



Herbal Medicine: **The Future is Natural**

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Acting President, National Academy of Science and Technology
Professor, Department of Chemistry, Ateneo de Manila University

The History of Drugs



“Doctor, I have a stomach ache.”

What doctors have prescribed through the ages:

2000 BC: *“Here, eat this root!”*

1900 : *“That root is dirty.
Here, swallow this pill!”*

2000 : *“That pill is synthetic.
Here inject this antibiotic!”*

2016 : *“That antibiotic is ineffective.
Here, eat this root!”*



The background is a collage. The left side is filled with a dense pattern of white, round pills. The right side features various green herbs, including leafy plants and bundles of dried grasses, set against a light green background.

Herbal Medicine: **The Future is Natural**

Outline

1. Herbs: From Wellness to Medicine
2. Herbal Medicine Systems of the World
3. Opportunities and Challenges of Herbal Medicine

The background of the slide is a collage. The left side is filled with a dense pattern of white, round pills. The right side features a collection of various green herbs, including leafy plants, stems, and small flowers, arranged in a somewhat organized but natural-looking fashion. The overall color palette is light and natural, with white, green, and light beige tones.

Herbal Medicine: The Future is Natural

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Herbals: from Wellness to Medicine



Medicine



Cosmetics,
Spices, Teas,
Beverages



Dietary
supplements



Traditional
herbal
products



Ampalaya Plus
Ampalaya + Banaba + Luyang Dilaw



Herbal
medicines



Pure drugs



Herbals: from Wellness to Medicine

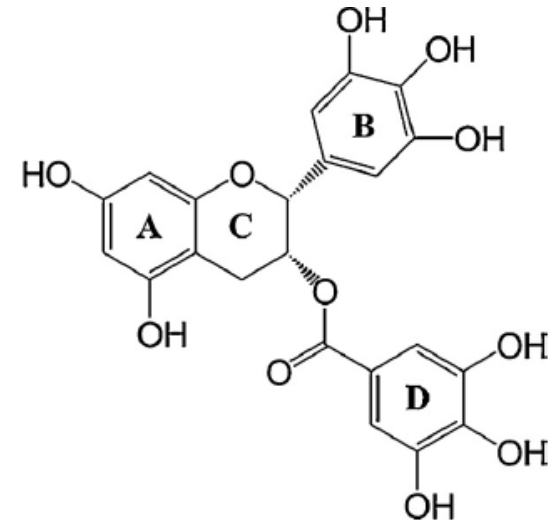
INTEGR MED RES 3 (2014) 16-24

Anticancer effects and molecular mechanisms of epigallocatechin-3-gallate

Kyoung-jin Min*, Taeg Kyu Kwon*

Epigallocatechin-3-gallate (EGCG) is a type of catechin found in green tea. EGCG exhibits a variety of activities, including anti-inflammatory, antidiabetes, antiobesity, and antitumor.

Some of these effects are associated with the modulation of reactive oxygen species (ROS).



Herbals: from Wellness to Medicine

Carcinogenesis

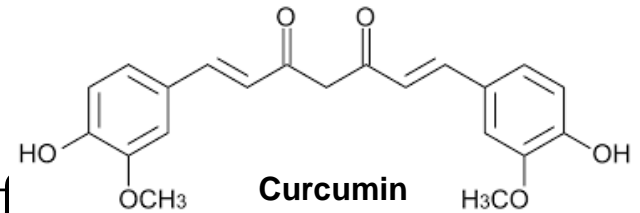
Integrative Cancer Research

(1993) 14 (3): 493-496.

Effect of turmeric and curcumin on BP-DNA adducts

M.A. Mukundan, M.C. Chacko, V.V. Annapurna and K. Krishnaswamy¹

Turmeric significantly reduced the level of BP—DNA adducts of benzo[a]pyrene (a carcinogen). This provides support for the anticarcinogenic and chemopreventive properties of turmeric.



Herbals: from Wellness to Medicine

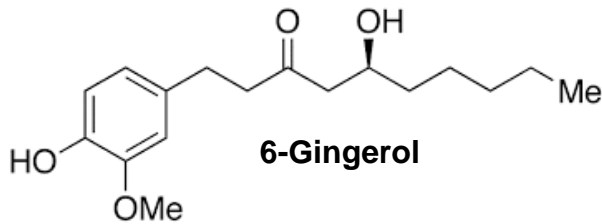


British Journal of Nutrition (2006), 96, 660–666

DOI: 10.1079/BJN20061849

Anti-diabetic and hypolipidaemic properties of ginger (*Zingiber officinale*) in streptozotocin-induced diabetic rats

Zainab M. Al-Amin, Martha Thomson, Khaled K. Al-Qattan, Riitta Peltonen-Shalaby and Muslim Ali*



At a dose of 500 mg/kg, raw ginger was effective in lowering serum glucose, cholesterol and triacylglycerol levels in diabetic rats. Additionally, raw ginger is effective in reversing diabetic proteinuria. Thus, ginger may be of great value in managing the effects of diabetic complications in human subjects.

Herbals: from Wellness to Medicine

Experimental Chemotherapy

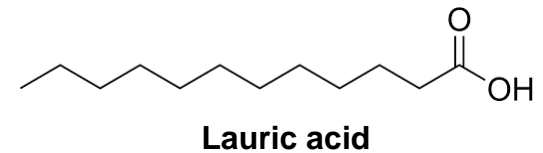
Chemotherapy
DOI: 10.1159/000356067

Received: January 3, 2013
Accepted after revision: September 30, 2013
Published online: ■■■■

Induction of Apoptosis by the Medium-Chain Length Fatty Acid Lauric Acid in Colon Cancer Cells due to Induction of Oxidative Stress

J.K. Fauser^{a,b} G.M. Matthews^{c,d} A.G. Cummins^b G.S. Howarth^{a,c}

Conclusion: Compared to butyrate, lauric acid displayed preferential antineoplastic properties, including induction of apoptosis in a colorectal cancer cell line.



Herbals: from Wellness to Medicine

Vol.123:No.4

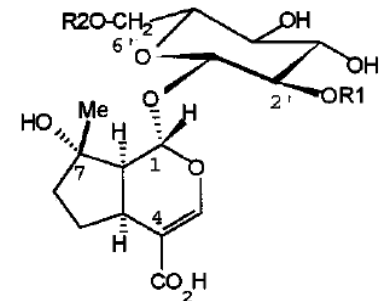
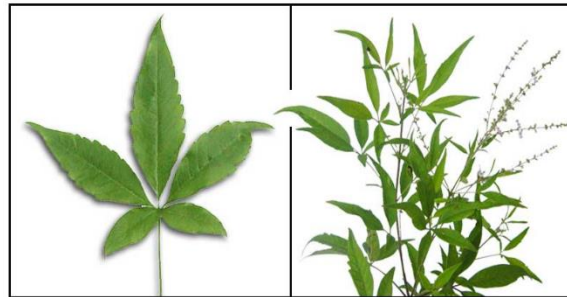
PHILIPPINE JOURNAL OF SCIENCE

IDENTIFICATION OF FOUR IRIDOIDS IN THE PHARMACOLOGICALLY-ACTIVE FRACTION OF VITEX NEGUNDO, L.

