FEATURE ARTICLE

CHEMISTRY OF NATURAL PRODUCTS: A VERITABLE APPROACH TO THE DEVELOPMENT OF DRUGS FOR COMBATING CURRENT AND FUTURE DISEASES OF GLOBAL HEALTH IMPORTANCE

Karniyus S. Gamaniel[1*], Kudirat B. Mustapha[1], and Taiwo E. Alemika[1,2]

[1]*National Institute for Pharmaceutical Research and Development (NIPRD), Idu, Abuja. Nigeria.*
[2]*Department of Pharmaceutical Chemistry, University of Jos, Jos. Nigeria.*

Being a paper presented at the 38th Annual International Conference of the Chemical Society of Nigeria (CSN) and 5th Federation of African Societies of Chemistry (FASC) Congress held September 2015 in Abuja, Nigeria. Prof. K.S. Gamaniel is the DG/CEO of NIPRD.

Abstract

The earth's resources, especially natural products, are no doubt important materials from which mankind continues to derive numerous benefits. Natural products, especially plants have historically served as sources of pharmaceuticals, either as drugs or as leads. Even with the advent of newer technologies such as combinatorial chemistry, robotics, high throughput screening (HTS), bioinformatics, and *in silico* molecular modelling, natural products still play a crucial role in drug discovery. This is because they provide an unparalleled range of chemical diversity on which the newer technologies find leverage. Thus in combating current, emerging and future diseases of global importance (such as malaria, pain, Alzheimer's, HIV/AIDS, Lassa fever, Ebola virus disease, and Zika virus disease) natural products still remain the veritable resource scientists can, and indeed, must rely on.

Keywords: Natural Products; Chemistry; Medicinal Plants; Drug Development

Introduction

Natural resources and products derived from them are useful raw materials obtained from the earth. Human beings cannot make natural resources; rather we use and modify them in ways that are beneficial to us. Some examples of common natural resources in Nigeria are: natural gas; petroleum; coal; various metal ores (including tin, iron ore, niobium, lead, zinc, limestone); and plants (Table 1). Nigeria is endowed with a fair share of all the various categories of the natural resources listed in Table 1. For instance, Nigeria is the 7th world largest producer of petroleum fuel derived from its natural resources.

Plants as useful natural products

Turning to plant resources and human health, medicinal plants and traditional knowledge of their use can be an important component of our national economic development strategy for the promotion of general health and

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* Corresponding author. *E-mail*: ksgama@yahoo.com   *Tel*: +234 (0) 8055000150

conservation. It is estimated that about 5,000 plant species exist in Nigeria, ranking it eleventh in Africa for diversity. Out of this number of species, 205 are considered endemic, making the country the ninth highest in ranking among 42 African countries.

Table 1: Natural resources and products/ services derived from them

Natural Resource	Products or Services derived from them
Plants	Wood, paper, cotton clothing, fruits, vegetables, pharmaceuticals, phytomedicines
Air	Wind energy
Animals	Foods (milk, cheese, steak, bacon) and clothing (wool sweaters, silk shirts, leather belts)
Coal	Electricity
Minerals	Coins, wire, steel, aluminium cans, jewellery
Natural gas	Electricity, heating
Oil	Electricity, fuel for cars and airplanes, plastic
Sunlight	Solar power, photosynthesis
Water	Hydroelectric, energy, drinking, cleaning

The estimated World market for herbal medicines based on traditional knowledge is up to US$60 billion (30% of world pharmaceutical sales). Africa accounts for only 1.2% of the world's total pharmaceutical sales. Nigeria has comparative advantage in this area and can easily capture a significant proportion of the huge market through the development of the herbal pharmaceutical industry.

According to NAFDAC records, the number of herbal products imported into Nigeria as at 2012 was 502. The products were imported mainly from USA, Europe, China, India, S. Korea and S. Africa. Export of herbal products from Nigeria is virtually non-existent although records also indicate that there are 196 herbal product manufacturers in the country.

There is no doubt that rigorous scientific research and development studies offer a great opportunity to develop new drugs and strategies that could result in expanded access to clinically proven products. In this regard, the chemistry and biology of natural products is very imperative.

Herbal medicines are often prepared in the form of mixtures and many scientists resent the idea of dealing with mixtures in herbal medicine research, which differ substantially from the pure active components of allopathic medicines. These scientists prefer to isolate pure chemicals before subjecting them to scientific validation. Yet, research on herbal medicine products cannot be conceived merely because of the need for novel active drug molecules; people who are already using the products should benefit from the research. Thus initiating research on such products with the sole aim of striking a pure chemical entity goes contrary to the principles of research bioethics.

Addressing the challenges posed by conducting analytical research on herbal traditional medicines might offer a new opportunity to support product development and public health. Therefore, this paper wishes to draw attention to the largely untapped resource of medicinal plants in Nigeria and other parts of Africa, and the need to engage both our knowledge of chemistry and biology appropriately to exploit them sustainably towards national health and economic development.

Natural products in drug development

Natural products have been a source of leads for the development of many of the most effective drugs currently available for the treatment of a variety of human diseases and significantly impacted on healthcare and prevention of diseases. The two most effective drugs against malaria (quinine and artemisinin) were derived from plants. The ancient civilizations of the North Africans, Chinese and Indians provided written evidence for the use of natural sources for curing various diseases.

Natural sources of drug products can be broadly classified into four Categories

1. Microbial world e.g. Cephalosporin derived from *Cephalosporium acremonium*
2. Plant sources e.g. Paclitaxel from *Taxus brevifolia* (anticancer)
3. Marine sources e.g. Discodermolide from *Discodermia dissoluta* (possesses a strong antitumor activity)
4. Animal sources e.g. Epibatidine from African clawed frog (is ten times more potent than morphine).

