Innovation in Malaria Control:

The Unfolding Story of Herb 25

Herbal Point Services

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Herbal Point Services

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Dedication

This book is dedicated to my family for their encouragement in the establishment and development of Herbal Point Services.

And also to the individuals and organisations making contributions in diverse ways to develop therapies and interventions aimed at reducing or eliminating the burden of malaria in Africa.

Table of Contents

Acknowledgements

It is the contributions of certain individuals that made this project possible; first, my husband, Prof. Idris Bugaje and my elder brothers, Alhaji Sani Nuhu and Alhaji Salisu N. Muhammad. Pharmacist Nelson Okwonna, who did the scripting of this book, capturing the events as they were, is also acknowledged. I recognize my students who worked on aspects of the drug development, the staff of the Department of Pharmacognosy and Drug Development, Ahmadu Bello University and other researchers who contributed to the success of the work. I have also received tremendous encouragement from Alhaji Turadu Dantata, of Kano and Dr Isah M. Abbas, then Registrar of the Ahmadu Bello University, Zaria.

FOREWORD

By

Prof. Ahmed Tijjani Mora, FPCPharm; FPSN; mni

Foundation Dean, Faculty of Pharmaceutical Sciences, Kaduna State University (KASU)(2012-2016)

Visiting Professor, Department of Clinical Pharmacy and Pharmacy Practice, College of Pharmacy, Igbinedion University, Okada(IUO), Okada, Edo State;

National President, Ahmadu Bello University Alumni Association;

National Chairman, Conference of alumni Association of Nigerian universities (CAANU);

Former Registrar and CEO Pharmacist Council of Nigeria (PCN),(2003-2012);

Conferred with the traditional title of *Wakilin Maganin Zazzau* by the Zazzau Emirate Council in September, 2013.

Sometimes in 1988, and as the then Chief Pharmacist and Head of Pharmacy Department at the now defunct Kaduna State Health Management Board (HMB), I was invited by the late Dr Frederick B. Adenika (1945-2003),one of the greatest minds in the subject of Pharmacy Management in Nigeria and a distinguished author, to join some notable Pharmacists and scientists for the Workshop at the NICON NOGA Hilton Hotel (now Transcorp Hilton hotel) Abuja at that time, Dr. Adenike was newly appointed pioneer Chairman of the Board of the National Institute of Pharmaceutical Research and Development (NIPRD), Idu, Abuja. It was his objective primarily to set an agenda for the

new Research Institute established by the Federal Government to research into many traditional-based herbal products as additional sources of medicament for cure, prophylaxis and management of medical conditions afflicting Nigerians in addition to the much promoted orthodox Western based pharmaceutical products .

That Workshop, which to me, with hindsight of knowledge now, was more like an informal brains storming gathering to galvanize ideas to assist the newly formed NIPRD in the absence of a similar Institute in Nigeria or indeed West Africa from which the new board of NIPRD under the late Dr. Adenika and/or the Management under its pioneer, Director/CEO Professor C.O.N Wambebe could draw experiences in kick starting the new research Institute.

There was no Dr.(Mrs.) Hadiza Nuhu among those invited to attend the NIPRD event in 1988; but here she is twenty nine (29) years later with a publication –'Innovation in Malaria Control - the Unfolding Story of Herb 25' which chronicles her success story basically as an entrepreneur and a pharmaceutical scientist of repute in the Pharmacognosy specialty nurtured in the famous Faculty of Pharmaceutical Sciences, Ahmadu Bello University (ABU), Zaria coming out with a pharmaceutical product essentially developed from an ubiquitous plant from the savannah vegetation region of Northern Nigeria – Azadirachta Indica leaves to treat malaria.

It was therefore a thing of joy to me and an honour to be requested by Dr. Nuhu to write the foreword to her publication. To be fair to NIPRD though, the Institution has produced only one product since its inception, I was close enough as it's next door neighbor in Idu, Abuja for eight (8) years when I served as the Registrar and CEO of the Pharmacist Council of Nigeria (PCN) (2003-2012) to appreciate at first hand, the many frustrations by the various management staff of the Institute in term of dearth of resources, especially financial and equipment with which to execute its mandate, which basically was to produce pharmaceutical products from our many herbal resources.

Dr. Nuhu has come to the rescue of Nigerians by tapping from the vast knowledge albeit from traditional sources of our many plant species to produce Herb 25, which has not only won several awards, but most importantly, saved hundreds and thousands of lives of patients afflicted with malaria.

Between the seven (7) and ten (10) million patients have been treated with Herb 25, and not one case of fatality from toxicity or of teratogenicity was reported. Herb 25 can therefore be said to be safe and effective; the every basic parameters required in any drug development project. To document the chronological development of the product in a very simple language as elucidated in the book –'Innovations in Malaria Control: The Unfolding Story of Herb 25' is yet another scientific breakthrough by Dr. Hadiza Nuhu, as it will certainly add to the very few

research studies in drug development in Nigeria which has eventually seen the light of the day as a patent with appropriate intellectual property belonging to Dr. Nuhu, as what she had accomplished in the area of drug development through innovative skills, entrepreneurship and of course dint of hard work, perseverance and doggedness, many thanks to her ever-supportive husband, and a good friend of mine, Professor Idris Muhammad Bugaje .

Ahmadu Bello University Zaria, and indeed and indeed the Faculty of Pharmaceutical Sciences and its Department of Pharmacognosy and Drug Development has produced a World-Class African Scientist, and one has defied all infrastructural odds to produce a pharmaceutical product from plant origin for Prophylaxis and treatment of malaria.

As our distinguished Alumnus, Dr. Nuhu has made the ABU Alumni Association proud and we freely identify, and congratulate her in achieving this novelty. I recommend this book to all members of the health care profession especially pharmacists, doctors and nurses as well as students of health sciences in our Universities.

Pharm. Prof. Ahmed Tijjani Mora, B.Sc. (pharm); Ph.D.; FPCPharm; FPSN, mni (Wakilin Maganin Zazzau)

April, 2017.

Preface

About two decades ago, we set out on a journey to provide our community with a home-grown remedy for malaria; ours was a journey of faith and passion. Faith, because the obstacles were all too clear; passion, because we just couldn't walk away.

Though the support structures for indigenous research and its commercialisation were not readily available, we found courage mostly from the necessity of our contribution. Personally, that was my motivation; that we can do this and that it could make a difference.

The innovation that is Herb 25 was achieved by this simple understanding of our own capacity to, by the will of God, make a positive contribution in a resource poor setting where, though the challenges are much, the possibilities are also endless.

It is my desire that this book would inspire present and future research scientists to persevere at that which they believe to be true; to not quit in the deployment of their capacities, to reach out to other individuals who could help achieve their pursuit and to continue where others have stopped.

The story of Herb 25 is just beginning; we are happy to share it, knowing this could be the beginning of many great contributions by other research scientists who would find in this simple story, courage and perhaps, insight.

Receiving the 2008 National Honours Award of OON, on Herb 25:

CHAPTER ONE

The Beginning

Very rarely do individuals set out to achieve great accomplishments. Often what we count as accomplishments are products of the interplays between our environment, our capacities and our value systems, the latter being primarily a product of our upbringing and worldview.

The setting for the Herb 25 story is Northern Nigeria, Zaria, Kaduna State, to be precise. Zaria is home to the Ahmadu Bello University (ABU), acclaimed to be the largest university in Nigeria, more importantly though, the university houses the Faculty of Pharmaceutical Sciences.