FABIAN M. DAYRIT* and LOLITA G. LAGURIN
Philippine Institute of Pure and Applied Chemistry,
Ateneo de Manila University,
Loyola Heights, Quezon City

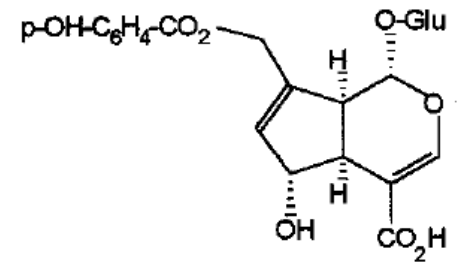
ABSTRACT

Four iridooids--2'-p-hydroxybenzoyl mussaenosidic acid, 6'-p-hydroxybenzoyl mussaenosidic acid, agnuside and lagundinin-- were identified in the pharmacologically-active fraction of the leaves of *Vitex negundo*, L. The data obtained for 2'-p-hydroxybenzoyl mussaenosidic acid modifies a previous assignment while lagundinin is a newly identified iridooid.

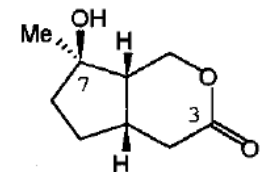


R1=COC₆H₄OH(para) R2=H
2'-p-Hydroxybenzoyl mussaenosidic acid (1)

R1=H R2=COC₆H₄OH(para)
6'-p-Hydroxybenzoyl mussaenosidic acid (2)



Agnuside (3)



Lagundinin (4)

Herbals: from Wellness to Medicine

Nat. Prod. Rep., 2000, **17**, 215–234

MILLENNIUM REVIEW

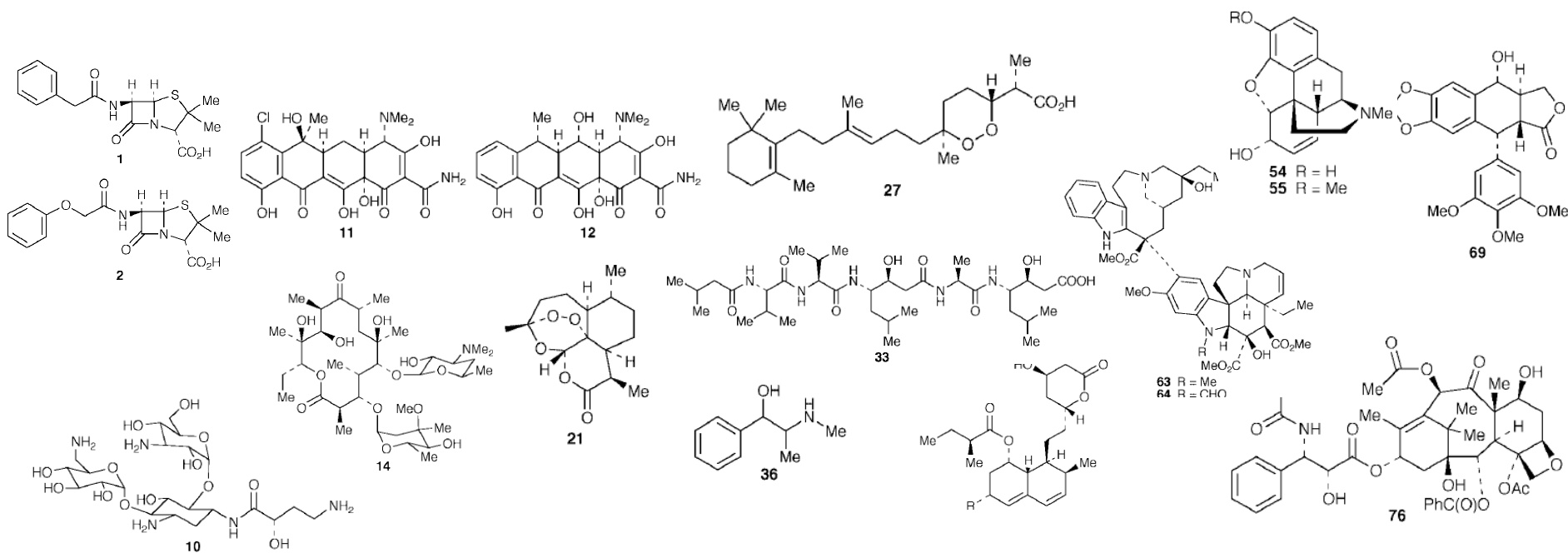
The influence of natural products upon drug discovery

David J. Newman,^{*a†} Gordon M. Cragg^a and Kenneth M. Snader^b

^a *Natural Products Branch, Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute, Rockville MD 20852, USA*

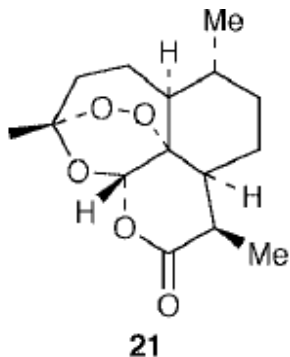
^b *Pharmaceutical Resources Branch, Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute, Rockville MD 20852, USA*

NPR



Drug

Artemisinin:
Anti-malarial



Plant



Artemisia annua

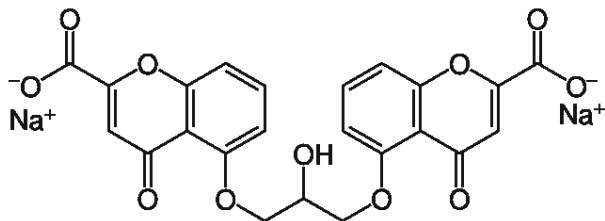
Traditional use

Chinese herb Qinghao; Chinese medicine for chills and fevers

Youyou Tu was awarded Nobel Prize in 2015 for discovery of artemisinin from ancient TCM text.

Cromoglycate:

Asthma prophylaxis

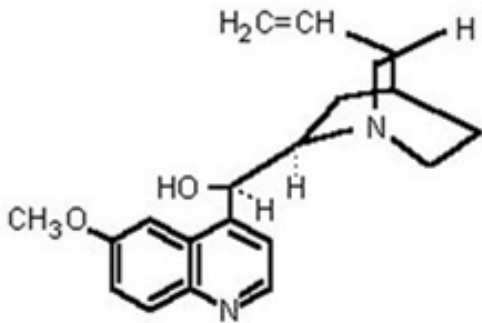


Ammi visnaga

Active ingredient of the khella plant. Middle Eastern remedies for asthma. Khellin has also traditionally been used in Egypt to treat kidney stones.

