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Continuing education programme in medicinal chemistry using open and distance learning

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Summary

There has been a considerable increase in demand for trained medicinal chemists in low- and middle-income countries (LMICs) in the last few years. In particular, a confluence of global, regional and local initiatives has created a need for professionals educated in medicinal chemistry in Africa, where hitherto there has been very little opportunity for training in this field. The international programmes now under way, that aim to strengthen the pharmaceutical innovation capacities of LMICs generally and especially to build Africa's capacity for pharmaceutical production and innovation, can only succeed if there is an adequate supply of professionals with high quality training in medicinal chemistry.

Open and distance learning provides a very flexible, cost-effective approach to delivering technical training, continuing education and high quality source materials that can be quickly, efficiently and cheaply up-dated to keep pace with advances in fast-developing field.

A distance training programme has been developed and piloted by one of the world's leading authorities in medicinal chemistry and is being disseminated in on-line and CD rom formats. The target audiences include synthetic chemists and researchers, as well as university teachers and technically trained managers, administrators, regulators, funders and others who are involved in the pharmaceutical innovation cycle and in pharmaceutical production, regulation, supply and monitoring at national level. Medicinal chemistry has a core role to play in building the knowledge capacities of all these professionals to discharge their functions competently.

1. The need for continuing education in medicinal chemistry

1.1 Chemistry for development

Science and technology generally are increasingly seen as important in national and global development, including the achievement of the Millennium Development Goals.[1] The core role of chemistry for development has been emphasized.[2]

Chemistry is a platform science. Through understanding the physical and chemical properties of matter, during the last two centuries chemistry has helped to give humanity an unprecedented degree of mastery over its physical environment. Chemistry interfaces with a range of pure and applied sciences, providing the basis for understanding the atomic and molecular aspects of these disciplines and underpinning the dramatic advances seen in recent decades in such diverse fields as medicine, genetics, biotechnology, materials and energy.

1.2 Medicinal chemistry

Medicinal chemistry encompasses the design and synthesis of compounds that contribute to the prevention and treatment of diseases and the promotion and maintenance of human health. Through structural modifications to adjust the physical, chemical and biological properties of molecules, medicinal chemistry underpins a range of inter-related pharmaceutical sciences which deal with drug

design, discovery and development, the formulation of bioactive compounds into appropriate dosage forms, drug uptake, distribution, metabolism and excretion, toxicology, etc. Improving health and advancing economically are intimately inter-connected[3] and medicinal chemistry makes major contributions to both of these:

- Advances in these fields have contributed enormously to improving life expectancy and the quality of life through the treatment of infectious diseases and metabolic disorders and the control of pain.[4]
- Industrial organic chemistry built on mid-19th century processes for manufacturing dyestuffs. By the 20th century it had expanded to include the synthesis of pharmaceuticals. The pharmaceutical industry employs millions of people and generates global prescription sales well in excess of US$ 600 billion per year.[5,6]

Traditionally, medicinal chemistry has been seen as an advanced science most relevant to high-income countries (HICs) where the major pharmaceutical companies were located. In less economically advanced countries, employment opportunities have often been in quality assurance rather than in fundamental discovery research. However, in the last two decades ***there has been a growing demand for medicinal chemistry in low- and middle-income countries*** (LMICs). Several factors are responsible for this major change:

1. ***The pharmaceutical industry*** has begun to develop very substantially in a number of LMICs, as a result of a several drivers:
    - To maintain global competitiveness, pharmaceutical companies have been shifting both the manufacture of chemicals and the research and development (R&D) of new products to LMICs where salaries and overhead costs are lower.
    - Pharmaceutical sales in LMICs have been a major growth area,[7] creating new markets and incentives for local and regional production.
    - A number of 'innovative developing countries', including Brazil, China and India, have established strong capabilities in pharmaceuticals. In the case of India, this was centred for many years in the generic drugs industry, through which India became the leading supplier of cheap medicines to other LMICs.[8] India is now focusing much attention and investment on developing its own innovative R&D-based pharmaceutical industry. China has also been a major manufacturer of bulk intermediates and products for pharmaceuticals and has a well-established, large internal market for modern as well as traditional medicines. Brazil has been a relatively new entrant to the field, but has already established itself as a major supplier of vaccines for both domestic and international markets and is now investing in expanding its drug development capabilities.
2. The advent of ***HIV/AIDS*** caused a major shift in approach by many LMICs. The anti-retroviral drugs (ARVs) needed for treatment were costing over US$10,000 per year in the 1990s and were unaffordable by LMICs, where most cases of HIV/AIDS were occurring. Pressure by some countries – South Africa, in particular – and threats to implement the flexibilities provided under the Trade-Related Intellectual Property Rights (TRIPs) international trade agreements (including local manufacture without royalty payments to patent holders), led to some pharmaceutical companies lowering their prices. But ARVs remained largely unaffordable in LMICs. In the short term, the humanitarian need to provide lifelong treatment of people living with HIV/AIDS has been met by the establishment of the Global Fund for AIDS, TB and Malaria to purchase drugs for LMICs, and the provision of generic versions of front-line ARVs at less than US$200 per year by Indian manufacturers. Overall, these developments have led to a considerable increase of attention to issues around equitable access to medicines.[9]
3. HIV/AIDS, TB and malaria have received increasing attention, especially since the setting of the MDGs and in particular through the provision of funding by the Bill and Melinda Gates Foundation and the establishment of some international public-private partnerships. However, ***a range of other infectious diseases that occur predominantly or exclusively in LMICs have continued to be relatively neglected***. These include leishmaniasis, trypanosomiasis, schistosomiasis and Guinea Worm. The new Gates Grand Challenges[10] recognise the need for a wider approach encompassing vaccines, drug resistance, etc. The opportunities are increasing for medicinal chemists in LMICs to become involved in research to address these challenges, not only because of the ***development of centres of excellence*** in their own countries (e.g. by the Pan Africa Chemistry Network[11]), but also because of the evolving approach of ***open source development of***

drugs,[12,13,14] which enables scientists in widely distributed locations to collaborate in international research programs.

4. There has been a confluence of issues related to HIV/AIDS in particular and to the ***strategic and economic importance more generally of establishing capabilities for drug manufacture and, ultimately, drug development in LMICs***. A World Health Organization (WHO) Commission on Innovation, Intellectual Property Rights and Public Health[15] was followed by an Inter-Governmental Working Group on Public Health, Innovation and Intellectual Property,[16] which negotiated a Global Strategy and Plan of Action (GSPOA).[17] The eight elements of the GSPOA, designed to promote innovation, build capacity, improve access and mobilize resources, include:
    - prioritizing research and development needs
    - promoting research and development
    - building and improving innovative capacity
    - transfer of technology
    - application and management of intellectual property to contribute to innovation and promote public health
5. The ***growing demand for innovation in pharmaceutical production that is relevant to and conducted by LMICs themselves*** has resulted in the establishment of the African Network on Drugs and Diagnostics Innovation (***ANDI***). This was launched in 2008 by the WHO Special Programme of Research and Training in Tropical Diseases (TDR) and supported by the European Union[18] as a sustainable platform for stimulating and funding R&D innovation in Africa. It was recognized that *"significant, but isolated, product discovery and development activities are ongoing"*, that there are important African initiatives underway in lead discovery and development, particularly for natural products, but no single African country or institution has demonstrated the capacity to move from basic research to the registration and commercialization of a new drug; *"However, consultations with many experts suggest that this can be achieved through a strategic mechanism to support relevant, continent-wide activities in a coordinated and structured manner"*.[19] The ANDI business plan projects spending rising to over US30 million/year by the 6th year of operation.[20] Similar regional networks are envisaged for Asia and Latin America.[18]
6. Initiatives in the last few years by the Organization for Economic Cooperation and Development**,** ***the government of the Netherlands, the African Union and its new Partnership for Africa's Development and the Council on Health Research for Development, in collaboration with Ministers of Science and Technology in Africa, have resulted in a concerted*** action plan to develop Africa's capacity for pharmaceutical manufacturing**.**[21]

1.3 Educational need

The conjunction of global, regional and local factors outlined above has resulted in a major upswing in the need for people with training in medicinal chemistry in many LMICs and especially in Africa. The range of professionals who require an in-depth knowledge of modern approaches to medicinal chemistry includes not only synthetic chemists and researchers actively engaged in the field, but also university teachers and technically trained managers, administrators, regulators, funders and others who are involved in the pharmaceutical innovation cycle and in pharmaceutical production, regulation, supply and monitoring at national level. Medicinal chemistry has a core role to play in building the knowledge capacities of all these professionals to discharge their functions competently.

Globally, relatively few degree courses specialise specifically in medicinal (or pharmaceutical) chemistry, but many university degrees in disciplines such as chemistry, pharmacy and pharmacology include units on medicinal (or pharmaceutical) chemistry at BSc and MSc levels. At least in North America and Europe, medicinal chemistry is often presented to undergraduate students whose career plans are to be health practitioners (pharmacists, physicians, and industrial chemists) so its subject matter is often presented from an applications viewpoint rather than from a fundamental viewpoint. Among LMICs, India[22] is unique in offering more than 500 courses in pharmaceutical chemistry at Masters level. Elsewhere in LMICs, and especially in Africa, few courses are available.