Dr Hadiza Nuhu, OON

Dr. Hadiza Nuhu was employed at the Faculty in 1988 as a Graduate Assistant in the Department of Pharmacognosy and Drug Development, Faculty of Pharmaceutical Sciences.

Pharmacognosy is the study of medicinal drugs derived from plants or other natural sources. The American Society of Pharmacognosy defines pharmacognosy as "the study of the physical, chemical, biochemical and biological properties of drugs, drug substances or potential drugs or drug substances of natural origin as well as the search for new drugs from natural sources."

Though they often do not get the credit, more than 50% of drugs in clinical use today have their origin from nature – mainly from plants and microbes. Hence, pharmacognosy research scientists and lecturers are by default, enmeshed in the intricacies of drug development.

Prior to her employment at ABU Zaria, Dr. Hadiza Nuhu had completed her undergraduate studies at the then University of Sokoto (Now, Usman Danfodio University), graduating in 1985 with a Second-Class Upper Honours Degree in Botany, clinching an award by Zamfara Textiles Industry for the Best Graduating Student in the Faculty of Science of the University.

Zaria provided the context for the development of Herb 25 because as a Pharmacognosy lecturer, Dr. Nuhu was the harbinger of wisdom on herbal drug development, and as a mother living in Zaria, she was at the same time exposed to the realities of her immediate environment.

Zaria, apart from the academic institutions, is primarily an agrarian society. In 1980, the incidence of poverty in Nigeria, using the lower than US $1 per day income level, was 27.2%; in North Western Nigeria, the rate was slightly higher at 37% and this figure has increased progressively since then to 69.4% in 2010 (CBN and NBS).

Access to health care in such settings is luxury, not because there are no hospitals, but rather because the poor simply could not afford it.

Up until 2005, Nigeria did not have a social health insurance system, though an Act establishing one was passed in 1999, it was not until 2005 that the National Health Insurance Scheme (NHIS) became active and even at that, the level of coverage is still abysmally low at just about 5% of the population.

There is a strong correlation between Out-Of-Pocket-Expenditure (OOPE) and poverty in developing nations.

In these settings, incidences of illness constitute both a financial shock and a reduction in capacity to earn due to morbidity. In these settings, patients also pay more for health care leading to a vicious cycle of poverty and illness. Often, children and mothers are the most affected in this setting. Childhood mortality in such setting, as expected, is quite high.

According to the Word Bank database, between 1980 and 1995, the childhood (under five) mortality rate in Nigeria was 210 (out of 1000 live births), in other words, mothers buried a fifth of their children before the age of five. Note that this data would be worse for Northern Nigeria with a much higher poverty and illiteracy rate.

Though this figure has reduced to 109 (2015), it is still very high, particularly when compared to other African nations like South Africa, with a child mortality rate of 40 (out of 1000 live births), (2015).

Of these under-five deaths, preventable or treatable infectious diseases such as malaria, pneumonia, diarrhoea, measles and HIV/AIDS account for more than 70 per cent of the currently estimated one million under-five deaths in Nigeria.

So, naturally, women came to Dr. Nuhu with their medical problems, after all, she is a lecturer at the Faculty of Pharmaceutical Sciences!

Dr. Nuhu and her family fortunately were quite willing to help, both with finance for health care and every day general counsel for their indigent neighbours at Zangon Shanu, Jama'a Ward, just adjacent to the University.

One case out of the many distressing encounters that helped nudge her towards the path of drug development was the case of a 38-year-old woman who had come knocking with her child of about 18 months. The woman needed money and Dr. Nuhu had obliged her. At the clinic, the child was diagnosed with malaria; however, they had come too late. The baby died.

In some other cases, though, the interventions were timely; however, these events essentially got Dr. Nuhu to start considering why she couldn't develop a herbal medication that would help the immediate community. Two things were on her mind – access and cost.

Over the years, she had seen many research works end up on the book shelves of the Faculty. It was worrisome that despite the volume of undergraduate and post-graduate dissertations, somehow, none of Nigerian universities has been able to make significant

contribution in drug development. Working in the Faculty of Pharmaceutical Sciences, she saw the potentials. Also, prior to that moment, she had moved with her husband to England for his postgraduate studies and had observed with keenness, the painstaking efforts western researchers dedicated to their work and the resultant effects.

Thankfully, her husband was a Chemical Engineer working as a research scientist and lecturer, also at the University. Though he wondered at her commitment to such a venture, he didn't discourage her. She had evaluated the all-too present need, the required capacities to execute a successful intervention and for her subject, she chose malaria.

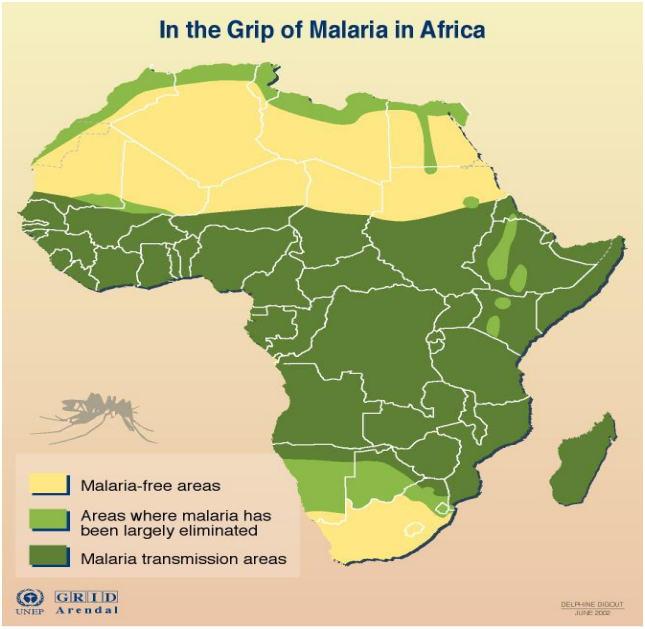
Dr. (Mrs) Hadiza Nuhu, OON with husband at ABU Award Function

The choice for malaria was obvious – it is a well-known, preventable disease that had been shown to be treatable and had even been eradicated in certain countries. She was determined to find a treatment from the wealth of herbal resources in Nigeria.

CHAPTER 2

A Closer Look at Malaria

Malaria is a global problem. Today, 40% of the world's population is at risk of malaria, majority of who live in the world's poorest countries.



Sources: A. Platt McGinn, *Malaria, Mosquitoes, and DDT,* World.Watch, Vol.15. No.3, May-June 2002.

Figure 1: Areas in Africa in the Grip of Malaria
Source: Platt McGinn, 2002.

The apparent correlation of malaria with poverty is not a coincidence, most of the developed world had found

means to resolve their malaria problem. The widespread uses of insecticides like DDT and medication therapy – quinine, were instrumental to the elimination of malaria particularly after Second World War (WWII).

According to the World Health Organisation (WHO), Official Register of areas where malaria elimination has occurred, twenty-seven countries and one territory have been able to achieve this feat. Most of this happened between 1955 and 1987. Within 2007 and 2015, five countries also, have been able to achieve malaria eradication.

In other words, the existence of malaria is more about the failure of leadership in developing countries, than the lack of tools to achieve this. For no apparent reason, Africa was left out of the Global Malaria Eradication Programme that was implemented between 1955 and 1969.