Drug

Quinine:
Anti-malarial



Plant

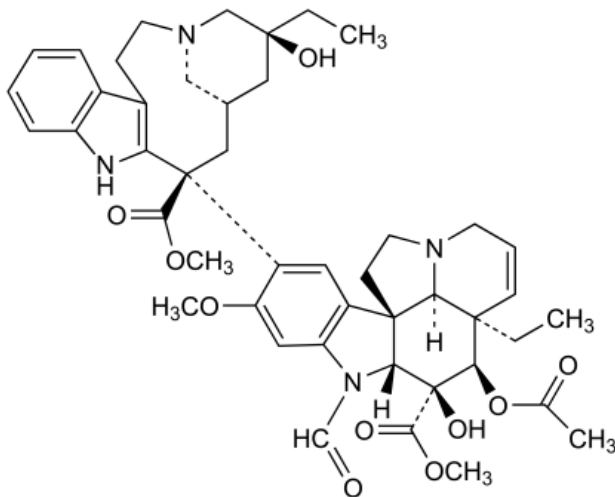


Cinchona spp.

Traditional use

From the bark of the cinchona tree. Traditional remedy in South America for the treatment of fevers and shivers. There is renewed interest in cinchona. There is a cinchona plantation in Mt. Kitanglad, Bukidnon.

Vincristine:



Vinca spp.
(periwinkle)

Rosy periwinkle was originally investigated for its folk use as an anti-diabetes drug. It was eventually discovered to have strong anticancer properties.

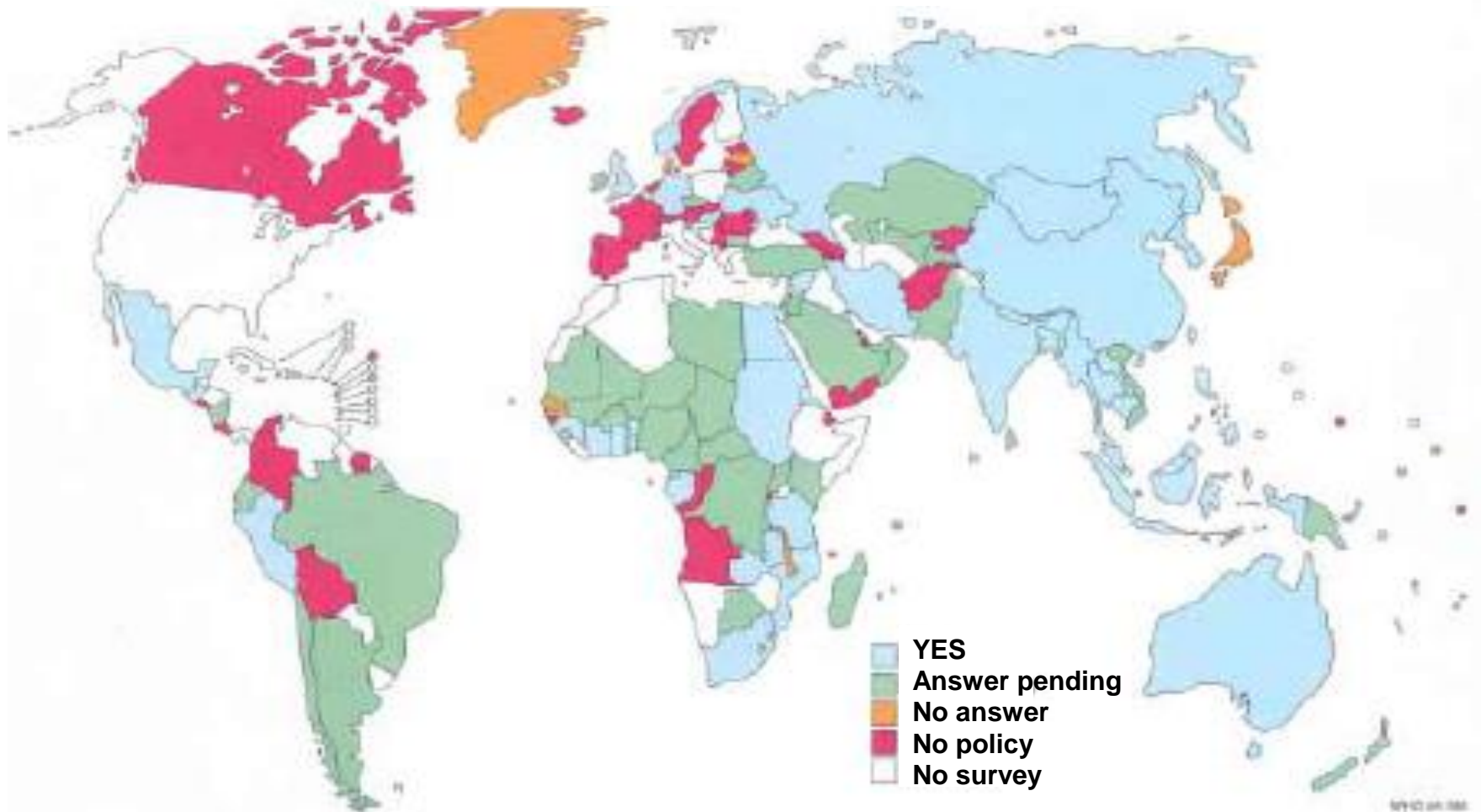
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National policy on traditional medicine and complementary/alternative medicine WHO, 2005

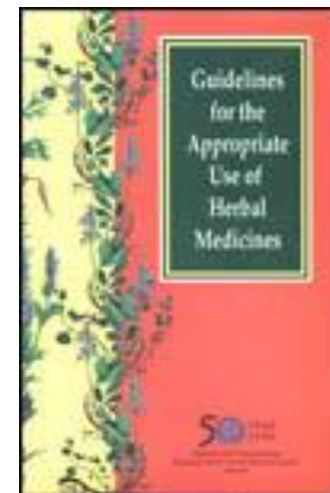
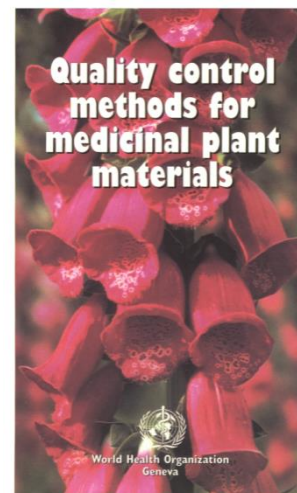


Map 2. Member States with national policies and those pending

Overview of Herbal Medicine Regulations in the World

http://www.holisticonline.com/Herbal-Med/hol_herbalmed-drugreg.htm

- WHO recognizes the important and historical role of herbal medicine in health. Herbal medicine is a major form of treatment for more than 70% of the world's population.
 - The *Guidelines for the Assessment of Herbal Medicines* states that a substance's historical use is a valid way to document safety and efficacy in the absence of scientific evidence to the contrary.
 - Appropriate use
 - Quality control methods
 - Recommended labeling



