

Medicine Challenges for the XXI Century and Forceful Use of Medicinal Plants

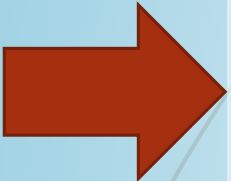
Cusco - September 16th to 22nd - 2018

Prof. Maurizio Grandi, PhD., M.

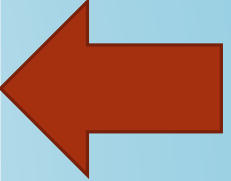
La Torre – Torino Italy

What is **HEALTH**?

- According to the World Health Organization (WHO), in **1948** **Health** was defined as:



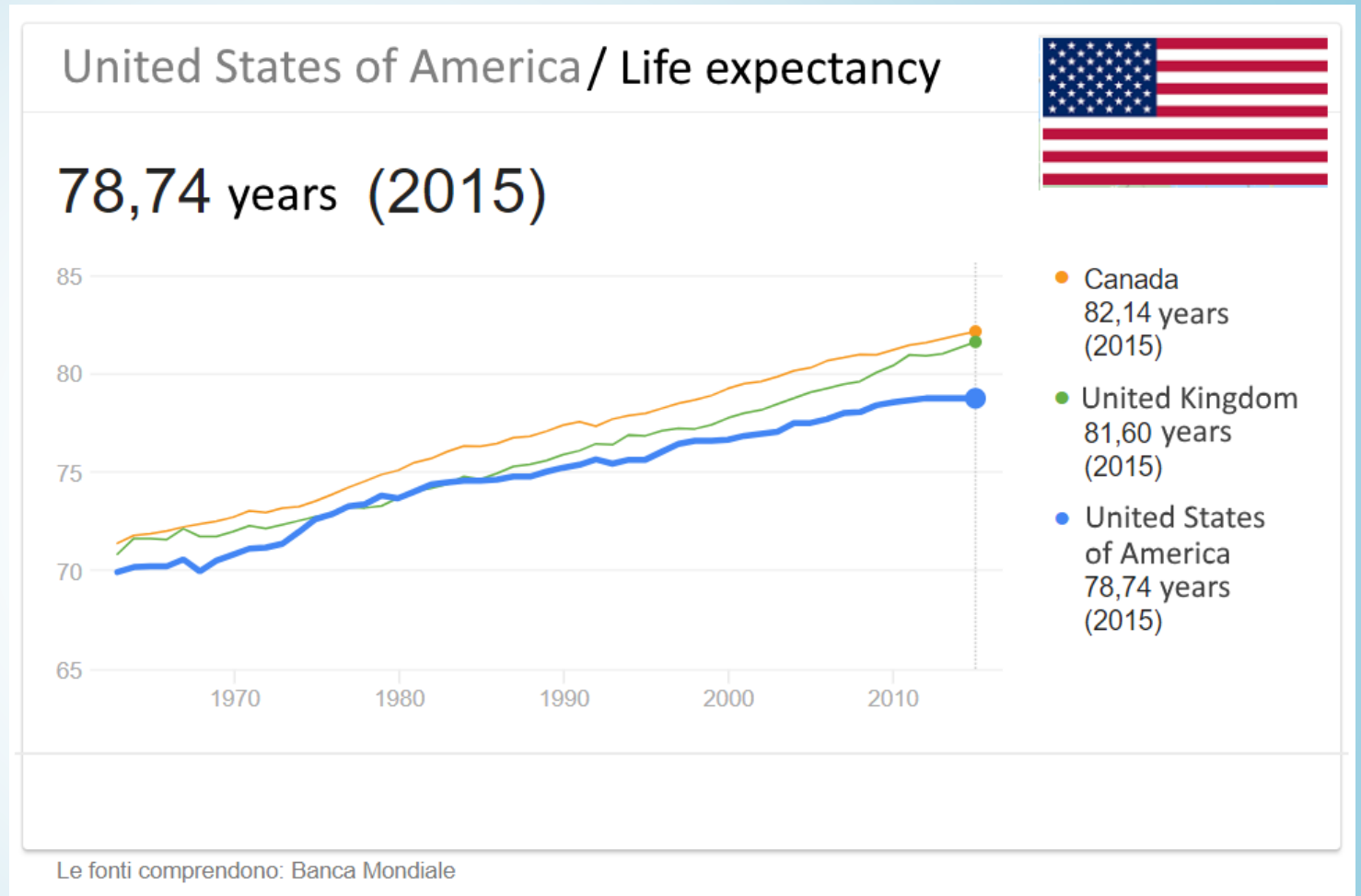
“A state of complete physical, mental, psychological, emotional and social well-being”.



- This attitude has led to unsustainable pharmaceutical costs in industrialized countries and has raised ethical issues.
- It has caused an incredible amount of **over-medication**.
- The number of people who end up in the hospital each year in America following adverse reactions is over 2.2 million:
 - about 20 million unnecessary antibiotics are prescribed every year.
 - 7.5 million are people who undergo unnecessary medical and surgical procedures.
 - Almost 9 million people are hospitalized unnecessarily.

Life Expectancy

- In the United States, **health costs** per citizen are **four times higher** than in Greece or Chile.
- Yet the average life expectancy in America is **two years lower** than that of Greece and Chile.



There is no direct correlation between how much is spent in medical treatment and life expectancy.

Opioid drugs in the U.S.A.

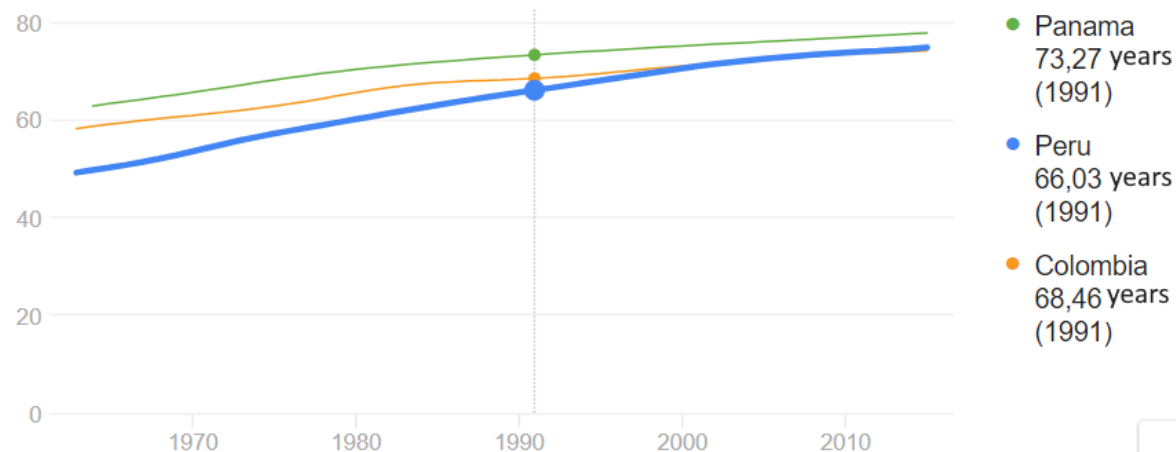
- Life expectancy in the United States has decrease for two years in a row due to the crisis caused by the spread of **opioid drugs** and related drugs in recent years.