Malaria Free Countries	Eradication Time Frame
Bulgaria, Cyprus, Dominican, Grenada, Hungary, Italy, Italy, Hungary, Jamaica, Netherlands, Poland, Romania, Saint Lucia, Spain, Taiwan, Trinidad and Tobago, USA< Venezuela	1955 – 1972
Australia, Brunei, Cuba, Mauritius, Portugal, Reunion, Singapore, Yugoslavia.	1972 – 1987
Armenia, Maldives, Morocco, Turkmenistan, United Arab Emirates.	2007 – 2015
Argentina, Azerbaijan, Costa Rica, Georgia Iraq, Kyrgyzstan, Oman, Paraguay, Sri Lanka, Syria, Georgia, Tajikistan, Turkey, Uzbekistan.	Achieved zero incidence rate in 2014.

Adapted from WHO Malaria Eradication Database

Epidemiology

Malaria is an acute febrile illness. In a non-immune individual, symptoms appear 7 days or more (usually 10–15 days) after the infective mosquito bite. The first symptoms – fever, headache, chills, vomiting and

diarrhoea – may be mild and difficult to recognize as malaria. It may degenerate to jaundice and anaemia.

The disease is diagnosed by a blood test and can also be contacted via blood transfusion. Complications could arise due to malaria infections particularly involving P. falciparum to include kidney or liver failure, coma and death.

Infants, children under five, pregnant women and people living with HIV/AIDS are most susceptible to malaria.

In most cases, malaria is transmitted through the bites of female Anopheles mosquitoes. There are more than 400 different species of Anopheles mosquito.

The disease is caused by one of the four species of the one celled parasite called plasmodium; these are P. vivax, P. malariae, P. ovale and P. falciparum. Among these, it is only the infection by P. falciparum that is potentially fatal. Similarly, this is the species that is active across sub-Saharan Africa.

Anopheles mosquitoes lay their eggs in water which hatch into lava eventually emerging as adult mosquitoes. The female mosquitoes seek a blood meal to nurture their eggs. Transmission is more intense in

places where the mosquito lifespan is longer (so that the parasite has time to complete its development inside the mosquito) and where it prefers to bite humans rather than other animals. According to the WHO factsheet, the long lifespan and strong human-biting habit of the African vector species is one of the main reasons why nearly 90% of the world's malaria cases are in Africa.

Transmission also depends on climate conditions that may affect the number and survival of mosquitoes, such as rainfall patterns, temperature and humidity.

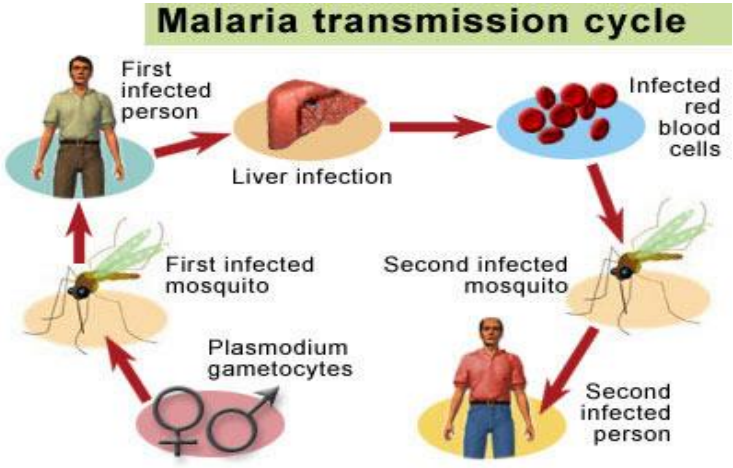


Figure 2: Malaria Transmission Cycle

Countries in the Antarctica region, because of their extreme climate conditions are relatively not affected by mosquitoes. In many places, transmission is seasonal with the peak during and just after the rainy season.

Human immunity is another important factor, especially among adults in areas of moderate or intense transmission conditions. Partial immunity could be developed over years of exposure, and while it doesn't provide complete protection, it does reduce the risk that malaria infection will cause severe disease. For this reason, most malaria deaths in African occur in young children.

Individuals with sickle cell trait (Hb AS) possess some level of immunity against cerebral malaria and the preponderance of the sickle cell trait in Africa is believed to be an adaptive mechanism to malaria.

Prevention and Therapy

The risk of the disease can be reduced by preventing mosquito bites through vector control - use of mosquito nets, insect repellent, drainage and treatment of stagnant water.

Antimalarial medicines (chemoprophylaxis), can also be used to prevent malaria for individuals travelling from

malaria free regions to malaria endemic areas. This suppresses the blood stage of malaria infections, thereby preventing malaria disease. However, individuals living in endemic regions cannot continue taking these medications on a daily or weekly basis due to drug toxicity.

For pregnant women living in moderate-to-high transmission areas, WHO recommends intermittent preventive treatment with sulfadoxine-pyrimethamine, at each scheduled antenatal visit after the first trimester. Similarly, for infants living in high-transmission areas of Africa, 3 doses of intermittent preventive treatment with sulfadoxine-pyrimethamine are recommended for prevention, delivered alongside routine vaccinations.

Despite the increases in DDT resistance and the acclaimed toxicity profile of the chemical, DDT is still widely in use, however, the WHO recommended insecticides for vector control are pyrethroids.

In recent years, mosquito resistance to pyrethroids has emerged in many countries. In some areas, resistance to all 4 classes of insecticides used for public health has been detected (WHO).

The best available treatment, particularly for *P. falciparum* malaria, is artemisinin-based combination therapy (ACT). WHO recommends that all cases of suspected malaria be confirmed using parasite-based diagnostic testing (either microscopy or rapid diagnostic test) before administering treatment. Resistance to ACTs have also been reported and the incidence is gradually rising.

Africa leads the world with 90% incidence rate (i.e. reported new cases of malaria), compared to South East Asia (7%) and Eastern Mediterranean (2%) regions. Africa also leads in malaria mortality rate (i.e. death) at 92%; South East Asia and Eastern Mediterranean have 6% and 2% respectively.

Progress is being made, however. Between 2010 and 2015, malaria incidence rate (new malaria cases) fell by 21% globally and in the African region, whereas, under this same period, mortality rates fell by an estimated 29% globally and by 31% in the African region, demonstrating increased commitment to treatment and access to medicines.

Children under 5 years of age are particularly susceptible to malaria illness, infection and death. In 2015, malaria killed an estimated 303, 000 under the

age of five globally, including 292,000 in the African region. Between 2010 and 2015, the malaria mortality rate among children under the age of five fell by an estimated 35% (WHO, 2016). Nevertheless, malaria remains a major killer of under-fives, claiming the life of a child every two minutes (WHO, 2016).

Nigeria, a country of over 170 million people, with 64% of its population living in extreme poverty in rural areas without access to portable water and adequate healthcare has more reported cases of malaria and deaths due to malaria than any other country in the world. The disease is responsible for 60% of patients visits to health facilities, 30% of childhood deaths, 25% of deaths in children under the age of one and 11% maternal deaths. The financial loss due to malaria annually is estimated to be 132 billion naira in form of treatment costs, prevention and loss of man-hour which have created a negative dent on its economic growth (NMCP, 2016).

At the time Dr. Nuhu began her research, the mortality rate from malaria was even much higher than it presently is. A key concern to her then and now is the issue of disease resistance. Malaria has had a history of developing resistance to treatment, hence, the need for Nigeria, the country with the biggest malaria burden in

the world to have a pipeline of drugs in anticipation for an eminent malaria resistance epidemic.

Besides developing an arsenal of therapeutic agents; some research scientists have argued that we look more carefully at the way we look at malaria therapy considering this looming epidemic and the chronic nature of our exposure to mosquitoes – the vector for malaria disease.