Herbal medicine systems of the world



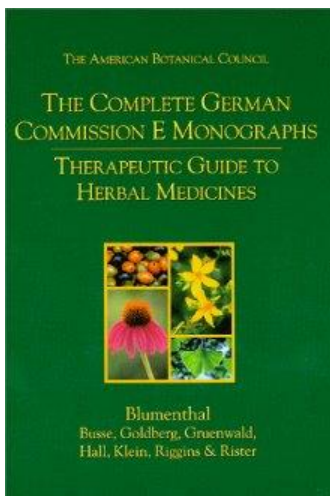
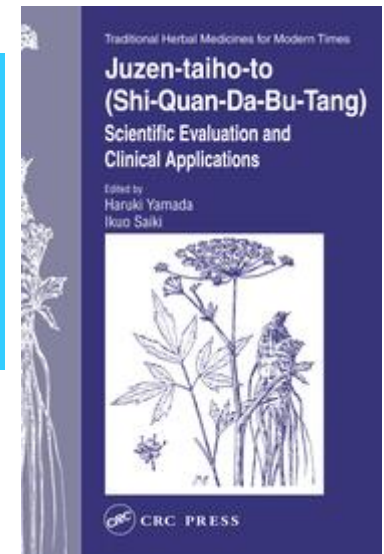
Ayurveda (Sanskrit: "the science of life") originated in northern India over 5,000 years ago and is part of Indian culture. It includes a system of herbalism, diet, yoga, detoxification, and psychological interventions.

Traditional Chinese medicine (TCM) is rooted in the ancient philosophy of Taoism and dates back more than 2,500 years. The *Chinese Materia Medica* lists thousands of medicinal plants, including leaves, roots, stems, flowers, and seeds, which are often combined in formulas as teas, capsules, liquid extracts, or powders.



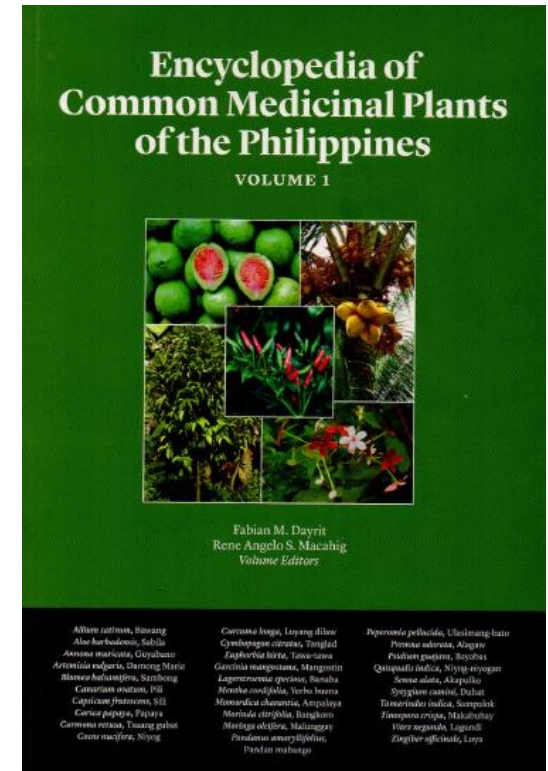
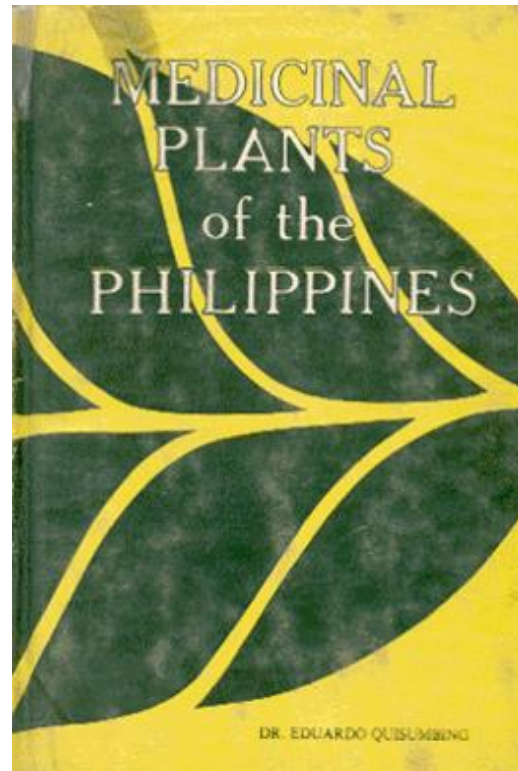
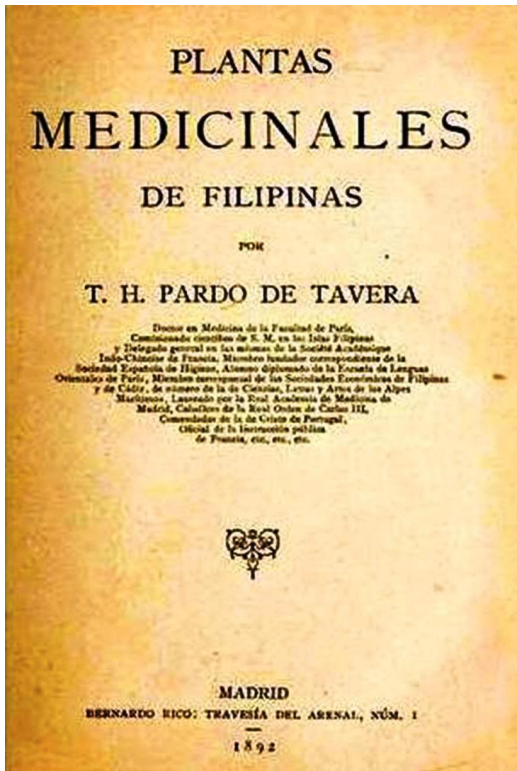
Herbal medicine systems of the world

Japan: Kampo is playing an increasingly important role in Japan's modern-day health care, including its national health insurance system and the medical community



Germany: The German Commission E was formed in 1978 to evaluate the safety and efficacy of herbals. The Commission E monographs are used by physicians, pharmacists, regulatory agencies, consumers and the herbal industry.

Herbal medicine systems of the world



Dr. Eduardo A. Quisumbing
(1895-1986)
National Scientist

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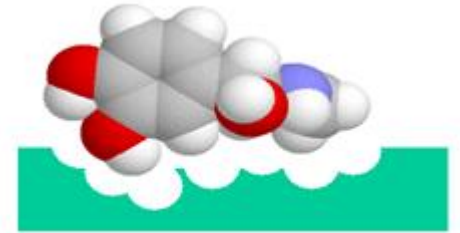
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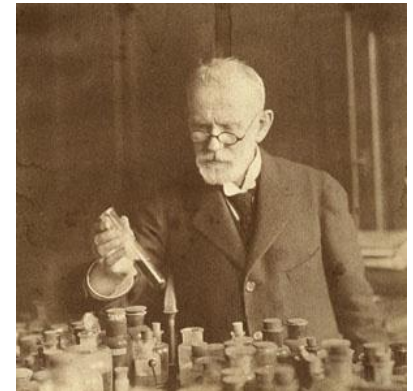
Western Pharma: Lock & Key Paradigm



Emil Fischer (1852-1919, Nobel Prize in Chemistry 1902) proposed the "**Lock and Key Model**" to visualize the substrate-enzyme interaction.