Center for Disease Prevention and Control (CDC)

- In the United States the abuse of opioid drugs has become a problem especially during the years of the **economic crisis** in the poorest areas of the country, when many people did not have money to cure themselves and became **dependent** on **pain medication** with high concentration of opiates.
- Several such drugs have become illegal and people ended up obtaining them illegally or replacing them with **heroin**, a relatively inexpensive and distant drug relative to opioid drugs.
- In the United States, heroin overdose deaths increased by **533%** from 2002 to 2016, from 2,089 to 13,219.

Peru / life expectancy

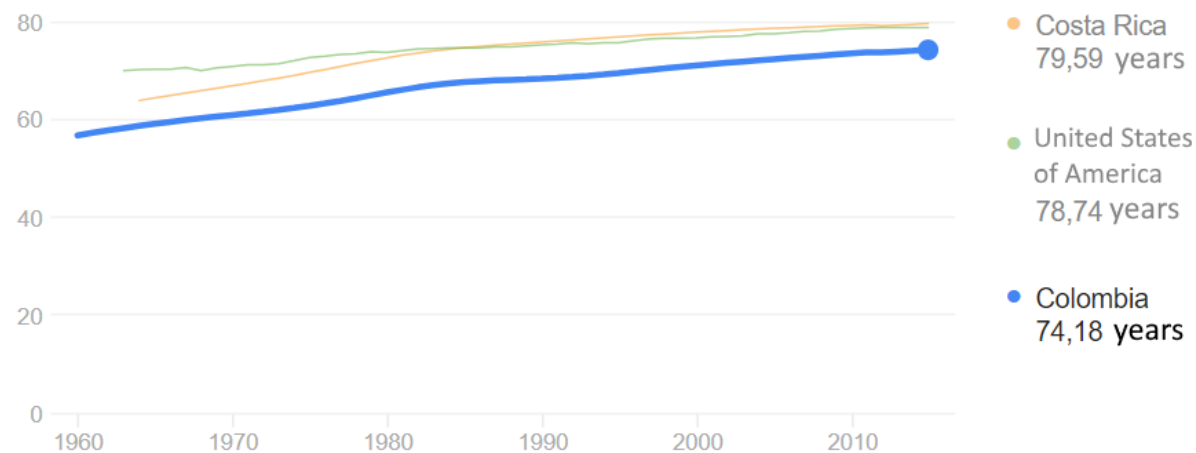
74,78 years (2015)



Average life expectancy Peru and Colombia

Colombia / life expectancy

74,18 years (2015)



Coca




“No es soroche, es la emoción de estar tan cerca del cielo”







- The indigenous peoples know how to effectively cope with the effects of high altitude.
- **Coca** is the best natural medicine to combat altitude sickness.
- It was even considered sacred because of its curative powers and is still used in the same way now as it was in the time of the Incas.
- It contains iron, vitamins A, B, B2 and calcium, among other nutrients.
- Coca makes it easier for the bloodstream to absorb oxygen, suppresses hunger, combat fatigue, headaches and can ease the stomach.
- Chewing leaves (which can be *bitter*) or drinking coca tea (mate) is very common.
- ***How do we use the coca leaves in the western world?***