The significance of sustainable development of natural drug products

It is imperative to note that plant extracts and products contribute in four major areas to human health and wellbeing:
1) Foodstuffs,
2) Flavoring agents and spices,
3) Perfumes and cosmetics,
4) Pharmaceutical and biological agents

The exploitation of natural resources would no doubt provide significant commercial prospect to:
1) Global pharmaceutical companies,
2) Small to medium size biotechnology companies,
3) Botanical supplement companies,
4) Food industry.

It is worthy of note that the African societies/cultures cherish the medicinal value of these natural resources in view of its ease of accessibility, low cost and believed high efficacy. However, several factors have hindered the development and utilization of the great potential locked up in our natural resources. These include: colonial suppression – such that traditional medical practice is seen as sub-standard and 'second-rate' compared to orthodox medicine; inadequate development of the traditional sector – which again is an offshoot of the previous point.

The continuing growth and application of Chinese and Ayurvedic medicine has however shown the need for the development of African traditional medicine and collaboration with Western/orthodox medicine. The tools of modern research, Good Manufacturing Practice and other tools of modern science can be used profitably to develop our natural resources in a sustainable way into products contributing to National, Regional and global healthcare of humankind. This calls for, among other things, the need for indexing eco and ethno-information of plants, chemistry and biology of their products in such way that information can be analyzed and accessed globally in real time.

Of course the processes involved are not without their challenges. For instance, there is a problem regarding access to active principles. They are often extracted and analyzed only as a single component in time, ignoring daily metabolic flux, seasonal variation in enzyme activities, and the biosynthetic genes which are present, but not fully functional. Development of methodology able to characterize the majority of constituents in an extract without isolation may help in the process of extracts validation and standardization.

While there are important ecological concerns regarding genetically modified crops, they

present economically effective way to bring preventative healthcare to humankind. There are numerous fungi, bacteria and in some cases, algae, symbiotically associated with plants, which are capable of independent biosynthetic production. Investigation of this potential will enhance the production of active agents in a sustainable manner.

Resurgence of Natural Product Chemistry

Natural products, especially secondary metabolites from plants, have been isolated by chemists and used as biologically active pharmacophores. Some recent examples include: amphotericin B (antifungal); cyclosporin A (immunosuppressive); erythromycin (antibiotic); lovastatin (anticholesterolemic); paclitaxel (antitumour); and tacrolimus (immunosuppressive).

However, from the 1990s, there was a shift away from natural product drug discovery. This could be attributed largely to the popularity of combinatorial chemistry, holding the promise of huge chemical diversity and new leads. This looked even more desirable against the perceived challenges in the journey from natural product to orthodox drugs. Challenges such as lack of plant knowledge (as ageing traditional medicine practitioners die and ethnobotanical knowledge is lost); low yield of bioactive compounds; expensive synthesis; and generally long, expensive drug discovery process all contribute to further diminish interest in natural product programmes. In some cases, such as at Abbott Laboratories, natural product programmes were even suspended!

However, as several combinatorial chemistry programmes matured, the gains made have not been as fantastic as expected. For instance, in 2007, only 17 new drug entities were approved, compared to 53 in 1996. Moreover, combinatorial chemistry has been largely successful only in specific drug discovery programmes (such as in the search for HIV protease inhibitors) where main chemical structures with desired activities are already known. Thus combinatorial chemistry has been unable to replace natural products as the primary source of chemical diversity.

In the light of the above, drug discovery has entered a new phase in which, although the modern tools of chemistry and biology (such as robotics, bioinformatics, HTS, biotechnology, molecular biology and combinatorial chemistry) are still being deployed, chemists and pharmacists are turning their attention back to nature. Promising candidates from the renewed search include huperizine A, triptolide, celastrol, capsaicin and curcumin.

Thus as the challenge to find biologically active compounds and develop them into drugs subsists, there is renewed interest in natural products. It is expected that this renewed popularity will continue into the foreseeable future because natural products continue to serve as a veritable source of novel drug leads, which is the inspiration on which the newer technologies find leverage.

The Example of NIPRD

Since 1989 when the National Institute for Pharmaceutical Research and Development (NIPRD) became operational, the vision and mission of the Institute has evolved and expanded in keeping with the global trend on research and development of phytomedicines, pharmaceuticals and biological products. The Institute has therefore been in the forefront of research and development in Nigeria in partnership with other professional key players. The Institute has been able to leverage on alliances forged with both local and international agencies. Notable examples of such agencies include: The United States of

America National Institute of Health (NIH)/ National Institute of Allergy and Infectious Diseases (NIAID); African Network of Drugs and Diagnostics Innovations (ANDI); African Centre of Excellence in Phytomedicine Research and Development (ACEPRD) at the University of Jos; African Institute of Biomedical Science and Technolgy (AiBST).

The contribution of the Chemical Society of Nigeria (CSN) in the promotion of sustainable product development is uniquely recognized, being a major stakeholder in global health matters. Thus there is a need for closer collaboration between NIPRD and CSN towards shaping the chemistry of natural resources into sustainable product development in helping to combat the global health challenge.

Conclusion

Indeed, international efforts and investment in new medicinal agents will require the creation of numerous new alliances. These alliances must work on both local and global level and involve individuals who can set aside their ego for the greater good. Therefore, the alliances should be composed of international agencies, government agencies, pharmaceutical companies, academic institutions, nongovernment organizations, scientific societies and private foundations.

Such collaborations would be expected to yield programs to assist developing countries to potentiate their facilities and enable scientists evaluate natural product-based medicinal agents in a sustainable manner. This would significantly improve global healthcare systems.

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