Moringaling Philipines Foundation Inc.

5th MORINGA Congress

THEME OF CONFERENCE

MORINGA, WORLD'S SUPERFOOD

KEYNOTE SPEAKER

Dr. Jed Fahey of the Johns Hopkins University, USA

Mimosa, Clark, Pampanga
November 21-22, 2013
Visit www.moringaling.net or call 026215391;09258430033

5th Moringa Congress
Clark, Philippines
November 22, 2013

The Potential Medicinal Value of *Moringa oleifera* and the Need to Preserve Its Vanishing Germplasm Resources

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Dietary Approaches to the Prevention of Chronic Disease

Moringa: The Strength of the Scientific Evidence for Medicinal Effects

Understanding Moringa Germplasm Diversity

Dietary Approaches to the Prevention of Chronic Disease

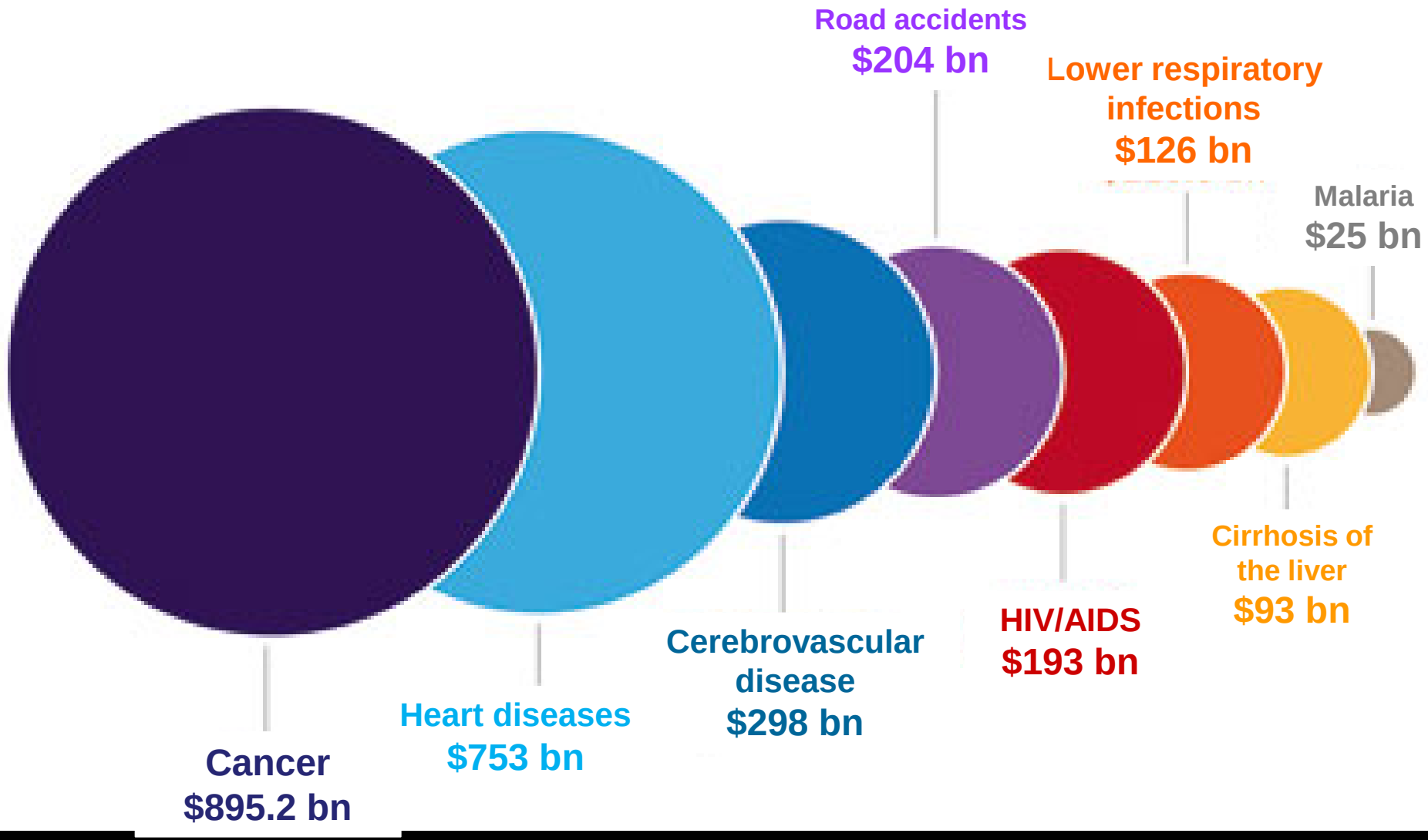
Moringa: The Strength of the Scientific Evidence for Medicinal Effects

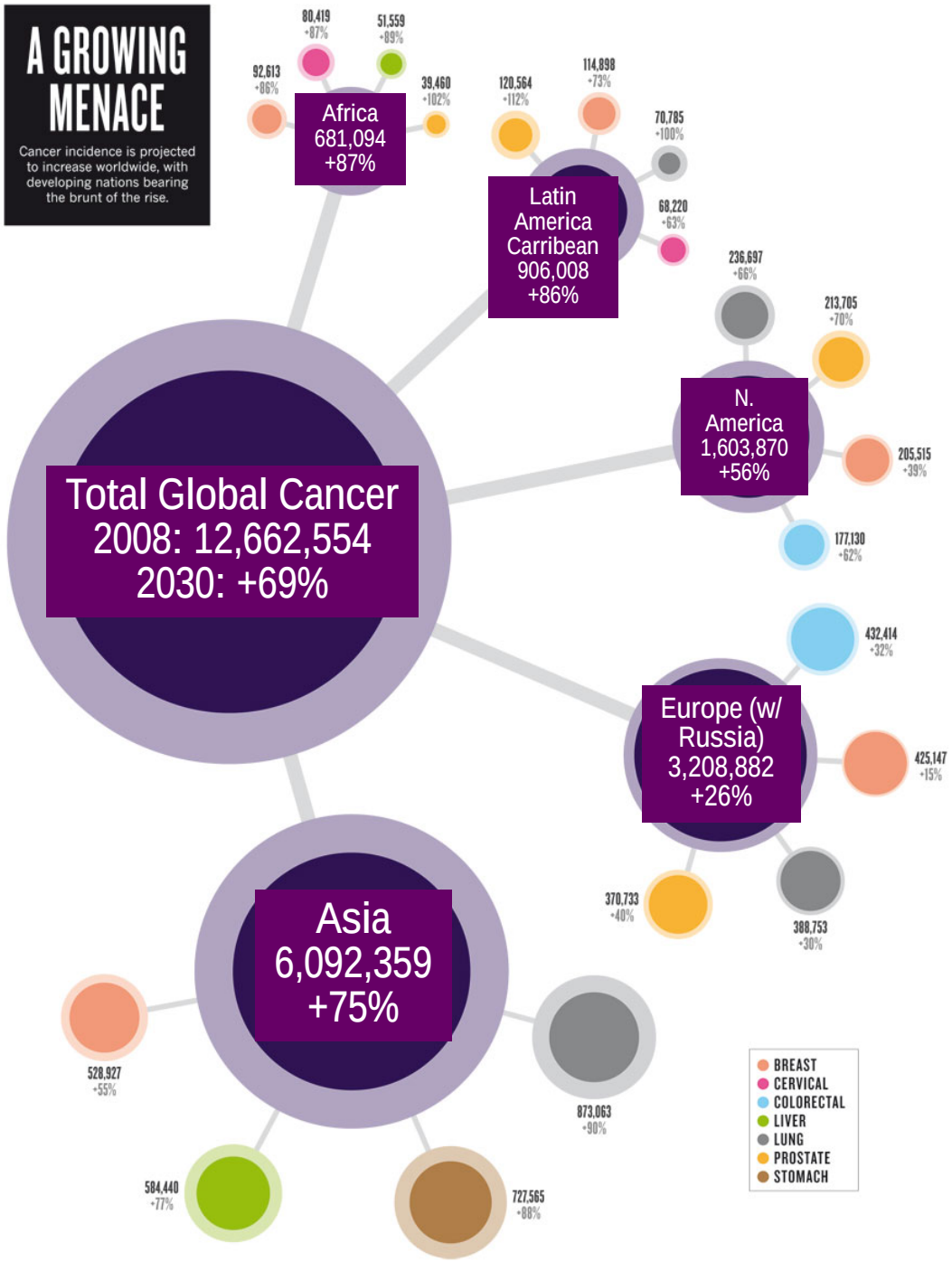
Understanding Moringa Germplasm Diversity

Jed W. Fahey, 11/22/2013 Presentation
5th Moringa Congress, Clark, Philippines

GLOBAL ECONOMIC CHRONIC DISEASE BURDEN

The burden of cancer, calculated as the cost of years lost from ill-health, disability or early death, outweighs all other health concerns.





O'Callaghan (2011)
Nature 471: s2-s3.

Proportion of Cancers Attributed to Different Factors

Factor	Best estimate (%)	Plausible Range (%)
Tobacco	33	25 - 40
Diet including obesity & inactivity	30	20 - 60
Infection: viral, bacterial, parasitic	18	10 - 25
Reproductive factors and hormones	7	5 - 10
Ionizing radiation, especially imaging	6	4 - 8
Heredity	5	2 - 8
Occupation--reaffirmed	3	2 - 8
Alcohol	3	2 - 4
UV light	1	0.5 - 1
Pollution	<1	<1 - 2
Medicines	<1	<1- 2
Industrial products	<1	<1 - 2
Food additives	<1	-2 - 1

Prevention → Ideally, by modifying exposure

Doll & Peto, 1981; 1996; Levine et al, 1989; Li et al., 1991; Pisani et al., 1997; Key et al., 1997; Parkin et al., 2006; **GS Omenn, 2011**

Prevention
Lifespan vs. *Healthspan*

As starvation and contagious diseases are being reduced, lifespans are increasing . . . but . . . these conditions are rapidly being replaced by conditions associated with food and with chronic stress and the oxidative and inflammatory conditions associated with that stress.

So while lifespan may be increasing, *healthspan is not increasing commensurately.**

**healthspan: the enjoyment of good health, or aging with minimal handicap and near full function for the duration of a vigorous and productive natural life*

Fahey & Kensler (2013) American Medical Association Virtual Mentor 15(4): 311-318.

Prevention
Lifespan vs. *Healthspan*

The chronic diseases of aging are overwhelming the health care systems of the world.

These, and similar statistics for other chronic diseases, are progressively defining medicine by its ability to deliver long-term health care, but not as a tool for extending *healthspan*.

Fahey & Kensler (2013) American Medical Association Virtual Mentor 15(4): 311-318.

PREVENTION WORKS!

Priorities of CDC's Heart Disease and Stroke Prevention Program

Mortality Rates for Cancers and Heart Disease 1975-2006

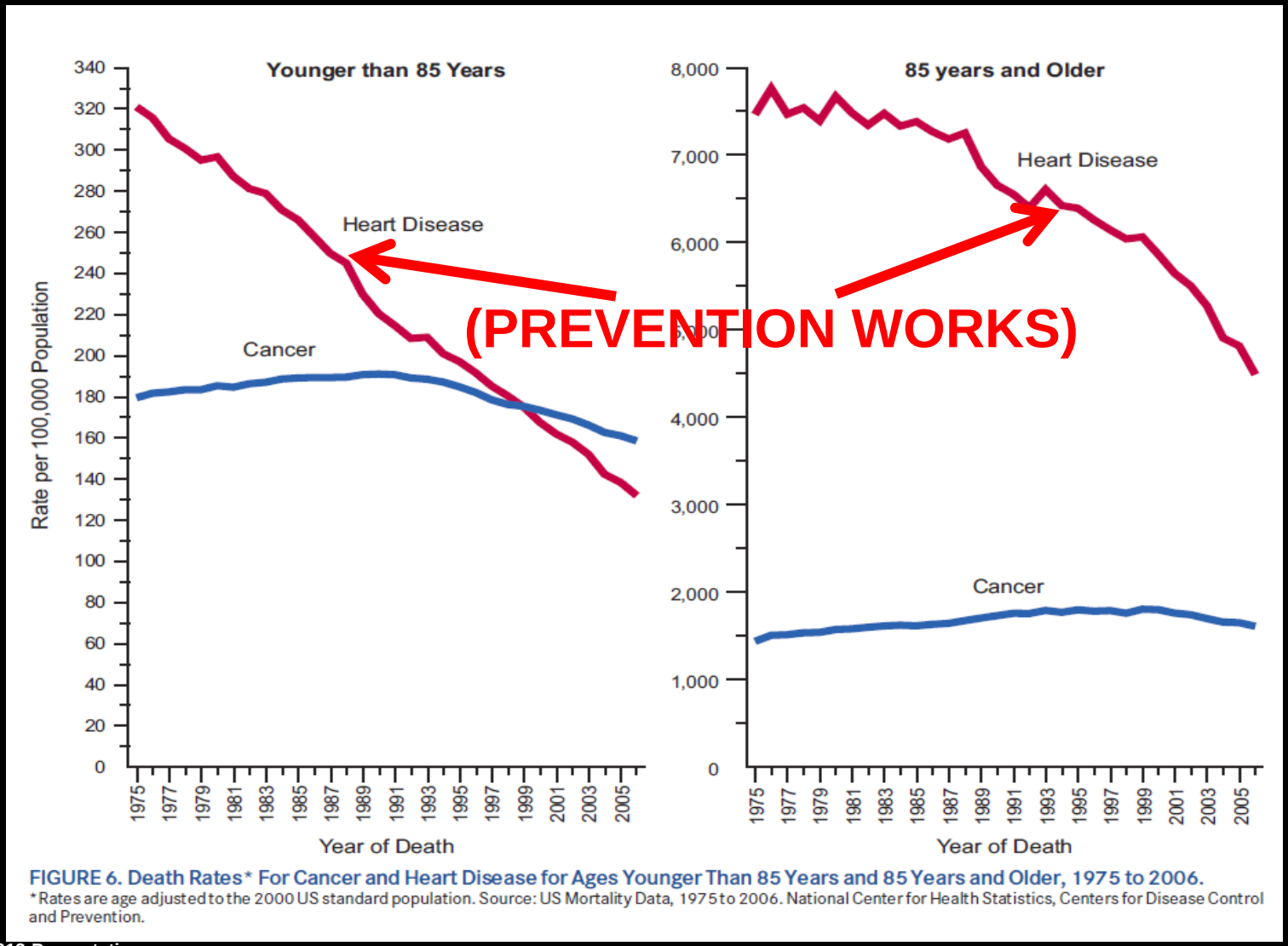
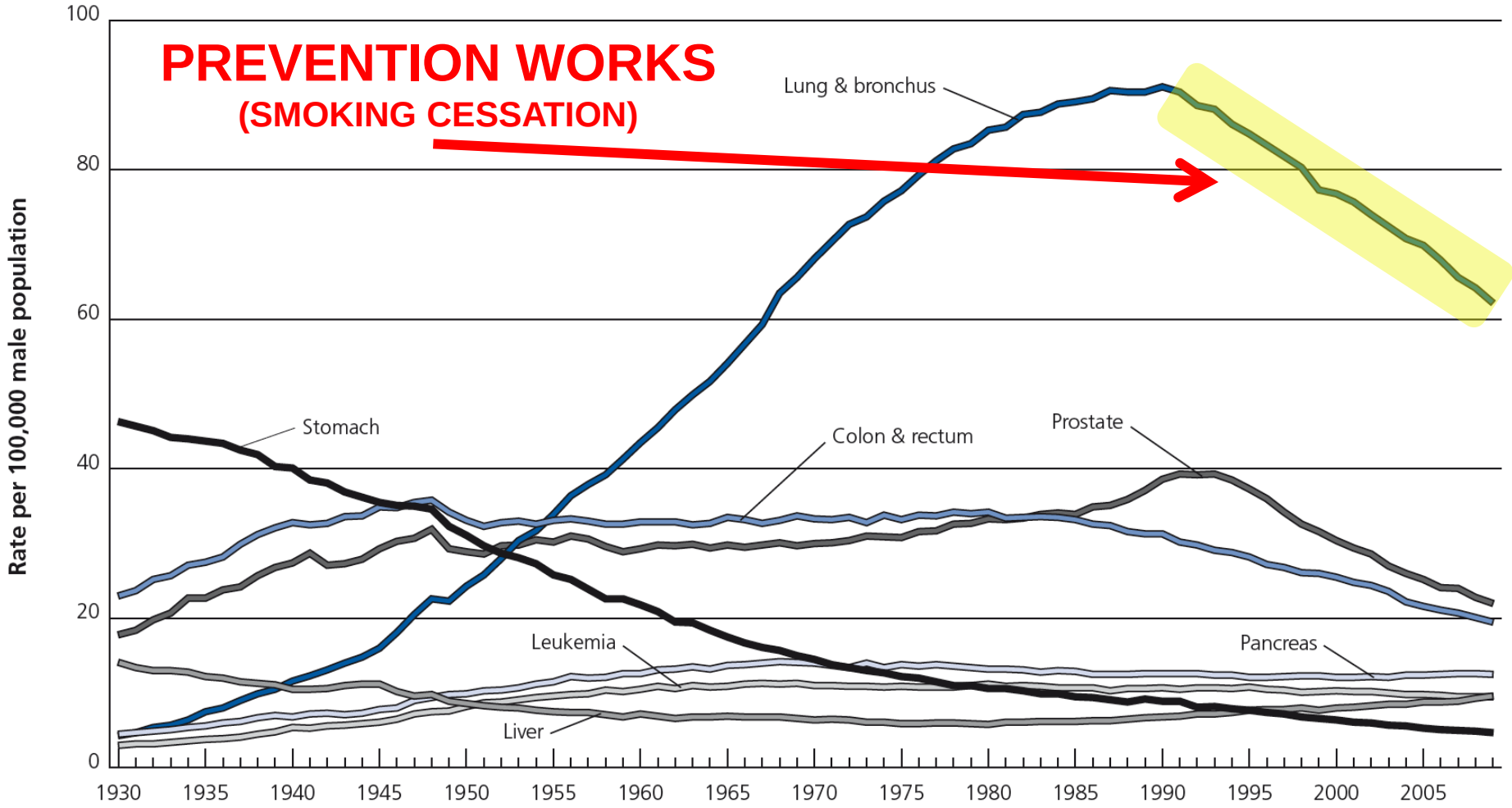


FIGURE 6. Death Rates* For Cancer and Heart Disease for Ages Younger Than 85 Years and 85 Years and Older, 1975 to 2006.
*Rates are age adjusted to the 2000 US standard population. Source: US Mortality Data, 1975 to 2006. National Center for Health Statistics, Centers for Disease Control and Prevention.

Age-adjusted Cancer Death Rates*, Males by Site, US, 1930-2009



*Per 100,000, age adjusted to the 2000 US standard population.

Note: Due to changes in ICD coding, numerator information has changed over time. Rates for cancer of the liver, lung and bronchus, and colon and rectum are affected by these coding changes.

Source: US Mortality Volumes 1930 to 1959, US Mortality Data 1960 to 2009, National Center for Health Statistics, Centers for Disease Control and Prevention.

Prevention: Framing the Battle

Cancer development is a continuum. It is like a smoldering barn full of hay that, before it bursts into flames is NOT a safe place to be.

Michael Sporn (2011; *Nature* 471: S10-11)

We need an approach that is prescriptive, rather than proscriptive. 'Chemoprevention' connotes all the negatives (DON'T eat charred meat, NEVER smoke, AVOID hazardous situations, MINMIZE time in the sun, etc.), whereas 'chemoprotection' connotes being proactive and taking positive [dietary] steps to protect your health.