Professor David T. Okpako in a 2015 article noted that in the olden days, our forebears treated the symptoms of malaria – fever, aches and pain (FAP) and that this treatment could be equivalent to cure.

He argued that such successful treatment of malaria-induced FAP is equivalent to cure in Africans living in continuous contact with the anopheles mosquito. He also noted that Africans already have partial immunity conferred on them by anti-plasmodium antibodies and numerous genetic protective adaptations e.g., sickle cell trait and glucoe-6-phosphate dehydrogenase enzyme deficiency. In such people, he argued, all that is needed is a successful amelioration of the malaria-induced inflammation with chemotherapy (some mediators of inflammation, e. g., the cytokine, tumour necrosis factor and TNF actually suppress immune activity in the

sufferer). The resulting surge in anti-plasmodium immune activity in such people would eliminate the parasite, resulting in a cure of the disease.

Moreover, the immune status of the individual against the plasmodium was strengthened after every bout of malaria-induced FAP, and successive attacks would be less severe in a process of natural attenuation of the parasite.

This, he argued, was how Africans living in malaria endemic areas came to attain a state of biological equilibrium with the disease before European introduction of modern chemotherapy with plasmodicidal drugs less than 500 years ago.

The main point is that the current drug that seeks to eliminate the parasites, with which we could get infected the next day, puts an unnecessary pressure on the plasmodium to develop a resistance.

Herbal treatment, with their relatively lower plasmodicidal suppression, do not provoke the plasmodium into mobilising its considerable arsenal of resistance mechanisms, which is what happens when we use plasmodicidal anti-malaria drugs such as chloroquine and the ACTs whose aim is to kill the plasmodium.

The occurrence of the malaria multi-drug drug resistance we see in *Plasmodium falciparum,* he argued, is a defence reflex against extinction by an ancient parasite that sees itself threatened.

Historical Perspectives on Malaria and Mosquitoes

Without a doubt, mosquitoes are the most widely discussed arthropods in Nigeria's historical account. To understand the full impact of the mosquito problem and the relevant role Herb 25 plays as an antimalarial for both treatment and prevention, a review of historical developments in the battle against malaria would be necessary.

Scientists began to understand the parasitic nature of the illness in 1880, when plasmodium parasites were found in the blood of a malaria patient by Alphonse Laveran. However, it was only until 1897 that mosquitoes were found to be the carriers of the plasmodium after a research by Renold Ross.

The term 'Malaria' appeared in English literature first in 1829 and its origin is from Medieval Italian, meaning "bad air" – "mala aria". It was associated with swamps and marshland and was earlier referred to as marsh fever.

The argument against the use of insecticides like DDT to clear malaria from swamps and other incubating centres in developing countries included the toxicity profile of the chemicals, the relatively large effort required to implement such an exercise and the increasing resistance to the insecticide. Note, however, that all eradications of malaria were achieved via the use of DDT and that these countries were either not in the tropics or were islands.

We are of the opinion though that the continued existence of the malaria problem is more from the lack of resource commitment than any other thing.

Malaria and Traditional Medications

Medicinal Plants have been the most promising malarial treatment for mankind till date. All present day standard antimalarial therapies, such as quinine, artemisinine, etc. have been obtained from plants. For thousands of years, traditional herbal remedies have been used to treat malaria in Africa and elsewhere in the world.

Quinine became the predominant malaria medication until the 1920s when other medications were developed. In the 1940s, Chloroquine replace quinine as the treatment of both uncomplicated and severe

malaria until resistance supervened first in South East Asia and South America in the 1950s and then globally in the 1980s.

In Africa, where more than 80% of the population rely on traditional medicine, malaria is widely treated with different species of plants. Many of these plants have not been studied and perhaps some of them may have better antimalarial activity than Cinchona (source of quinine) and Artemisia annua (source of artemisinine). The search needs to be sustained until a solution is found among the vast flora of Africa.

The safety and continued efficacy of some of the traditional treatments after hundreds of years of use, made Dr. Hadiza Nuhu to believe that a search is not only worthwhile but may lead to an answer that will address this enormous problem.

Preparing for the Failure of ACTs

As earlier said, malaria presently accounts for more deaths and morbidity in Nigeria than in any other country in the world. At least, a whopping 300,000 individuals die annually from malaria in Nigeria. That is about 34 individuals per hour.

With more than a million malaria episodes in Nigeria each year, if we do not have a cure for malaria, in one year alone, we would be facing an epidemic of monumental proportions.

Presently, there is no long term strategic commitment by public institutions in Nigeria to prepare for this day.

According to the 2013 WHO World Malaria Report, parasite resistance to artemisinine has now been detected in four countries of the Greater Mekong sub-region: Cambodia, Myanmar, Thailand and Vietnam. In Cambodia's Pailin Province, resistance has been found to both components of multiple ACTs, therefore, special provisions for directly observed therapy using a non-artemisinin-based combination (atovaquone+proguanil) have been introduced.

A similar report in October 2016 confirms these findings. However, though there has not been any official study to confirm the existence of resistance to ACTs in Nigeria, clinicians are gradually reporting delayed malaria clearance with ACTs.

Taking a cue from the development of ACTs, there is great wisdom and urgency in looking at herbal remedies for answers. Hence, Herb 25 is not only relevant as

medication of the day, but is also, an arsenal for the day of reckoning.

Practical Issues in Combating Malaria

The various approaches in addressing malaria and prospects for evaluation are summarised in Tables 1 and 2.

Table 1: Approaches to Malaria Treatment

S/N	APPROACH	PROBLEMS	PROSPECTS
1	Vaccinations	Not yet established.	RTS, S/AS01 is the most advanced vaccine candidate against P. falciparum would be rolled out in 2017 with moderate efficacy.
2	Insecticide treated nets	Insufficient, impractical and not very conducive to many.	Limited, at best preventive. Highly Recommended.
3	Vector Control by Spraying Indoor and outdoor spraying.	Resistance development to common insecticides.	Limited, requires concerted large scale efforts. Best Approach.
4	Chemotherapy (ACTs)	Growing resistance and relatively expensive.	Uncertain; New agents are urgently needed; not affordable to many

From the above, the future of malaria control doesn't look particularly bright for Africa, even with the progress with vaccine development. Also, at present, Africa is yet to show leadership in any of these areas.

A serious rethink of the approaches and resource allocation is therefore necessary for avoiding a possible worsening of the status quo. Looking inwards, African medicinal plants offers certain opportunities; some of which are shown in Table 2.

Table 2: Prospects and Problems of Herbal Medicines in Malarial Control

S/N	APPROACH	PROSPECTS	PROBLEMS
1	Vector Control	High prospects. Numerous plants have shown insecticidal properties. Development of stable, safe mosquito repellent ointments and creams. Can also be impregnated into nets.	Non-stability of available repellents and low investment in research and intellectual property frameworks.
2	Standardized Chemotherapeutic Agents	Over 1200 species identified to have antimalarial property.	Insufficient political support and resource allocation.

		Plants are currently used by more than 80% of the population. Likely to be cost-effective. Herb 25 is a notable example; the only NAFDAC registered herbal drug for malaria.	Need for increased investment in research and development.
3	Unstandardized use of medicinal plants	Complicated.	Poses serious implication to health, open to abuse. Could lead to increased drug resistance. Moral duty of government to regulate the standards.