Legenda





Rete fissa del radar di controllo a terra

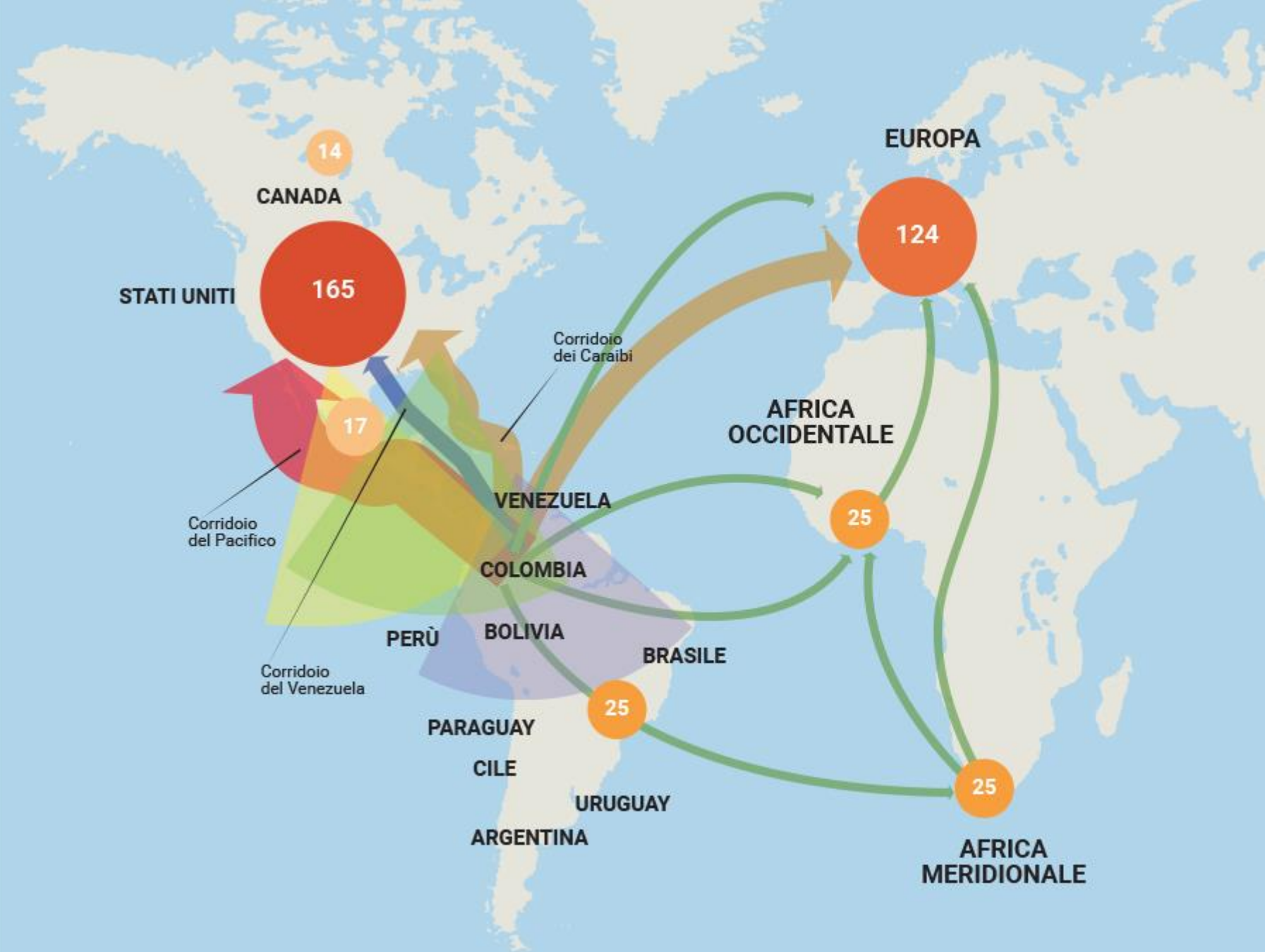
-  Caraibi 2
-  Amazzonia
-  Caraibi 1

Traffico di cocaina

-  140 tonnellate
-  60 tonnellate
-  15 tonnellate
-  6 tonnellate

Consumo di cocaina

-  160 tonnellate
-  120 tonnellate
-  20 tonnellate
-  10 tonnellate



A new definition of **HEALTH**

- Now there is a new definition of HEALTH, presented in 2011, but very few people are aware of it.



“The ability to adapt and manage oneself in the face of social, physical and emotional challenges”.



- The new definition could lead to a **more rational use** of resources with positive outcomes on people's health.
- “Health is a human right, nobody should be sick or die because of poverty, or because they can not access the health services they need”

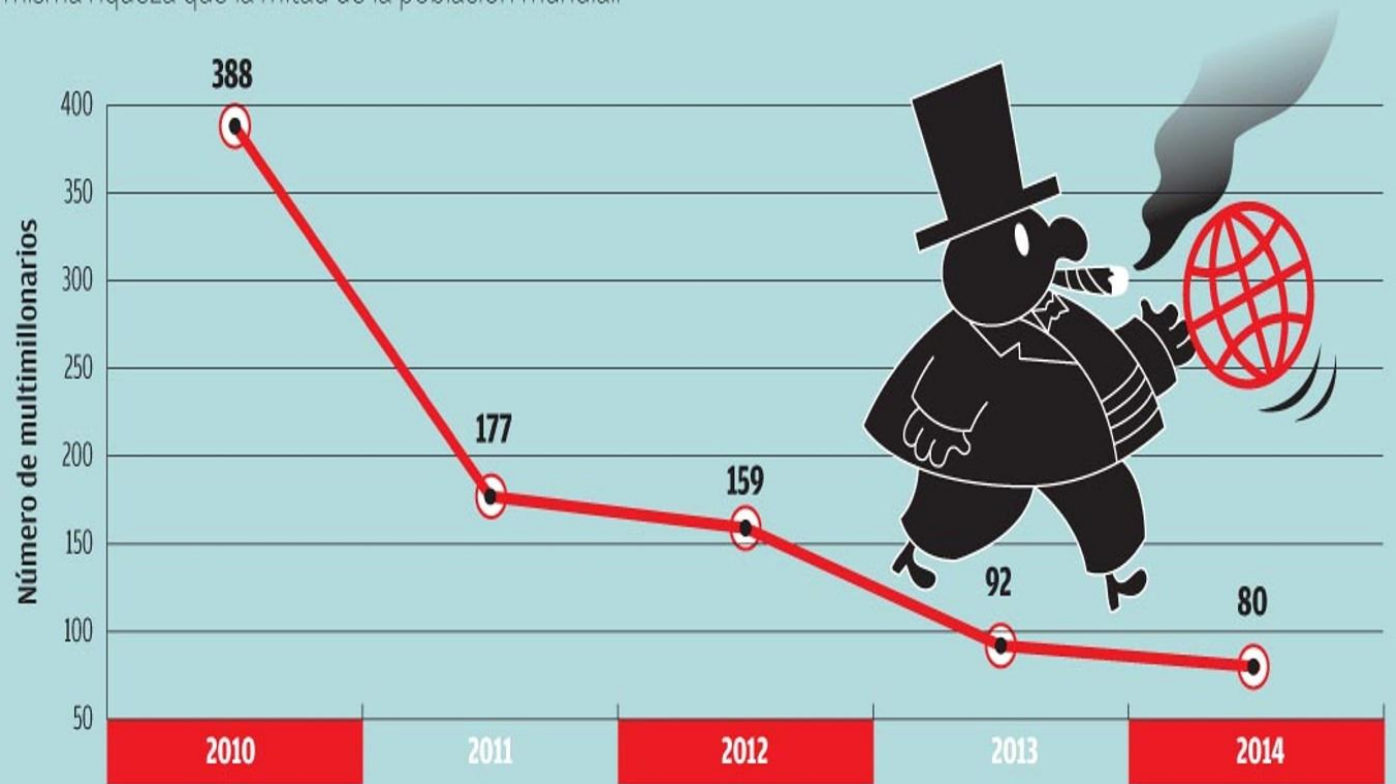
WHO director, the Ethiopian Tedros Adhanom Ghebreyesus

Is **HEALTH** a right or just a cost?

- The 64 [2016] richest people in the world possess half the wealth of the planet.
- In some countries, up to 70% of health costs are paid directly by the citizen.
- The **WHO** claims that "about 100 million people fall into a state of 'extreme poverty' (under \$1.90 a day) due to health care costs"
- 5.6 million children under five died last year → 5,000 deaths per day. 1/3 of which due to preventable and treatable diseases: **pneumonia, diarrhea** and **malaria**.

MÁS RIQUEZA EN MENOS MANOS

➤ Según Oxfam, cada vez menos gente controla un mayor monto de recursos. Actualmente, 80 multimillonarios tienen la misma riqueza que la mitad de la población mundial.



Fuente: Oxfam | Gráfico: Eduardo Salgado

DARK
COLUMBIA
DAILY TRIBUNE
CAGLECARTOONS.COM
4/7

02007

WELL, I
LEFT YOU
HALF!

WHAT ARE YOU,
GREEDY?



Indigenous People

On the borders of Peru, Brasil and Bolivia live the highest concentration of uncontacted peoples of the Earth.

- Isconahua
- Matsigenka
- Matses
- Mashco-Piro
- Mastanahua
- Murunahua (or Chitonahua
- Nanti
- Sapanawa
- Nahua
- and many others...

Indigenous Peoples in Latin America

By the year 2010, an estimated 45 million indigenous people lived in Latin America, accounting for 8.3 % of the region's population. The United Nations has championed the promotion of their rights through the use of different resources and special regulations for this purpose.