Paul Talalay (ca. 1985)

Principles of Chemoprotection[1]

1. All aerobic cells are constantly stressed by:

   - REACTIVE OXYGEN INTERMEDIATES
   - TOXIC DNA-DAMAGING CARCINOGENS
   - INFLAMMATION/INFECTION
   - RADIATION (UV, Ionizing)

   That can lead to cancer and chronic degenerative diseases

2

1. Paul Talalay
2. Albrecht Dürer

Principles of Chemoprotection

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   Can lead to cancer and chronic degenerative diseases

2. **Cells contain protective "Phase 2" (Nrf2-dependent) genes that do not normally operate at maximum capacity, but can be induced by a wide variety of chemical agents, including many dietary phytochemicals**

3. **Upregulating these enzymes is highly protective and reduces the risk of cancer and chronic degenerative diseases. A key feature (product) of these enzymes is the cellular antioxidant glutathione (GSH)**

Principles of Chemoprotection

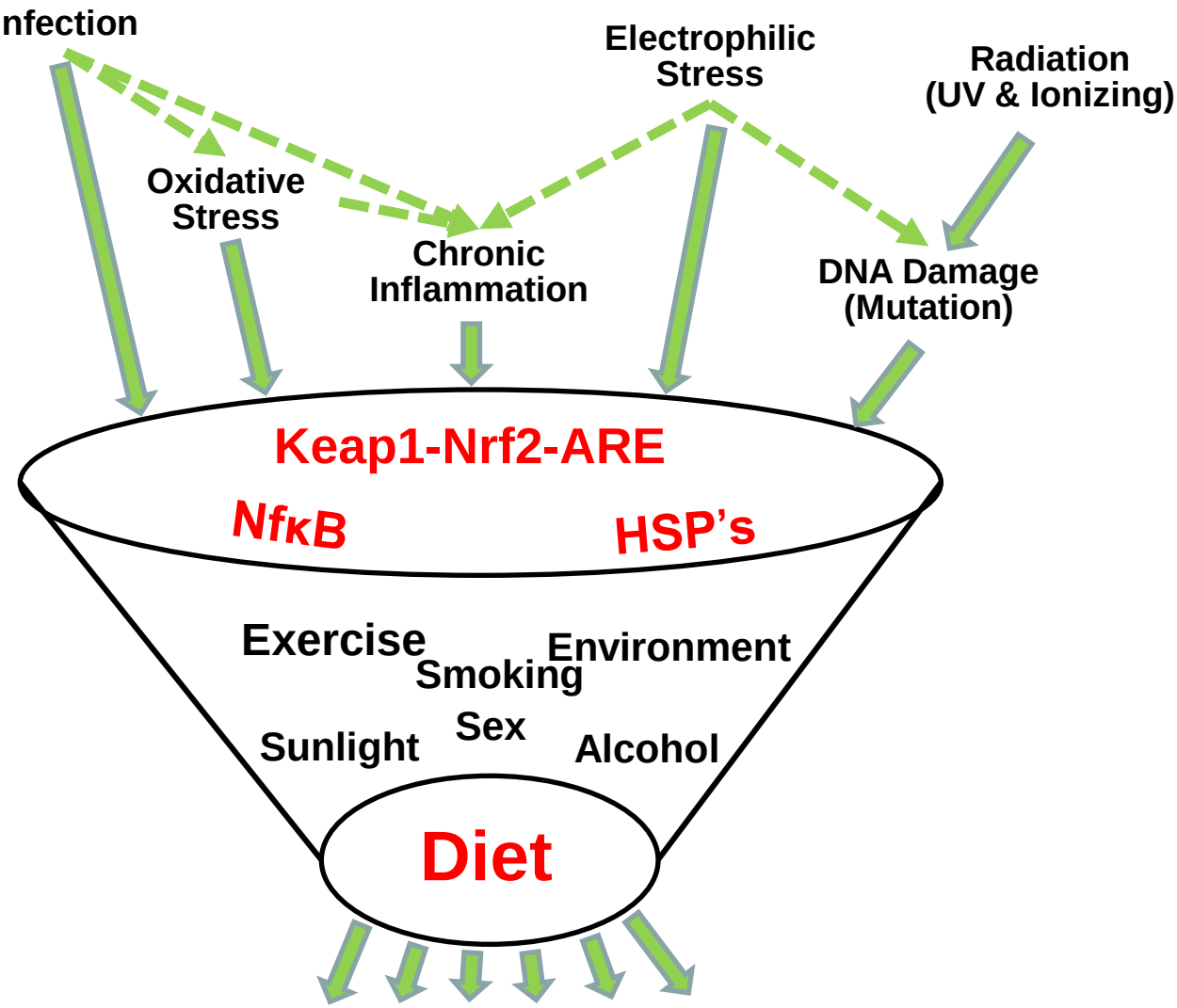
4. Susceptibility to carcinogen damage is controlled – at least in part, by balance between Phase 1 enzymes that activate and Phase 2 enzymes that detoxify carcinogens.
5. Susceptibility can be reduced (chemoprotection) by manipulating balance between the two families of enzymes

Phytochemicals, Chronic Disease and Metabolism

Processes Central to Disease Pathophysiology

Effectors

Corporeal & Behavioral Modifiers



Chronic Diseases including Cancer

There is overwhelming epidemiological evidence that high fruit and vegetable consumption reduces risk of cancer and other chronic diseases.

We and others have obtained overwhelming evidence that edible plants contain inducers of the Phase 2 (cytoprotective enzyme) response.

"Green Chemoprevention"

•Use of dietary means to deliver chemoprotective phytochemicals makes good sense; chemoprevention by whole foods, or simple extracts of whole foods, presents unprecedented opportunities to solve unmet global problems.

•The overwhelming advantage of green chemoprevention* is that it is frugal, realistic, and economically sustainable in underserved and economically deprived populations which will become the major targets of chronic illness in the foreseeable future. Thus, it can serve rich and poor alike.

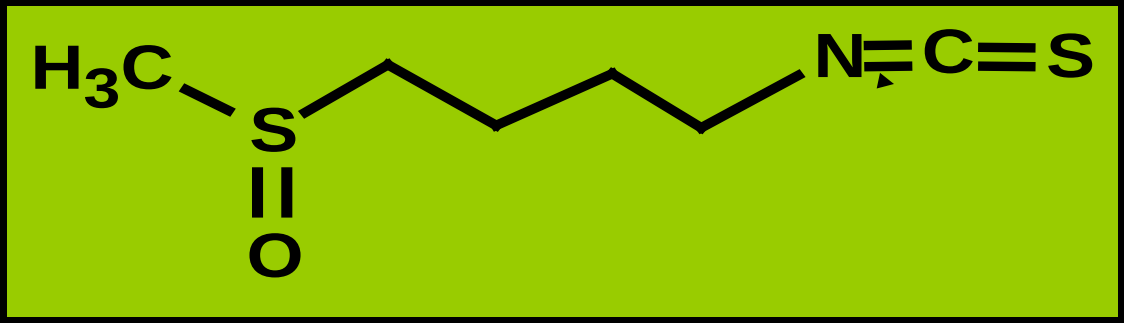
**Compared to developing pharmaceuticals to protect theoretically healthy individuals.*

Fahey, Talalay & Kensler (2012) *Cancer Prev Res 5(2):179-188.*
Fahey & Kensler (2013) American Medical Association Virtual Mentor 15(4): 311-318.

Background of our work with phytochemical-rich plants

A variety of edible plants, especially crucifers (e.g. broccoli) contain inducers of the Phase 2 (cytoprotective enzyme) response.

Sulforaphane

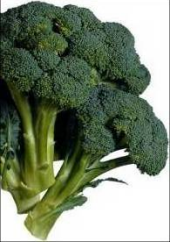


An isothiocyanate (“mustard oil”) isolated from broccoli is the principal and very potent Phase 2 cytoprotective enzyme inducer.[1]

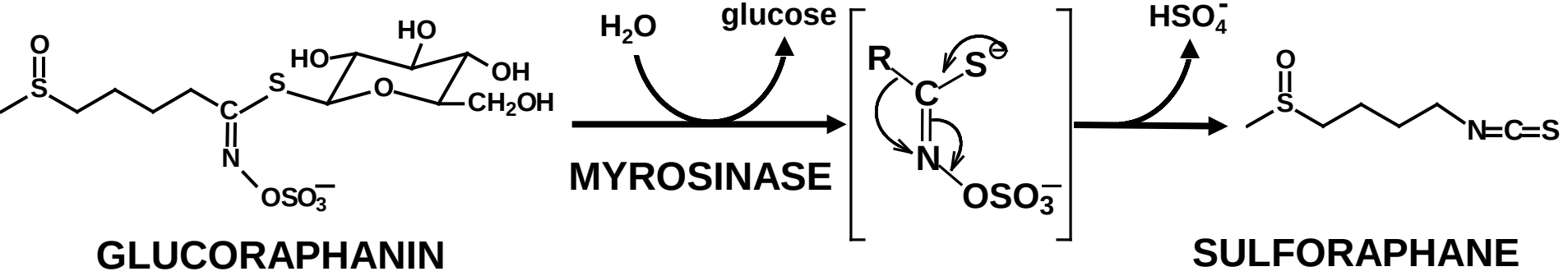
Later, its precursor (glucoraphanin) was found in very high levels in broccoli sprouts.[2]

Sulforaphane was then shown to be a highly selective antibiotic vs. *Helicobacter pylori*.[3]

1. Zhang, Talalay, Cho & Posner (1992) PNAS
2. Fahey, Zhang, Talalay (1997) PNAS
3. Fahey et al. (2002) PNAS



The “Mustard-Oil Bomb”



GLUCORAPHANIN

SULFORAPHANE

- water soluble
- heat stable
- non-reactive

and / or

Gut Microflora

- not very water soluble
- heat-sensitive
- reactive

Fahey et al (2001) *Phytochemistry* 56(1): 5-51

Although sulforaphane (from broccoli) and other isothiocyanates (including those from Moringa) are not direct antioxidants, they activate transcription of phase 2 cytoprotective genes, whose products provide chemically versatile, often catalytic, and prolonged indirect antioxidant protection.

We ultimately developed broccoli sprouts as a dietary source of chemoprotective activity, exploiting *green chemoprevention* or *frugal medicine.*

How to Move Forward?

The first use in a clinical intervention was with broccoli sprouts grown at the study site.

But many bridges had to be crossed in order for us to move forward with clinical trials.

Challenges for Green Chemoprotection

- Efficacy
- Cost
- Taste → Cultural Acceptability
- Delivery (Logistics & distribution)
- Clinician buy-in
- Control of food product integrity
- Safety (responsibility and liability)
- Regulatory paradigm shift (IRBs and FDA)

CHALLENGE

Who Will Pay for Trials?

Early participation of pharmaceutical companies, is unlikely (*and we would not welcome it*) because the intellectual property considerations which have been central to their enormous success do not exist.

But food manufacturers, packers, distributors, formulators, retailers, and their suppliers (e.g., seed producers) should assume responsibility for sponsoring phytochemical-based prevention trials.

Fahey, Talalay & Kensler (2012) *Cancer Prev Res 5(2):179-188.*

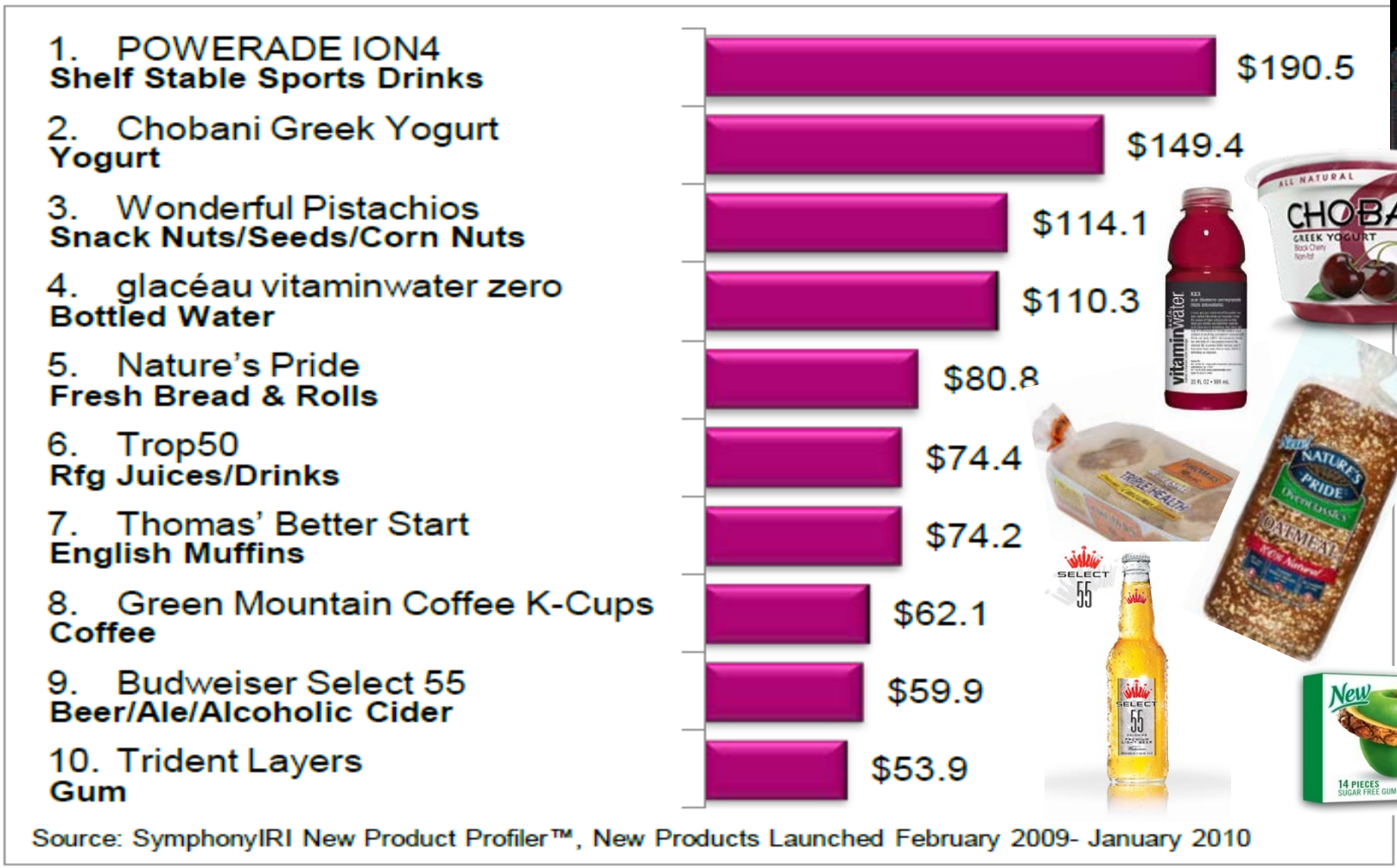
The Food Industry is the 3rd largest manufacturing industry… after transportation equipment (#1), and petroleum/coal products (#2).

$600 Billion Grocery

$400 Billion Food Service

Courtesy of M. Gillette

Most Successful New Products in 2010



2010 New Product Pacesetters: Top 10 Food & Beverage Brands

Year-One Dollar Sales ($ Mil) Across Food, Drug and Mass (Excluding Walmart)

Courtesy of M. Gillette

CHALLENGE

Clinician buy-in

- Inflexible crossing-over between:
  - Physicians & pharmaceuticals

    AND
  - Nutritionists/dieticians & food

- Clinicians tend not to recommend dietary approaches or natural products.

- Back to the future: "*Let thy food be thy medicine and medicine be thy food*" (Hippocrates)

In early broccoli sprout studies, fresh sprouts were administered to small numbers of subjects:

Riedl (2008)
3 days of oral broccoli sprout smoothies . . .

Galan and Silverman (2004)
7/9 (6/9) subjects “cured” of *H. pylori*

Yanaka, Fahey, et al. (2005, 2009)
Significantly reduced biomarkers of *H. pylori* infection

Riedl, Saxon, Diaz-Sanchez: (*Clin. Immunol. 2008*)

Oral sulforaphane increases Phase II antioxidant enzymes in the human upper airway

Day 1
Day 2
Day 3

Separate Cohorts (5 subjects each)

25 - 200 g by mouth, of broccoli sprout homogenate hydrolyzed with daikon myrosinase (corresponding to 12.5 – 100 µmol sulforaphane daily)

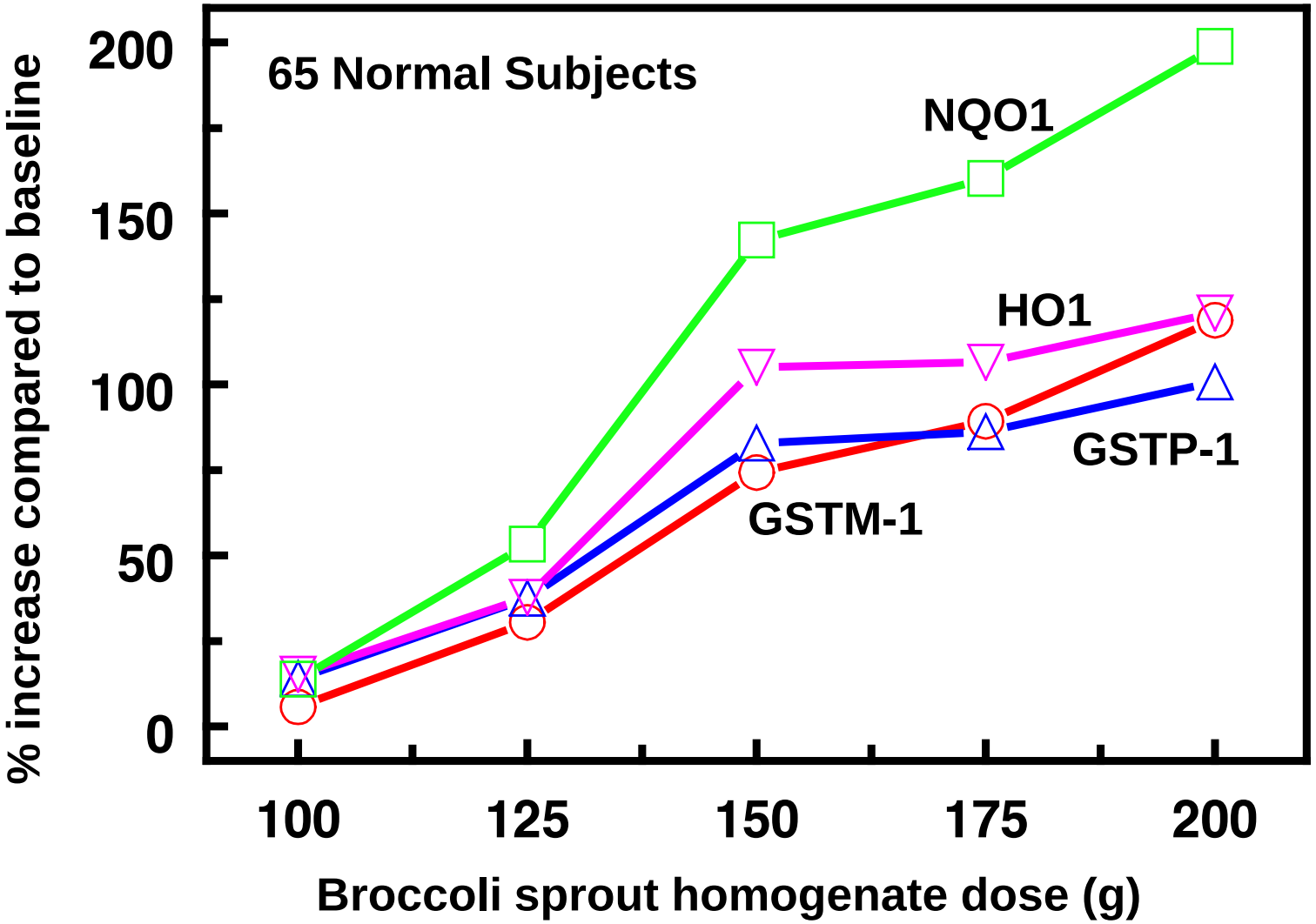
Placebo: 200 g alfalfa sprouts

Day 4

measured levels of mRNA in NASAL LAVAGE CELLS

NQO1
Glutathione Transferases (GSTM1 and GSTP1)
Heme Oxygenase (HO-1)

Oral Sulforaphane Increases Phase 2 Enzymes in Upper Airway as Measured in Mucosal Lavage