CHAPTER THREE

Making Herb 25

The search for a herbal antimalaria drug began in 1994 shortly after Dr. Hadiza Nuhu returned from the UK where she accompanied her husband for his PhD (1990-93). Hadiza Nuhu began by implementing an intensive literature review of the available herbal remedies used traditionally for malaria treatment.

She had a set of criteria for the ideal herbal remedy which included the following:

1. A history of safety and efficacy with traditional use
2. A leaf would be preferable – as it is easier to assure sustainability of supply.
3. A combination of more than one plant to reduce the risk of resistance.
4. Naturally abundant – also for the purpose of sustainability.

Over thirty (30) local plants were considered in this manner, after which, some satisfactory plants and plant mixtures were identified. A literature survey to confirm the safety and toxicity of these plants was also done. Some were also tested in the laboratory to determine

their Median Lethal Dose (LD_{50}) in a standard toxicity analysis procedure.

One combination – Sample Number 25, was particularly promising and was selected for further studies and that's how the name Herb 25 came about.

Herb 25

Herb 25 is a mixture of Nigerian medicinal plants taken as an infusion (hot water extract) for the prevention and treatment of malaria.

The key ingredient is Azadirachta indica leaves.

Treatment

The average adult dose is two teabags of 2g each taken at 12 hours' interval for 5 days and a maximum of 7 days.

The child dose is 1g tea bag at 12 hours' interval for 5 days and a maximum of 7 days.

Prevention

Half of adult dose to be taken for 3 days.

Toxicity Studies of Herb 25

A 2009 toxicity study by Professor N.D.G. Ibrahim and Dr. Sani Adamu at the Department of Veterinary Pathology and Microbiology, Faculty of Veterinary Medicine, ABU Zaria, showed that the aqueous extract of Herb 25 had a wide margin of safety and is regarded safe as an oral preparation for practically applied medical use.

Toxicological studies are based on the first principle of medicine which is “do no harm”; herbal medicines intended for use in human beings are required to be tested for toxicity by regulatory authorities. In Nigeria, the National Agency for Food and Drug Administration and Control (NAFDAC) is responsible for the registration of Herbal remedies for commercial use. A key NAFDAC requirement is a toxicity study.

A similar study was conducted in April, 2006 at the Department of Pharmacognosy and Drug Development, which determined the Median Lethal Dose (LD_{50}) to be 1265mg/Kg.

Antiplasmodial Studies

In 2011, a post graduate work by Mrs. Udoso Uduak Eyakeno at the Department of Pharmacognosy and Drug Development, Faculty of Pharmaceutical Sciences, ABU Zaria, comparatively evaluated the Antiplasmodial effects of Artemisia annua L. (Asteraceae) and Herb 25.

The study compared the Antiplasmodial effects of both 100mg and 200mg/Kg of A. annua and Herb 25. The study found that both possessed significant antiplasmodial activity with an average percentage suppression and mean survival times shown below.

Table 3: Comparing Effects of Artemisia annua and Herb 25 (Uduak, EU, 2011)

	Average Percentage Suppression		Mean Survival Time	
Dose	100mg /Kg	200mg /Kg	100mg /Kg	200mg /Kg
Artemisia annua	76.58%	84.31%	20.75 ± 0.86	23.00 ± 1.62
Herb 25	60.89%	71.90%	21.25± 0.65	20.00 ± 2.56

The outcomes were comparable with that of the standard – Artesunate at 10mg/Kg, hence, justifying the use of both drugs for anti-malarial therapy.

Efficacy on Plasmodium berghei

Another study in 2009, at the Centre for Biotechnology Research and Training, Ahmadu Bello University evaluated the efficacy of Herb 25 on Plasmodium berghei. The researchers evaluated for the presence or absence of the parasitaemia via both oral and peritoneal routes. At 100mg/Kg and 200mg/Kg, the extract showed a dose dependent clearance of the parasite via both oral and peritoneal routes with more than 2 months' survival duration compared to the controls that died a week after infection.

Plasmodium berghei is a protozoan parasite that causes malaria in certain rodents. Originally, isolated from thicket rats in Central Africa, P. berghei is one of four Plasmodium species that have been described in African murine rodents, the others being Plasmodium chabaudi, Plasmodium vinckei and Plasmodium yoelii.

Due to its ability to infect rodents and relative ease of genetic engineering, P. berghei is a popular model organism for the study of human malaria.

Clinical Observational Trials of Herb 25

In 2007, Professor Tony Elujoba of the Faculty of Pharmacy, Obafemi Awolowo University, Ile-Ife, fondly referred to as the 'Village Chemist' performed an observational study on some voluntary patients.

He performed an investigational laboratory examination of the bold film for the presence of malaria parasites before and after using the powdered drug sample of Herb 25.

Out of the 13 patients who completed the 5-day examination, all were relieved, except 1 who was referred and 2 others who were placed on alternative medication.

Pharmacovigilance

Prior to applying to NAFDAC, Dr. Nuhu committed to pharmacovigilance, i.e. a process of observing the clinical outcomes of the drug. This period lasted between 2004 and 2007 and involved the studies highlighted above, including the observational studies done at Herbal Points Services which had opened in 2004 and is discussed in the subsequent chapter.

By 2006, she was convinced of the safety and efficacy of Herb 25 and an application was made to the National Agency for Food and Drug Administration and Control (NAFDAC). The application was evaluated by NAFDAC, inspections were carried out and registration was achieved in 2007 with NAFDAC No: **NRN-A7-0155L** given to Herb 25**.**

Herb 25 remains the only herbal drug registered by NAFDAC for the treatment of malaria.

A Note on Drug Development

As earlier mentioned, natural products including plants, animals and minerals have been the single most productive leads for the development of drugs.

At present, some compounds derived from natural sources are currently undergoing clinical and preclinical studies. They have found applications notably as anti-inflammatory, cardiovascular, anti-diabetic, anti-obesity, anti-malarial, anti-viral, and anti-neoplastic agents.

For example, to develop a herbal drug derived from plants, as is the case with Herb 25, the first step is to collect and authenticate the materials. This is done via a herbarium as plants can look very similar. Hence, it is

required to have a herbarium specimen of the plant material for cross matching and authentication.

A herbarium is a collection of preserved plant specimens and associated data used for scientific study. The term can also refer to the building or room where the specimens are housed, or to the scientific institute that not only stores but uses them for research.

After authenticating the material, a pharmacognostic and phytochemical evaluation is performed to determine the physical and chemical composition of the medicinal plant material, these studies are very important as they provide information on the properties of the plant material.

A plant material is identified by its physical and phytochemical features. Phytochemical features ascertain the nature and quantity of chemicals in the plant material.

Next is the pharmacological evaluation and standardization. Pharmacology refers to the uses, effects and modes of action of drugs. In the case of Herb 25, the drug shows antiplasmodial activity.

The gold standard is the clinical trial. Clinical trials are employed to verify the safety and efficacy of the drug

on humans. There are three levels of clinical trials with varying complexity – phase 1, 2 and 3.

Observational studies – the kind conducted by the Village Chemist for Herb 25 are a kind of phase 1 clinical trial.

Herbal medicines, under Nigerian law, can be registered with NAFDAC without a clinical trial, provided there is evidence of traditional use and safety as shown by the toxicity studies. This exemption is because, technically, a history of traditional use shows that the drug is at least safe in humans. Such herbal remedies, however, often do not get prescribed by physicians and usually bear the mark "these claims have not been validated by NAFDAC".

Globally, drugs - including herbals, must pass the Phase 3 clinical trials to be treated as prescription medicine.

