

## Translational Medicine

- It is hypothesised that successful Translational Medicine will reduce “late” failure rates in phase 3 clinical studies.
- It will serve to accelerate drug discovery and lead to new therapies for patients.
- It will enhance disease research and drug development

## BIOMARKERS

- *Does the compound get to the site of action? Absorption*
- *Does the compound cause its intended pharmacological/functional effects Efficacy*
- *Does the compound have beneficial effects on disease or clinical pathophysiology? Efficiency*
- *What is the therapeutic window (i.e. how safe is the drug)? Safety*
- *How do sources of variability in drug response in target population affect efficacy and safety?*

### *Pharmacogenomics*

## Translational medicine: science or wishful thinking?

Martin Wehling

Clinical Pharmacology Mannheim, University of Heidelberg, Mannheim, Germany

*Journal of Translational Medicine* 2008, 6:31

- Despite increased efforts and investments into R&D, the output of novel medicines has been declining dramatically over the past years.
- "Translational medicine" as a fashionable term is being increasingly used to describe the wish of biomedical researchers to ultimately help patients.
- Improvement of translation is thought to become a remedy as one of the reasons for this widening gap between input and output is the **difficult transition between preclinical ("basic") and clinical stages** in the R&D process.

## Translational medicine: science or wishful thinking? (cont)

Martin Wehling

Clinical Pharmacology Mannheim, University of Heidelberg, Mannheim, Germany

- Animal experiments, test tube analyses and early human trials **do simply not reflect** the patient situation well enough to reliably predict efficacy and safety of a novel compound or device.
- This goal, however, can only be achieved if the translational processes are **scientifically backed up** by robust methods some of which still need to be developed.
- This mainly relates to biomarker development and **predictivity assessment**, biostatistical methods, smart and **accelerated early** human study designs and decision algorithms among other features.
- **It is therefore claimed that a new science needs to be developed called 'translational science in medicine'.**

## All Is Not Well in the World of Translational Research

• Ellis F. Unger, MD

FDA, Silver Spring, Maryland

Editor

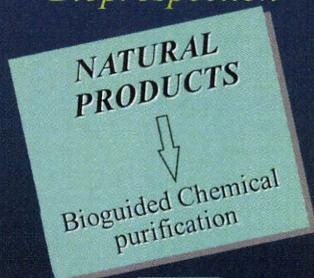
[ellis.unger@fda.hhs.gov](mailto:ellis.unger@fda.hhs.gov)

*Journal of the American College of Cardiology* Vol. 50, No. 8, 2007

It is not unusual for novel treatment strategies to fail in clinical trials, despite highly encouraging results in preclinical proof-of-concept studies. Typically, such "failures of translation" are blamed on the poor predictiveness of animal models. Often, however, the poor predictiveness of today's preclinical proof-of-concept studies is related not to limitations of the models but to investigator bias and a lack of scientific rigor. The resulting false-positive results only serve to mislead the field and impede medical progress. With the resurgence of translational research, it is useful to examine some of the problems that plague these studies and consider their solutions. With thoughtful planning, execution, and analysis, it is possible to generate reliable and predictive data from preclinical proof-of-concept studies. Through the application of the aforementioned principles, false-positive results will be less likely to misguide investigators, and the field will be advanced more rapidly.

## We Want a NEW MEDICINE

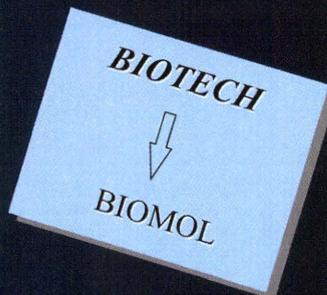
Bioprospection



Organic Synthesis



Biotechnology



Presumed Activity  
(folk medicine)

Theoretical Activity  
(genome indication)

## EFFICACY and SAFETY

## Why to invest in a new medicine?

### 1 . INNOVATION

- ✓ Safer medicine
- ✓ Higher specificity
- ✓ Improved Bioavailability
- ✓ New pharmacological effect