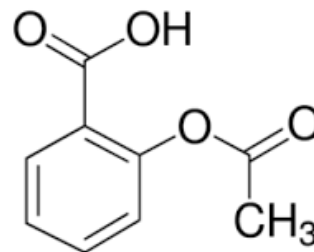
Paul Ehrlich (1854-1915, Nobel Prize in Physiology or Medicine 1908) proposed the paradigm of the "***magic bullet***" for drugs: ***a specific molecule for a specific target.***



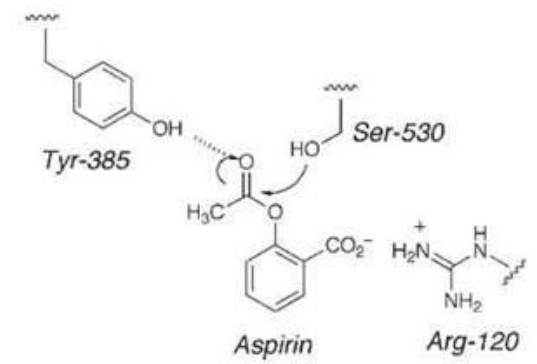
Western Pharma: Lock & Key Paradigm

The Reality: Compounds often affect several sites

Acetyl salicylic acid



- inhibits COX-1 by acetylating serine 530
- suppresses COX-2 transcription blocking prostanoid synthesis



Proc. Natl. Acad. Sci. USA
Vol. 96, pp. 5292–5297, April 1999
Pharmacology

Suppression of inducible cyclooxygenase 2 gene transcription by aspirin and sodium salicylate

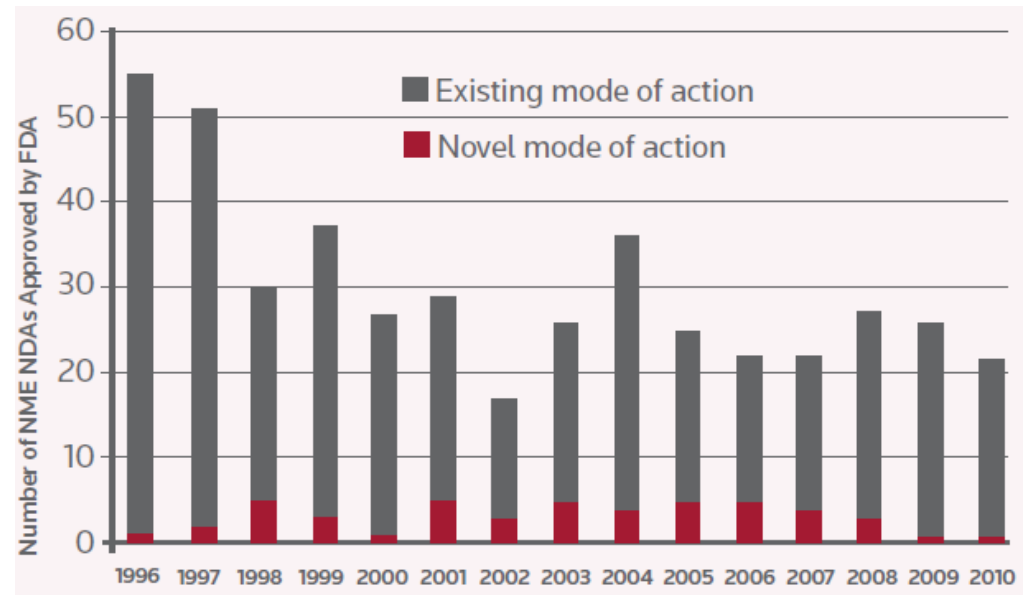
XIAO-MING XU*, LETICIA SANORES-GARCIA*, XIAN-MING CHEN*, NEVENKA MATIJEVIC-ALEKSIC*, MIN DU*, AND KENNETH K. WU*†‡

Western Pharma: Lock & Key Paradigm

... it doesn't work for everything!

Only 22 drugs reached the market in 2010 compared to almost 40 per year in the late nineties.

(source: The Changing Role of Chemistry in Drug Discovery, Thomson-Reuters, IYC Report 2011)



Charities chief: 'Pharma blockbusters are gone'

Incoming chief executive of the Association of Medical Research Charities lays out what the country needs.

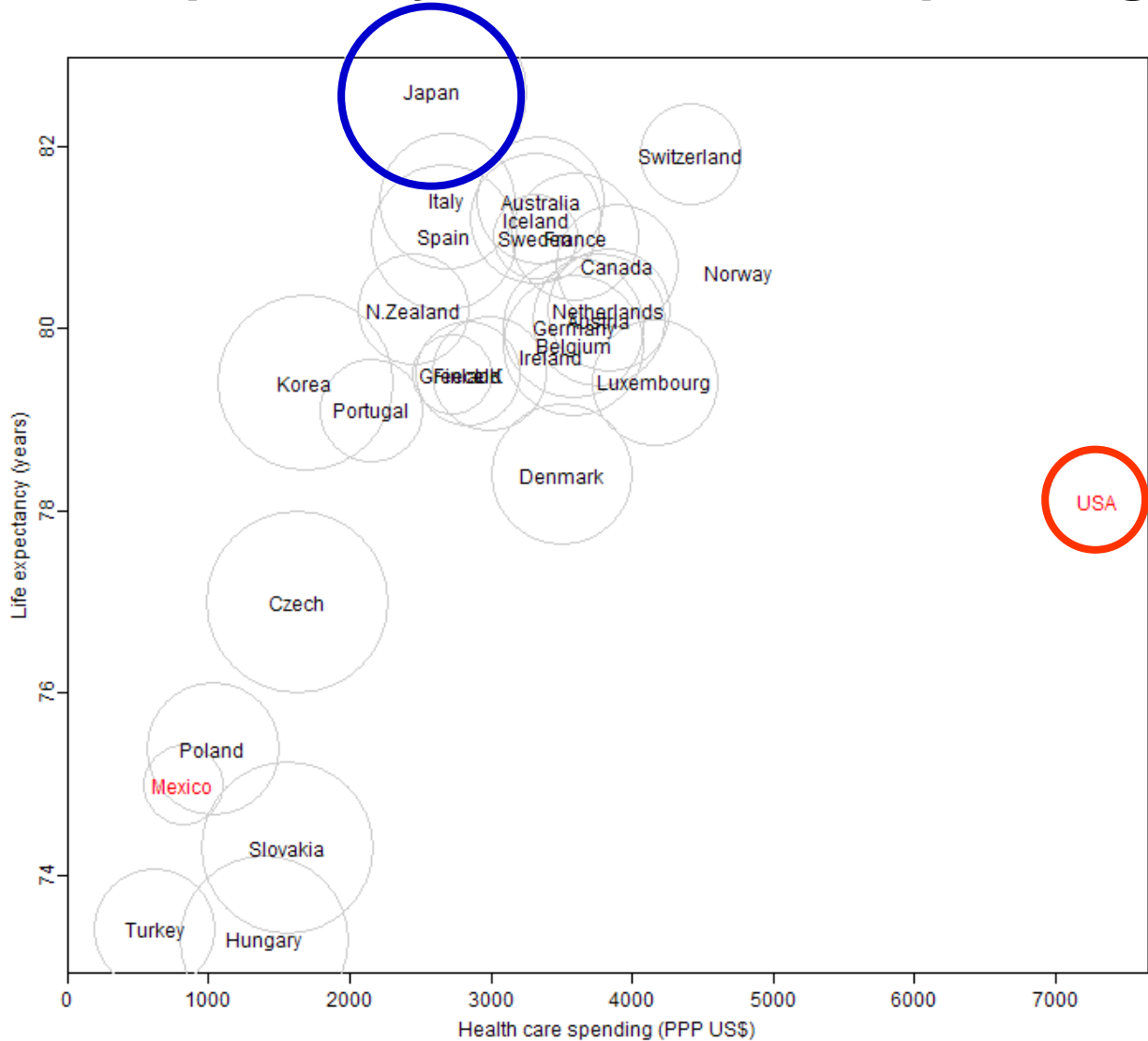
What is the biggest concern of your member charities at the moment?

