Phytomedicines

From translation of IKS to

Innovation for the Bioeconomy

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Innovation Partnerships in Science
Leading Phytomedicines

Profile

• 200 000 Traditional Healers; Over 20 000 MD’s

• Sangoma’s are spiritualists

• Inyanga’s are herbalists

• 3000 medicinal plants

• 300 medicinal plants traded: R4billion revenue

• 30 million patients

Applications

• HIV-AIDS, TB, Malaria

• Cancer, Pain, Depression

• Diabetes, Obesity, Heart Disease

• Inflammation and infertility
SENSE-MAKING

20% : Pharmaceutical Medicine

80% : Traditional Medicine
MARKET TRENDS

- Blockbuster drugs are diminishing.
- Only 21 NME were approved by FDA in 2008.
- Greater public expectations of drug safety
  - Merck’s Vioxx and Astrazeneca’s Ximelagatran
- Natural and Traditional Products may offer better routes to the discovery, development and delivery of new medicines.
- Plant-derived drugs such as Paclitaxel, Vincristine, Vinblastine, Artemisinin and Camptothecin account for an estimated $65 billion in sales.
- Phytomedicine Adaptogens.
- Phytomedicine Immunogens.
- Phytomedicine Adjuvants.
- Phytomedicine Multi-complexes.
- Phytomedicine Synergistics.

*Drug Discovery Today: Vol 14, August 2009*
PLANTS DEVELOPMENT PIPELINE PHYTOMEDICINES

From 2000-2010: R100m INVESTMENT NEEDED > 2010: R900m

BASIC SCIENCE

- Plant Selection
- Monographs
- Extraction
- Screening
- Fractions
- ID Actives
  - Alkaloids
  - Terpenes
  - Flavonoids
  - Glycosides
  - Tannins
- Character
- Analogs

DEVELOPMENT

- Animal Models
- Formulation
- PK ADME
- Mechanisms
- M-GMP
- Standardize

VALIDATION OF EFFICACY AND SAFETY

- GCP
- Phase 1
- Phase 2
- Phase 3
- Phase 4
- Patenting
- Registration

PHARMA AGRI BUSINESS

- Public, Private Partners

HEALTH CARE

- Health Policy and Management
- Healer-Doctor Training
- Facilitating Monitoring Access
- Surveillance

Establishment and completion of technology platform
Drug Discovery and Development Process

Expensive, time consuming, numerous bottlenecks

Reverse Pharmacology

Economical, efficient, less bottlenecks with potential registration of phytotherapy and phytomedicine

Translational Validation Model
Molecular Diversity
- within boundaries of drug-like properties
- greater number of chiral centres
- increased steric complexity
- greater molecular rigidity
- tend to follow Lipinski ‘rule of 5’

Privileged Structures
Selected by evolutionary pressures to interact with biological targets:
- binding affinities for receptor systems
- biochemical specificity

Advanced Technologies
- HTS
- Medicinal Chemistry
- Genomics and Proteomics
- Structural & Systems Biology
- Bioinformatics

Phytomedicines
DRUGS OF THE FUTURE
Amazing new medicines will be based on DNA
Find out how they will change YOUR LIFE
Tulbaghia alliacea and Cancer

Artemisia afra and TB

Lessertia frutescens and HIV
Leading Phytomedicines Methods

- HPLC
- 1D and 2D NMR
- LC-MS
- X-Ray Chrystallography
- Firefly Luciferase Bioluminescence
- ELISA
- Fluorescence Microscopy
**Tulbaghia alliacea Phytomedicine**

Marasmicin

- Marasmicin detected in *Tulbaghia alliacea*.
- Significant antifungal activity against 5 species:
  - *Candida albicans*
  - *Candida glabrata*
  - *Candida crusei*
  - *Cryptococcus neoformans*
- Specific *Tulbaghia alliacea* fractions powerfully induce apoptosis in leukemia cells.
- **Current Research:** Focused on optimizing a more potent *Tulbaghia alliacea* product.


**Artemisia afra Phytomedicine**

- **Artemisinin** was not detected in *Artemisia afra*.
- **DCM Fraction C8** inhibited mycobacterial replication
  - IC₅₀ = 1.9 µg/ml (M. aurum)
  - IC₅₀ = 2.0 µg/ml (M. tuberculosis)
  - MIC = 10.0 µg/ml
- C8 mostly sequiterpene lactones (Arsubin +Artemin).
- Aqueous extracts modulate pulmonary inflammation in TB-challenged mice.
- **Current research**: Focused on developing an aerosol *Artemisia afra* phytomedicine product.

*Tuberculosis* (2009): S33-S40
Sutherlandia Phytomedicine


Phytomedicine Project

- Phase II 100 HIV patient clinical trial.
- CD4>350; Viral Load >1000 mRNA copies/ml; 6 months.
- **Hypothesis:** Sutherlandia will delay the onset of AIDS.
- **Future Research:** Development of a better formulation of the Sutherlandia product.
- **Funding:** Secured: 2010-2012.
Hoodia gordonii
Phytomedicine

- Taken by San for centuries to still hunger and quench thirst, whilst crossing the desert.

- CSIR scientists ID P57, patented the drug and licensed it to the company Phytopharm (UK).

- Phytopharm (UK), licensed Unilever (Dutch) the right to develop and market the first herbal diet drug, with revenues of >$1billion per year.

- CSIR has acquired the right to now completely commercialize P57 through further research, development and innovation partnerships with several stakeholders.
*Pelargonium sidoides*

Phytomedicine

Umckaloabo® registered as a drug:

Germany : 2005

Switzerland : 2007

Indications: Bronchitis and Sinusitis