### 2. SOCIO-ECONOMICAL

- ✓ Low price
- ✓ Accessible
- ✓ Competitive

### 3. Better "COMPLIANCE"



## BIOTROP

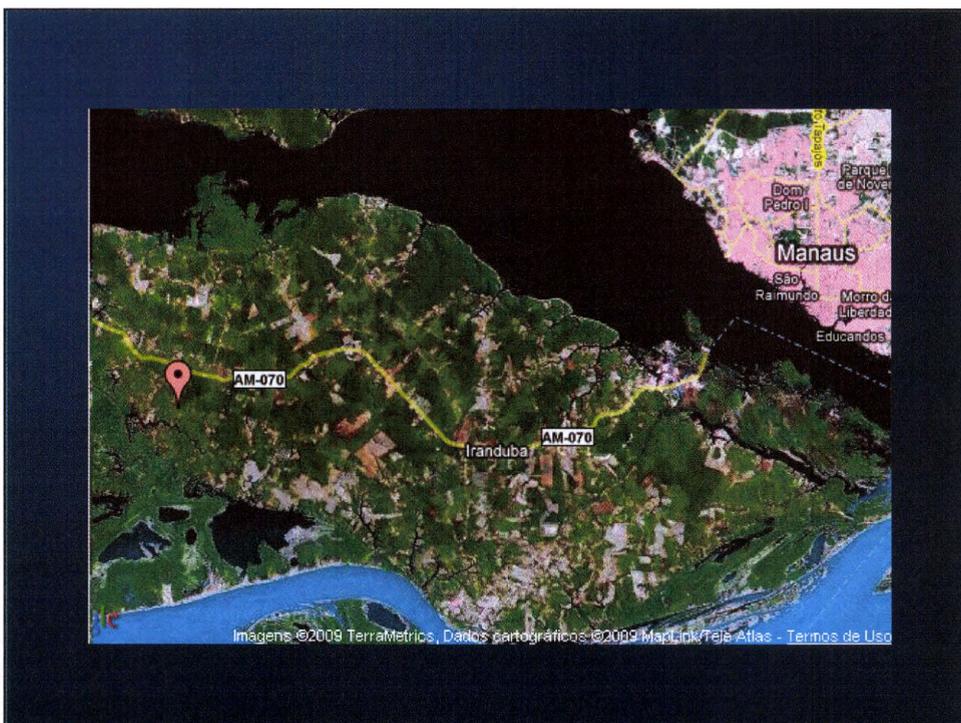
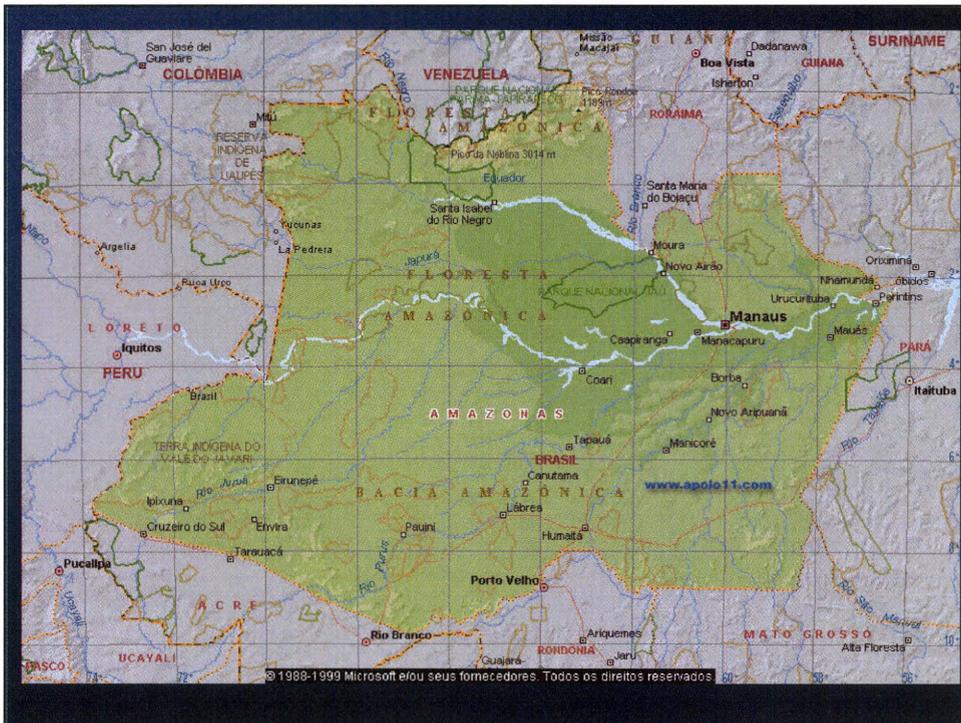
A SCIENTIFIC PROJECT TO BE  
DEVELOPED IN THE AMAZON REGION

INNOVATIVE AND  
SOCIOECONOMICALLY DRIVEN

## MALARIA

ENDEMIC

*P. vivax*



## Medicinal Plant

*Ampelozizyphus amazonicus*

*Quassia amara*

*Geissospermum laeve*

*Cecropia glazioui*

*Virola surinamensis*

## Extraction

Water (tea)

ethanol

(fermented/distilled)

