



Research review paper

Plant-made therapeutics: An emerging platform in South Africa[☆]

Edward P. Rybicki^{a,*}, Rachel Chikwamba^b, Muffy Koch^c, James I. Rhodes^d, Jan-Hendrik Groenewald^d

^a Institute of Infectious Disease & Molecular Medicine and Dept of Molecular & Cell Biology, University of Cape Town, Private Bag X3, Rondebosch, 7701, South Africa

^b Plant Biotechnology Research Group, Biosciences Division, Council for Scientific and Industrial Research, PO Box 395, Pretoria 0001, South Africa

^c 4502 Donnelly Drive, RR#4, Merrickville, ON, Canada K0G 1N0

^d Biosafety South Africa, 105 Wentworth, Somerset Links Office Park, De Beers Avenue, Somerset West 7130, South Africa

ARTICLE INFO

Available online 3 August 2011

Keywords:

Plant-made therapeutics
Biopharming
Biosafety
Transgenic plants
Vaccines
South Africa

ABSTRACT

The field of plant-made therapeutics in South Africa is well established in the form of exploitation of the country's considerable natural plant diversity, both in the use of native plants in traditional herbal medicines over many centuries, and in the more modern extraction of pharmacologically-active compounds from plants, including those known to traditional healers. In recent years, this has been added to by the use of plants for the stable or transient expression of pharmaceutically-important compounds, largely protein-based biologics and vaccines. South Africa has a well-developed plant biotechnology community, as well as a comprehensive legislative framework for the regulation of the exploitation of local botanic resources, and of genetically-modified organisms. The review explores the investigation of both conventional and recombinant plants for pharmaceutical use in South Africa, as well as describing the relevant legislative and regulatory frameworks. Potential opportunities for national projects, as well as factors limiting biopharming in South Africa are discussed.

© 2011 Published by Elsevier Inc.

Contents

1.	Background	450
1.1.	Exploitation of traditional phytomedicines	450
2.	Recombinant molecules from plants	451
2.1.	Background	451
2.2.	Initiatives in plant based protein expression	451
2.3.	Biopharming at the University of Cape Town	451
2.4.	Biopharming at the Council for Scientific and Industrial Research	452
2.5.	Biopharming at the University of Pretoria	453
2.6.	Biopharming at Stellenbosch University	453
3.	Biosafety considerations for biotherapeutics-producing plants	453
3.1.	Background	453
3.2.	Risk analysis for TPPs	454
3.3.	Characteristics and risks of different production platforms	454
3.4.	General approaches to manage these risks	455
3.5.	Regulatory overview for PMT organisms and products in South Africa	455
3.5.1.	Current regulatory environment	455
3.5.2.	Overview of current South African biosafety regulations	455
4.	The future of biopharming in South Africa	456
4.1.	Opportunities	456
4.2.	Challenges	457

[☆] For: Biotechnology Advances (Elsevier) Special Issue on Production of Foreign Proteins in Plant Cells: Challenges and Opportunities.

* Corresponding author. Tel.: +27 21 6503265.

E-mail address: ed.rybicki@gmail.com (E.P. Rybicki).

4.2.1. Funding	457
4.2.2. Infrastructure	457
4.2.3. Entrepreneurship and commercial product development	457
5. Concluding remarks	457
References	457

1. Background

South Africa has a long history of exploiting its plant diversity in the form of herbal medicines—which is possibly as old as humankind itself, given current speculation as to the origins of modern humans (Henn et al., 2011). Probably ever since there were people in the land, native plants have been used by traditional healers. European and other settlers in the 1600s subsequently simply adopted much of the native pharmacopoeia, given the huge distances and unreliable delivery schedules of their familiar medicines. The advent of modern pharmacology, however, pushed many of the South African plant medicines into the background, as purified and synthesised pharmaceuticals largely took the place of dried herbs and herbal extracts, which again became the stock in trade only of traditional healers. This led to a parallel market in medicines and therapeutics, with synthetic and purified, formulated products being prescribed by university-trained medical personnel to higher income patients, and the lower income and unemployed rural groups accessing the traditional products.

However, there has recently been a major resurgence in interest in indigenous phytomedicines, with a number of international and local initiatives actively exploring the country's botanical resources, with an emphasis on working with traditional healers to exploit known medicinal plants, as well as screening unique southern African plants more generally for pharmacologically active compounds. A significant number of novel products are in development, some are in clinical trial, and a few are in the market already.