Indigenous people recognized by the UN

- 300 million people living in 75 countries.
- They represent over 5000 languages and cultures.
- They make up only 4% of the world's population, but they hold up to 90% of the world's cultural diversity.
- There are no more than **100** uncontacted tribes in the world. The majority live in this area (Brazil – Peru).

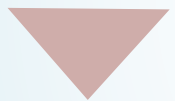


"The rainforests hold answers to questions we have yet to ask."

Saying in Surinam

- ▶ We have to look at the way we live from a different prospective.
- ▶ Our planet is built on ideas, inspiration, dreams, myths, intuition, brought from human imagination all the way to awareness.
- ▶ If we ignore our word heritage, we risk losing cultures, languages, part of the spirit of the world. We have to think in terms of "**Forest of the mind**".
- ▶ Every few weeks an elder dies and with him die ancient knowledge and information.

The protection
of human
history is linked
to that of our
natural
habitat.



The custodians
of our past are
the only
possible guides
for our future.



2/3 of all global
biological resources lie
in the 17
"biological countries"
inhabited by most of the
indigenous peoples of
the world.

Not a supermarket

- **Farmers, small producers and indigenous people** feed the world and they keep it cool.
- They provide up to 70% of the world's food source using up only 30% of its natural resources.

Via Campesina in Cop23 and WTO, Argentina, Nov 2017

- "We have to break with the historical paradigm that views Amazonia as an inexhaustible source of supplies for other countries without concern for its inhabitants."

Pope Francis



The Nahua



In the 80s, the oil explorations conducted by Shell forced the isolated tribe of the **Nahuas** to a **first contact**.

Since then, almost **half** of the tribe members have died.

Up to 80% of Peruvian Nahua tribe poisoned by mercury

A 2008 report suggests that gas extraction could earn it 230 million dollars annually and 90 million dollars in income tax revenue.



In humans, mercury damages the central nervous system, kidneys and brain and can lead to birth defects.

Miners use mercury to separate gold from rock and sediment. Mercury is also released into the air by burning fossil fuels.

Liver cancer

- ▶ Young people with an average age of 25 and children who generally do not have hepatitis B or C virus.
- ▶ The majority have giant tumors larger than 10 cm.
- ▶ They come from the Andean side of the country. Apurimac in the south-east.



West-East highway

► The 227-kilometer highway connects Peru and Brazil. It cuts the forest in two, endangering the planet's biggest **green lung**, and the entire Earth's climate balance.

► In Southeast Peru, biodiversity includes two million square kilometers of rainforests and savannahs generated by the sources of three large river basins:

Juruà, Purus and Madeira.

► They are home to indigenous groups still living a voluntary isolation, a treasure to be preserved.

► The road isolates indigenous animals and cultures and attracts hundreds of miners, traffickers, mercenaries and woodcutters (mahogany trees and other fine wood).



Highway connecting Brazil to Peru

➤ The highway that connects Puerto Esperanza and Inapari on the border with Brazil could cause the deforestation of 2,750 square kilometers.


➤ The populations of Puerto Maldonado is now called **Madre de Dios**.

➤ 350 indigenous people, belonging to over two hundred different linguistic groups live in the 5.5 million square kilometers.



The next **Synod** announced by Pope Francis will be in the **Amazon** - October 2019

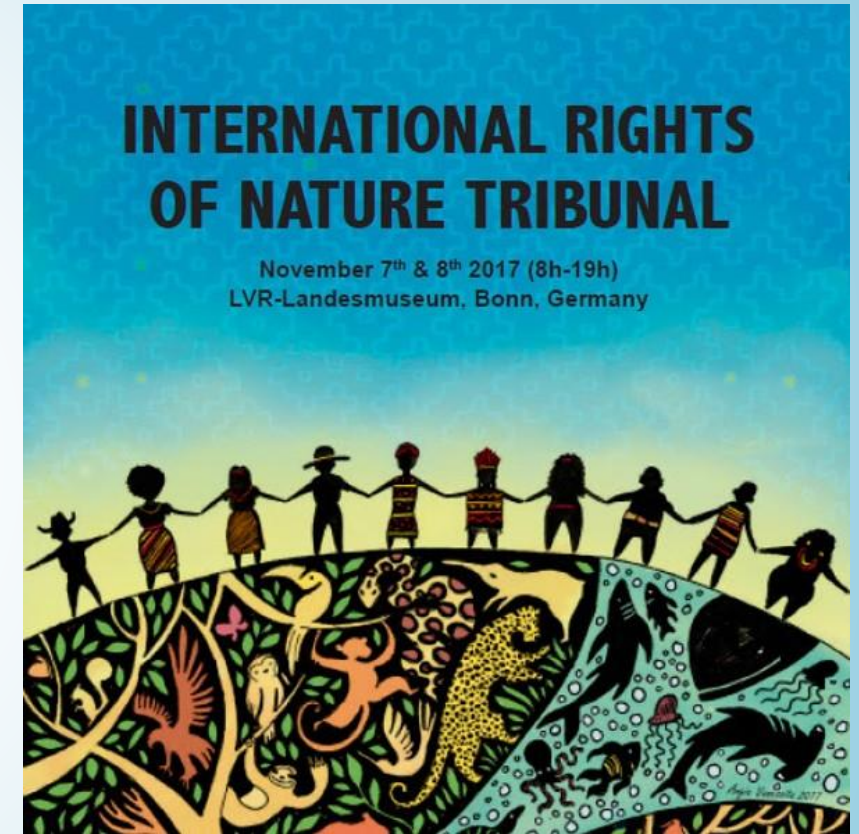
- "Soybean plantations are the business of the moment.
- There is no hesitation in destroying millions of hectares of forest to produce soy that the multinationals then transport to China and North America.

- 
- Even precious wood is not recovered, there is only the hurry to make room and go further, destroying all these extraordinary resources, plants and animals that for indigenous peoples are sources of life, with which they have **lived in balance for millennia**.
 - By this I do not mean that there should be no economic activities in the forest, but [...] a different use of resources respecting nature...
 - Another big problem is corruption... »

The guardians of the Earth

- On paper, the climate agreement adopted in Paris two years ago recognizes **the importance of human rights** and the role of **indigenous peoples** and local communities in providing **solutions** to **climate change**. Unfortunately this is only true in writing and doesn't seem to be applied.
- Science shows that by recognizing the right to land, the indigenous people can ensure a less dramatic climate change effectively and inexpensively. But if they claim their rights, too often they are **brutally killed, jailed or persecuted**.

Forest Day Conferences of the Parties to the UN Framework Convention on Climate Change (UNFCCC) held in 2017 under the presidency of the Fiji Islands in Bonn, Germany.