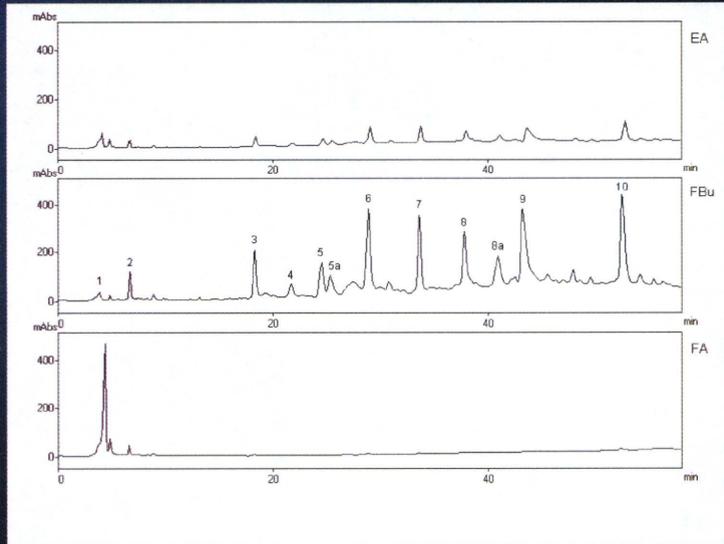
## PURIFICATION OF FBut in HPLC

FBut

HPLC prep  
column C18  
gradiente water/ACN 10 to 20%  
45 min, 20% to 60 min

F1	F2	F3	F4	F5	F6	F7	F8	F8a	F9	F10
1.0%	1.5%	4.0%	1.7%	6.1%	9.2%	6.5%	7.0%	3.2%	14.2%	8.8%

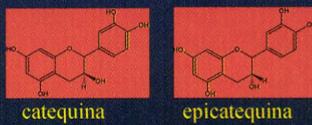
*C. glazioui*



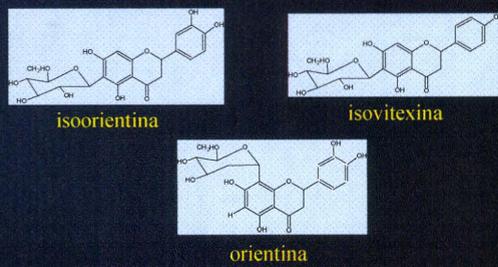
IDENTIFICAÇÃO DOS COMPOSTOS ISOLADOS DE *C. glazioui* Sneth