Riedl et al. (2008) Clin Immunol

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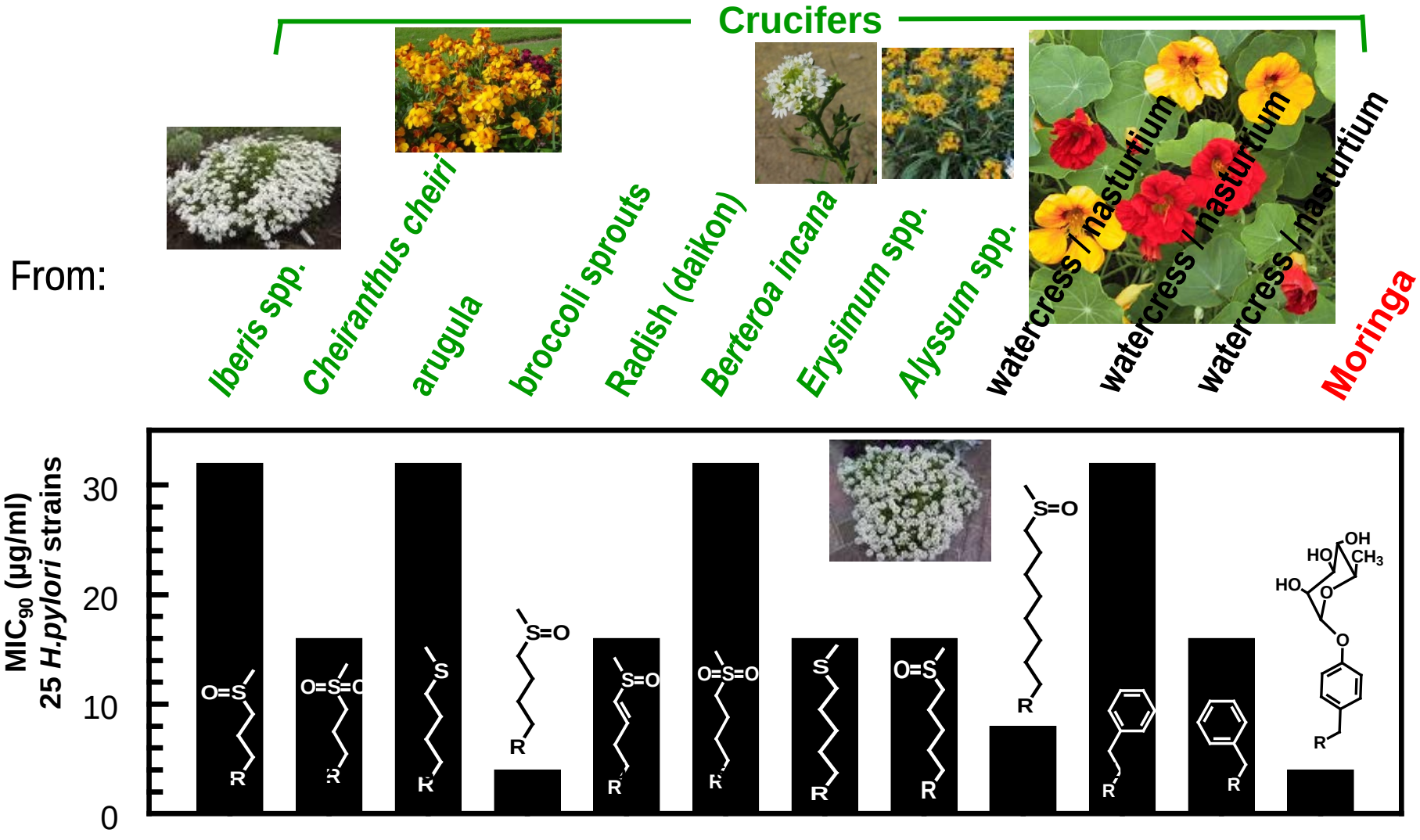
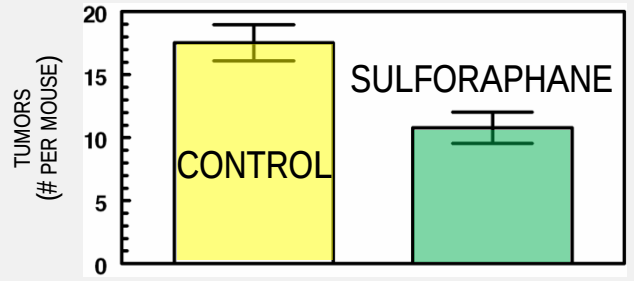
Antibacterial potency of a variety of plant-derived isothiocyanates against *Helicobacter pylori*



Haristoy, Fahey, Scholtus, Lozniewski (2005) *Planta Medica* 71: 326-330.
Fahey et al. (2002) *Proc. Nat. Acad. Sci. USA* 99(11): 7610-7615.

BROCCOLI & MORINGA

GASTRIC TUMORS PER MOUSE FORESTOMACH (CHEMICAL CARCINOGENESIS MODEL)



We discovered that sulforaphane is a highly effective antibiotic against all 48 strains of *H. pylori* tested

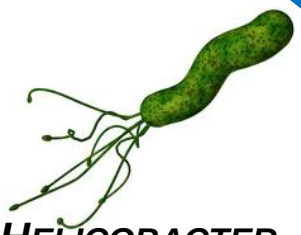
It is equally effective against strains resistant to the 2 antibiotics most commonly used to treat *H. pylori* infections in people.

Helicobacter is recognized as a carcinogen by the W.H.O.

Infected individuals have 3- to 6-fold higher risk of gastric carcinoma.

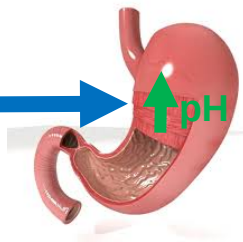
ISOTHIOCYANATES

ANTIOBIOTICS & PROTON PUMP INHIBITORS
(WHICH ARE EFFECTIVE ONLY 75-90% OF THE TIME)



HELICOBACTER PYLORI

UREASE



GASTRITIS → ULCER → STOMACH CANCER & LYMPHOMA

ASYMPTOMATIC INFECTION

UREA

Jed W. Fahey, 11/22/2013 Presentation
5th Moringa Congress, Clark, Philippines

Patient Characteristics and Test Results Following Broccoli Sprout Therapy

- **Subjects received 14, 28, or 56 g fresh broccoli sprouts (~84 - 336 µmol) 2x/day, for 7 d.**

- ***H. pylori*-positive patients were identified by stool antigen testing or gastric biopsies.**

- **7of 9 (78%) patients were HpSA^{neg} immediately after the completion of therapy and 6 remained negative at day 35.**

- **UBT was completed on 6 patients →**
  - **2 were neg., 2 pos., and 2 indeterminate.**

- **Endoscopic gastric biopsies were obtained from 1 patient with an indeterminate breath test and the tissue was negative for *H. pylori* by immunohistochemical staining.**

Galan et al. (2004) *Dig Dis Sci* 49: 1008-1010.

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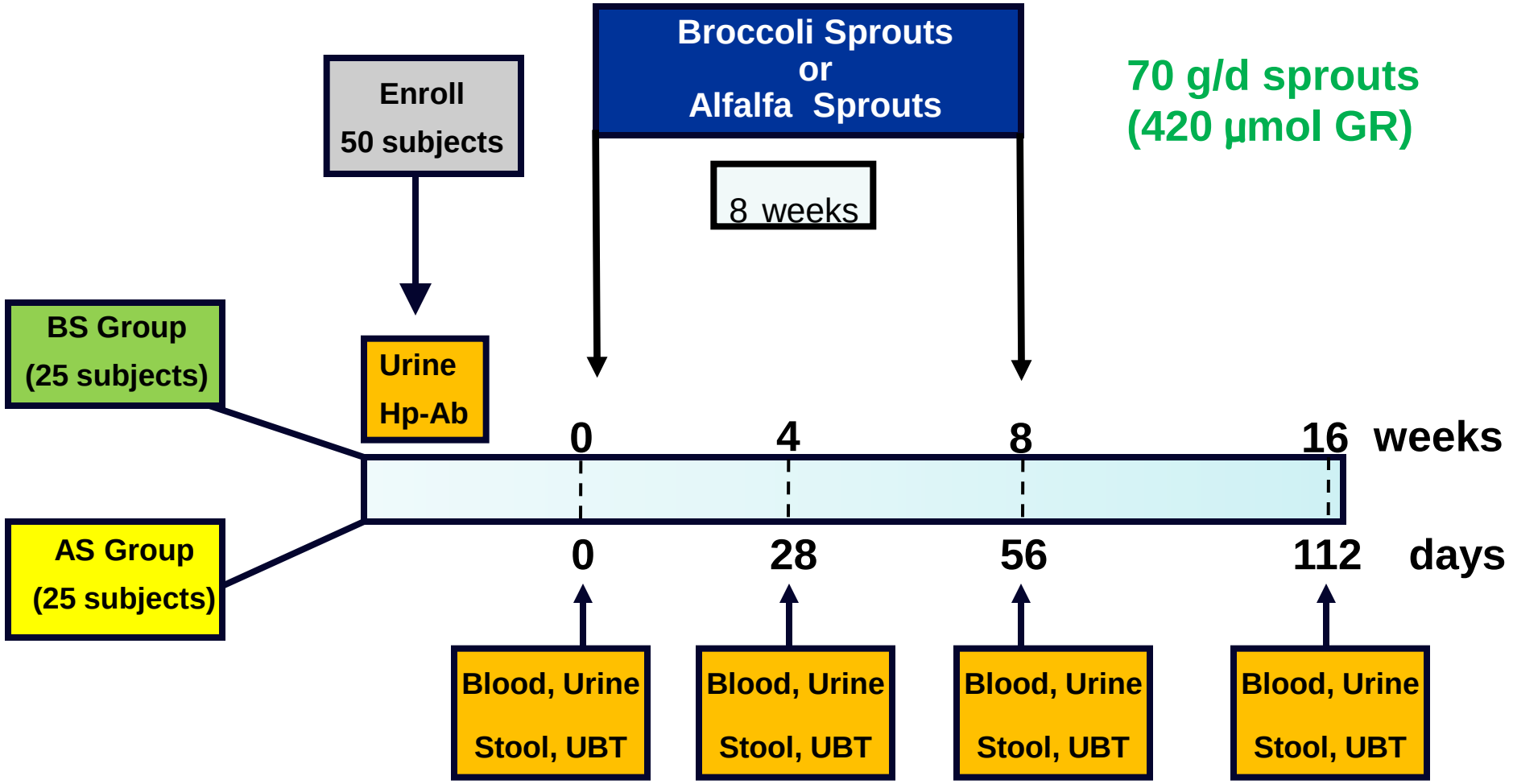


Treatment of *H. pylori*-infected humans with fresh broccoli sprouts reduces gastric colonization, inflammation, and *H. pylori* stool antigens

Yanaka, Fahey et al. (2009) *Cancer Prevention Research*

Sulforaphane Effects on *H. pylori* Infection: A Small Clinical Trial

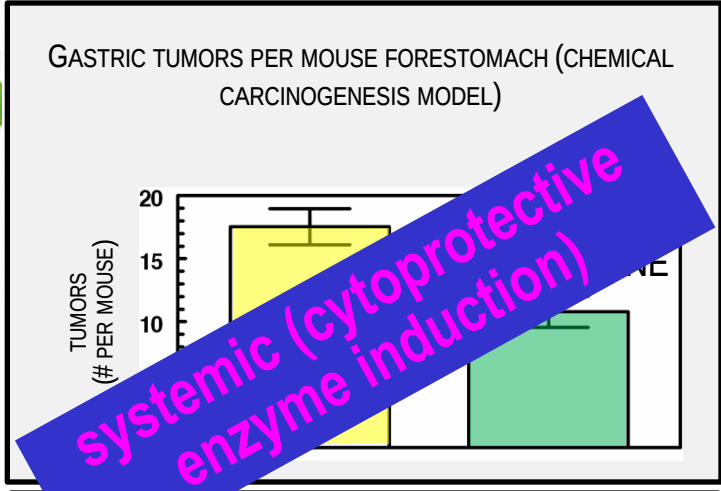
- 50 subjects infected with *H. pylori* were randomly assigned to eat either broccoli sprouts (400 µmol sulforaphane/glucoraphanin or alfalfa sprouts (No SF/GR)
  (70g/day x 60 days)
- Hp colonization was measured by stool antigen, and urea breath test
- Degree of gastritis was evaluated by measuring serum levels of pepsinogen
- Measurements were performed just before the intervention, 1 and 2 months into the intervention, and 2 months after the intervention

Broccoli sprouts, but not alfalfa sprouts:

1) Decreased Hp stool antigen during the intervention
2) Decreased UBT score during the intervention
3) Decreased PG I and II during the intervention
4) These values recovered to initial levels at 2 months after intervention

Yanaka, Fahey et al. (2009) *Cancer Prevention Research*

BROCCOLI & MORINGA



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antibiotic

antibiotic

urease inactivator

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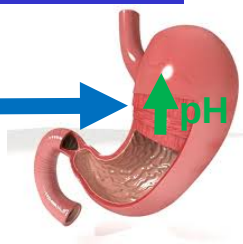
UREASE



UREA

GASTRITIS → ULCER → STOMACH CANCER & LYMPHOMA

ASYMPTOMATIC INFECTION

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CHALLENGE

Cultural Acceptability

Fresh sprouts are OK in Japan and Korea, but not in US or China, and not for longer duration trials

Concentrated extract (BSE)* is more controllable and reproducible

*BSE = a freeze-dried (lyophilized) Broccoli Sprout Extract which we make at, or via Johns Hopkins University

Preparation of BSE for use in clinical interventions:

Provide seeds of known provenance and GR/SF titer HOW?

Contract to grow large batch 3d old sprouts HOW?

Boiling water extract WHERE?

± Treat with myrosinase HOW?

Freeze-dry WHERE?

QA testing (microbial, metals, phytochemical titer) WHAT? WHERE? HOW MUCH?

Dosify ± masking, and packaging

- water
- juice (e.g. mango, lime, pineapple) HOW? WHERE? WHO?
- gel-caps

Fahey, Talalay & Kensler (2012) *Cancer Prev Res 5(2):179-188.*

Clinical Trials with BSE:

>25 trials worldwide, 13 of them with approved INDs

Clinical Interventions Using SF-Rich Broccoli Sprout Extract (BSE) --- ± INDs

CANCER PREVENTION

- Stomach cancer prev. (Vanderbilt, Tsukuba, Tohoku, Balt.)
- Liver cancer prev. (China)
- Air toxics prev. (China)
- Breast cancer prev. (Balt.)
- Breast cancer therapy (Balt.)
- Colon cancer prevention (OSU)
- Prostate cancer prev. (Fred. Hutchinson; JHU; OHSU; OSU)
- Bladder cancer treatment and prev. (RPCRC Buffalo)
- Skin cancer prev. (Balt., Scotland)

NON-CANCER

- Skin treatment (Balt.)
- COPD treatment (Balt., Philly, Buffalo)
- Drug metabolism (U Wash)
- Asthma treatment (Balt.)
- GR→SF conversion (Balt.)
- Allergic airway prev. (UCLA)
- Autism (Boston, Balt.)
- Parkinson's (planning stage)
- X-ray irradiation damage (Balt.)

3 broccoli sprout (BSE) trials in China:

(2002) water MADE ON-SITE

(2003) water MADE ON-SITE

(2009) dilute mango juice CARRIED IN

(2011) dilute pineapple/lime juice CARRIED IN

Kensler, Egner, Groopman (2012) *China Cancer*: 21(10): 732-743.
Egner et al. (2013) *Prog. Chem.*: (*in press*)

Dietary Approaches to the Prevention of Chronic Disease: Chemoprevention *vs*. Chemoprotection *vs*. Green Chemoprotection

The prevention of chronic and degenerative diseases (like cardiovascular disease, cancer, chronic obstructive pulmonary disease {COPD}, asthma, stroke, obesity, Alzheimers, and diabetes) has in the last 30 years overtaken treatment of the scourges of starvation and a variety of infectious and communicable diseases as an urgent health priority in much of the world.

However, they both continue to coexist in many sections of many countries and they are overwhelming those nations' health care systems. The diseases associated with smoking, overeating, and sedentary lifestyles are but two of the most glaring and obvious examples worldwide.

We have for many years been studying edible plant-based (dietary) approaches for prevention that seek to impede, block, or even reverse the early steps in disease progression, including the molecular steps involved in its initiation. The use of a food-centered approach can be sustainably applied in underserved poor populations as well as in the personalized medicine that is catching on in richer countries. In fact, we cannot afford not to change our approaches.

We discovered that broccoli sprouts are an exceptionally rich source of inducers of the enzymes that detoxify carcinogens, and developed techniques to detect these inducers and assess their metabolism in humans.

More recently, we determined that one of these inducers, the isothiocyanate sulforaphane has selective and potent antibiotic activity against *Helicobacter pylori* (a causative agent of dyspepsia, peptic ulcer disease and stomach cancer) and it is equally effective against multiply antibiotic resistant strains.

We have just discovered that it inactivates urease (a major pathogenesis factor of this bacterium) by an apparently independent mechanism.

We have developed, characterized, and supplied preparations rich in specific phytochemicals for a large number of animal and clinical studies.

Sulforaphane comes from an inert precursor "glucosinolate" storage molecule only when that molecule is acted upon by an enzyme that is present both in the plant tissue (but kept separate until the plant is bruised or chewed), in an explosive reaction dubbed the "mustard oil bomb".

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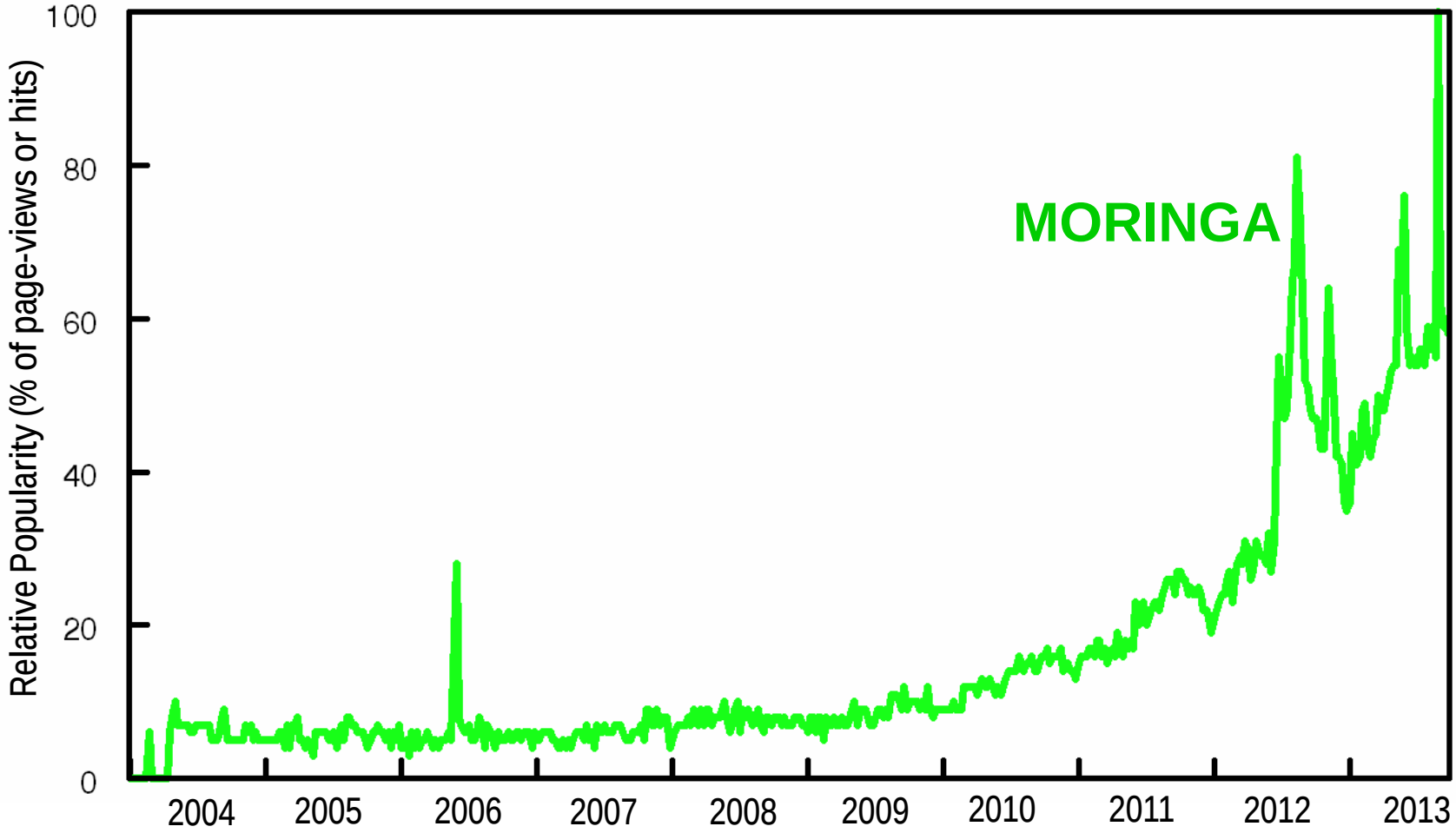

