



editorial



Walter Rangel Campos



Pedro Pina Catarino



Heinrich C. Hoppe

New frontiers in ethnomedicine: exploring the Angolan

indigenous pharmacopeia for novel antimalarial drugs

These are exciting times for science in Angola. After decades of war and monolithic thinking the tide is finally turning. The oil-rich nation has greatly benefited from the sharp increase in Brent crude oil prices and production over the past 15 years, effectively providing the financial means for many to go abroad, largely to access a better education. Portugal, the former colonial power was the destination of most, followed by Brazil, South Africa and more recently the UK and the USA. There also seems to be a renewed interest toward education by seasoned professionals as many pursue advanced degrees at the later stages of their careers.

The increased political stability coupled with double-digit economic growth and high remuneration packages in the face of a global financial crisis prompted many young and dynamic graduates to return home. It also made Angola a very attractive destination of choice for many largely Portuguese-proficient professionals fleeing the harsh financial realities and bleak career prospects in their home countries. The brain gain has been significant, especially in less mainstream fields like Laboratory Sciences. There is still, however, a palpable shortage of talented and experienced M.Sc. and Ph.D. graduates to lead meaningful research projects.

Further compounding this shortage of human capital is the limited number of research laboratories, although visible efforts are being undertaken to overcome this hurdle. Nonetheless, for the first time in recent history we have the most important resource needed to turn the tide and launch research science in the country: scientists.

A sign that the tide is turning is the recent sharp increase in peer-reviewed publications coming from Angola. Although the contribution from Angolan scientists and institutions is (with very few exceptions) small and often limited to sample collection and preparation, they are steps in the right direction. It gets people interested in research science and helps to attract much-needed political and financial support to recruit talented graduates and equip our labs. This is vital if we want to start doing real and relevant research directed at providing answers to some of our most pressing public health issues.

One of our most unrelenting public health emergencies is malaria. The parasite is holoendemic in the country and the leading cause of morbidity and mortality, accounting for up to 60% of all hospital outpatient visits, admissions and deaths [1,2]. There were 3.68 million confirmed cases in 2010 alone out of a total population estimated at under 20 million. Studies indicate that *Plasmodium falciparum* is the main culprit, responsible for over 90% of all infections. However several cases of patients simultaneously infected with all four different species of the parasite found in the country, have been observed (Fernanda Dias Monteiro *et al.*, unpublished). Further magnifying this problem is the increased incidence of infection with drug-resistant strains reported by clinicians countrywide. These indicators suggest that we need to resort to every available strategy from vector control to host behavior change and pharmacological intervention to combat a disease that effectively holds the country at ransom.

Currently, the overwhelming majority of rural Angolans resort primarily to traditional medicinal remedies and practices to combat the disease. The limited availability of drugs is partially responsible, yet there is also a strong cultural belief in the healing properties of the indigenous pharmacopeia. We therefore contend that there must be some medicinal remedies that are of therapeutic significance beyond their placebo effect to symptomatic patients infected with the parasite.

A bilateral research-science oriented agreement was recently made between the Republic of Angola and the Republic of South Africa to promote collaboration, by co-funding feasible projects. The Department of Health Science and Technology of the Angolan-based University, Instituto Superior Politécnico de Benguela (ISPB) joined forces with the Department of Biochemistry, Microbiology and Biotechnology of the University of Rhodes in South Africa to take advantage of this funding opportunity. Together we have submitted a proposal to investigate the antimalarial properties of traditional remedies used in Angolan folklore medicine.

ISPB scientists working with very limited resources have already published findings on the bactericidal and antiparasitic properties of *Cymbopogon citratus* (lemon grass) [3,4]. Currently they are cataloging and compiling an herbarium of Southern Angolan medicinal plants with the help of the Council of Traditional Healers in Angola.

Rhodes University has a long history of research excellence and as such the necessary technical skills and human resources to foster skill transfer to the ISPB. By tapping into Rhode's expertise we aim to introduce the following techniques at the ISPB: mammalian tissue culture; *in vitro* antimalaria susceptibility assays and HPLC fractionation. This will be accomplished through a technical exchange program and validation of the results obtained at the ISPB by Rhodes University. We will also attempt to identify the

chemical composition and structure of the most promising hits, although the cost and logistical challenges of implementing mass spectrometry and NMR spectroscopy at the ISPB place them beyond the scope of this project at the current time.

This work aims to be part of a national validation algorithm to incorporate traditional remedies in standard therapy protocols. Remedies with a favorable *in vitro* profile showing robust antimalaria activity and high Therapeutic Index will be standardized and fast tracked into small-scale clinical trials to provide further evidence of their effectiveness. This practice may be questionable in modern-day medicine but the historical empirical evidence of its effectiveness is unquestionable. Furthermore, in a region where even the cheapest drugs are not accessible to most, resorting to more readily available traditional remedies, even if of limited effectiveness, will save lives and help to alleviate poverty.

The likelihood of finding novel antimalaria agents, albeit remote, cannot be excluded. Plants used in traditional medicine have provided the backbone of contemporary antimalaria therapy [5]. Quinine, derived from the tree bark of *Cinchona calisaya* native to the tropical Andes forests of South America, was the predecessor of both the 4-aminoquinolines and the 8-aminoquinolines. Artemisinin, first isolated from the sweet wormwood *Artemisia annua* and native to temperate Asia, is a powerful drug that rapidly decreases blood stage parasites. Nowadays, artemisinin derivatives are used in combination therapy where their short plasma half-life and rapid action are combined with a second drug with a longer half-life to complete the clearance of the parasitemia and forestall the emergence of drug-resistant strains. This approach buoyed antimalaria therapy in an arena of widespread resistance to historically used drug classes.

Out of the three most populated regions in the world affected by the parasite, that is, South America, South-East Asia and Sub-Saharan African, only the latter has failed to yield a novel antimalarial therapeutic agent. This region currently is, and probably always was, the most severely affected of all and as such a significant number of the indigenous remedies target this disease. This combined with the fact that few reported attempts have ever been made to explore the antimalaria properties of its traditional pharmacopeia makes this region an obvious target for these efforts.

High throughput screening of synthetic libraries and rational drug design has yielded significant numbers of hit compounds [6], but not yet added to our clinical armamentarium of antimalaria drugs. This is most probably because of the significant effort and investment required to progress drugs through preclinical and clinical development, contrasted with a limited return on investment for big pharma for obvious economic, social and political reasons. Faced with this unfortunate lack of interest, every effort, in the public and nonprofit sector, however small, becomes more significant.

Research is not a luxury, much less the sole responsibility of developed nations. It is therefore imperative that collaborative efforts and funding initiatives such as ours become more mainstream so that we can pool our limited resources toward confronting common challenges.

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Walter Rangel Campos*

Pedro Pina Catarino

Department of Health Science and Technology,
Instituto Superior Politécnico de Benguela (ISPB),
Av Governador Moutinho T-125, Benguela, Angola

Heinrich C. Hoppe

Department of Biochemistry, Microbiology & Biotechnology,
Rhodes University, PO Box 94, Grahamstown 6140, South Africa

*Corresponding author

email: wrcampos2003@yahoo.com (W. Rangel Campos)