The paradigm needs to change. The old model of the pharmaceutical blockbuster — we develop something, we get it to market, we get it out there, it's a billion dollars — that is gone.



Aisling Burnand

Life expectancy vs. Healthcare spending

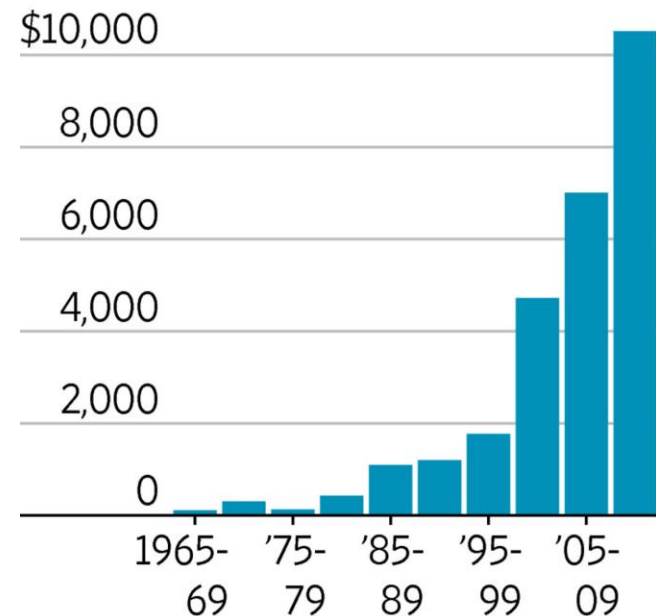


(<http://www.stat.columbia.edu>)



A Month of Meds

Median price* of cancer drugs approved during each five-year period, for a month's supply



*initial price upon approval, in 2014 dollars

Source: Peter Bach at Memorial Sloan Kettering Cancer Center

THE WALL STREET JOURNAL.

SUSTAINABLE DRUGS AND GLOBAL HEALTH CARE

Geoffrey A. Cordell

Natural Products Inc., Evanston, IL 60203, U.S.A.

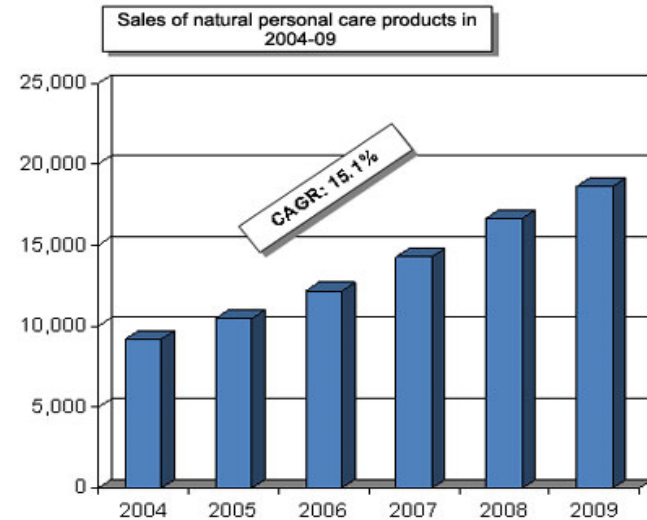
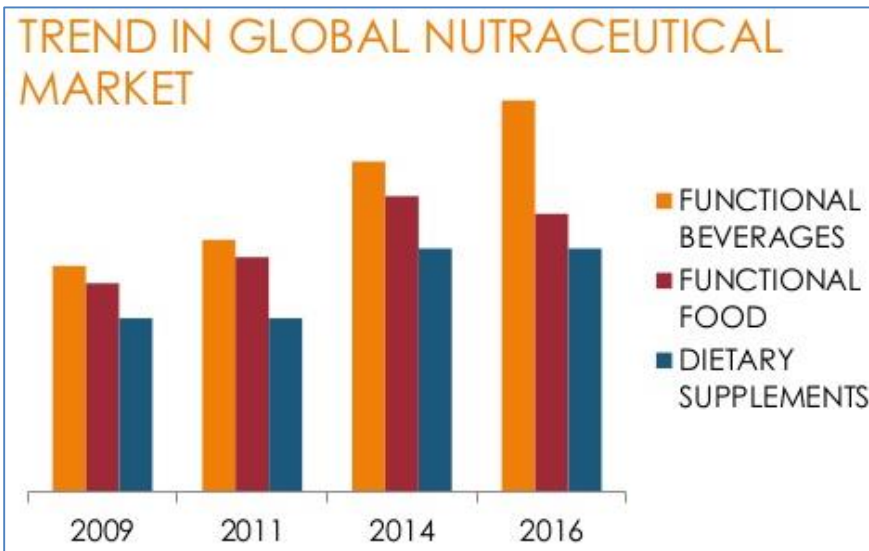
- The annual per capita cost of health care in the US is approx. \$6,096 (~PhP300,000).
- The pharmaceutical industry has a large environmental footprint.
- The estimated cost of drug development ranges from \$800M to \$1.7B with an estimated average development time of 14 years (Berndt et al. MIT, 2005).

➤ *Can we afford the US-style drug development system?*

The Natural Products industry is growing

The natural health products industry has been growing at the rate of about 15% per year.

(www.globe-net.com)



**All data in manufacturers' sales, unless otherwise indicated, manufacturers' sales refers to the price received by the marketer before distributor and/or retail markups.
The above figure only includes four key regions: United States, Europe, Asia, and Brazil.*

Global nutraceutical market

- 2011: \$142 B
- 2017: \$205 B (projected)
- Estimated growth rate: 6.3%

(Mitali Singh)

The Natural Products industry is growing ... but more science is needed!