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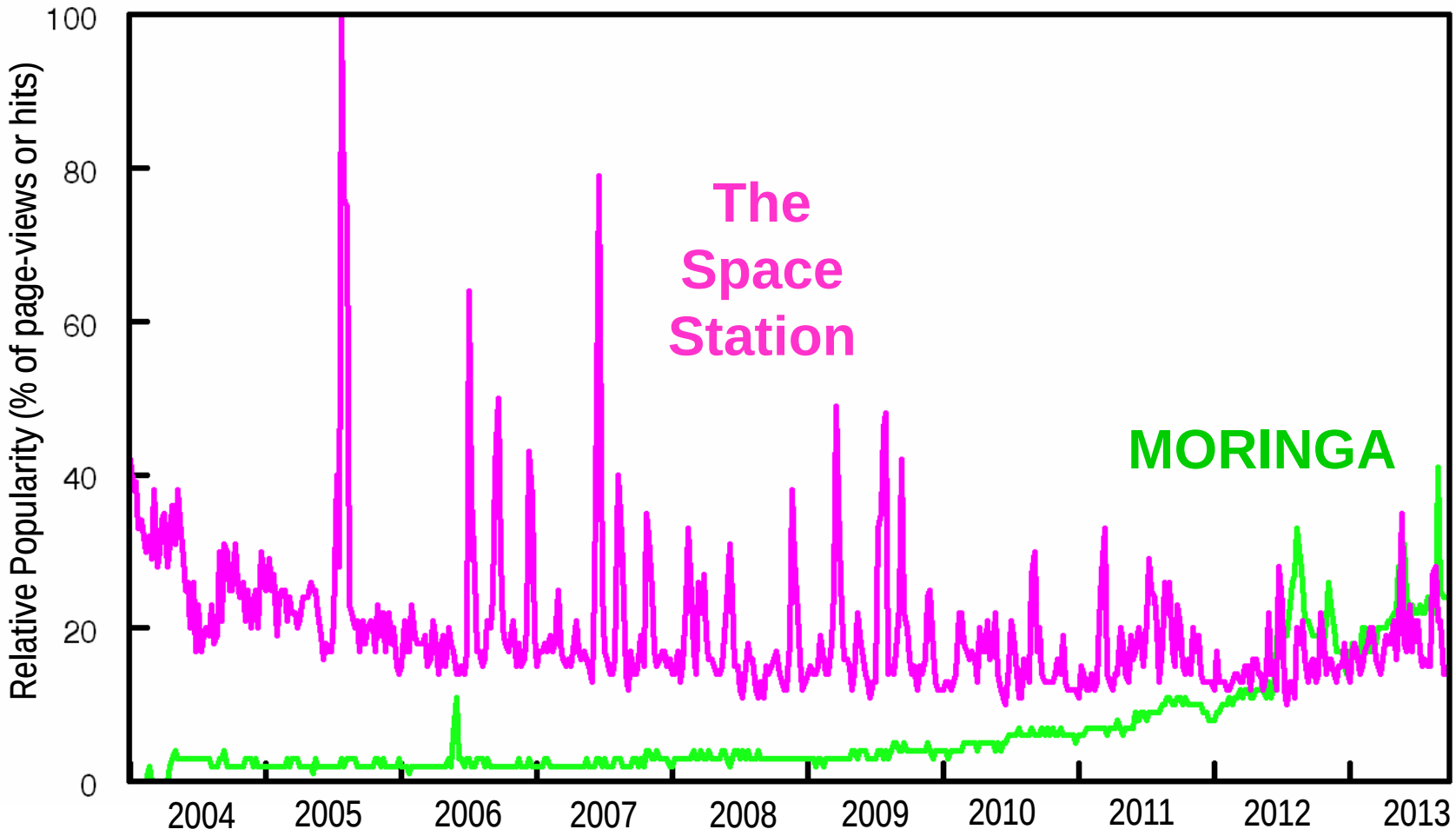
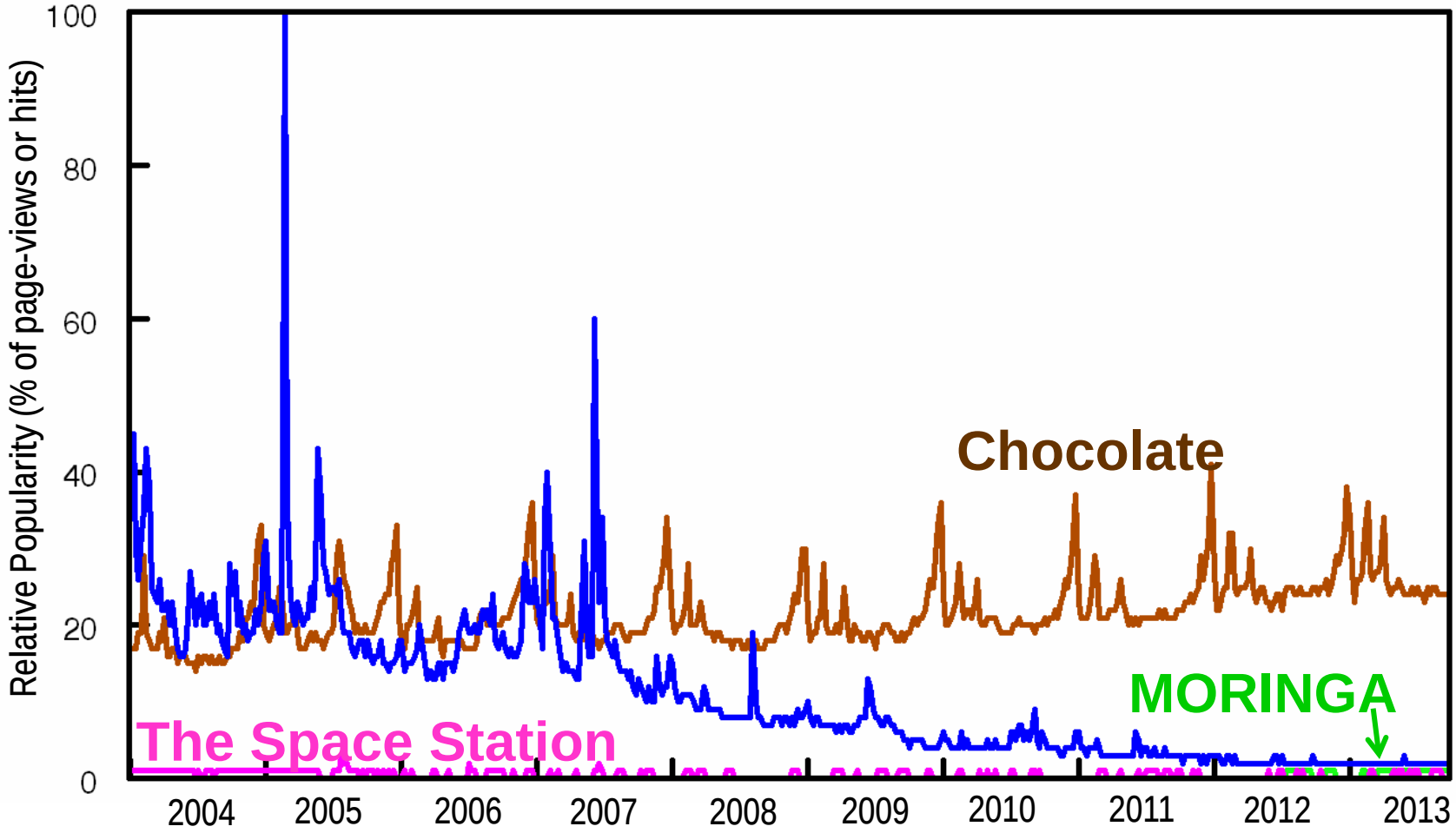
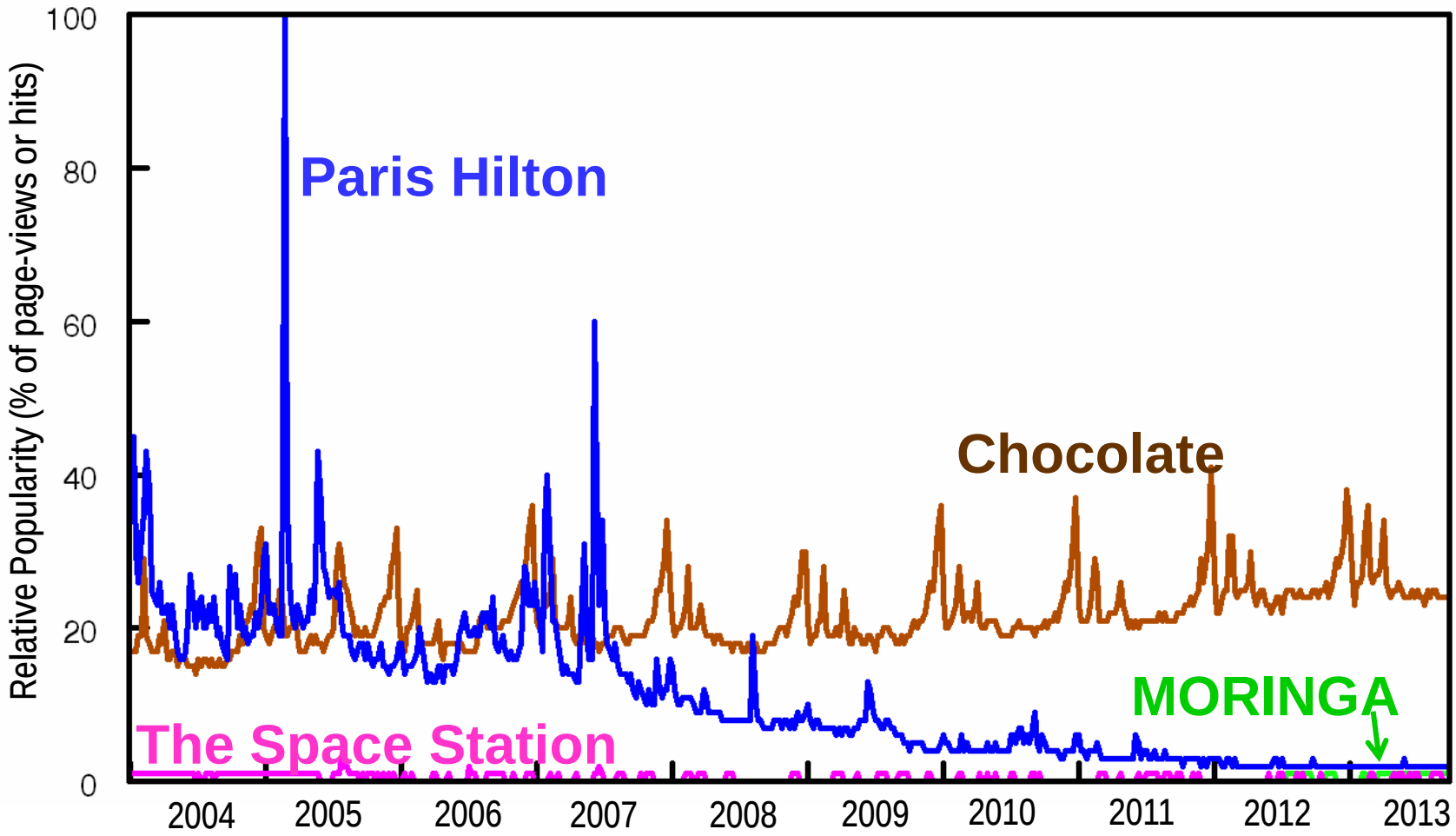


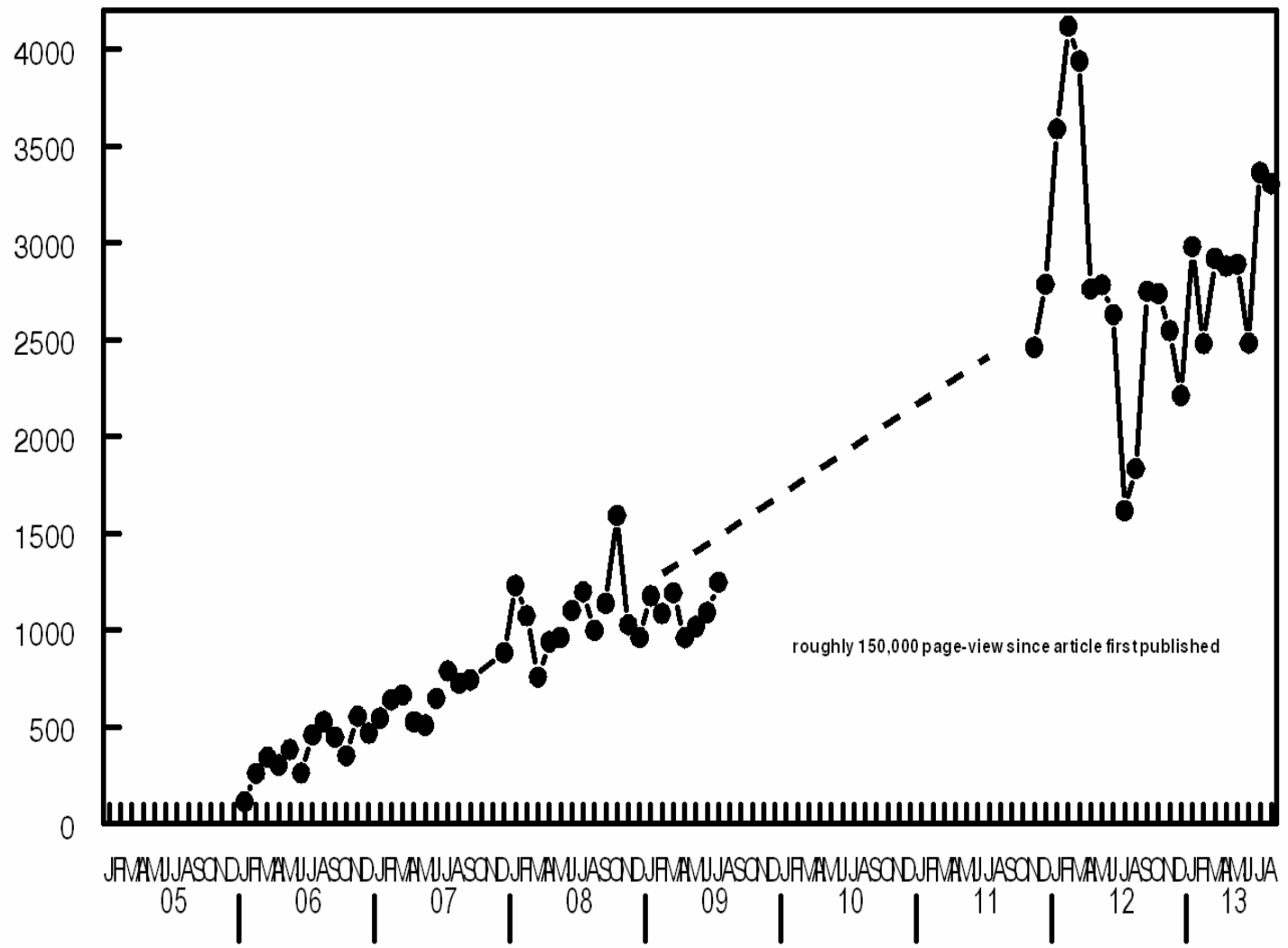
Google Trends® Popularity



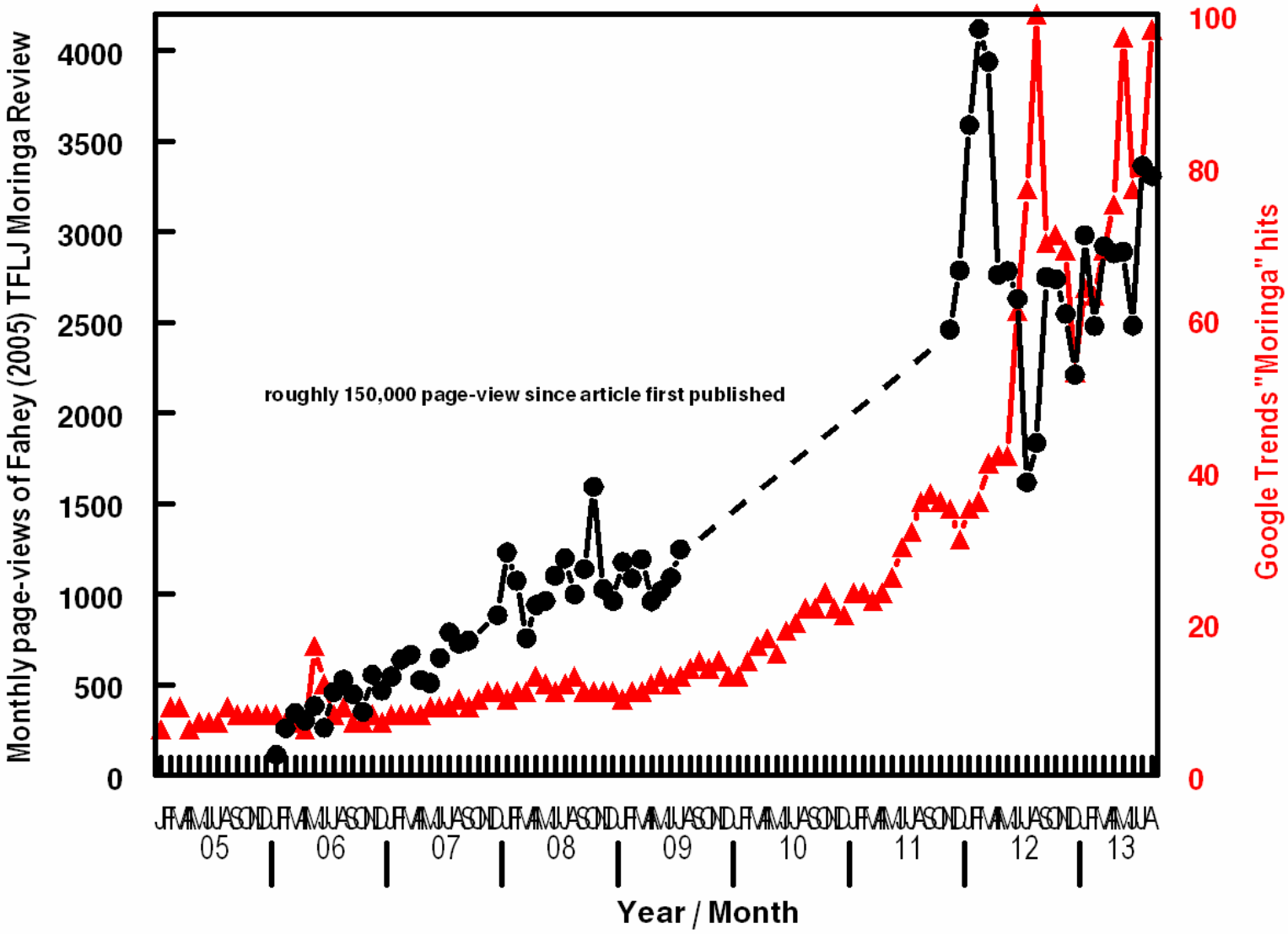
Google Trends® Popularity



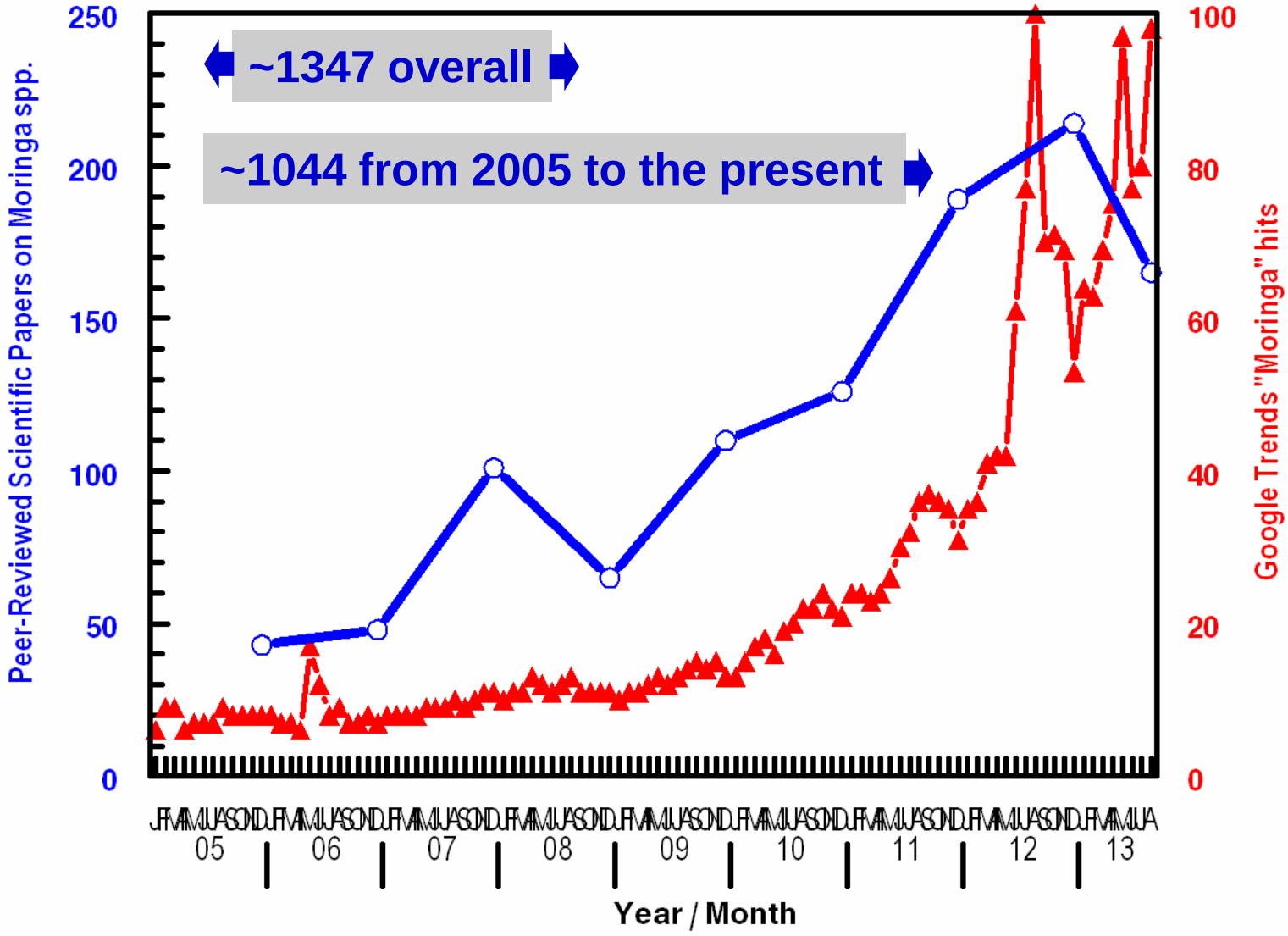
Monthly Page-Views of Fahey (2005) TFLJ Moringa Review