CLIMATE CHANGE - FALSE ENERGY SOLUTIONS - FINANCIALIZATION OF NATURE - WATER RIGHTS IN MADRID - DEFENDERS OF MOTHER EARTH - LIGNITE MINING IN GERMANY - AMAZON THREATS (ECUADOR, BRAZIL, BOLIVIA-TIPNIS AND FRENCH GUYANA) - NAFTA'S IMPLICATION ON NATURE

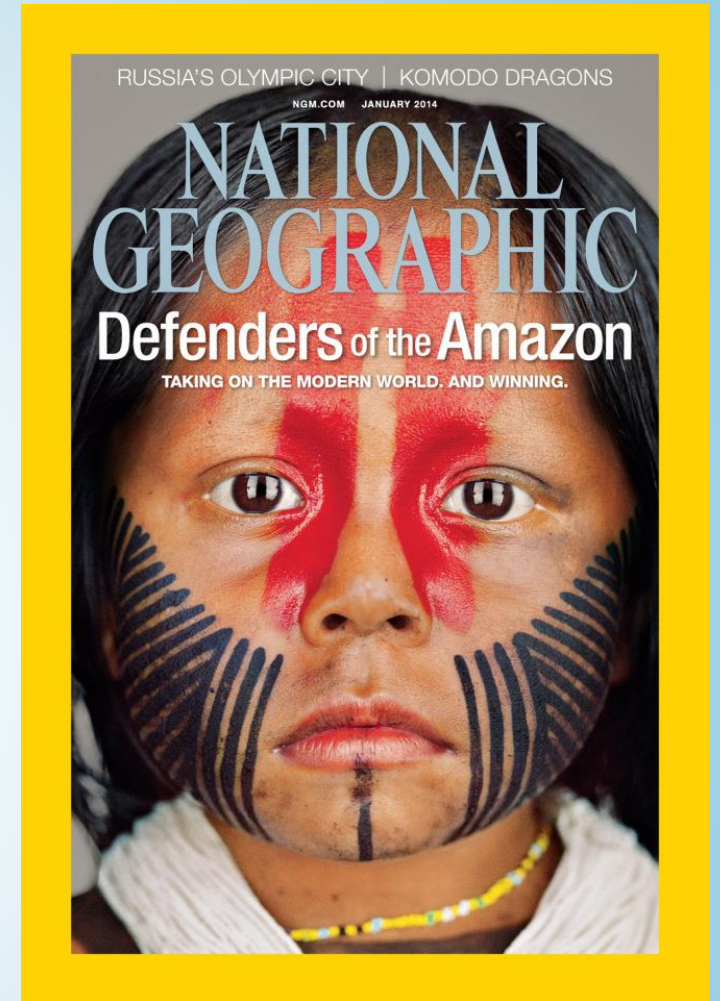
November 7th & 8th 2017 (8h-19h)
LVR-Landesmuseum, Bonn, Germany
LVR-Landesmuseum Bonn, Colmantstr. 14-16, 53115 Bonn
Registration: <http://therightsofnature.org>

The Defenders

Of the 185 **defenders** of the Earth killed in 2015, more than half were killed in South America:

- Guatemala (10%)
- Colombia (10%)
- Mexico (9%)
- Brazil (9%)
- Peru (8%)
- Honduras (6%)

Mining companies, agribusiness, oil, gas and coal companies and dam builders remain the most dangerous companies for the **defenders**.



The year 2018, is the 20th anniversary of the UN Declaration on Human Rights of the Defenders.

Global Witness

INTELLECTUAL PROPERTY RIGHTS



- In the **United Nations Conference on the Environment of Rio de Janeiro in 1992**, the biggest discussion was on «intellectual property rights»: who benefits from the commercialization of natural resources?
- Laws were made so that at least a percentage of profits should go back to the country and to the people who discovered the plants used for healing.
- Unfortunately it is difficult to do so in practical terms.

TRIPS – Trade-Related Aspects of Intellectual Property Rights

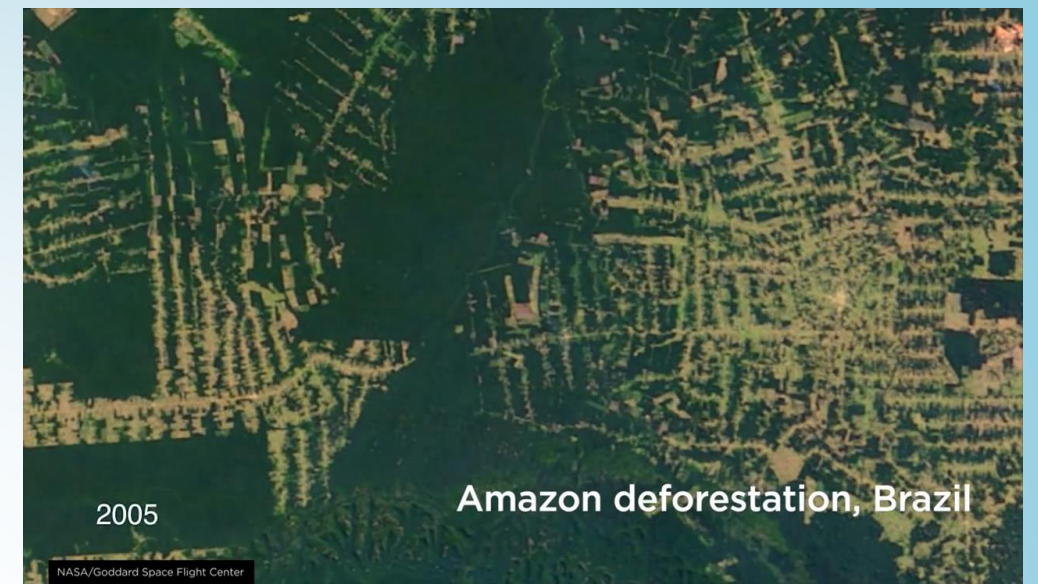
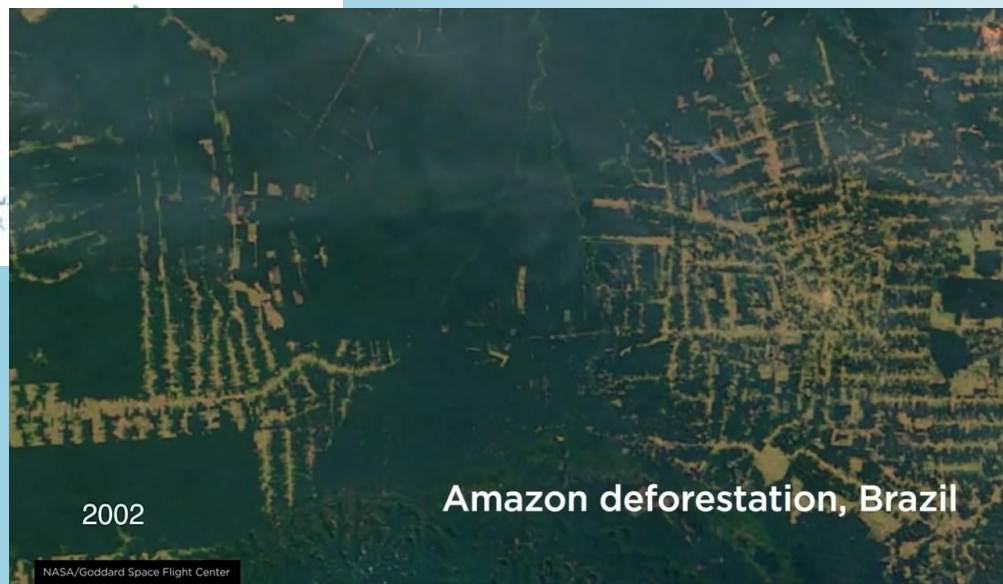
Patentable Subject Matter