- 13C - RNM
- 1H - RNM
- LC - MS

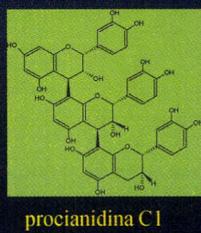
FLAVANÓIS



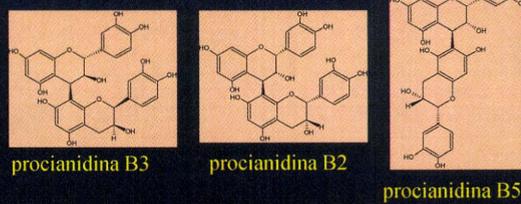
FLAVONÓIDES



PROCIANIDINA TRÍMERO



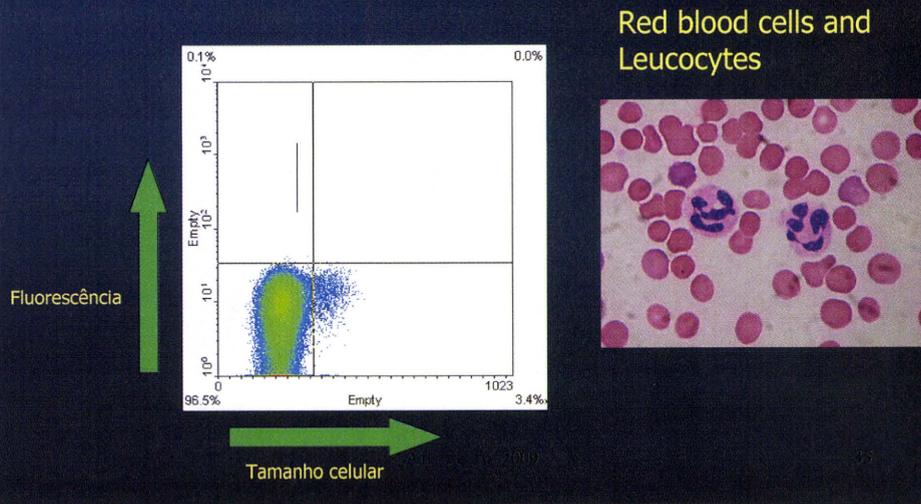
PROCIANIDINAS DÍMERO



## Citômetro de Fluxo (Flow cytometer)

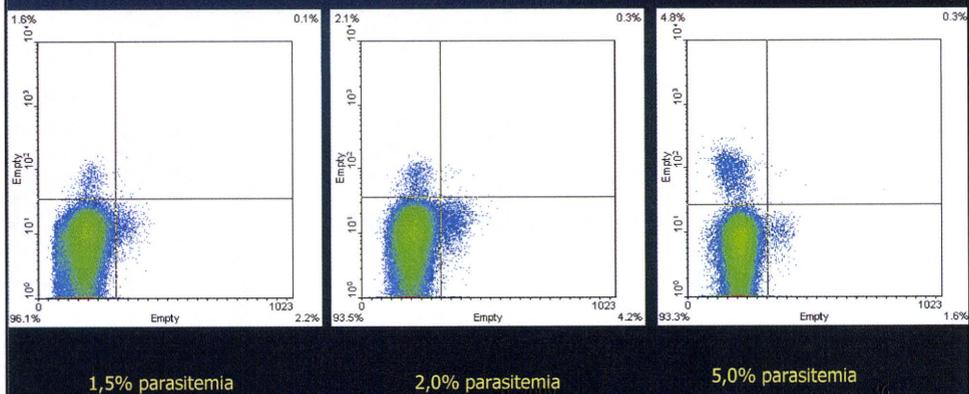
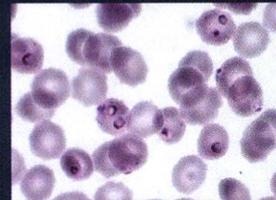
Blood samples + Acridine Orange [1 $\mu$ M]

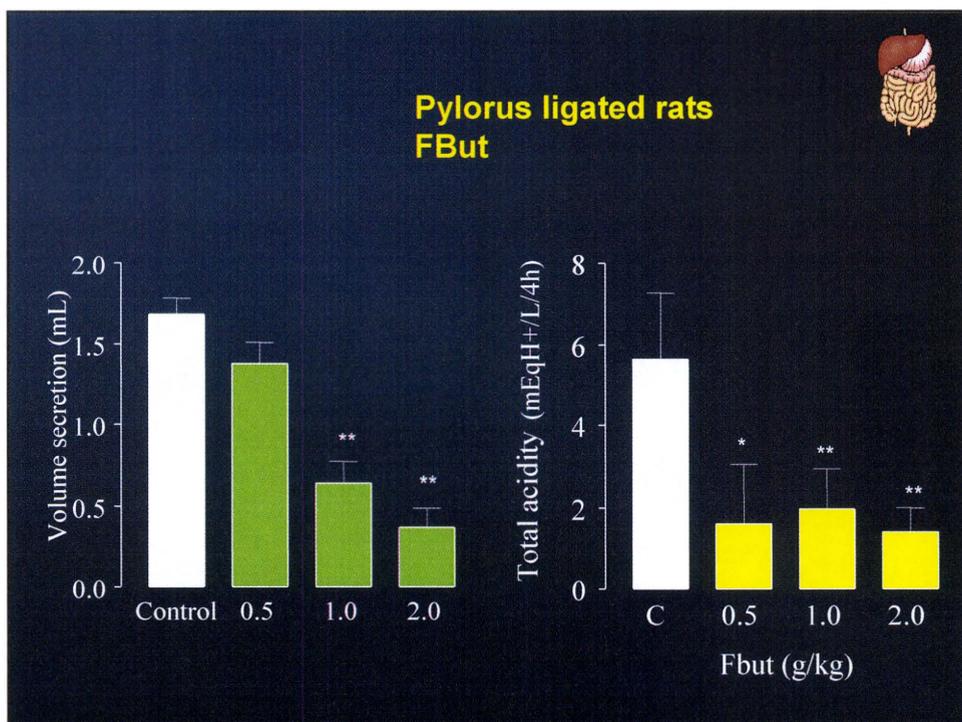
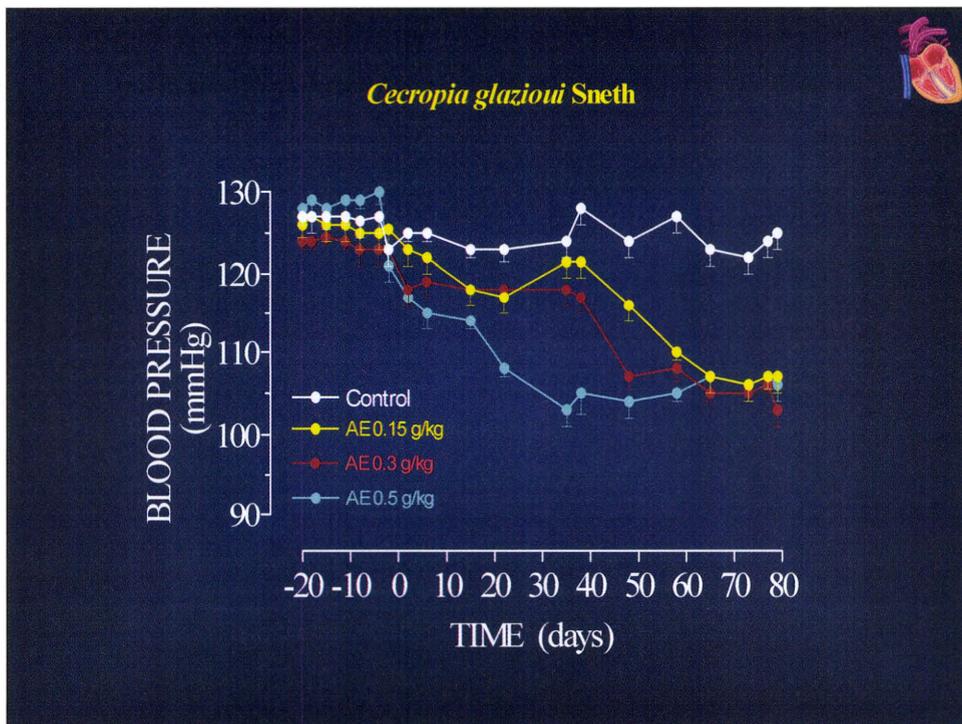
Program analysis: WinMDI 2.8