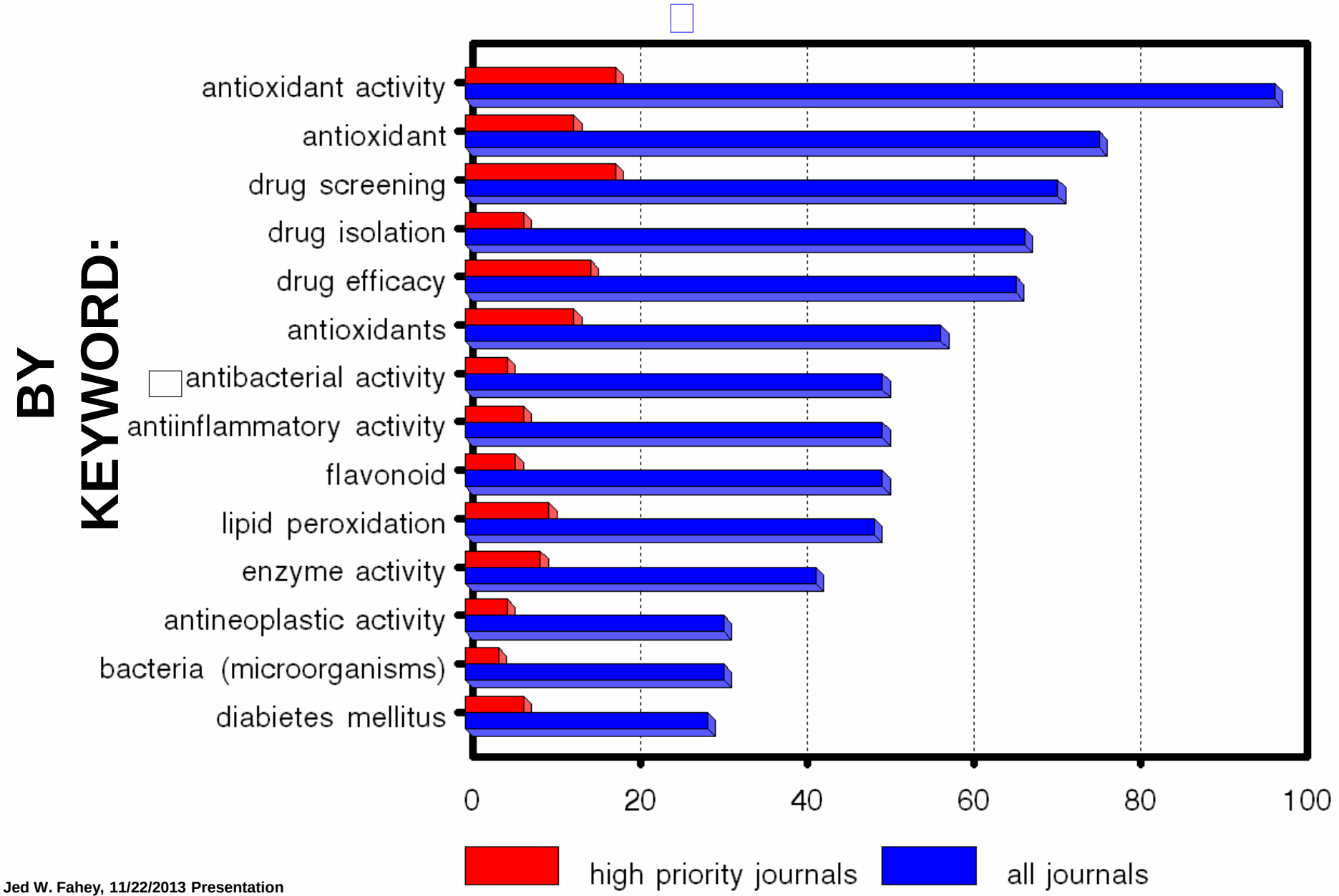
Moringa "Popularity" -- 2005-present



Moringa "Popularity" -- 2005-present



Moringa peer reviewed papers: in all (*n*=1347); in "high priority"(*n*=127) journals; "clinical or human" studies (n=2)



Moringa: The Strength of the Scientific Evidence for Medicinal Effects

Moringa has the very same "mustard oil bomb" as the cruciferous vegetables.

It is at the center of the exciting medicinal chemistry of that species, which presents very many possibilities for disease treatment and prevention.

We have also discovered that the main isothiocyanate from Moringa is every bit as potent an antibiotic against *H. pylori* as sulforaphane.

There are in fact huge numbers of anecdotes about Moringa as an indication for a variety of conditions.

Unscrupulous profiteers play off of the placebo effect (i.e. the fact that 1 out of 3 people taking a given preparation, extract, juice, or capsule for the treatment of a condition will report that the condition “got better” or changed, as a result of taking that preparation), to make all sorts of spurious claims of efficacy.

Types of Epidemiological Evidence

[cell culture and animal (pre-clinical) studies]

Descriptive Studies

ACS, IARC, surveillance programs

Ecological Studies

relationships among populations, not between people; correlative

Migrant Studies

captures macro-environmental effects (vs. genetic)

Cross-Sectional Studies

descriptive; provide data on entire population under study

Case-Control (or Retrospective) Studies (longitudinal or descriptive)

retrospective; on diagnosed individuals vs. not-diagnosed individuals; problems with recall bias and selection bias

Cohort Studies (to support existence of assoc. b/w suspected cause & disease)

prospective; or can be retrospective from archived records; huge & expensive to provide statistical power to evaluate cancer endpoints

Randomized Controlled Trials (RCT)

intervention; “gold standard” & “double blind”; can backfire if based on flawed assumptions (e.g. CARET and ATBC)

Meta-Analyses & Pooled Analyses

single estimate; distillation; dose-relationship; heterogeneity; ↑power

The Strength of Scientific Evidence

(to focus on a dozen or so individual studies)

Nutritional value

Antioxidant potency

Antibiotic properties

Anti-diabetic indications

Cardiovascular protective potential

Anti-asthmatic potential

Chemoprotective potential

(An example of some of the recent non-clinical nutrition studies)

Food Science & Nutrition

Open Access

Comparative study on nutrient composition, phytochemical, and functional characteristics of raw, germinated, and fermented *Moringa oleifera* seed flour

Oluwole S. Ijarotimi[1], Oluwole A. Adeoti[1] & Oluwaseun Ariyo[2]

[1]Department of Food Science and Technology, Federal University of Technology, Akure, Nigeria
[2]Department of Human Nutrition, Faculty of Public Health, College of Medicine, University of Ibadan, Ibadan, Oyo State, Nigeria

Food and Nutrition Sciences, 2013, 4, 991-997
http://dx.dor.org/10.4236/fns.2013.49128 Published Online September 2013 (http://www.scirp.org/journal/fns)

Scientific Research

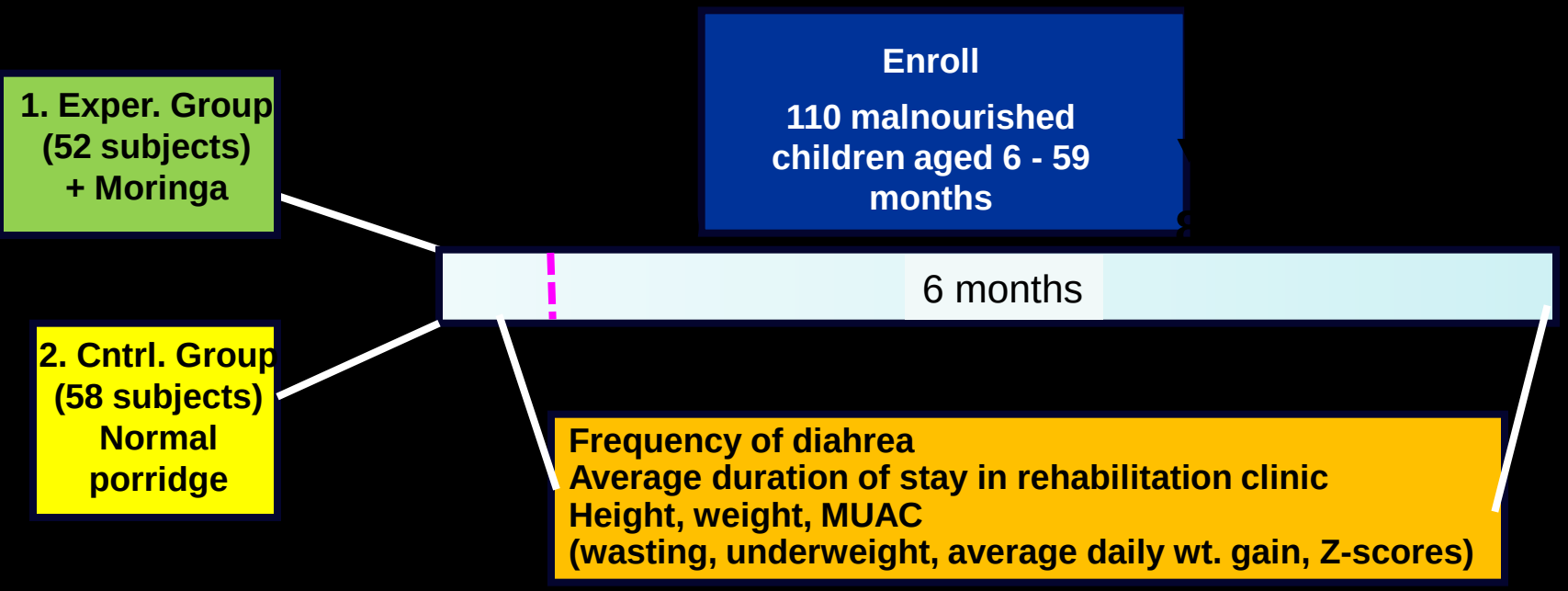
Nutritional and Clinical Rehabilitation of Severely Malnourished Children with *Moringa oleifera Lam.* Leaf Powder in Ouagadougou (Burkina Faso)

Urbain Zongo[1*], Steve Léonce Zoungrana[2], Aly Savadogo[1], Alfred S. Traoré[1]

[1]Department of Biochemistry-Microbiology, University of Ouagadougou, Ouagadougou, Burkina Faso; [2]Department of Gastroenterology, Clinique de L'amitié, Ouagadougou, Burkina Faso.
Email: *e.gaagvander@zgt.nl

Received June 17th, 2013; revised July17th, 2013; accepted July 24th, 2013

10 g/day dry *M. oleifera* leaves



Zongo et al. (2013) *Food and Nutrition Sciences* 4: 991-997.

- Quicker recovery of weight-for-age and weight-for-height
- Greater improvement in wasting and underweight metrics.
- Average daily weight gain:
  - 8.9 g/kg/d Moringa vs. 5.7 g/kg/d standard porridge
- Average length of care at inpatient rehabilitation unit:
  - 36 days Moringa vs. 57 days standard porridge
  - (acceptable value = <28 d)
- No sig. difference in height or ΔMUAC over course of study
- Profound change in frequency of diarrhea
  - 8% w/ Moringa vs. 80% standard porridge

Zongo et al. (2013) *Food and Nutrition Sciences* 4: 991-997.

MEDICINE

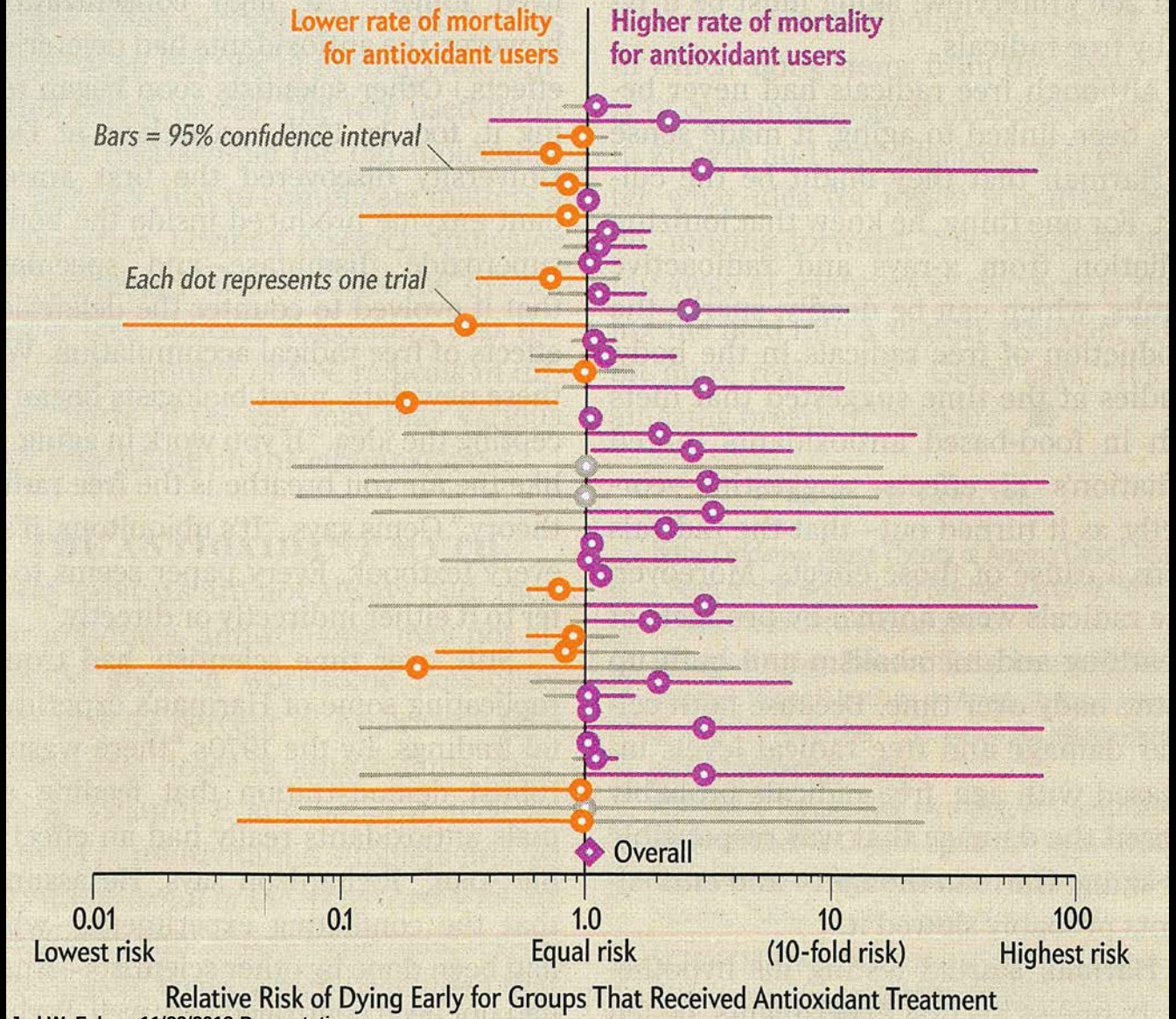
The Myth of Antioxidants

The hallowed notion that oxidative damage causes aging and that vitamins might preserve our youth is now in doubt

By Melinda Wenner Moyer

Bottom Line: Taking Some Vitamins Can Shorten Life Span

In 2007 researchers reviewed 68 of the most scientifically rigorous studies of vitamins and reported that pooling the data from the 47 trials with the least scientific bias resulted in a 5 percent increase in the rate of early death. Further analysis linked the increased risk to beta-carotene, vitamin A and vitamin E.

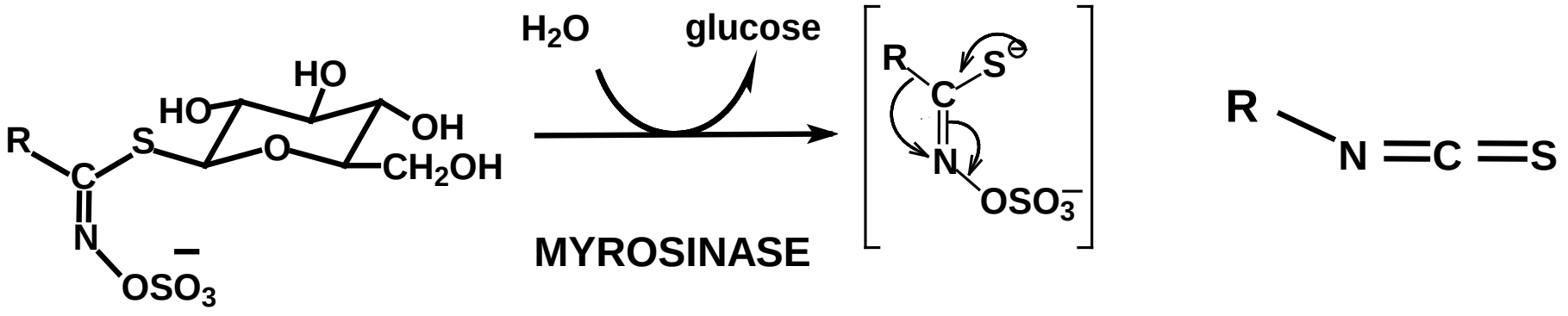


Jed W. Fahey, 11/22/2013 Presentation
5th Moringa Congress, Clark, Philippines

Original study:

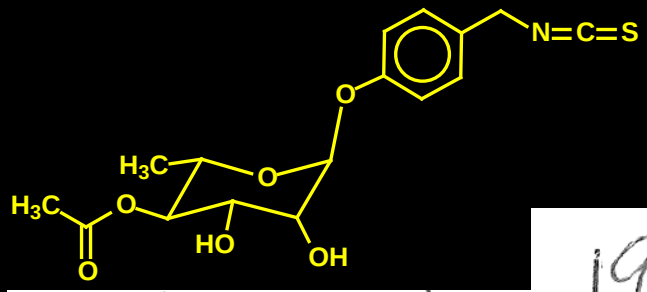
The Strength of Scientific Evidence

Moringa contains the same so-called “mustard-oil bomb” that the cruciferous plants such as broccoli, mustard, and horseradish contain.



GLUCOSINOLATE

ISOTHIOCYANATE



Philippine Journal of Science 119: 23-32 1990

STUDIES ON *MORINGA OLEIFERA* SEEDS, PART I. THE ANTIBIOTIC COMPOUND AND ITS DEACTIVATION IN AQUEOUS SOLUTION.