Article 27 - Paragraph 3

Members may also **exclude** from **patentability**:

... (b) plants and animals other than micro-organisms, and essentially biological processes for the production of plants or animals other than non-biological and microbiological processes. However, Members shall provide for the protection of plant varieties either by patents or by an effective sui generis system or by any combination thereof. The provisions of this subparagraph shall be reviewed four years after the date of entry into force of the WTO Agreement.

In some states of Latin America a plant discovery or a method of production **known** to the indigenous communities is considered *res nullius* – *nobody's thing*. Therefore the intellectual property is not awarded to the people.



20 thousand hectars of land are destroyed every day (FAO).
In the past 15 years, 3% of the primary forests has been destroyed.



The Big Pharma Project

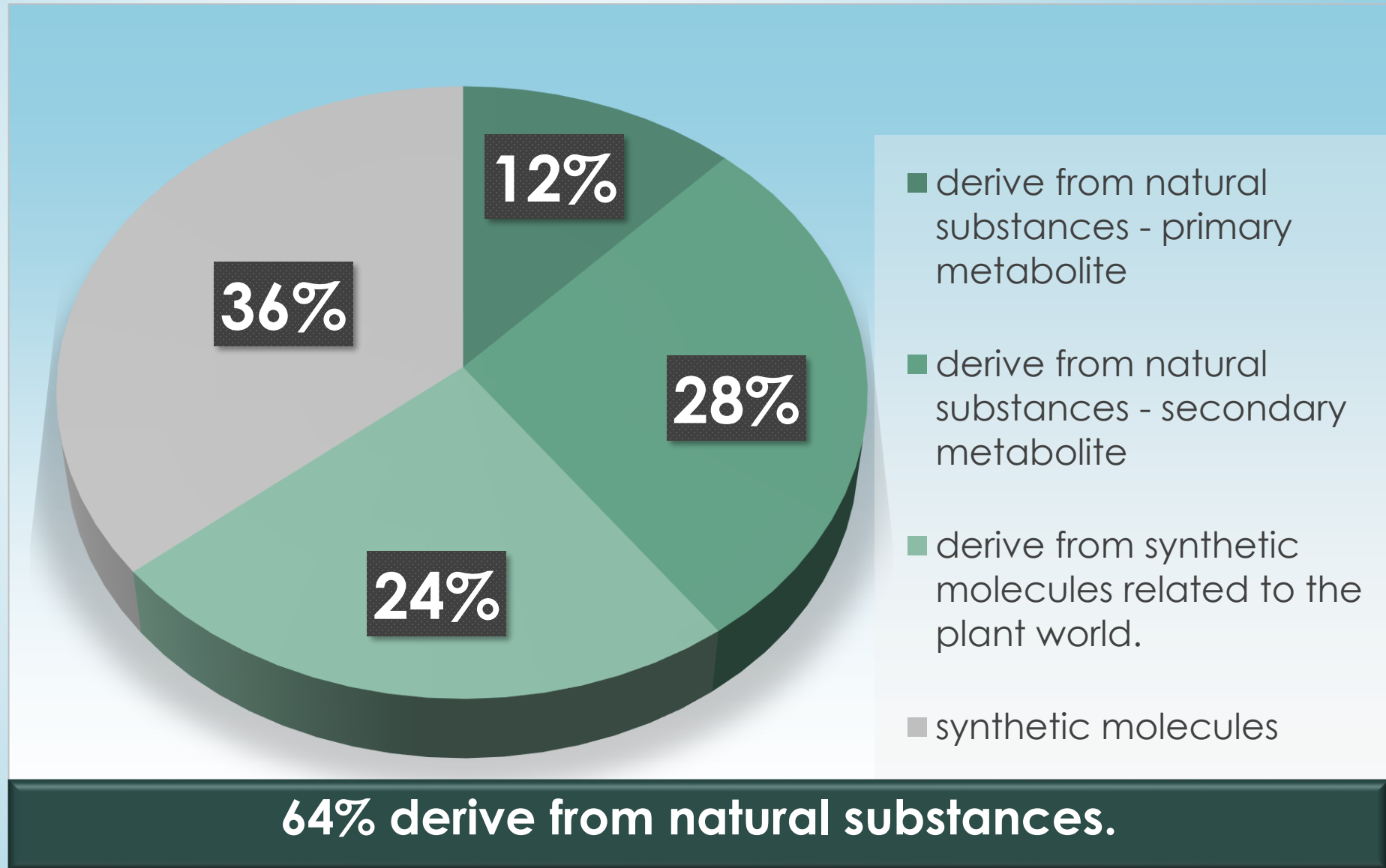
► is a research carried out in six countries that demonstrates the pharmaceutical industry's methods to prolong the monopolies of manufacturing and selling of drugs that earn the highest income in Latin America but block access to healthcare for the most vulnerable populations.



Amazon just acquired online pharmacy PillPack and entered the pharmacy business

- "Just as science has been revolutionized by gene therapy or new treatments, I think the drug delivery channel should also be revolutionized by improvements based on technology or efficiency," said Brent Saunders, CEO of Allergan.
- Jeff Bezos bought into this idea to cut costs on generic pharmaceuticals.
- **Alibaba Health**, Asian colossus, already has a dedicated channel for online sale of pharmaceutical products.

