



Chemistry and Healthcare Innovation in Brazil

2011 is the International Year of Chemistry (IYoC), which is being celebrated by many countries throughout the world, including Brazil. Last month, conferences were held in Campinas and Sao Paulo that included four Nobel Prize Laureates in chemistry and international experts from the chemical science community. Such world class conferences attest to Brazil's growing scientific standing, which reflects the quality of chemistry teaching and research and also the scale of investment in future world class talent. A particularly exciting initiative is the *Ciências sem Fronteiras* Program¹ that was recently announced in Brasilia and which is already being put into practice. Thousands of studentships will be available for young Brazilian scientists to study abroad and there is also the intention to attract senior external researchers to seed laboratories in Brazil.

While funding bodies in Brazil have carefully considered future employment for skilled scientists, the 2011 IYoC provides a timely opportunity to speculate on prospects for chemical sciences in particular. Chemistry provides outstanding education and training at graduate and undergraduate levels and many chemists achieve successful careers in such diverse fields as finance and politics, for example. However, what are the prospects for the majority who wish to pursue science as a career? Academic positions are finite, while the industrial R&D base in Brazil may not have capacity to employ chemists on the scale envisaged. I will focus on prospects for chemists within the biomedical environment where they can play pivotal roles in translating biological discoveries into innovative drugs that meet the medical needs of the 21st Century.

The UK has a positive balance of payments of some \$7bn/year with respect to pharmaceutical imports/exports whereas corresponding figures for Brazil show a significant deficit that is growing. Generic capacity is some way below China or India, while basic pharmaceutical R&D has not enjoyed the same level of investment as other countries. However, the external environment is changing rapidly with major Pharma companies closing research sites and slashing R&D budgets. For example, at the time of merger, the combined annual research spending for Pfizer and Wyeth was over \$11bn, but future investment will shrink to \$6-7bn/year. While the economic and personal consequences of downsizing are obvious, few opinion leaders seem to have realised that the flow of new drugs will slow to a trickle that will not meet medical needs over the next decades. A radical new paradigm for drug discovery

and development is urgently required that recognises the risks and time scales involved, but also the need for a sustained return on investment.

Brazil has a unique opportunity to drive such an exciting initiative given strong commitment to the chemical excellence that translates new biology into much needed medicines. Novel small molecules will be essential to delineate the relevance of complex biological pathways to human disease, since proper target validation will have a tremendous benefit on driving laboratory research to clinical success. For the foreseeable future, synthetic molecules will still provide the cost effective oral medicines that are the bedrock of healthcare systems, despite the clinical and commercial success of some biological therapies. Chemistry space must also be significantly expanded to access the numerous disease targets that are beyond conventional drug templates. It is sobering to realise that the human genome comprises some 23,000 genes but only 266 have been modulated by current drugs and a wealth of biological targets await innovative chemistry intervention.

Drug discovery is most effectively practised when top quality scientists from key disciplines such as biology, chemistry and metabolism are integrated into multidisciplinary teams with common objectives and a hunger for new medicines. Of course, some components can be contracted out, but there is no substitute for co-localisation of core teams where informal scientific challenge and debate are naturally part of daily research routines. The lack of integration of biology and chemistry is well illustrated by the pioneering research of Silva and Ferreira in Riberao Preto on snake venoms which led to the identification of angiotensin converting enzyme (ACE), but US medicinal chemists translated their discovery into ACE inhibitors and A2 antagonists that achieved outstanding clinical and commercial success.²

One approach for Brazil would be to embed experienced industrial scientists within biomedical centres by establishing new chairs of medicinal chemistry with supportive infra-structure to facilitate translation of basic biology into new medicines. This could provide a step towards creating a network of Therapeutic Centres of Excellence where multidisciplinary teams work together on diseases of high medical need, and where education and training of future drug discoverers can be delivered. The value of experienced pharmaceutical scientists should not be underestimated and recent downsizing of UK Pharma may provide a unique opportunity for medicinal chemists

with proven track records to contribute to the development of world class drug discovery capability in Brazil. *Ciências sem Fronteiras* program also offers pathways for students to train abroad and for external scientists to seed relevant research projects in Brazil. The successful 70s CNPq-NAS program could provide an additional model involving experienced scientists from the UK and other countries. In addition to an outstanding record for pharmaceutical innovation, the UK scientific community includes world class centres such as the Structural Genomics Consortium, Cambridge Crystallographic Data Base and the European Laboratory for Bioinformatics as well as numerous academic groups with relevant synthesis and drug discovery expertise.

Consideration of therapeutic areas for focus is a complex issue, but neglected diseases often come to mind. However, traditional scourges such as Chagas disease and schistosomiasis will surely retreat as hygiene and social conditions continue to improve, while malaria is relatively well served through significant investment by the Gates Foundation in the Medicines for Malaria Venture.³ TB is also receiving due attention, but progress has been limited by a paucity of targets and the difficulty for drug molecules to penetrate the mycobacterium. On the other hand, the three leading causes of death across the world are still cardiovascular, cerebrovascular and chronic obstructive pulmonary diseases, while obesity and diabetes are reaching epidemic proportions. However, Pharma is turning away from some of these serious conditions even though cost effective new drugs are urgently required, while ageing populations will make additional demands for proper treatment for Alzheimer's and Parkinson's diseases and other neurological disorders. Innovative drugs that address such high priority medical needs will bring significant personal, economic and social benefits.

Drug discovery and development pose significant challenges, but the demise of traditional Pharma demands a radical new paradigm if we are to improve life expectancy for our most vulnerable communities and to enhance quality of life all round. This editorial offers a personal perspective on the current situation and future options and suggests that synergy between Brazil's ambitions and UK academic and industrial experience may offer a unique, and mutually beneficial, way forward.

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References

1. The "*Ciência sem Fronteiras*" program is an initiative of the Brazilian government sponsored by the National Council for Scientific and Technological Development (CNPq). It is an agency linked to the Ministry of Science and Technology (MCT), dedicated to the promotion of scientific and technological research and to the formation of human resources for research in the country. Available at: <http://www.cienciasemfronteiras.cnpq.br/web/guest/opograma> .
2. Ferreira, S. H.; Rocha e Silva, M.; *Experientia* **1965**, *21*, 347. DOI: 10.1007/BF02144709. <http://ukpmc.ac.uk/abstract/MED/5870517>. With the permission of author Ferreira, S. H., the original article "Potentiation of bradykinin and eledoisin by BPF (bradykinin potentiating factor) from *Bothrops jararaca* venom (PMID:5870517)" is available under request.
3. The Medicines for Malaria Venture - MMV, a not-for-profit public-private partnership, was established as a foundation in Switzerland in 1999. Available at: <http://www.mmv.org/> .