. I want also to appreciate Prof. Deji Femi Pearse who recruited me from University of Ife in 1984 to join the first college Dean of School of Pharmacy, UNILAG that eloquent and prolific scientist – Prof E. E. Essien. May the God Almighty reward all of you abundantly.

Within the Faculty of Pharmacy, I have served at different times as the head of department of Pharmaceutics and Pharmaceutical Technology and also as the Acting College Dean School of Pharmacy and more recently Dean, Faculty of Pharmacy. I hereby

publicly acknowledge the support of all staff of the school/faculty both academic and non academic. I thank you all for your support and if I stepped on any toes, please accept same as an act of God i.e. inevitable.

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Mr. Vice-Chancellor, Sir, distinguished ladies and gentlemen, members of the press, I thank you all for your attention and for honouring our invitation.

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