Pharmaceutical products registered from 1981 to 2002



- 62% of all **anticancer drugs**
 - 71% of all **antibacterial drugs**
- come from natural substances

More than half of all medicine found on pharmacy shelves contain plant compounds



- The Amazon is the world's largest tropical forest and home to a quarter of all botanical species on this planet. More than 250,000 species.
- About 80% of individuals from developed countries use traditional medicine which has compounds derived from medicinal plants.
- Medicinal plants contain organic compounds which provide definite physiological action on the human body.
tannins, alkaloids, carbohydrates, terpenoids, steroids and flavonoids
- These compounds are synthesized by primary or secondary metabolism of living organisms.
- Secondary metabolites are chemically and taxonomically extremely diverse compound with sometimes obscure functions.

This is ETHNOBOTANY



- For over three and a half billion years Nature has created extraordinary chemical compounds and new technologies are facilitating our ability to discover them, study them, manipulate them and use them, like never before.
- **Ethnobotany** is the study of a region's plants and their practical uses through the traditional knowledge of a local culture and people. An ethnobotanist thus strives to document the local customs involving the practical uses of local flora for many aspects of life, such as plants as medicines, foods, and clothing.
- *Richard Evans Schultes*, often referred to as the "father of ethnobotany", explained the discipline in this way:

“Ethnobotany simply means... investigating plants used by societies in various parts of the world”.

PHARMACEUTICAL DRUGS IN THE THIRD MILLENNIUM

The budget must be lowered compared to traditional clinical trials and standards.

Even if extended to 30,000 people, the trials would never be able to consider all the variables existing in the human being.

The new methodologies must be adopted by regulatory bodies, redesigning the rules of the game and the methodology of clinical studies.

The forms of protection of know-how will change, overcoming the patent, taking into account open borders, science, and states.

Sustainability is at stake. The system can no longer afford exaggerated costs for the development of just one new molecule.

The Pharmaceutical Industry

- The aspect of "Natura Magistra" is often underestimated or ignored by the pharmaceutical industry.
- We need to use the opportunity presented by the European legislation on the traditional medical product of plant-based origin and not get stuck on the **non-patentability**.
- The pharmaceutical industry too often prefers to include modified active ingredients only for commercial reasons.
- The new methodologies question the very idea of a therapeutic area.
- The results of the research will help decide which pathogens the potential drug can be used for.

- Random selection
- or
- taxonomic selection

A part of a plant
(roots, leaves, bark, seeds...)

1 molecule is
isolated

To be used in **only**
1 therapeutic area

We know the **active molecule**,
but not its toxicity nor its
therapeutic area.

- Anthropological selection

Indigenous
people have
used for many
treatments

Interesting
plant
(all parts)

Interesting
molecule
1

Interesting
molecule
2

Interesting
molecule
3

Interesting
molecule
etc...

Therapeutic
area
1

Therapeutic
area
2

Therapeutic
area
3

Therapeutic
area
etc...

We know its **toxicity** and its **therapeutic area**,
but not the active molecule.

Chemical warfare

“A majority of the world's insects live in the Amazon rain forest, and the fact that the forest has not been devoured by this entomological onslaught is testament to these plant' abilities as chemical warriors. Plants protect themselves by producing an astonishing array of chemicals that are toxic to insects, thereby deterring predation. When ingested by humans, these same plants and their chemical weapons may act on a variety of ways in the body: they may be nutritious, poisonous, or even hallucinogenic. And in some cases they are therapeutic.”

Tales of a Shaman's Apprentice: An Ethnobotanist Searches for New Medicines - Mark J. Plotkin



**Plants cannot hide nor can they run.
Vegetal poison is nature's way of allowing
plants to continue their life process.**

If it's bitter it's good for you...

- Many of the human body's powerful reactions are a direct response to plant **alkaloids**, a class of chemical compounds most common in tropical plants.
- **4000** species belonging to **350** families produce alkaloids.
- These molecules have had a major impact on every culture if not every person on the planet.
- Alkaloids are characterized by a molecular structure that must include a **nitrogen** atom and at least **two carbon** atoms.
- The **bitterness** was frequently a clue for people the world-over that a plant had therapeutic properties.



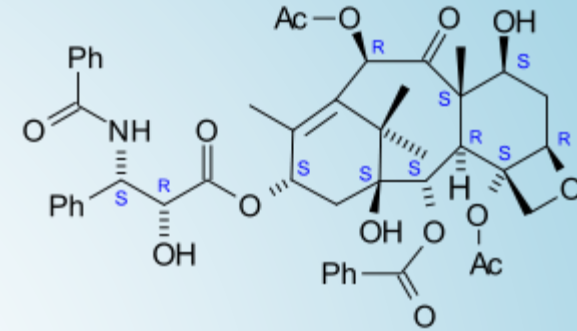
TAXOL

- Taxol is a chemotherapy medication used to treat a number of types of cancer.
- It comes from the bark and needles of the *pacific yew tree* in the American northwest, which must be cut down.
- Taxol selectively interferes with the division of **cancer** cells

by attacking the microtubules that thread and pull chromosomes apart during cell division.

Native Americans

- The **Potawatomi** tribe treated venereal diseases by crushing the leaves and applying them directly to the sores.
- **Chippewa, Iroquois, and Menominee** tribes eased pain caused by arthritis and rheumatism by boiling the branches and leaves of the yew and then bathing in the steam.



15% of the 300,000 known plants have a documented therapeutic activity, but there are many more...

- Pollution and environmental looting with deforestation has contributed to the destruction of 60,000 species in the last century.
- The need of proper certification, the lengthy registrations standards built for today's "globalized" market, on the "molecular" models of the western nations, slow down the spread of herbal products especially in developing countries.

From idea to shelf...

- At least 20 years.
- A **clinical trial** – requires testing on 30,000 patients.
- Too much money invested to isolate only 1 active molecule.
- The registration procedures require thousands of pages of documentation, pharmacological, toxicological and clinical tests - from \$800,000,000 to \$10,000,000,000 - over 25 years.
- The costs are higher than the income of an average laboratory, where the investment for research must exceed 10% of the turnover.