## Citômetro de Fluxo

Amostra Sangue Parasitado





NORTH OX Med &

**COS**

*Natural Hits for diverse biological targets  
The Amazonian CRD for pharmacology and safety evaluation*

*challenging the rain forest  
for*

*Pharma and skin protection hits*

*Phytoproducts development*

International Symposium on Standardization of Traditional  
Medicine. 17-18 November 2010. Toyama. Japan

## Herbal Medicine Projects in Latin America and Peru

MBA Pharmacist Diana Flores  
Scientific University of South  
Latinpharma /GTZ Project Consultant

Toyama, November 18, 2010



## The world-wide market for botanical products

US \$228 billion in the food industry  
Botanical supplements 12 billion.  
Botanical functional foods 15 billion.

US \$850 billion in the pharmaceutical  
industry  
Drugs from botanical precursors 31  
billion

US \$27  
billion

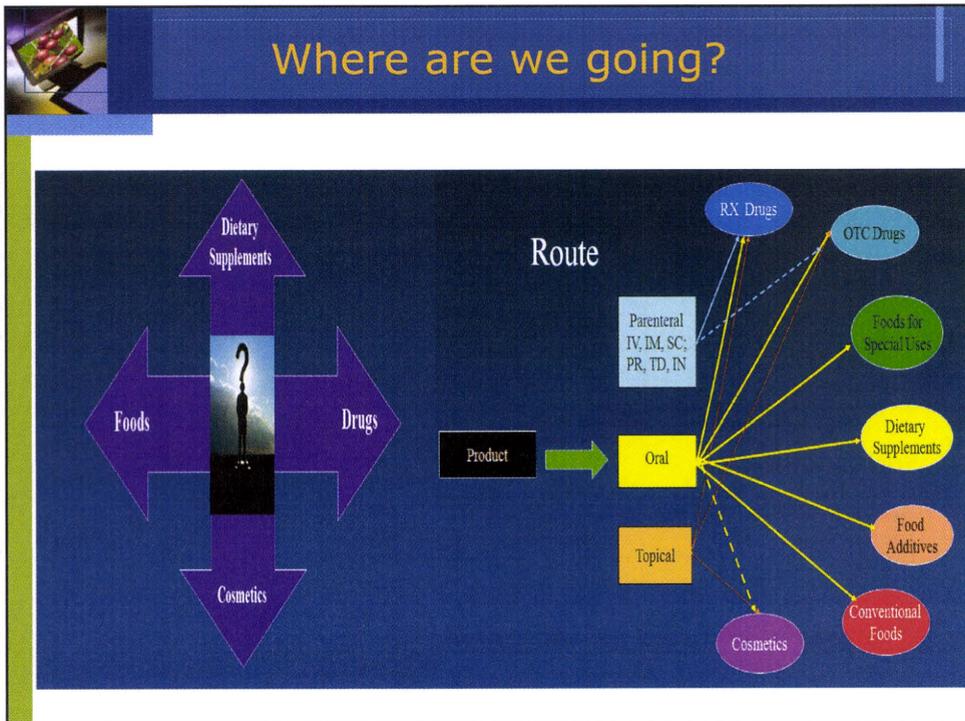
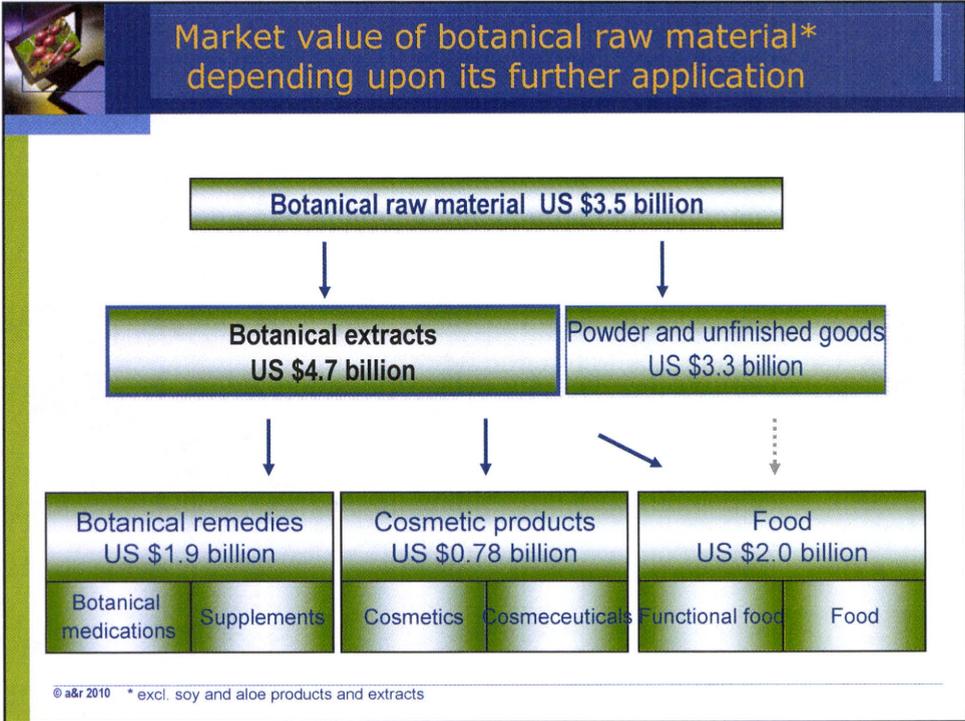
US \$86 billion  
in botanical  
products