This poses s some challenges because of the relatively non-proprietary nature of herbal medicines and the cost of implementing these clinical trials. Clinical trials are very expensive and drug firms expect to make profit, hence, drug candidates are expected to have some level of proprietary protection to attract investment.

Hence, it is the chemicals in herbal remedies and not necessary the extracts themselves that are the subject of most clinical trials on drugs of herbal origin. However, evidence abounds for the efficacy of these extracts.

Generally, very few pharmaceutical companies are involved in drug discovery screening from natural sources. This neglect may be due to the high cost involved in isolation and identification of pure compounds, difficulty in collection, the complex nature of plants, and absence of clear-cut regulatory guidelines for natural products.

In the conventional drug discovery process, a single pure active constituent is isolated, purified and standardized. However, multi-constituent herbal formulations can also be standardized with newer techniques such as DNA fingerprinting, High-Pressure Thin Layer Chromatography (HPTLC), and Liquid Chromatography–Mass Spectroscopy (LCMS).

Production of Herb 25

The production process of Herb 25 is similar to that of most herbal medicinal plants and involves collection of the plant material, sorting, drying, size reduction, classification, storage and packaging.

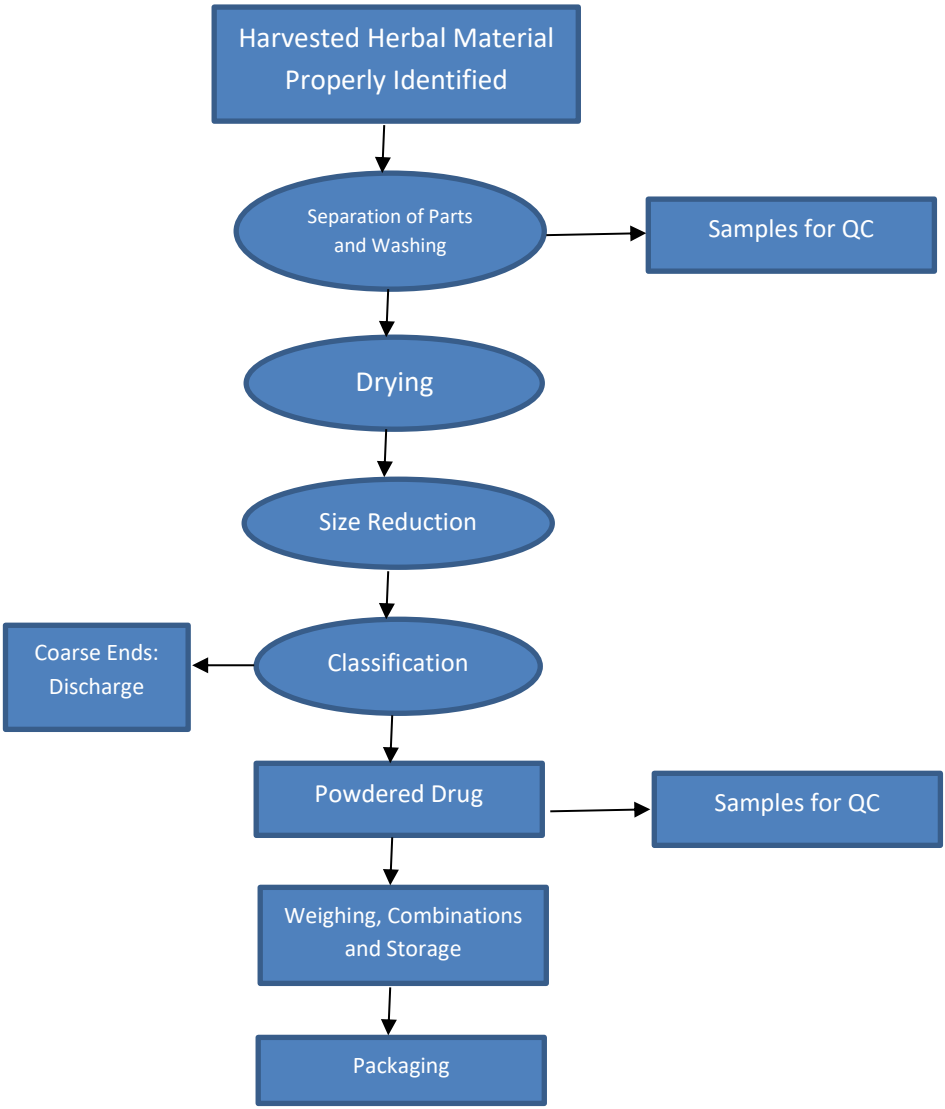
Each of the process involves a quality control process to ensure conformity to the established standards.

When plants are collected from the wild, there is a risk that they have been incorrectly identified, hence, they would need to be verified for proper identification. One advantage to using wild plants however is that they are unlikely to contain any pesticide residues. Plant materials for Herb 25 are collected from the wild.

The sorting of the plant materials and washing are to remove unwanted plant materials, dust and other unwanted particles.

The plant materials are then dried and size reduced, after which they are classified and coarse ends discharged. The powdered materials are then weighed, mixed thoroughly, stored and then packaged into tea bags.

Figure 3: Process Flow Diagram for Herb 25 Production



CHAPTER FOUR

Herbal Point Services

Health care services in Nigeria consist of a wide range of providers in the public and private sectors. In the public sector, Nigeria operates a decentralised health system run by the Federal, State and Local Governments. The Federal Government co-ordinates the affairs of the University Teaching Hospitals and Federal Medical Centres through the Federal Ministry of Health, while the State Government manages the various General Hospitals. The Local Government focuses on Primary Health Centres and Dispensaries and are supported by a parastatal under the Federal Ministry of Health - National Primary Health Care Development Authority (NPHCDA).

The private sector also participates in health care provision in Nigeria by playing strategic roles: They include private for-profit clinics, health maintenance organisations, hospitals, pharmacies, pharmaceutical marketing and manufacturing firms. Non-governmental organisations (NGOs), community based organisations (CBOs), religious and traditional health care providers also constitute part of the health care industry.

The role of research and development (R&D) in promoting rapid economic transformation and solving the numerous health challenges has long been recognised. Private and public research organisations constitute a vital component of the health care ecosystem; they contribute in the areas of drug development, clinical trials, epidemiological data management, teaching and learning.

Herbal Points Services represents one of the leading private herbal drug research and development organisations in Nigeria.

Established in 2004 by Dr. Hadiza Nuhu, the Herbal Point Services had the following mandates:

1. To develop the dream of the antimalaria product.
2. Documentation of ethnomedical practices in Nigeria.
3. Development of alternative medicine from traditional medicine plants for Nigerians.
4. Value addition to Nigerian medicinal plants already in use in Nigeria, e.g. bitter leaf, moringa, etc.

In 2007, with the registration of Herb 25 as the first drug to be developed by any Nigerian university, Herbal

Point Services achieved a major milestone. Herb 25 is also acknowledged to be the only registered anti-malaria medication developed from Nigeria.

The company launched the product in 2010 at Arewa House, Kaduna.

Figure 4: Packet and Carton of Herb 25

Herbal Point successfully established a standard herbarium and through intensive research and development has developed standard medicinal herbal preparations for various ailments such as high blood pressure, diabetes, liver ailment, malaria, diarrhoea and typhoid fever.

Herbal Point, since its establishment in 2004, has played home to hundreds of screening of medicinal plants and documentation of viable and abundant local medicinal plants such as Mahogany (madaci), Guera senegalences (sabara), Kigelia africana (rawaya), Erythrina senegalensis (minjirya), Stegnaotaenia araliaceaa (ararrabi), Salvadora persica (tazargade), etc.