FABIAN M. DAYRIT[a], ANGELA D. ALCANTAR[a,b], IRENE M. VILLASENOR[c],

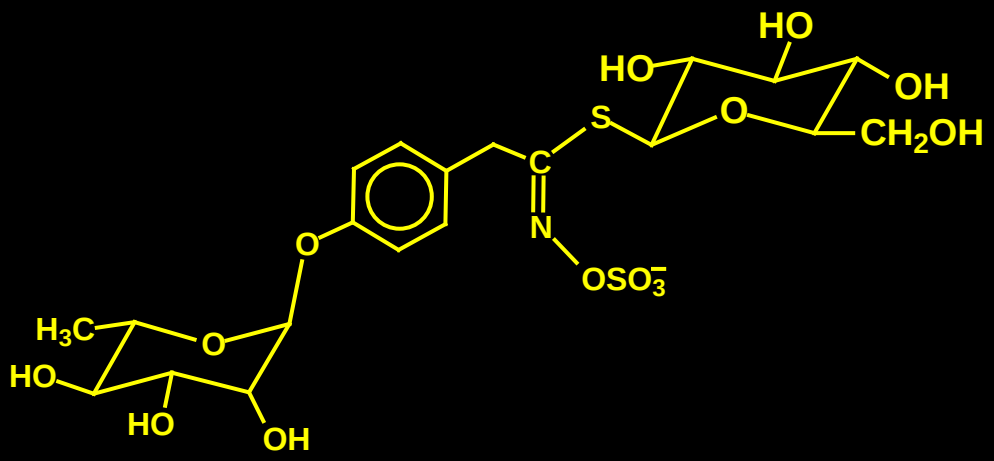
[a] *Department of Chemistry, Ateneo de Manila University, P.O. Box 154, Manila*
[b] *present address: Department of Chemistry, Xavier Univesity, Cagayan de Oro City*
[c] *Institute of Chemistry, University of the Philippines, Diliman, Quezon City*

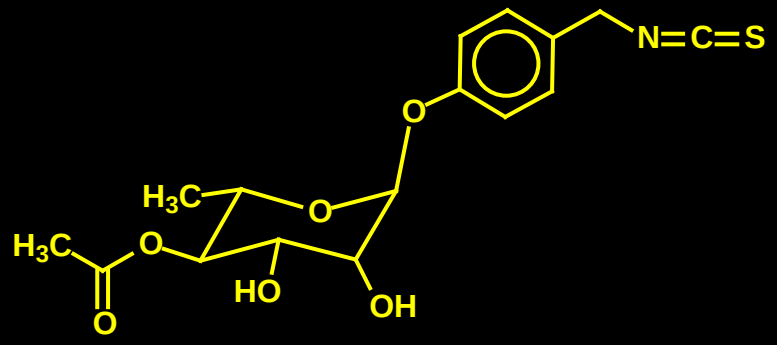
ABSTRACT

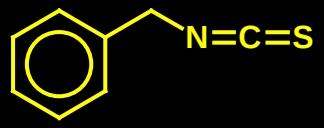
4-[α-L-Rhamnosyloxy]benzyl isothiocyanate, *A*, and 4-[α-L-rhamnosyloxy]phenylacetonitrile, *B*, were isolated from the raw seeds of *Moringa oleifera* by hot water extraction. *A* was found to be active against *Bacillus subtilis* but inactive against *Escherichia coli*. *B* was inactive against both organism.

When left to stand in an aqueous methanol solution, A decomposes and loses its antibacterial activity.

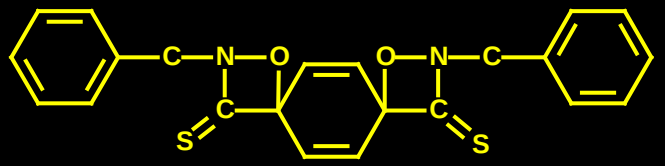
the rhamnosylated glucosinolates & isothiocyanates

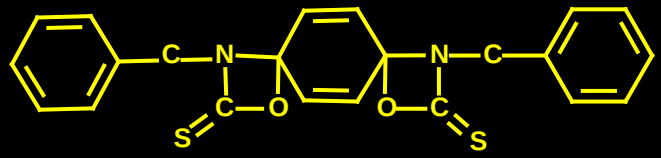






Pterygospermin





[1] G.S. Chatterjee, S.R. Maitra, Sci. Cult. 17 (1951) 43–44.
[2] P.A. Kurup, P.L.N. Rao, J. Ind. Inst. Sci. 34a (1952) 219–227.
[3] P.A. Kurup, P.L.N. Rao, Ind. J. Med. Res. 42 (1954) 85–95.
[4] R.R. Rao, M. George, Ind. J. Med. Res. 37 (1949) 159–167.
[5] U. Eilert, B. Wolters, A. Nahrstedt, J. Med. Plant Res. 42 (1981) 55–61.

The pterygospermin structures suggested by Kurup and Rao, are not viable with regard to isolation, storage and characterization. The pathway to decomposition matching the one originally proposed by Kurup and Rao has been identified computationally, and the activation barriers are indeed high enough to allow for kinetically stable structures. However, for each of the suggested structures a lower-energy route has been identified, leading to half-life times in the order of seconds to a couple of hours. Thus, calculations seem to rule out the possibility for a long-term storage and isolation/characterization of those structures.

Howarth& Benin (2011) *Computational Theoret Chem* 965: 196-201.

Computational and Theoretical Chemistry 965 (2011) 196–201

Contents lists available at ScienceDirect

Computational and Theoretical Chemistry

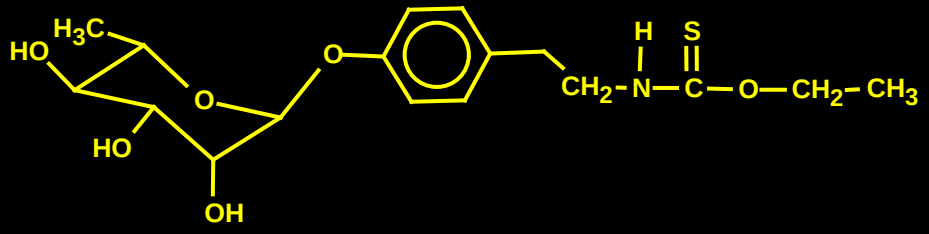
journal homepage: www.elsevier.com/locate/comptc

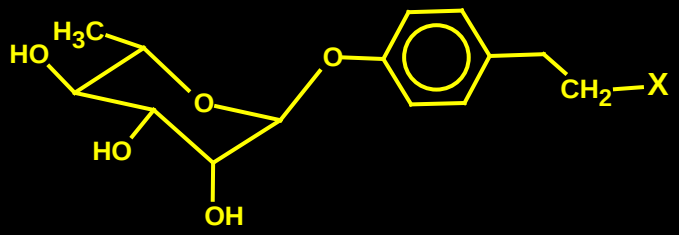
Theoretical investigation of a reported antibiotic from the "Miracle Tree" *Moringa oleifera*

Michael Horwath, Vladimir Benin *

Department of Chemistry, University of Dayton, 300 College Park, Dayton, OH 45469-2357, United States

Niazimicin, and the rhamnosylated thiocarbamates: niazinin, niazimicin, niaziminin, niazirin, etc.





Faizi (1992) J Chem Soc Perkin Trans 1: 3237-3241.
Faizi (1994) J Chem Soc Perkin Trans 1: 3035-3040.
Faizi (1994) J Nat Prod 57(9): 1256-1261.
Faizi (1995) Phytochemistry 38(4): 957-963.
Faizi (1997) J Nat Prod 60(12): 1317-1321.
Guevara (1999) An antitumor promoter from *Moringa oleifera Lam. Mutation Research 440: 181-188.*

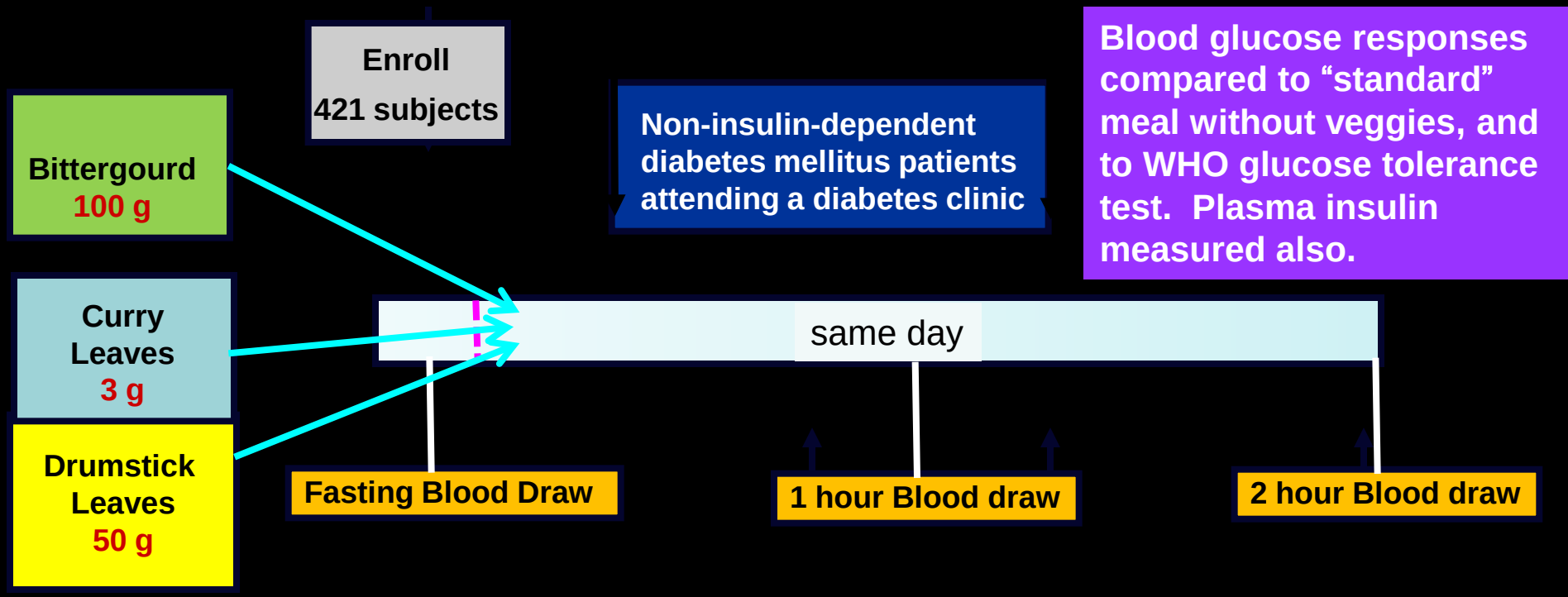
International Journal of Food Sciences and Nutrition (1993) **44**, 191–196

241

Effect of some Indian vegetables on the glucose and insulin response in diabetic subjects

Felicia William,[1] S. Lakshminarayanan[2] and Hariprasad Chegu[1]

Departments of [1]Biochemistry and [2]Medicine, Sri Ramachandra Medical College and Research Institute, Madras 600 116, India



Effect of some Indian vegetables on the glucose and insulin response in diabetic subjects

Experimental:

- **6 - T2DM and 6 control non diabetic subjects**
- ***M. oleifera* added to standardized meal after overnight fast**
- **? 1- and 2- h pos-prandial blood glucose ± 75g oral glucose load**

Result:

- **No difference in plasma insulin AUC**
- **Only *M. oleifera* elicited significantly lower glycemic response than:**
  - **standard meal (21% lower)**
  - **WHO glucose tolerance test (75 g glucose) (44% lower)**
- **(Bitter gourd (*Momordica charantia*) and curry leaves (*Murraya koenigii*) did not work).**

William et al. (1993) *Int. J. Food Sci. Nutr.* 44: 191-196.
As interpreted by Mbikay (2012) *Frontiers Pharmacol.* 3(24): 1-12.

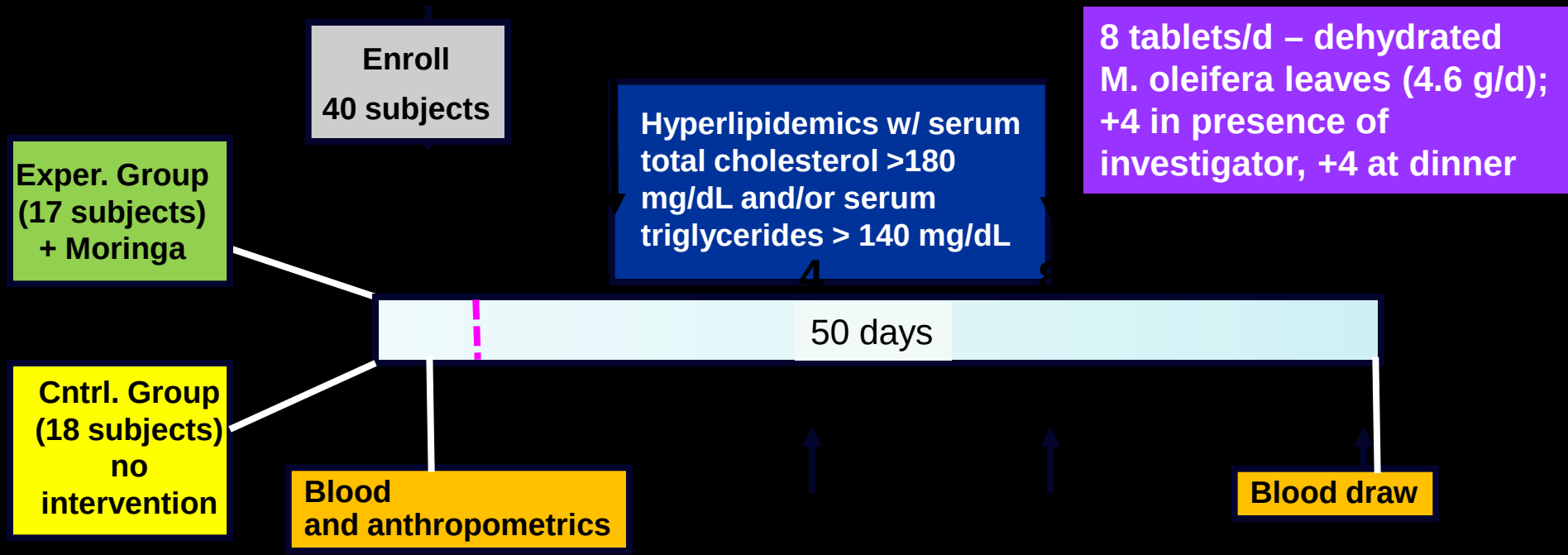
Journal of Herbal Medicine and Toxicology 4 (1) 165-172 (2010)
ISSN : 0973-4643

Original Article

IMPACT OF ANTIOXIDANTS FROM DRUMSTICK LEAVES ON THE LIPID PROFILE OF HYPERLIPIDEMICS

Vanisha S Nambiar*[1], Parul Guin[1], Shilpa Parnami[1], Mammen Daniel[2]

[1]Department of Foods and Nutrition, A WHO Collaborating Center for Health Promotion, [2]Department of Botany, The Maharaja SayajiRao University of Baroda, Vadodara- 390002, Gujarat. India.
*Corresponding author email: vanishanambiar@gmail.com



Parameter (mg/dL)	Experimental		Control	
	PRE	POST	PRE	POST
TC	187.14±2.92	184.00±3.14	186.14±2.42	184.49±1.60
Non-HDL	149.08±2.95	143.60±3.19	146.23±2.5	144.38±1.69
LDL/HDL	3.27±0.19	2.99±0.18	2.68±0.05	2.59±0.05

Nambiar et al (2010) *J Herbal Med Toxicol* 4(1): 165-172.

Int J Health Nutr 2011 2(1): 1-5

International Journal of Health & Nutrition

www.academyjournals.net

Original Article

Anti Diabetic Property of Drumstick *(Moringa oleifera)* Leaf Tablets

V.Veeranan Arun GIRIDHARI[1], D. MALATHI[2], K. GEETHA[3]

[1]Assistant professor (Food science and Nutrition), Regional Research Station, Tamil Nadu Agricultural University, Aruppukottai-626107.India;
[2]Professor, Dept. of Food science and Nutrition, Tamil Nadu Agricultural University, Coimbatore-641003.India;
[3]Assistant professor (Food science and Nutrition), A.D. A.C&R.I, Tamil Nadu Agricultural University, Trichy-9.India

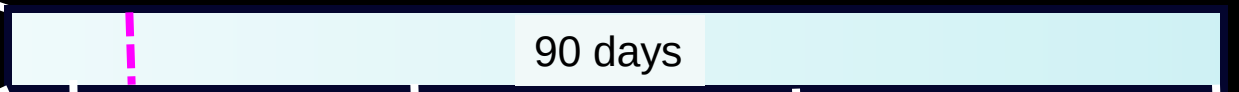
Enroll 60 subjects

Sedentary hypoglycemic T2DM subjects on oral sulfonylurea; 20>BMI>25; 40-58 yrs old; on standardized, calorie-restricted diet

2 tablets/d – dehydrated, powdered *M. oleifera* leaves (?? g/d); 1 after breakfast, 1 after dinner

Exper. Group (30 subjects) + Moringa

Cntrl. Group (30 subjects) no intervention



Blood and anthropometrics

Blood draw

Group	Initial	30 d.	60 d.	90 d.
Mean post-prandial blood glucose (mg/dL)				
CONTROL	179 ± 36.09	169 ± 36.73	167 ± 35.44	163 ±3 4.08
EXPERIMENTAL	210 ± 48.83	191 ± 48.64	174 ± 36.77	150 ± 21.10
Mean glycated hemoglobin (HbA_{1c} %)				
CONTROL	7.38 ± 0.60			7.36 ± 0.59
EXPERIMENTAL	7.81 ± 0.51			7.40 ± 0.63

All measures significant compared to the initial values;
However, note lack of good treatment allocation / randomization

Giridhari et al (2011) *Int J Health Nutr 2*(1): 1-5.

The Bioscan 5 (2) : 211-214, 2010
AN INTERNATIONAL QUARTERLY JOURNAL OF LIFE SCIENCES

HYPOGLYCAEMIC EFFECT OF *MORINGA OLEIFERA* AND *AZADIRACHTA INDICA* IN TYPE 2 DIABETES MELLITUS

D. JALAJA KUMARI
Department of Foods and Nutritional Sciences,
Acharya Nagarjuna University, (A.N.U), Guntur - 522 510
E-mail: jalaja9krishna@yahoo.com

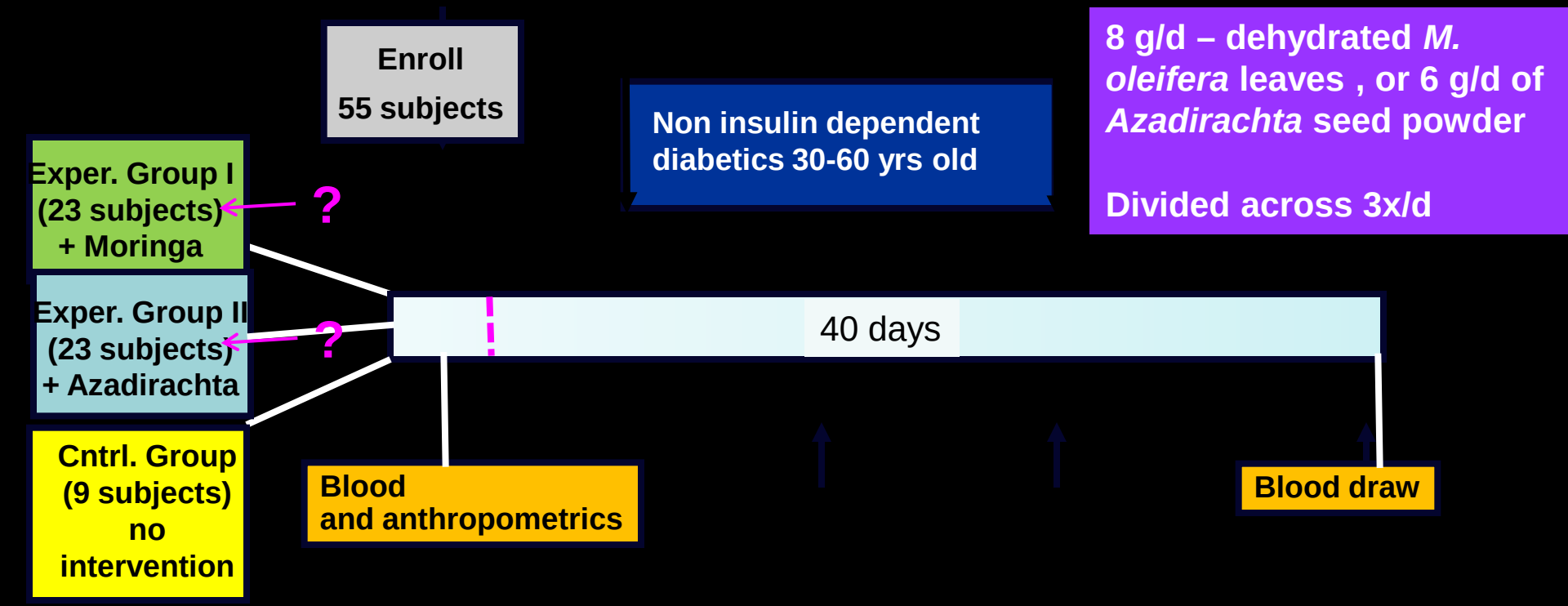


Table 4: Mean blood glucose levels of the experimental and control groups

Groups	Herbal powdersGlucose	Blood (mg/dL)	Initial	Final	't' value
Experimental Group II	Moringa Oleifera Leaves	Fasting	162 ± 9.0	117 ± 21.3	5.94**
		Post Prandial	219 ± 77.4	163 ± 49.4	2.9*
Experimental Group I	Azadirachta indica Seeds	Fasting	149 ± 63	135 ± 71.7	2.6*
		Post Prandial	252 ± 84.5	229 ± 91.5	6.9*
Control Group	No herbal powder Supplementation	Fasting	159.5 ± 6.8	159 ± 7.4	4.09NS
		Post Prandial	224 ± 3.7	251 ± 59.0	1.7 NS

* Significant at 5 per cent ** Significant at 1 per cent NS- Not significant.