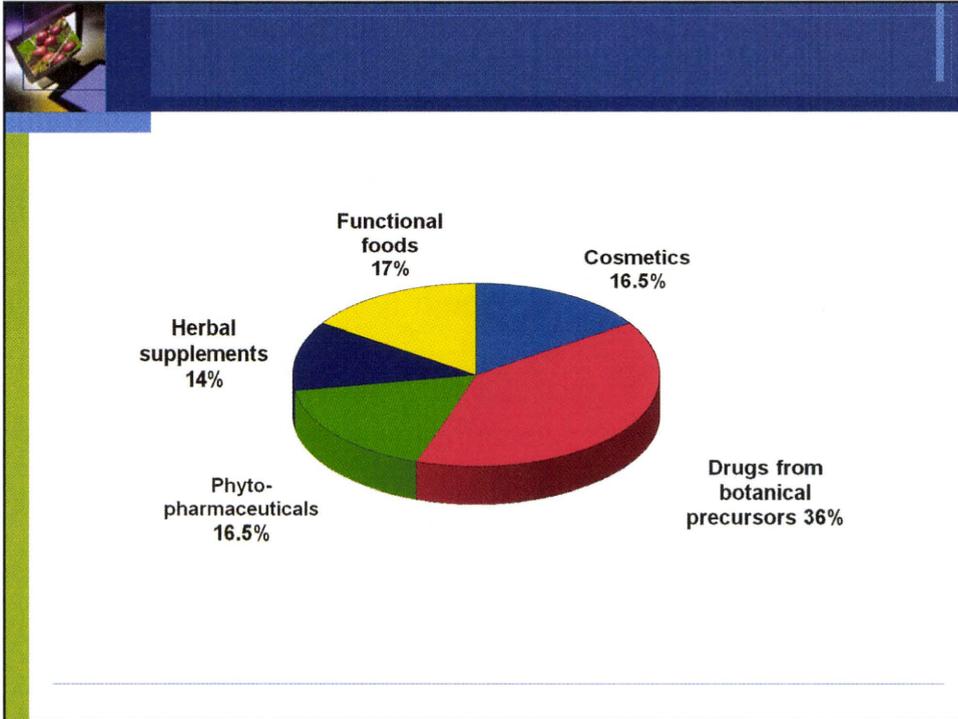
US \$45  
billion

**WHO 's KEY FACTS**  
Herbal medicines are the  
most lucrative form of  
traditional, medicine,  
generating billions of  
dollars in revenue.

US \$14 billion

US \$270 billion in the cosmetics  
industry  
Botanical beauty and skin care  
products 14 billion





- ## WHO'S KEY FACTS
- ❖ More than 100 countries have regulations for herbal medicines.
  - ❖ Counterfeit, poor quality, or adulterated herbal products in international markets are serious patient safety threats.

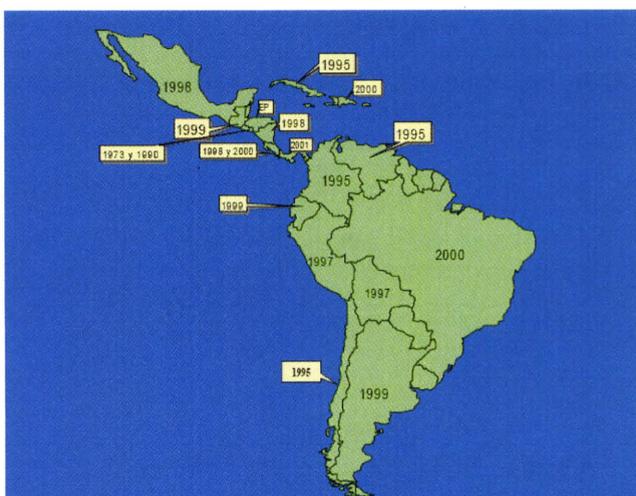


## WHO's KEY FACTS

- ❖ According to WHO, from 192 surveyed countries only 53 has some form of regulation for traditional medicine and among these only 18% include it in their national pharmacopeia (2002).
- ❖ Traditional medicine is the only one resource that poor and isolated population have and it is an alternative for the rest of people