Tungkulin ng
DEPARTMENT OF HEALTH
na alagaan ang kalusugan ng bayan.

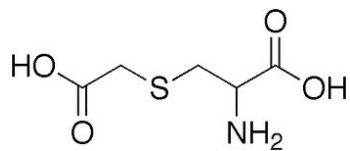
MAHALAGANG PAALALA:
ANG FOOD/DIETARY SUPPLEMENTS AY
HINDI GAMOT
AT HINDI DAPAT GAMITING PANGGAMOT
SA ANUMANG URI NG SAKIT.

*Mas mainam pa ring makakuha ng nararapat
na bitamina at mineral sa mga pagkain.*

Bago subukan uminom ng
Food/Dietary Supplements
sumangguni muna sa lehitimong duktur.

The Natural Products industry is growing

... but more science is needed!



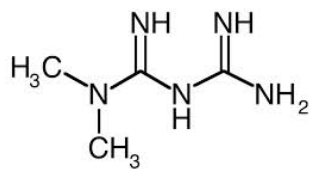
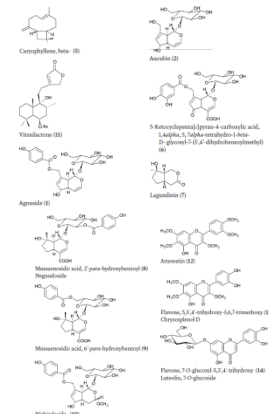
Carbocisteine



VS.

**VITEX
NEGUNDO L.
LAGUNDI
LEAF**

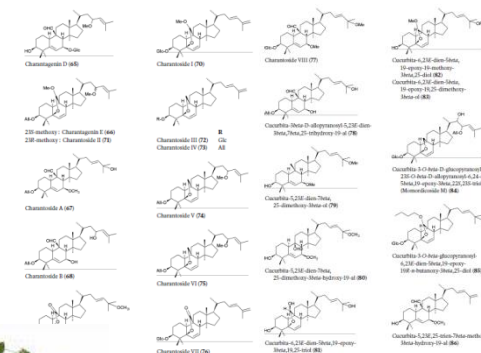
300 mg / 5 mL Syrup



Metformin



VS.



VS.



Challenges of Herbal Medicine

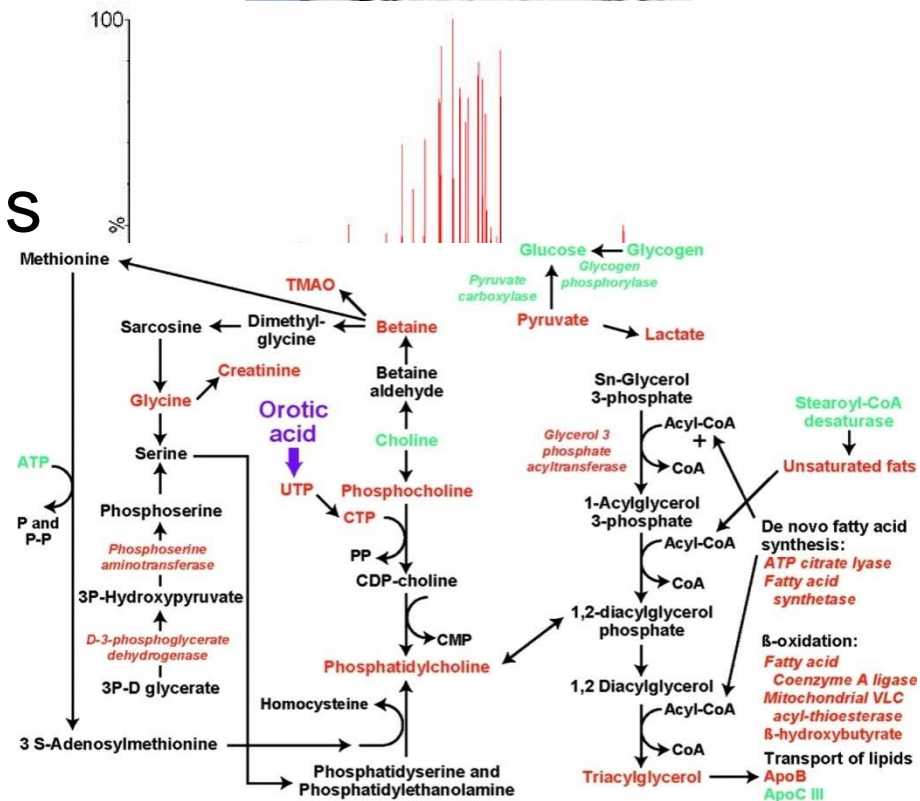
Modern science + Tradition + Affordability

➤ Validation of health claims



➤ Phytochemical analysis

➤ Identification of active substance(s); determination of mechanism(s) of action



Challenges of Herbal Medicine

Modern science + Tradition + Affordability

- Ensure the safety and efficacy of herbal products



Ten Leading Causes of Morbidity in the Philippines, 2002
(www.hero.org.ph)

- Address major diseases

Cause	Male	Female	Both Sexes	
	Rate**	Rate**	Number	Rate*
1. Pneumonias	931.1	881.7	734,581	924.0
2. Diarrheas	981.1	842.7	726,310	913.6
3. Bronchitis/ Bronchiolitis	748.1	798.8	629,968	792.4
4. Influenza	565.9	622.7	484,388	609.3
5. Hypertension	339.8	427.3	304,690	383.2
6. TB Respiratory	161.0	113.6	114,221	143.7
7. Diseases of the Heart	58.2	67.0	52,237	65.7
8. Malaria	53.5	42.6	39,994	50.3
9. Chickenpox	33.8	35.6	28,600	36.0
10. Measles	30.5	29.0	24,639	31.0

Synergy: Paradigm of Natural Products?

Indian Journal of Experimental Biology
Vol 48, March 2010, pp. 208-219

Drug development from natural products: Exploiting synergistic effects

Gudrun Ulrich-Merzenich^{a*}, D Panek^b, H Zeitler^b, H Vetter^a & H Wagner^c

^aMedical Polyclinic of the Rheinische Friedrich-Wilhelms-University of Bonn, Wilhelmstr. 35-37, D-53111 Bonn, Germany

^bInternal Medical Clinic I (CETA) of the Rheinische Friedrich-Wilhelms-University of Bonn,
Sigmund-Freud-Str. 25, D-53227 Bonn, Germany

^cDepartment of Pharmacy, Centre of Pharma Research, Ludwig-Maximilians-University,
Butenandstr. 5-13, House B, D-81377 Munich, Germany

Outlook and conclusions

In future drug development from natural products will not necessarily rely only on the discovery and analysis of new structures from nature's extremely rich biodiversity, but can systematically explore combinatory drug regimes. The introduction of the high throughput-technologies makes this possible. Their use has already changed our conceptual framework of drug targets, drug action and our understanding of the pathology of diseases (in favour of using phytomedicine).