Table 5: Mean blood lipid levels of the experimental and control group

Groups	Herbal powders	Blood lipids levels(mg/dL)	Initial ± S.D.	Final ± S.D.	't' value
Experimental Group II	Moringa Oleifera leaves	Serum total cholesterol	261 ± 20.0	224.0 ± 22.6	6.26 * *
		Serum triglycerides	130 ± 14.2	112 ± 13.9	4.8 * *
		HDL - C	57.0 ± 18.5	62.0 ± 19.7	2.24 NS
		LDL - C	171.0 ± 16.9	122.0 ± 2.9	3.62 *
		VLDL – C	26.0 ± 2.8	22.0 ± 2.9	3.6 *
Experimental Group I	Azadirachta indica seeds	Serum total cholesterol	204 ± 21.4	204 ± 30.1	4.90 * *
		Serum triglycerides	136 ± 34.3	122 ± 36.9	4.53 * *
		HDL - C	45 ± 11.4	46 ± 10.4	0.79 NS
		LDL - C	157 ± 11.4	134 ± 21.6	4.69 * *
		VLDL – C	27 ± 7.1A	24 ± 7.4	4.96 * *
Control Group	No herbal powder Supplementation	Serum total cholesterol	244 ± 34.9	241 ± 34.7	1.56 NS
		Serum triglycerides	138 ± 18.0	133 ± 19.6	4.12 * *
		HDL - C	52 ± 8.9	52 ± 8.0	0.01 NS
		LDL - C	164 ± 34	162 ± 35.0	2.03 NS
		VLDL - C	27 ± 3.7	27 ± 3.9	0.23 NS

"Significant reduction in:

- mean blood lipids
- fasting blood glucose
- post-prandial blood glucose"

Kumari (2010)
***Bioscan* 5(2): 211-214.**

frontiers in
PHARMACOLOGY

REVIEW ARTICLE
published: 01 March 2012
doi: 10.3389/fphar.2012.00024

Therapeutic potential of *Moringa oleifera* leaves in chronic hyperglycemia and dyslipidemia: a review

Majambu Mbikay [1,2] *

[1] *Chronic Disease Program, Ottawa Hospital Research Institute, Ottawa, ON, Canada*
[2] *Department of Biochemistry, Microbiology and Immunology, Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada*

Contents lists available at SciVerse ScienceDirect

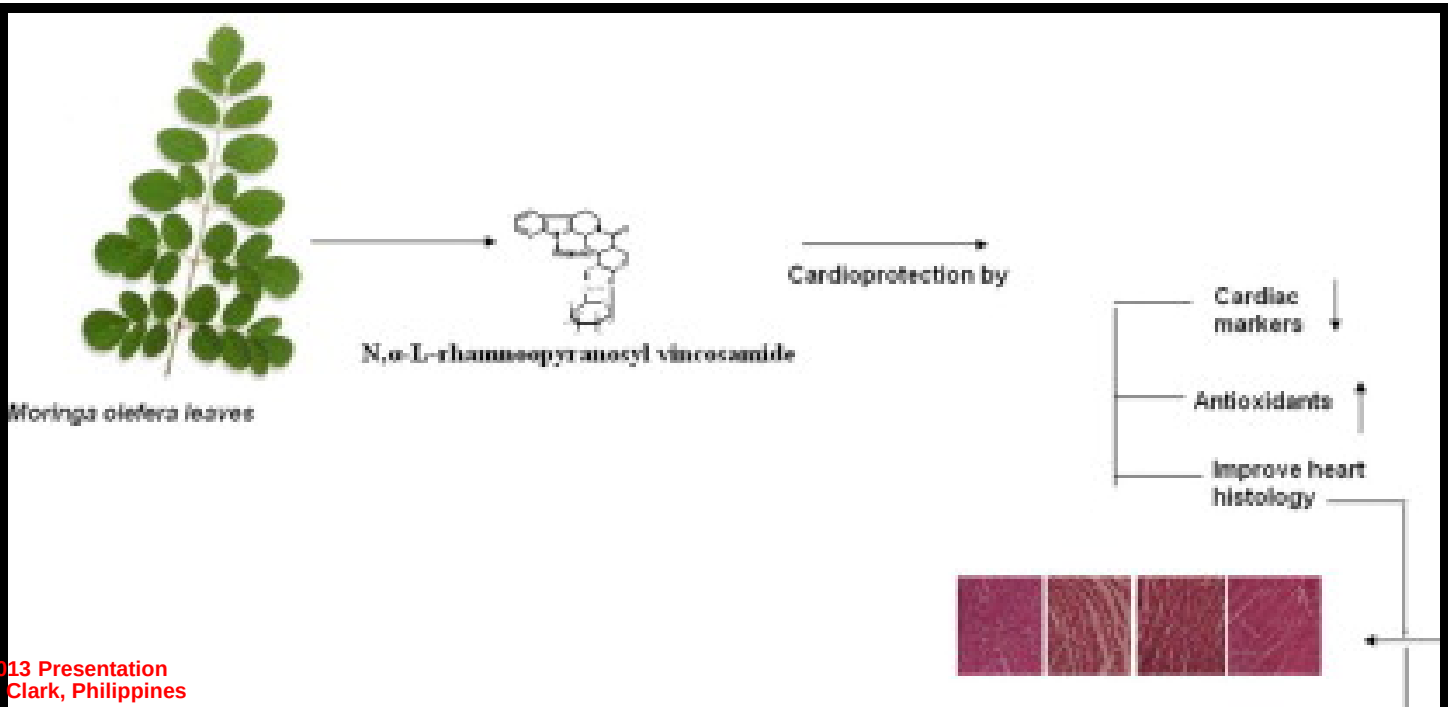
Bioorganic & Medicinal Chemistry Letters

journal homepage: www.elsevier.com/locate/bmcl

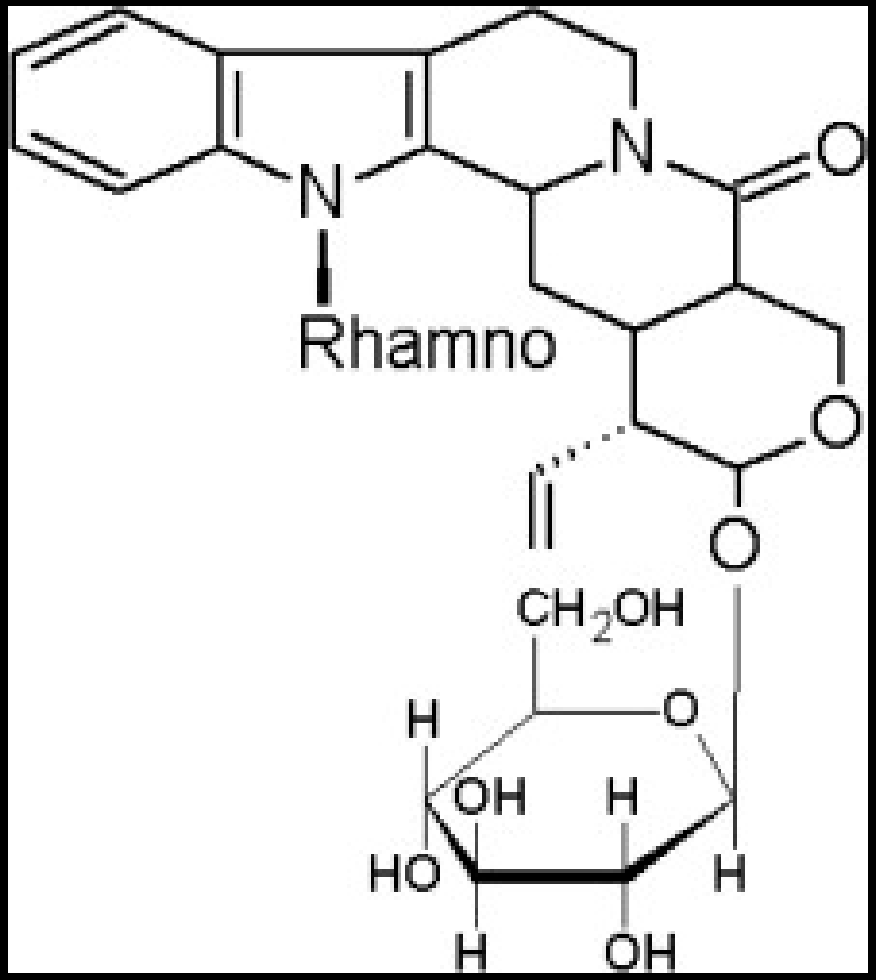
Cardioprotective potential of *N*,α-L-rhamnopyranosyl vincosamide, an indole alkaloid, isolated from the leaves of *Moringa oleifera* in isoproterenol induced cardiotoxic rats: In vivo and in vitro studies

Sunanda Panda [a,*], Anand Kar [a], Pratibha Sharma [b], Ashok Sharma [b]

[a] School of Life Sciences, Devi Ahilya University, Indore 452017, India
[b] School of Chemical Sciences, Devi Ahilya University, Indore 452017, India



N,α-l-rhamnopyranosyl vincosamide.



Panda, Kar, Sharma, Sharma (2013) *Bioorg Med Chem Lett* 23: 959-962.

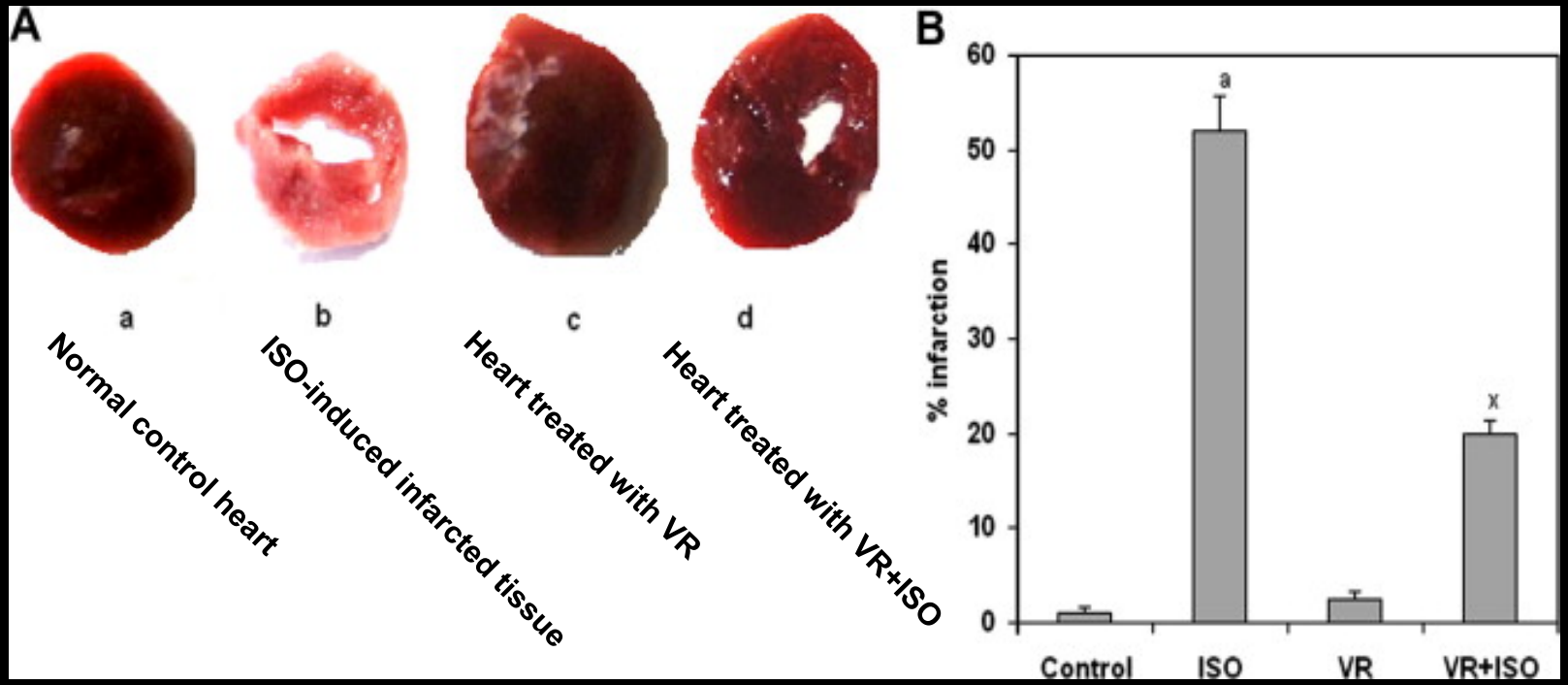
The mechanism of cardio protection seems to involve the prevention of the disruption in cardiac myofibrils, possibly through a reduction of oxidative stress leading to improved cardiac contractile function.

Isoproterenol generates free radicals and stimulates lipid peroxidation, a causative factor for damaging the myocardial tissues.

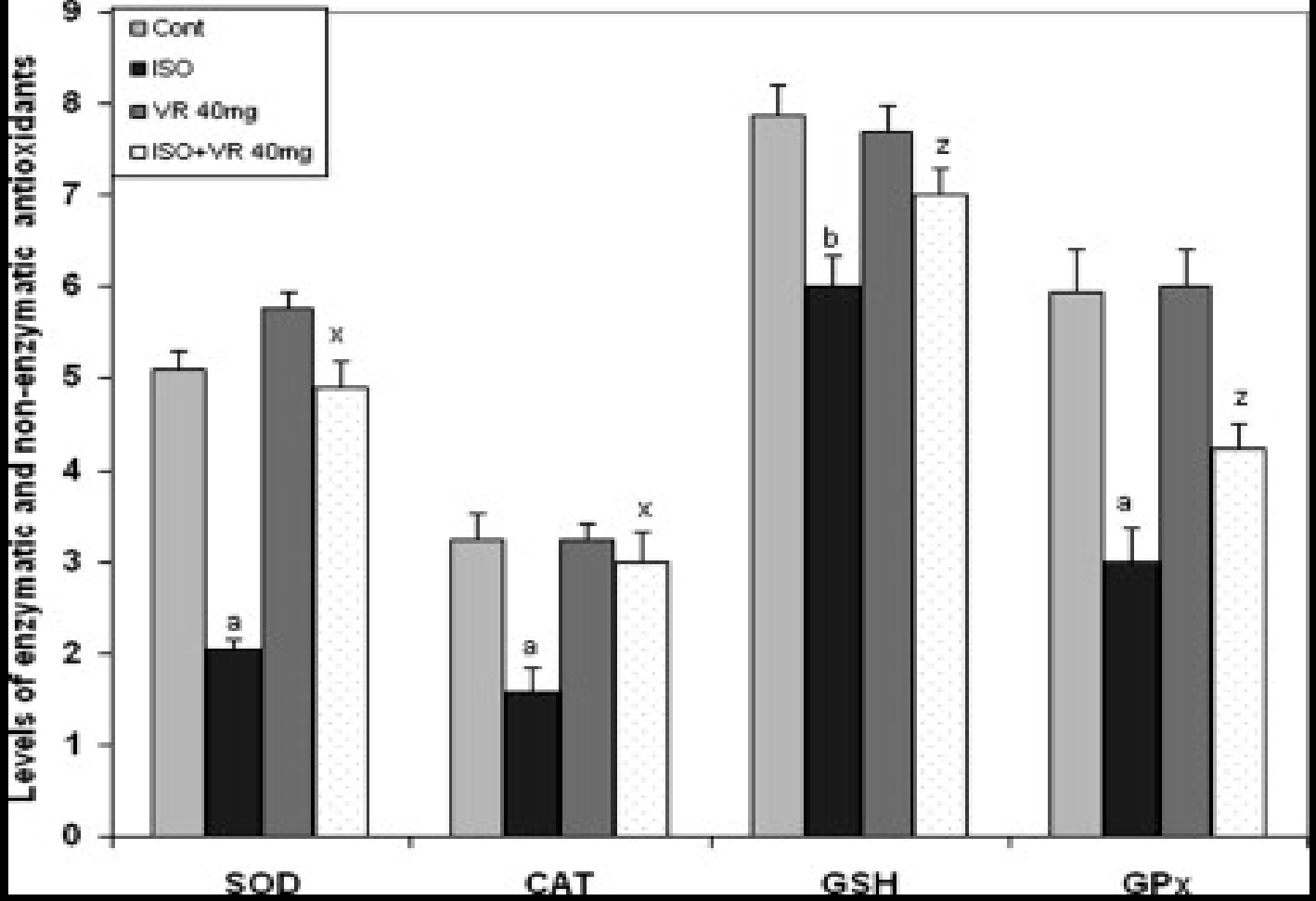
Thus, it appears that the beneficial action of the indole alkaloid from Moringa is mediated through its free radical scavenging property.

Panda, Kar, Sharma, Sharma (2013) *Bioorg Med Chem Lett* 23: 959-962.

Triphenyl tetrazolium chloride (TTC) staining assay in rat heart.



Panda, Kar, Sharma, Sharma (2013) *Bioorg Med Chem Lett* 23: 959-962.



Changes in:

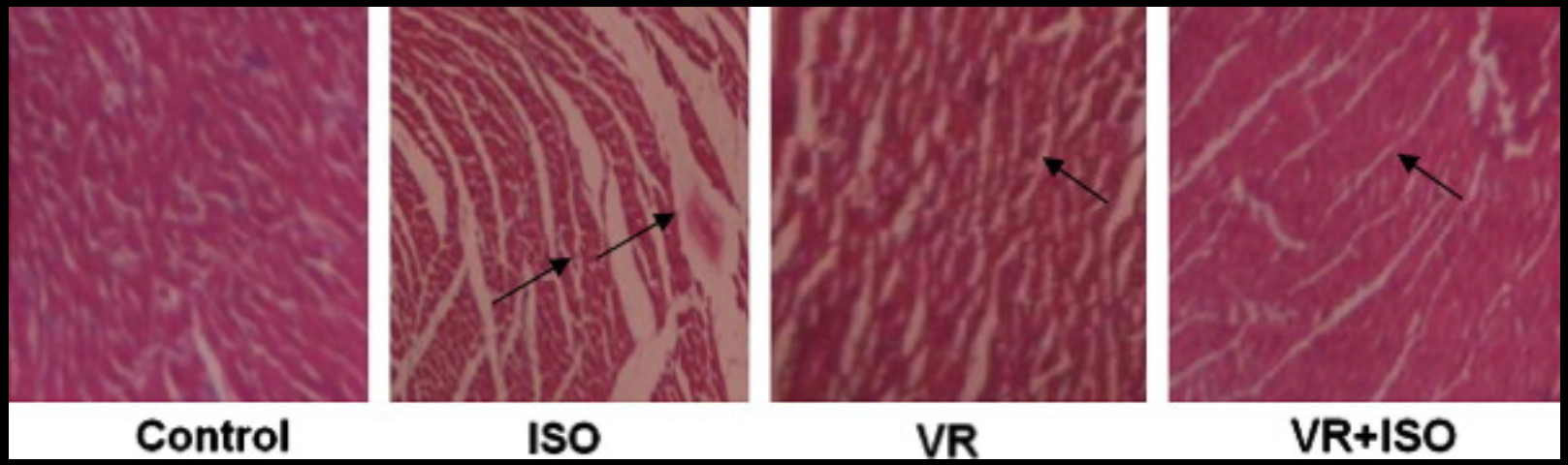
SOD (U/mg protein)

CAT (μM H_2O_2 decomposed/min/mg protein)

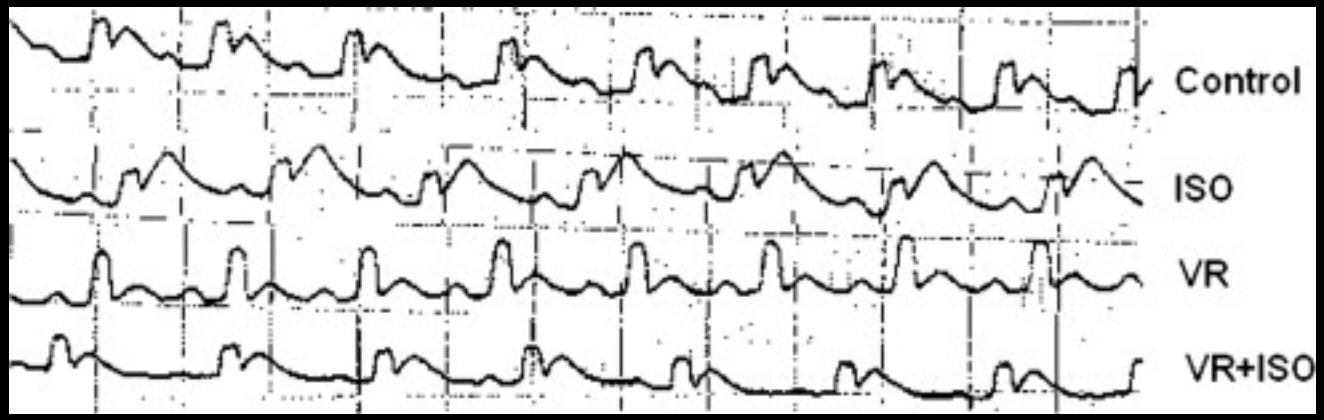
GSH (μM GSH/mg protein)

GPx (μmoles of glutathione oxidized/mg protein)

Panda, Kar, Sharma, Sharma (2013) *Bioorg Med Chem Lett* 23: 959-962.