Guided by the principles of safety, efficacy and affordability, Herbal Point Services has endeavoured to stay true to its vision of contributing to the alleviation of the health burden of its immediate society and that of the nation at large. The leadership of the organisation recognises the huge potential for herbal remedies in Nigeria and the need to preserve the knowledge base.

Besides Herb 25, which has earned Dr. Hadiza Nuhu the National Merit Award of the Officer of the Order of Niger, (OON), the organisation, under her leadership,

has also successfully formulated various herbal preparations. Examples are shown in Table 4:

Table 4: Some Other Herbal Preparations Being Processed for Registration by NAFDAC

S/N	Product	Pharmacological Activity
1	Herb 1	A herbal tea for treatment of piles and for vitality
2	Herb2	A herbal tea for treatment and control of high blood pressure
3	Herb 5	A blood sugar reducing capsule
4	Herb 10	A herbal antibiotic tea
5	Herb 16	An ulcer treatment capsule
6	Herb 24	A herbal liver invigorating tea
7	Herb 55	An anti-typhoid herbal tea
8	Herb 27	Feminity Booster
9	Moringa leaf powder	
10	Black seed (habbatus sauda)	
11	Blood boosting herb	
12	Liver invigorating herb	
13	Foeniculum vulgare (Hulba) Capsules	
14	Garlic Capsules	
15	Bitter leaf (Vernonia amygdalina)	
16	Cassia occidentalis Tea (Rai-Rai)	
17	Hibiscus sabdariffa Tea (Zobo)	

Herbal Points Services, by the grace of God, has recorded tremendous goodwill from both her immediate customers in Zaria and numerous customers all over Nigeria who have come to rely on these products, particularly the antimalaria drug – Herb 25 as their medicine of choice.

In recognition of Dr. Hadiza Nuhu's efforts in developing Herb 25, the organisation and herself, have been the subjects of numerous awards; a summary of these are made in Chapter 6.

CHAPTER FIVE

Key Partners

A. Department of Pharmacognosy and Drug Development, ABU, Zaria.

Dr Hadiza Nuhu (Mrs) has been a lecturer and researcher in the Department since May 1988. Dr U. Katsayal and Prof Hajara Ibrahim have been supporting the work on Herb 25. Presently, Prof Hajara Ibrahim is chairing a research group that is working on taking Herb 25 to the next level with new formulations into tablets and possible palatable syrups for children.

B. Centre for Biotechnology Research and Training, ABU, Zaria

During Dr. Hadiza Nuhu's sabbatical in the National Research Institute for Chemical Technology (NARICT), Zaria, its Director General, Dr E.M. Okonkwo commissioned this Centre to investigate Herb 25 to determine its antiplasmodial activity. This was successfully done under the supervision of Prof Andrew Nok, its Director at that time.

C. Department of Veterinary Pathology and Microbiology, ABU, Zaria

The National Research Institute for Chemical Technology, Zaria, under its Neem Promotion Project, also commissioned this Department to carry out toxicological studies and assessment of Herb 25 in the Department. This was carried out effectively by Prof. NDG Ibrahim and Dr. Sani Adamu.

D. National Agency for Food and Drug Administration and Control (NAFDAC)

NAFDAC has the mandate to regulate and register all foods and drugs, herbal and otherwise in Nigeria. The agency carried out its mandate well with respect to Herb 25 and even offered advices on ways to improve the processing and related matters.

E. Engagement of Onel Consults Limited

In April, 2010, Herbal Points Services engaged the services of Onel Consults Limited to evaluate possibilities for some business development interventions including:

1. Engagement of key stakeholders for a clinical trial
2. To seek out potential technical and funding partners

Prior to this engagement, the lead Pharmacist in the organisation – Nelson Okwonna, had been greatly influenced by Dr. Nuhu to embrace a career in drug development consulting, with a key focus on the Nigerian Pharmaceutical Research sector.

One of the first key stakeholders to be engaged was the National Health Research Ethics Committee (NHREC) under the Ministry of Health to ascertain a suitable clinical facility.

The NHREC is responsible for accrediting Health Research Ethics in Nigeria's health organisation. The NHREC, at every time had a list of accredited centres for a clinical research.

A clinical research accredited centre usually would have its own Health Research Ethics Committee responsible for the approval of every clinical research in the facility.

After the accredited institutions, Aminu Kano Teaching Hospital, Kano, was selected as the ideal location for the trial of Herb 25, considering the proximity and familiarity to the client.

The next step was to locate a principal investigator**.** Clinical trials are led by Principal Investigators who should be independent of the firm conducting the trial and should be knowledgeable in the field. After much search, Prof. Abdulrazaq Habib was selected as the Clinician to lead the study. Prof. A Habib is a Professor of Human Medicine and a specialist on tropical diseases. He is also a member of the National Drug Safety Advisory Committee.

Onel Consults sought and acquainted him with the objectives of the study and he was enthusiastic about the plans. Following this was to develop a study plan; the treatment protocol for consideration by the Health Research Ethics Committee of the institution.

At the same time, efforts were taken to constitute the other members of the team, including a clinical pharmacologist.

Based on WHO requirement, in preparing for the clinical trial, it was important to demonstrate the following:

1. Evidence of traditional use. This was to be achieved by citing both published works and oral data from traditional practitioners. This information is the most important data as it

reduces the stringent requirement on toxicological assessment.

2. Method of traditional use: processing and dosage procedures.
3. Experience with use; here Herbal Point Services would cite the long years she has used this product in addition to the traditional usage.
4. Observed toxicity with use if any.
5. Presence of other adjunct therapy or procedure with traditional use.
6. Any other available toxicological or pharmacological data showing rationale (in vivo assays). These should not be necessarily works done for Herbal Point Services, any published work is accepted.
7. Availability of a chromatographic fingerprint.
8. A herbarium specimen filed with an approved herbarium.

Concurrent efforts were made to mobilise necessary funds and technical partnership for the study which is yet to be undertaken at the time of writing this book, however, some valuable lessons were learned.

Attempted Engagement of Dr. Ramesh Pandey for collaboration on further development of HERB 25

Dr. Pandey was the CEO of Xechem Pharmaceuticals; Xechem licensed the only drug developed in Nigeria and marketed globally – NIPRISAN, which the company sold as NICOSAN.

The aim of engaging Dr. Ramesh Pandey was primarily technical collaboration, with potentials for financing considering his experience in the sector.

Two meetings were held with him to this effect and a summary would be made here:

a. Dr. Pandey offered to take-over the entire work and license the invention.
b. This was not satisfactory and the consultancy firm advised Dr. Hadiza Nuhu against taking this path. A counter-offer was made for a collaborative partnership where both parties had mutual ownership of both the research and commercialization process.
c. The meetings therefore ended in a stalemate as no further headway was possible. We believed Prof. Pandey's insistence on licensing the product even when the study

was not yet completed was very disadvantageous.

d. The conclusion then was that:
    1) "GDPAU's offer now will not satisfy the stated objective of Herbal Point Services (HPS)"
    2) A satisfactory agreement would be one that allows Herbal Point Services to maintain a certain degree of control and ownership of marketing and further development rights
    3) Such an agreement should include HPS's right or co-right for products developed from the research work done with funds generated from HERB 25 grant proposals.
    4) Dr. Pandey indeed could make things happen but HPS need to get a better deal structure.