Synergy: Paradigm of Natural Products?

Rasoanaivo et al. *Malaria Journal* 2011, **10**(Suppl 1):S4
<http://www.malariajournal.com/content/10/S1/S4>

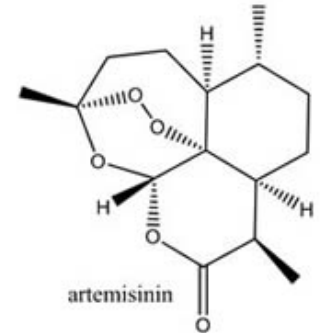


REVIEWS

Open Access

Whole plant extracts versus single compounds for the treatment of malaria: synergy and positive interactions

Philippe Rasoanaivo^{1*}, Colin W Wright², Merlin L Willcox^{3,4}, Ben Gilbert⁵



Results: There is evidence for several different types of positive interactions between different components of medicinal plants used in the treatment of malaria. Pharmacodynamic synergy has been demonstrated between the *Cinchona* alkaloids and between various plant extracts traditionally combined. Pharmacokinetic interactions occur, for example between constituents of *Artemisia annua* tea so that its artemisinin is more rapidly absorbed than the pure drug.

Some plant extracts may have an immunomodulatory effect as well as a direct antiplasmodial effect.

Synergy: Paradigm of Natural Products?

African Journal of Biotechnology Vol. 6 (25), pp. 2886-2896, 28 December, 2007

Review

The challenges of overcoming antibiotic resistance: Plant extracts as potential sources of antimicrobial and resistance modifying agents

T. Sibanda, and A. I. Okoh*

¹Applied and Environmental Microbiology Research Group (AEMREG), Department of Biochemistry and Microbiology,
University of Fort Hare. P/Baq X1314, Alice 5700, South Africa.

- Antimicrobial agents from plants most likely evolved through **different mechanisms** than antimicrobial agents derived from microorganisms and may act differently.
- There is a need to revisit antimicrobial agents from medicinal plants and understand them using the principles of synergy.

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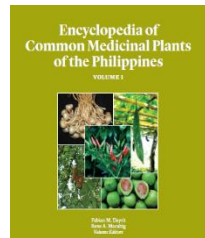
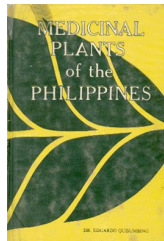
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Summary

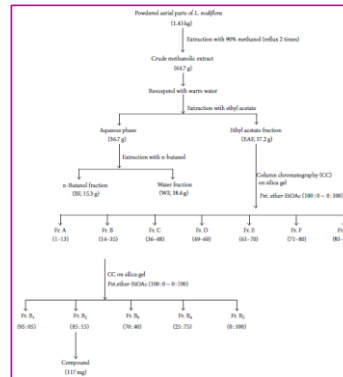
✧ Traditional use is an efficient and rational starting point for research on medicinal plants.

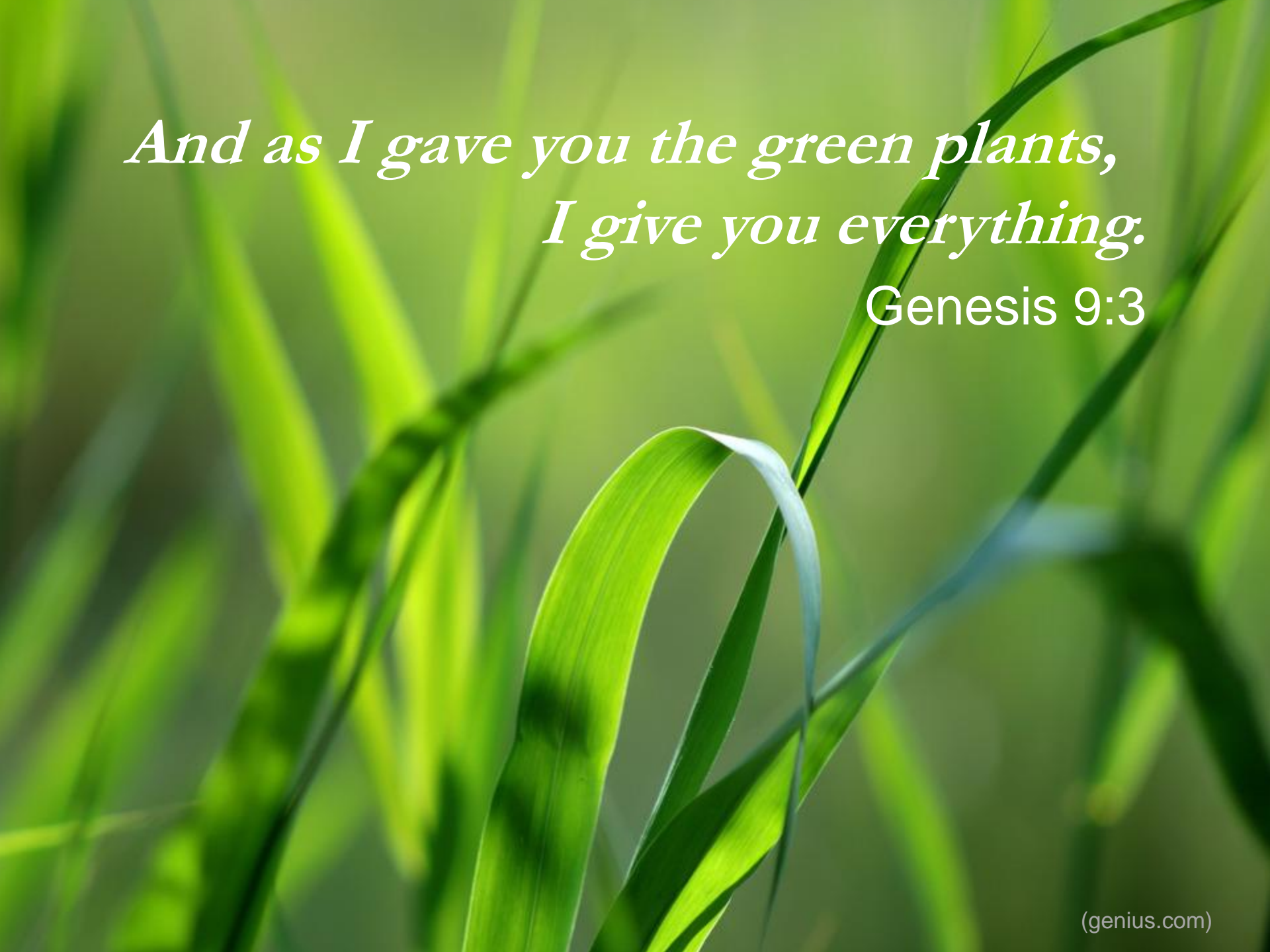


✧ There is a wide range of herbal products that can be developed.



✧ New paradigms and methods must be developed.





*And as I gave you the green plants,
I give you everything.*

Genesis 9:3