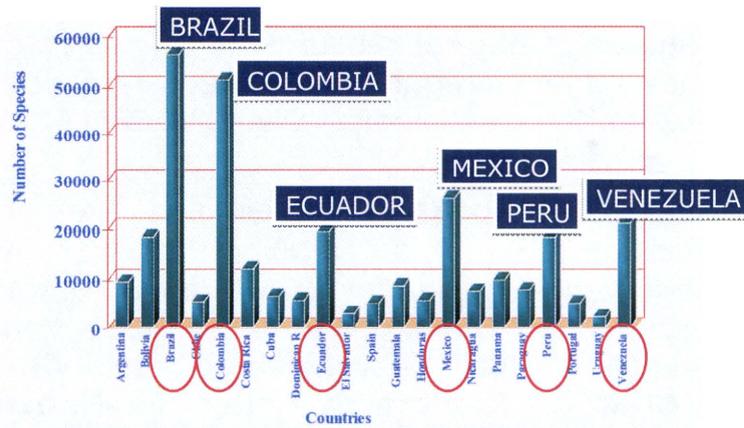


## Issue of regulations



Source: Gupta M, Garcia M, Cáceres A; ICS-UNIDO Training Course, Panama 2005

## Number of Species at Iberoamerican countries



Source: Total and endemic species data: World Conservation Monitoring Center (WCMC) Species Database, unpublished data (WCMC, Cambridge, U.K., December 1999). Threatened species of plants and world total for plants: WCMC species Database, unpublished data (WCMC, Cambridge, U.K., December 1999). These figures are generated from the dataset underlying the data published in K.S. Wilbur and H. J. Gilbert (eds.), 1999 IUCN Red List of Threatened Plants (IUCN, Gland, Switzerland and Cambridge, U.K., 1998) compiled by WCMC. Number of species per 10,000 square kilometers calculated by the World Resources Institute using land area figures from the Food and Agriculture Organization of the United Nations (FAO), FAOSTAT On-Line Statistical Service (FAO, Rome, 1999), available online at: <http://www.fao.org>. (a) Higher Plants include flowering plants, conifers and cycads, and ferns-alleles. (b) Values are standardized using a species-area curve: WORLD RESOURCES 2000-2001. (c) Russell A. Mittermeier, Patricio Robles Gil y Cristina Goetack, MEGADIVERSIDAD CEMEX, México, 1998.

## Herbal Medicines

- ❖ The Convention on Biological Diversity was inspired by the world community's growing commitment to **sustainable development**. It represents a dramatic step forward in the conservation of biological diversity, the sustainable use of its components, and the fair and **equitable sharing of benefits** arising from the use of genetic resources.
- ❖ WHO: "Guidelines for the Assessment of Herbal Medicines" (1991). The objective is to define basic criteria for the **evaluation of quality, safety and efficacy of herbal medicines** as well as elements for packing and labeling in order to assist national regulatory authorities.



## Herbal Medicines

- ❖ The use of natural resources involving traditional knowledge is regulated by item j) article 8 of Convention on Biological Diversity CBD (1992).
- ❖ At the Andean Region level, it is mentioned at Decision 391 and Decision 486 of Andean Community of Nations (CAN) about a Common Regimen on Industrial Property. Latin American countries have laws that establish the **Protection Regime of Collective Knowledge of Indigenous Populations** Linked to Biological Diversity (2002).