The potential partnership brokered by Onel Consults Limited didn't happen because of the nature of the deal structure and unfortunately, there was no subsequent meeting of minds.

CHAPTER SIX

Impact and Recognition

In modern medicine, herbal medicine suffers an institutional bias; they are not widely accepted as medicines in Nigeria and in most developed nations with notable exceptions like Germany and China though.

They are often classified as “herbal supplements”, a classification that can be very misleading. However, after the 2015 Nobel Prize in Medicine which was awarded to Tu Youyou for the development of artemisinin, herbal medicines have gained more recognition around the world.

Note that the development of Artemisinin was from Artemisia annua (Qinghao), a type of wormwood native to Asia, which has been shown to inhibit plasmodium growth. Tu’s work essentially was to improve the method of extraction of the plant,

The discovery of the anti-malarial drug “HERB 25” by Dr. Hadiza Nuhu, OON, also, should be seen in this light – the bringing to light of medication that has been so close to us.

On the impact of Herb 25, like the work of Tu Youyou, it also has huge effect for those living under the burden of malaria. Herb 25 is playing a vital role in resolving the malaria problem, and with increasing resistance to Artemisia Combination Therapies (ACTs), as earlier mentioned; there is need to have a product chain of new antimalarial drugs. Herb 25 fulfils this need.

The prospects for Herb 25 is quite much and with the right investments and collaborations, the medication can be a centre piece of anti-malaria therapy in days to come.

Reception

Herb 25 has enjoyed a level of recognition since its inception and registration with NAFDAC in 2007.

With a distribution centre in Kumasi, Ghana, Herb 25 is growing in recognition across West Africa with prospects of reaching other sub-Saharan countries in a few years. Locally, Herb 25 has become a household name in major cities most especially in the North West and North Central geopolitical zones of Nigeria.

With pharmaceutical outlets in over 10 major cities in Nigeria including Abuja and Enugu, Herb 25 has had

widespread use across the six geopolitical zones of Nigeria.

Recognition

Herb 25, its inventor Dr. Hadiza Nuhu, OON and Herbal Point Services have enjoyed a great wealth of National Honours some of which are:

- "Officer of the Order of the Niger" honoured by the President and Commander in Chief of the Armed Forces of the Federal Republic of Nigeria (Late) Alhaji Umar Musa Yar'adua, GCFR, in 2008.
- Local Raw Materials Content Award for Producing Anti-Malarial Drug (Herb 25) from Nigerian Medicinal Plants, honoured by the Raw Materials Research and Development Council, Abuja 2009.
- Great African Patriotic Achievers Merit Award by the African Update International Magazine, 2009.
- Award for Excellence for contribution to National Development Goals by the Organisation for Promoting MDG's and the Seven Point Agenda of the Federal Government, 2009.

- African Professional Managers Golden Award, 2009.
- Ahmadu Bello University Vice Chancellor's Award for outstanding research on malaria, 2015.

Dr. Nuhu responding to the Vice Chancellor's Award 2015

On the media platform, Herb 25 product has been in the Nigerian and foreign media in forms of;

- Health Programmes— Voice of America since 2007 interview.
- Documentaries such as the National NTA documentary on 'Women in Focus' in 2014 (available on YouTube).

- Ahmadu Bello University Mass Communication Students' winning a national documentary award (2014) organised by BOB TV, having worked on Herb 25 (available on YouTube).
- News items and interviews on various radio stations in Kaduna and Kano states.
- Numerous Contributory Articles and testimonials in various news dailies especially Daily Trust, published by Media Trust Limited.

With increasing awareness and general acceptability of medicinal herbal drugs on both National and International stage, Herb 25 and Dr. Hadiza Nuhu, OON will continue to play a vital role in drug development.

CHAPTER SEVEN

Challenges and Future Projections

The Herb 25 anti-malaria project has achieved some important milestones and with them, many challenges. Some of these are discussed in this chapter.

Challenges

According to the World Health Organisation, approximately 80 %of African population use some form of herbal preparation in one form or another and the worldwide market for herbal products is about $131 Billion. Despite this, there are still major challenges that must be overcome before the successful integration of herbal remedies into mainstream medicine in Nigeria.

With Herb 25, there were many challenges faced from conception, ranging from research, product development, commercialization and registration of the product with NAFDAC. Other challenges included finance, logistics and access to appropriate machineries, among others. There were other challenges from academic colleagues, medical scientists and clinicians who thought it was impossible or unnecessary to venture into such a project, especially when there was no reference point to start with.

Dr. Hadiza Nuhu, as a lady with the burden of a large family to cater to and a day-job as a lecturer, had to joggle a lot of challenging concerns to make her dream a reality.

Finance was the most challenging of all as every step and protocol needed funds. However, with support from family members and some concerned individuals, especially the sabbatical support received from NARICT, these were overcome.

The current challenge of taking Herb 25 to the next level also requires funding to carry out clinical studies and formulation studies that may lead to tabulation, capsulation and/or syrup production.

Drug development in itself is a lengthy, multi-disciplinary and costly process entrenched with a high degree of uncertainty of drug success.

Much scientific advancement in healthcare have been driven by innovations in different areas by understanding the pathogenesis of a disease, diagnosis of the disease and treatment of the disease which must be cost effective and affordable for whatever class of individual the drug is developed for.

Usually, the process requires a multi-disciplinary approach. No one specialty is enough to lead the process from start to finish. As shown with the Herb 25 study, the journey of meeting the observed need began with ethnomedical studies of existing therapies, then pharmacognostic studies, then pharmacology and eventually, clinical observational studies. All these were matched with the temerity of entrepreneurship and academic rigour. It was a fire that would easily have been quenched by the many seeming obstacles and the "Nigerian environment" issues. Yet, this has shown that our problems, though overwhelming, can be overcome with deliberate efforts, consistency and a large dose of optimism.

The challenges of developing Herb 25 encapsulate the challenges of herbal drug development in Nigeria and entail the following:

1. Low Investment in Research Commercialisation.
2. Relatively poor culture of innovation in academic institution
3. Relatively low level of interdisciplinary collaboration on drug development
4. Poor Intellectual Property Protection Structures
5. Poor rate of adoption by industry
6. Difficult Operating Environment

These challenges, however, are not necessary barriers but we would achieve greater productivity from our investments in the academic institutions if they are properly addressed.

The key emphasis is on recognising that the success observed so far with Herb 25 was possible because the much-needed delicate balance between academic research, entrepreneurship and traditional medicine knowledge was achieved.

The three pillars of Herb 25 Development

The intersection of these three is critical and is the necessary catalyst to sustain the momentum not just for Herb 25 but for other indigenous research efforts. Hence, the dedication to the development of Bio-entrepreneurs should be encouraged in our universities.

The opportunities in the herbal medicine industry in Nigeria are quite immense and not enough human and financial investments have been made in this industry.

The Future

Herb 25 has demonstrated so far that it is an antimalarial drug with great potentials in terms of efficacy and safety. There are good prospects to move it to the next level as a standard drug for antimalarial in Nigeria, Africa and beyond.

Herb 25 could compete with other antimalarial drugs in the world market, representing an important African contribution – helping to drastically address Africa's malarial burden. This is particularly important considering the increasing reports of resistance development to ACTs.

All stakeholders, particularly the Federal Government of Nigeria and its relevant agencies, have a responsibility to bring this vision to light; to help Herb 25 to attain its destiny as Nigeria's contribution to the global fight against malaria in this decade.

Herbal Points Services, would, as it had done in the past, continue on this path, till our task is done.

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