PAU-PEREIRA

Traditional Brazilian medicine

- Fever
- Indigestion and inappetence
- Malaria - prevention and treatment
- To strengthen the immune system
- Liver problems

Clinical trials

- Treatment of malaria
- Analgesic properties
- Treatment of memory deficit (Alzheimer's disease)
- **Anticancer** activity



CHARACTERISTICS

Pau-pereira or pao pereira

(*G. laeve* (Vell.) Miers; *G. vellosii* Fr. All. is a synonym)

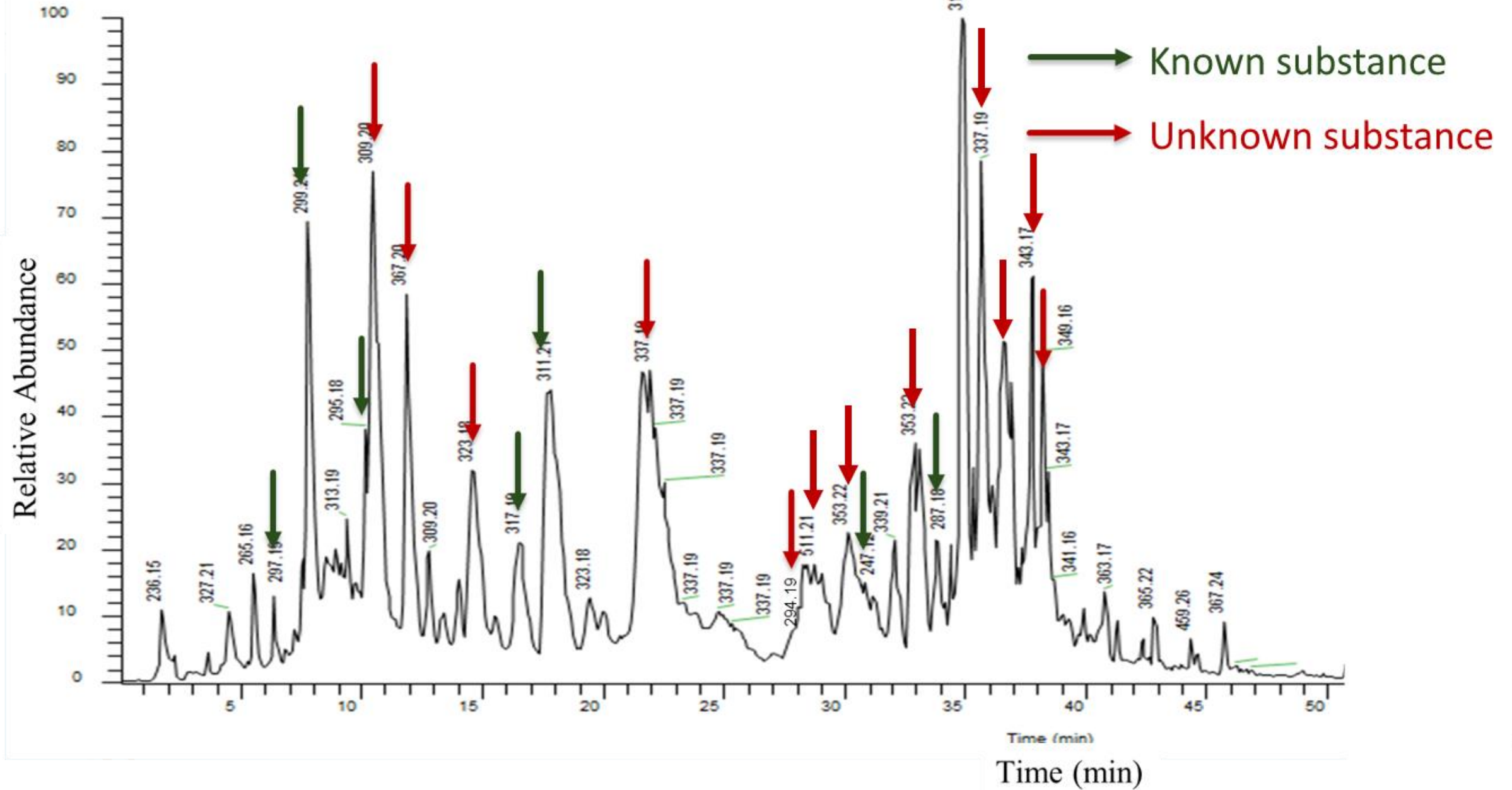
is the best known of approximately six **Geissospermum** species.

- The *Geissospermum Vellosii* (Pao Pereira) is part of the **Apocynaceae** family and of the genus **Geissospermum**.
- It is a tree present in the Amazon forest, especially in the territories of
Brazil, Bolivia, Suriname, Guyana and French Guiana.
- Pao Pereira grows spontaneously giving sprouts directly from the seed without any particular treatment.
- The bark of this plant flakes and regenerates continuously, so there is no need to cut the tree to remove the bark. The hydroalcoholic extract rich in alkaloids is obtained from the **bark**.



Accepted Name	Synonym	Distribution	Common name
G.Argenteum Woodson		N.South America: N.Brazil (AM,AP,RO) to Venezuela, Guianas	Maria congo (creolo) Pelowi (wayapi) Kongo ama (Palikur) Bitá udu(Aluku) Wataki (Wayana) Acariquara-branca, Acarirana, Quinarana, Pau-pereira (Portugais)
G. Fuscum Markgr.		S. Venezuela to N. Brazil	
G.Laeve (Vell.) Miers	G. Martianum Miers G. Vellozii Fr.All. Tabernaemontana laevis Vell.	N. South America: Guianas to Brazil (AP, PA, AM,MA, BA, DF, MG, ES, RJ)	Camarà de bilro, Camarà do Matto, Pau Forquiham Oinguaciba Pau- Puente Pau-pereira, Quinarana("false quinine"), Quina-quina (bitterness of quinine), Acariquara branca
G. Reticulatum A.H. Gentry		S. Venezuela, Peru, N.Brazil (AC, RO) to N. Bolivia	
G. Sericeum Benth & Hook. F.		N. South America: Guianas, Brazil (AP, AM, AC, RO, MA)	
G. Urceolatum A.H. Gentry		N.Brazil (PA,AM)	

Chromatogram Pau-pereira



Anti-cancer activity

Human prostate cancer, ovarian cancer in association with chemotherapy (Yu and Chen, 2014)

The mechanism of action based on the induction of **apoptosis** and the destabilization of the DNA of cancerous cells.

Partially through inhibiting NF- κ B activation in prostate cancer cells and may protect against CRPC.

Antinociceptive activity

The antinociceptive effect of the dichloromethane fraction involved an interaction with the serotonergic 5-HT_{1A} system.

Antimicrobial activity

against multi-drug-resistant *Staphylococcus* (MIC) of 5 μ g).
Pseudomonas aeruginosa (MIC 20 μ g)
S. aureus (MIC 80 μ g).

Anticholinesterase activity

Model is validated for the development of drugs used in the symptomatic treatment of Alzheimer's Disease.

The search for active substances is very promising, besides being a strategy for the discovery of **new antimalarial** drugs.

We need to change the way we think

- The **definition of HEALTH** has recently been updated.
- The distribution of wealth as it is, is no longer sustainable. The gap between those who are well and those who are not well is getting bigger.
- We need to invest, invest ourselves in a process that allows us to meet the needs of the present generation without compromising the possibility of those of future generations.
- Oh, you ordinary citizen! You have the responsibility of the decision-maker now. Small choices and great choices, day after day, can determine a change of mentality.



LA TORRE

PER CONOSCERE, ACCOGLIERE, CURARE



Thank you

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