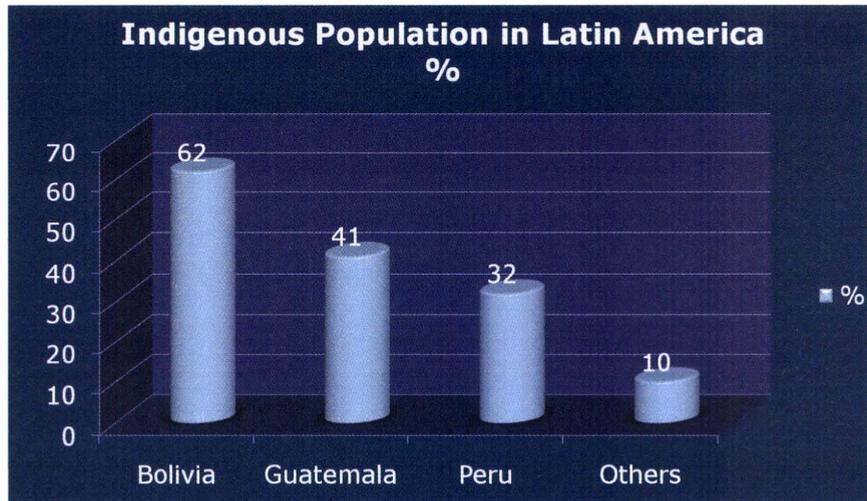


## Herbal Medicines

- ❖ As noted by the World Health Organization, it is critical to incorporate them into **primary health care strategies and ensuring that traditional medicines** and therapeutic elements of recognized utility are further researched for further pharmacological and clinic uses.
- ❖ **Aproximately 25% of worldwide biological diversity is concentrated at andean countries: Bolivia, Colombia, Ecuador, Peru and Venezuela.** In Peruvian case, this biodiversity is located specially at andean and amazon regions where high poverty levels are reported. That biodiversity represents potential development for major rural population.



## Indigenous Population: Percentage of total population



## Indigenous Population

Population range	Countries
4.6 to 8.5 Million	Peru, Mexico, Bolivia and Guatemala
0.5 to 1 Million	Colombia, Ecuador, Brazil, Chile and Venezuela
Less than 0.5 Million	Nicaragua, Honduras, Argentina, El Salvador, Panama, Paraguay, Costa Rica and Uruguay

Source UN, 2000 Census

According to UN, indigenous population at Latin America is greater than 30 Million people (2000 Census)



## Some active compounds obtained from Latin America region herbal medicines

- ❖ Psychotria ipecacuanha: emetine 1817
- ❖ Cinchona spp. : quinine 1820
- ❖ Erythroxylum coca : cocaine 1860
- ❖ Peumus boldus: boldine 1872
- ❖ Pilocarpus spp. : pilocarpine 1875
- ❖ Lonchocarpus nicou :rotenone 1895
- ❖ Gossypium spp. :gossypol 1937
- ❖ Carica papaya :papaine 1937
- ❖ Ficus antihelmintica :ficin 1938
- ❖ Stevia spp. :stevioside 1930



**INBio**  
Instituto Nacional  
de Biodiversidad

## INBio-Costa Rica

Company: Lisan S.A.

LDL: Costa Rica University

Activity control test: Costa Rica & Hospital Docente Clínico Quirúrgico

Joaquín Albarrán Domínguez-Cuba

Conservation of forest "bouganvillas", Women Association "El Abanico"



*Quassia amara*



*Justicia pectoralis*

PLANT/PART: *Quassia amara*, wood

REPORTED USES: used as a tonic (Coee *et al*, 1996)

BIOLOGICAL ACTIVITIES: Antiulcer activity (Tada *et al*, 1991)

CHEMICAL COMPOSITION: Bitter substances, sec-triterpene type; canthine alkaloids (Barbetti *et al*, 1990).

REFERENCES: Coee, F.G, Anderson, G.I. 1996. *Econ bot.*, 50 (1): 71-107

11451 plant species  
500 medicinal plants  
103 are comercializ.



## International Trade South – South & South - North

- ❖ We have to promote projects that involve latin american countries in order to develop herbal medicines value chain.



## BioTrade

- ❖ BioTrade Initiative (UNCTAD), jointly with national, regional and international partners, has supported the development of biodiversity-based sectors in developing countries, **particularly those businesses and local communities that depend on biodiversity for their living.**
  - ❖ Biotrade provides tools for the country's **sustainable development and conservation of native biodiversity.** The primary links of value chains are developed mainly in rural areas associated with people in extreme poverty and located in fragile ecosystems.
-

# BIOTRADE

BioTrade refers to those activities of collection, production, transformation, and commercialization of goods and services derived from native biodiversity under the criteria of environmental, social and economic sustainability.

## Principles

1. Conservation of biodiversity
2. Sustainable use of biodiversity
3. Fair and equitable sharing of benefits derived from the use of biodiversity
4. Socio-economic sustainability
5. Compliance with national and international regulations
6. Respect for the rights of actors involved in BioTrade activities
7. Clarity about land tenure, use and access to natural resources and knowledge

Value Chain Approach

Adaptive Management Approach

Ecosystem Approach



# Biotrade network

Activities are implemented by national, regional and international partners that foster BioTrade, its Principles and Criteria

Established a platform of national, regional and international public and private organizations working for the conservation & sustainable use of biodiversity, and a fair and equitable distribution of benefits

## Under development:

Costa Rica,  
Indonesia, Paraguay,  
Vietnam

## Latin America

- Bolivia
- Brazil
- Colombia
- Ecuador
- Peru
- Venezuela
- Guyana, Surinam

## Africa

- Botswana
- Malawi
- Namibia
- Mozambique
- South Africa
- Uganda
- Swaziland
- Zambia
- Zimbabwe