A more modern avenue for plant-derived therapeutics—namely, the use of plants as vehicles to make recombinant proteins and other molecules for use as therapeutics—is far less well explored in South Africa, and is in fact only really being investigated by two laboratories in the two main research hubs of the country. However, plant biotechnology in the wider sense is a thriving enterprise, with applications ranging from traditional and marker-assisted plant breeding, through micropropagation to cell culture and genetic manipulation for improved or novel traits such as virus resistance, metabolic pathway engineering and drought tolerance (see Rybicki, 1999; Thomson, 2008).

The regulatory environment for medicines in general, including plant-produced candidates, is well-developed, and legislation and procedures are modelled on best practise examples from the developed world. This is true too for genetically-modified plants: South Africa is presently one of the world leaders in terms of the proportion of major crops such as maize and cotton that are GM (James, 2010).

This review will therefore explore some aspects of the naturally-produced therapeutics pipeline in South Africa, as well as the use of plants for recombinant molecule production in more detail. The regulatory environment in South Africa, as well as biosafety considerations, will also be explored in detail. Important potential developments in biopharming in South Africa will also be discussed.

1.1. Exploitation of traditional phytomedicines

South Africa has some 30000 species of higher plants, comprising about 10% of the world total. Around 80% of these are endemic species (Goldblatt, 1978). As could be expected from such diversity, more than 3000 species are used for herbal medicines, for a market encompassing some 27 million people from a total population of

47 million (Light et al., 2005). It is not surprising, therefore, that pharmaceutical exploitation of this treasure chest has been going on for some time—and in fact, has been documented since the early days in South Africa of the Vereenigde Oostindische Compagnie (VOC; Dutch East India Company) (Scott and Hewett, 2008). South African reporting on ethnopharmacology has increased significantly in recent years (Light et al., 2005), and there are presently several local institutes and research groups dedicated to studying medicinal plants.

The University of Cape Town's Division of Pharmacology houses the South African Traditional Medicines Research Group (SATMERG), whose brief is to develop medicines particularly for the treatment of malaria, tuberculosis (TB) and diabetes mellitus. The group has published a recent review on investigating local flora for antimalarials (Pillay et al., 2008), and investigation of local and imported plants for antidiabetics (van de Venter et al., 2008). Highly active antimalarial compounds have been isolated from a variety of plants, including a diterpenoid from *Hyptis suaveolens* (Chukwujekwu et al., 2005), and sesquiterpene lactones from *Oncosiphon piluliferum* (Pillay et al., 2007)—however, potential problems were also identified with antagonistic effects between the traditional medicinal plant *Aspilia africana* and artemisinin, which is widely used for treatment of chloroquine-resistant *T. falciparum* (Waako et al., 2005). For antidiabetics, *Brachylaena discolor* was best of 11 species tested, with all plant parts giving high activity scores and negligible toxicity in stimulation of glucose utilisation in an *in vitro* model system.

The Council for Scientific and Industrial Research (CSIR) has an active and ongoing programme of high-throughput screening of a large library of extracts of indigenous plants for biological activity. The Bioprospecting Group of the Biosciences Division aims to identify potential new drugs from local biodiversity and indigenous knowledge based on medicinal plant use, and has worked closely with the UCT group on both antimalarials and diabetes drugs. Their focus is to research and validate traditional medicines to facilitate discovery of early-stage drug leads and further development of candidates through to proof of concept. Their emphasis is on the development of herbal treatments for HIV/Aids, malaria and TB, as these are seen as Africa's major infectious disease killer (Mamotte et al., 2010), as well as anticancer agents. In a major recent collaborative study with the US National Cancer Institute, 7500 plant extracts were screened for anticancer activity *in vitro* against human breast, renal and melanoma human cell lines, and the 6% that showed moderate activity were further screened against 60 human cancer cell lines (Fouche et al., 2008). The family *Asteraceae*, known to be rich in sesquiterpene lactones, provided the largest number of hits. The authors noted that 68% of the plant species which provided hits are reported to be used as traditional medicines—which could indicate that any medicinal use of plants is a useful guide for selection of plants for anticancer screening. A very recent investigation of *Siphonochilus aethiopicus*, anecdotally known to be effective against asthma, sinusitis, colds and flu, showed that extracts have anti-inflammatory and anti-allergic properties *in vitro* and *in vivo* in a mouse model (Fouche et al., 2011).

Possibly the longest-lasting systematic investigation of the medical potential of extracts of South African plants, which has been going on for more than 30 years, is at what is now the University of KwaZulu-Natal at Pietermaritzburg: there J (“Hannes”) van Staden and colleagues and collaborators have been working through a long list of native plants with medicinal history in order to catalogue activities ranging from antibacterial to antihelminthic and

Download English Version:

<https://daneshyari.com/en/article/14383>

Download Persian Version:

<https://daneshyari.com/article/14383>

[Daneshyari.com](https://daneshyari.com)