Medicinal chemistry is a dynamic subject drawing it subject matter from a variety of disciplines. The molecules that are prominent in today's medicinal practice were largely unknown even a few years ago and the approaches adopted for drug design are constantly evolving. The evolving nature of the field and the diversity of subjects from which its subject matter are derived places a particular burden on

practitioners who need to be contemporary in their treatment and understanding of the field. Teachers can rarely use the same set of notes more than once. Consequently, even for those who have received a sound education in medicinal chemistry there is a need for continuing education that is up-to-date and readily accessible to and affordable by a wide range of professionals.

2. Open and distance learning and medicinal chemistry

There is a need for the inclusion of modules on medicinal chemistry within existing degree programmes that are accessible to students in LMICs – and especially in Africa, where very few such courses exist at present. Furthermore, many of those requiring training in medicinal chemistry, including a wide range of scientists, legislators and scientifically qualified administrators, are not able to take full-time on-campus degree courses to upgrade their skills.

Open and distance learning (ODL) provides a highly flexible and cost-effective method for bringing high-quality training to all these groups. ODL involves a range of modalities – on-line, with or without support from tutors (which can be synchronous or asynchronous) or off-line via distributed CD roms. It offers a range of potential advantages over conventional, classroom-based education:

- ***Cost-effective:*** Eighty percent of jobs worldwide require technical and vocational skills, yet skills training is 14 times more expensive than general secondary education in Sub-Saharan Africa. The challenge is to provide cost-effective and flexible learning opportunities to large numbers of people[23] and the value and importance of ODL was recognised by UNESCO in its 2009 World Conference on Higher Education.[24] As noted by the Commonwealth of Learning[25] (COL: the only intergovernmental agency that focuses exclusively on using technology to expand the scope and scale of human learning), *"Achieving the MDGs will require a massive expansion of human learning. Traditional methods of education and training cannot address the scope and scale of the task. Technology has already revolutionised other areas of human life and the world must now harness it to learning and teaching."*
- ***Flexible:*** Remoteness from the centres of active research makes it difficult to interact with a significant cadre of active and like-minded practitioners. Traditional self-learning addresses this problem but often leaves the practitioner somewhat unsure of the strength and fundamental validity of conclusions drawn. In both on-line and off-line modalities, ODL courseware can be designed to be interactive, so that the learner is able to self-test, review, seek further details or explanations of unfamiliar terms and proceed at a self-determined pace and at times and in locations that are convenient for study.
- ***Suitable for training and up-dating of trainers:*** Currently, many educators in the field of medicinal chemistry have had their fundamental education in organic chemistry with an emphasis on synthesis. Consequently, they may be under-qualified in topics drawing upon cellular biology and physiology and unfamiliar with the latest, cutting-edge advances in theory and practice. To some extent these problems can be addressed by sabbatical experiences and attendance at international meetings but these are not continuously available to scientists and educators in LMIC and are comparatively very costly. Moreover, scientific meetings in the field of medicinal chemistry deal largely with specialized topics of current interest but are rarely comprehensive and systematic in coverage. The field of medicinal chemistry is rich in text books. However, these are expensive and quickly become out-dated. ODL – as web material or CDs (especially relevant in sub-Saharan Africa, where computer access and connect time can be costly) – can be rapidly, frequently and inexpensively up-dated to keep abreast of the latest advances.

Apart from the initiative by the Professor Lester Mitscher of the University of Kansas, Chair of the IOCD Working Group in Medicinal Chemistry, there have hitherto been few efforts to create ODL material for training in medicinal chemistry. Examples include work in HICs on course optimization[26,27] and specific teaching topics for inclusion in pharmacy and pharmaceutical science degree programs[28,29,30]

Within Africa, the Kwame Nkrumah University of Science and Technology offers open learning resources in health sciences[31] and the University of South Africa (the world's largest provider of distance education materials) has a course in medicinal plants within a biochemistry and physiology program,[32] but no high-level courses in medicinal chemistry are currently available in conventional or

ODL formats. The African Virtual University (AVU)[33] was created to increase access to higher education and training through the innovative use of information and communications technologies and aims to become the leading pan-African open, distance and e-learning network, The growing strength of the AVU, which has received support from a range of international development banks and foundations and has partnerships with institutions throughout the world, provides a clear prospect for ensuring the widespread delivery of ODL programmes across the continent.[34]

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