Changes in cardiac histology. Infiltration of inflammatory cells and maintenance of normal integrity of the cardiac muscles are marked in arrows.



Electrocardiographic (ECG) changes in normal and experimental animals.

Panda, Kar, Sharma, Sharma (2013) *Bioorg Med Chem Lett* 23: 959-962.

American Journal of Applied Sciences 9 (9): 1457-1463, 2012
ISSN 1546-9239

Moringa Oleifera Lam Mitigates Oxidative Damage and Brain Infarct Volume in Focal Cerebral Ischemia

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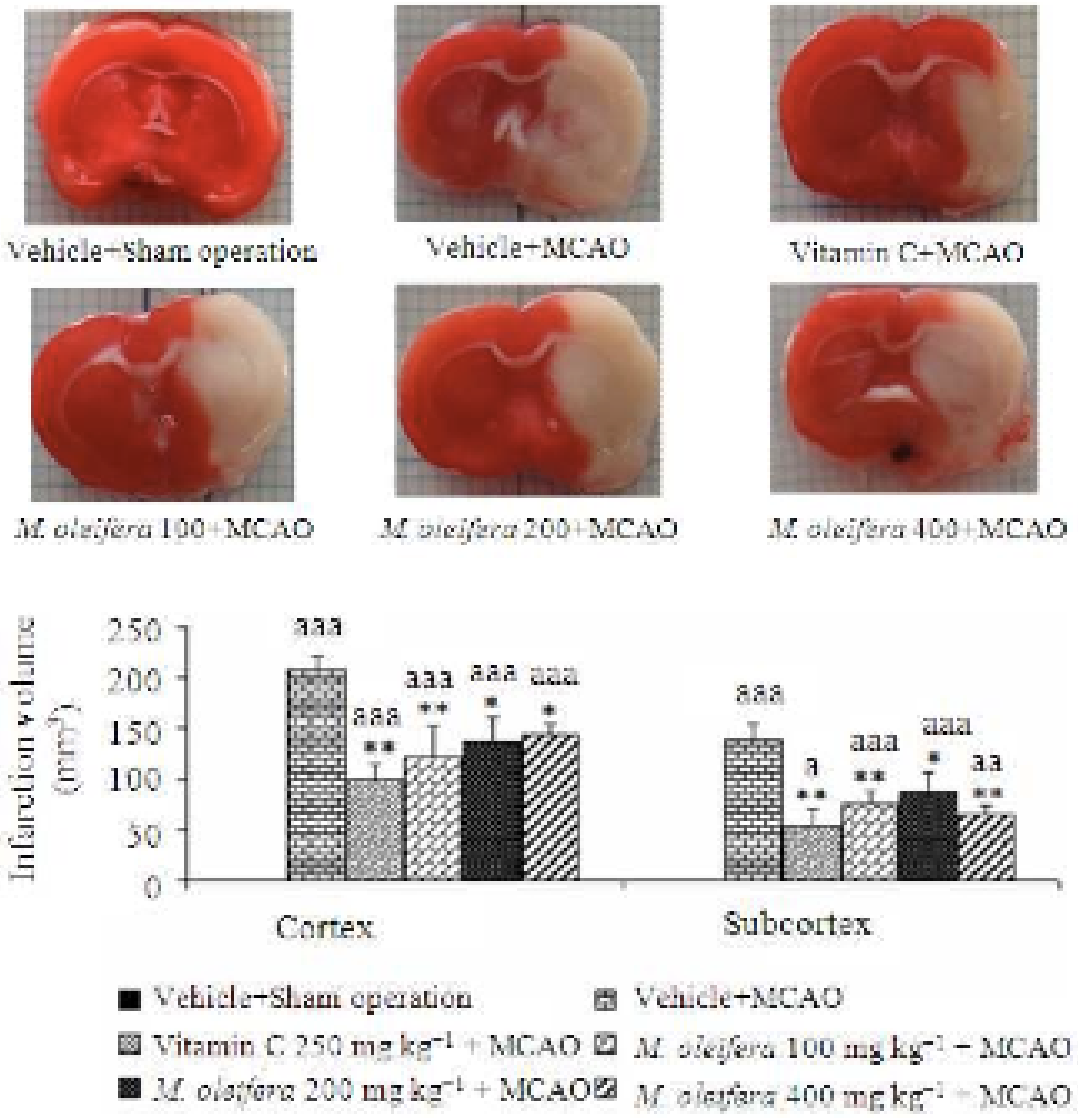

Fig. 1: The effect of Vitamin C, *M. oleifera* extract at the doses of 100, 200 and 400 mg kg^{-1} BW on the brain infarction volume. The coronal brain sections were determined using TTC staining. The data value are expressed as mean ± S.E.M. ^{a}: p-value<.05, ^{aa}: p-value<0.01, ^{aaa}: p-value<0.001; compared with vehicle plus sham operation. *: p-value<0.05, **: p-value<0.01; compared with vehicle plus MCAO

Kirisattayakul et al (2012) *Am J Appl Sci* 9(9): 1457-1463

Biomedical Research 2013; 24 (1): 127-130 ISSN 0970-938X

Effect of *Moringa oleifera* on undesireble skin sebum secretions of sebaceous glands observed during winter season in humans

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*Department of Biotechnology and Genetic Engineering, Kohat University of Science and Technology, Pakistan

Abstract

The present study was planned to test the efficacy of *Moringa oleifera* on undesirable skin sebum secreted by sebaceous glands during winter season in humans. For this purpose, an extract of *Moringa* leaves was prepared due to strong antioxidant activity. 3% *Moringa* leaves extract was incorporated in active cream and the base was without extract. The study was conducted during the winter season (October to January). A total of eleven healthy male volunteers with aged 20 to 35 years were contributed to accomplish this single blind study. The active cream and base were applied twice daily to the face (cheeks) for a period of 12 weeks. Also, the antioxidant activity of the plant extract alone and after addition in the creams was assessed using the stable free radical 1, 1-diphenyl-2-picrylhydrazyl (DPPH) assay. The instrumental measurements were carried out with photometric device (Sebumeter) with relative humidity (55–65%). The *Moringa oleifera* cream significantly reduces undesirable skin sebum during winter season in humans when applied ANOVA and paired t-sample test. Treatment with *Moringa oleifera* showed reduction of undesirable skin sebum secretions secreted by sebaceous glands during winter season in humans.

Research Article

Antiasthmatic activity of *Moringa oleifera* Lam: A clinical study

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Accepted: 07.03.2008

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ABSTRACT

The present study was carried out to investigate the efficacy and safety of seed kernels of *Moringa oleifera* in the treatment of bronchial asthma. Twenty patients of either sex with mild-to-moderate asthma were given finely powdered dried seed kernels in dose of 3 g for 3 weeks. The clinical efficacy with respect to symptoms and respiratory functions were assessed using a spirometer prior to and at the end of the treatment. Hematological parameters were not changed markedly by treatment with *M. oleifera*. However, the majority of patients showed a significant increase in hemoglobin (Hb) values and Erythrocyte sedimentation rate (ESR) was significantly reduced. Significant improvement was also observed in symptom score and severity of asthmatic attacks. Treatment with the drug for 3 weeks produced significant improvement in forced vital capacity, forced expiratory volume in one second, and peak expiratory flow rate values by 32.97 ± 6.03%, 30.05 ± 8.12%, and 32.09 ± 11.75%, respectively, in asthmatic subjects. Improvement was also observed in % predicted values. None of the patients showed any adverse effects with *M. oleifera*. The results of the present study suggest the usefulness of *M. oleifera* seed kernel in patients of bronchial asthma.

KEY WORDS: Bronchial asthma, *Moringa oleifera*, pulmonary function tests

(2008) *Indian J Pharmacol* 40(1): 28-31.

Finely powdered seeds – 3 g/d x 3 weeks

Open label

Noncomparative

20 patients (17-70 yrs old, male and female)

With mild-to-moderate bronchial asthma

Visiting outpatient clinic at hospital in Ahmedabad, India (Gujarat)

Agrawal & Mehta (2008) *Indian J Pharmacol* 40(1): 28-31.

- *Moringa oleifera* significantly improved
- Lung volume
  - 33%↑ FVC (forced vital capacity)
  - 30%↑ FEV1 (forced expiratory vol. – 1 sec)
- Pulmonary Function
  - 32%↑ PEFR (peak expiratory flow rate)
  - 20%↑ FEF (forced expiratory flow rate)
  - 35%↑ MVV (max. ventilatory vol.)
- Moringa oleifera decresed severity of asthma symptoms, resulting in significantly reduced:
  - ↓Dyspnoea
  - ↓Wheezing
  - ↓Chest tightness
  - ↓Cough

Agrawal & Mehta (2008) *Indian J Pharmacol* 40(1): 28-31.

Moringa: The Strength of the Scientific Evidence for Medicinal Effects

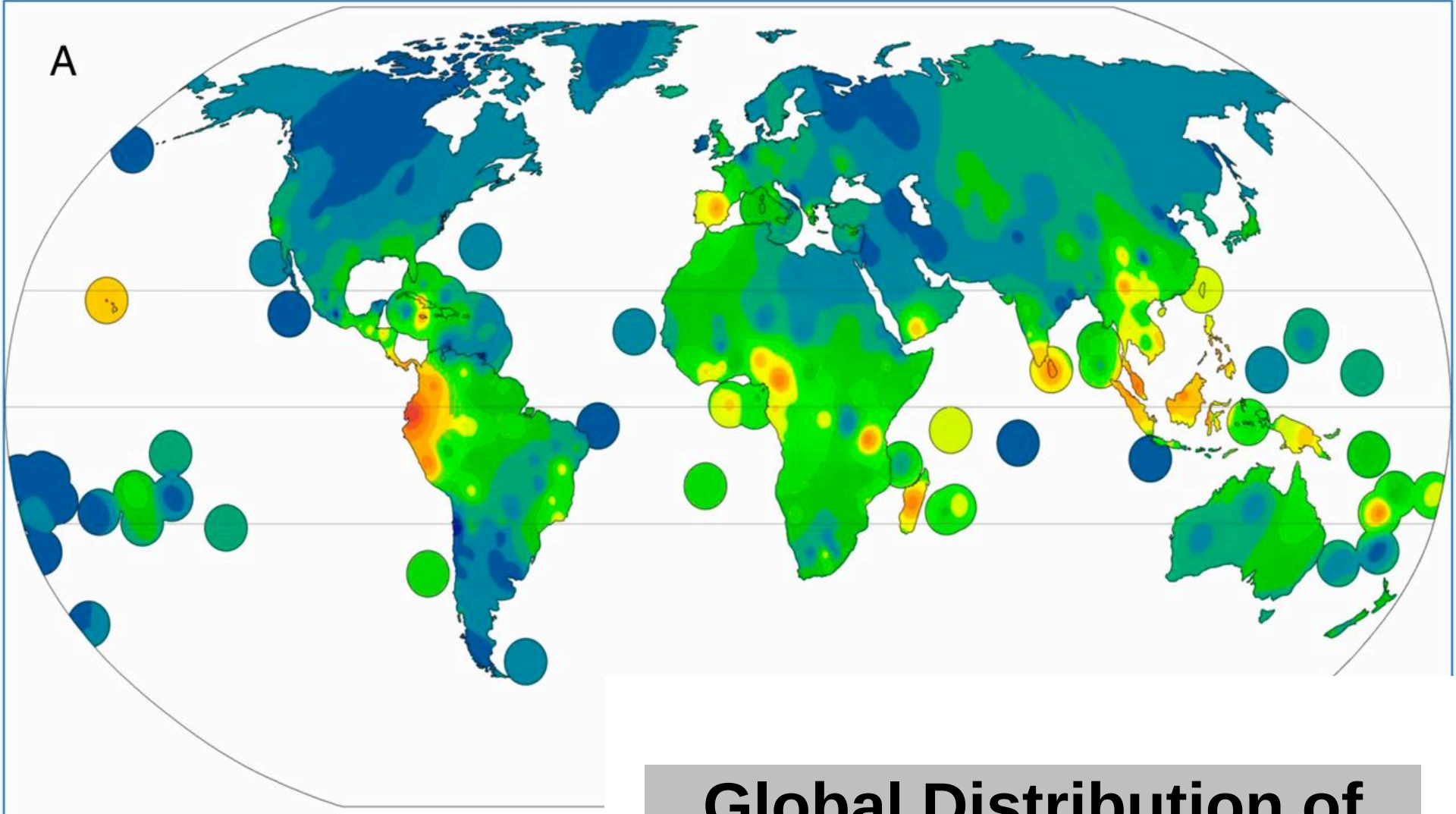
"We", in the community of Moringa-lovers, are hurting ourselves if we let this unscrupulous behavior taint what clearly is an extraordinary plant that truly does have great medicinal and nutritional potential if used appropriately.

"Appropriately" probably means consuming modest amounts of the leaves and/or seedpods in a balanced diet, or supplementing protein-poor diets with Moringa.

More concentrated preparations enriched in specific components or phytochemicals, by-and-large do still require additional clinical evidence, but if we approach it rationally and promote and fund high quality, scientifically rigorous studies, this will come in good time. This presentation will attempt to summarize some of the best currently available evidence in animal studies.

Understanding Moringa Germplasm Diversity

Jed W. Fahey, 11/22/2013 Presentation
5th Moringa Congress, Clark, Philippines



Global Distribution of Endangered Plants

Ibrahim M A et al. (2013) *PNAS* 110:16832-16837. (Oct 15, 2013)

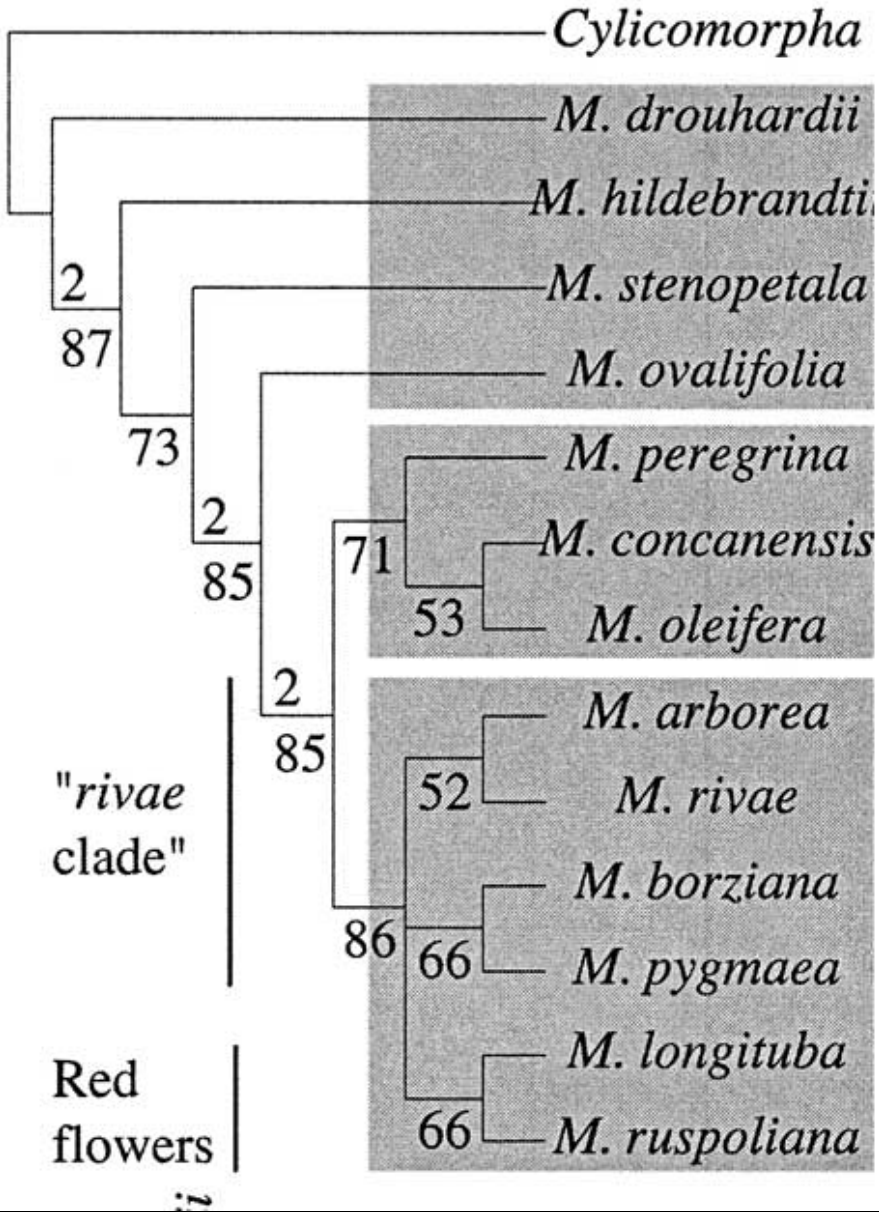
Medicinal Value of Plants

- 26% of new entities approved by the [US] FDA in 2010 were naturally derived
- over 60% of cancer therapeutics were derived from naturally occurring products
- 80% of the developing countries population relies on medicines derived from traditional plants for their pharmacopeia

Ibrahim M A et al. (2013) *PNAS* 110: 16832-16837.

Understanding Moringa Germplasm Diversity

- ***Moringa oleifera*** **is native only to a very small region in N.W. India and eastern Pakistan.**
- **There are 12 other closely related (i.e. genetically very similar) species of Moringa and many of them are edible, but are physically very different from *M.oleifera*.**
- **The domesticated Moringa that MPFI and all Moringa growers worldwide cultivate, represents only a small subset of the genetic diversity of the wild ancestors of *M. oleifera*.**
- **Intelligent use of Moringa requires knowledge of the genetic diversity present in the wild as well as in cultivation.**
- **Wild populations of domesticated organisms represent invaluable storehouses of genetic diversity that can be used to improve domestic stocks.**
- **The status of *M. oleifera* wild populations is particularly unclear due to its widespread dissemination, but it is critical to sort out for the use of- and the conservation of the species.**



bottle trees

NE, SW Africa, Madagascar

slender trees

Arabia, NE Africa, Indian subcontinent

tuberous trees, shrubs, and herbs

NE Africa

Bottle trees

Massive trees with bloated water-storing trunks and small radially symmetrical flowers.
M. drouhardii; Madagascar
M. hildebrandtii; Madagascar
M. ovalifolia; Namibia and extreme SW Angola
M. stenopetala; Kenya and Ethiopia

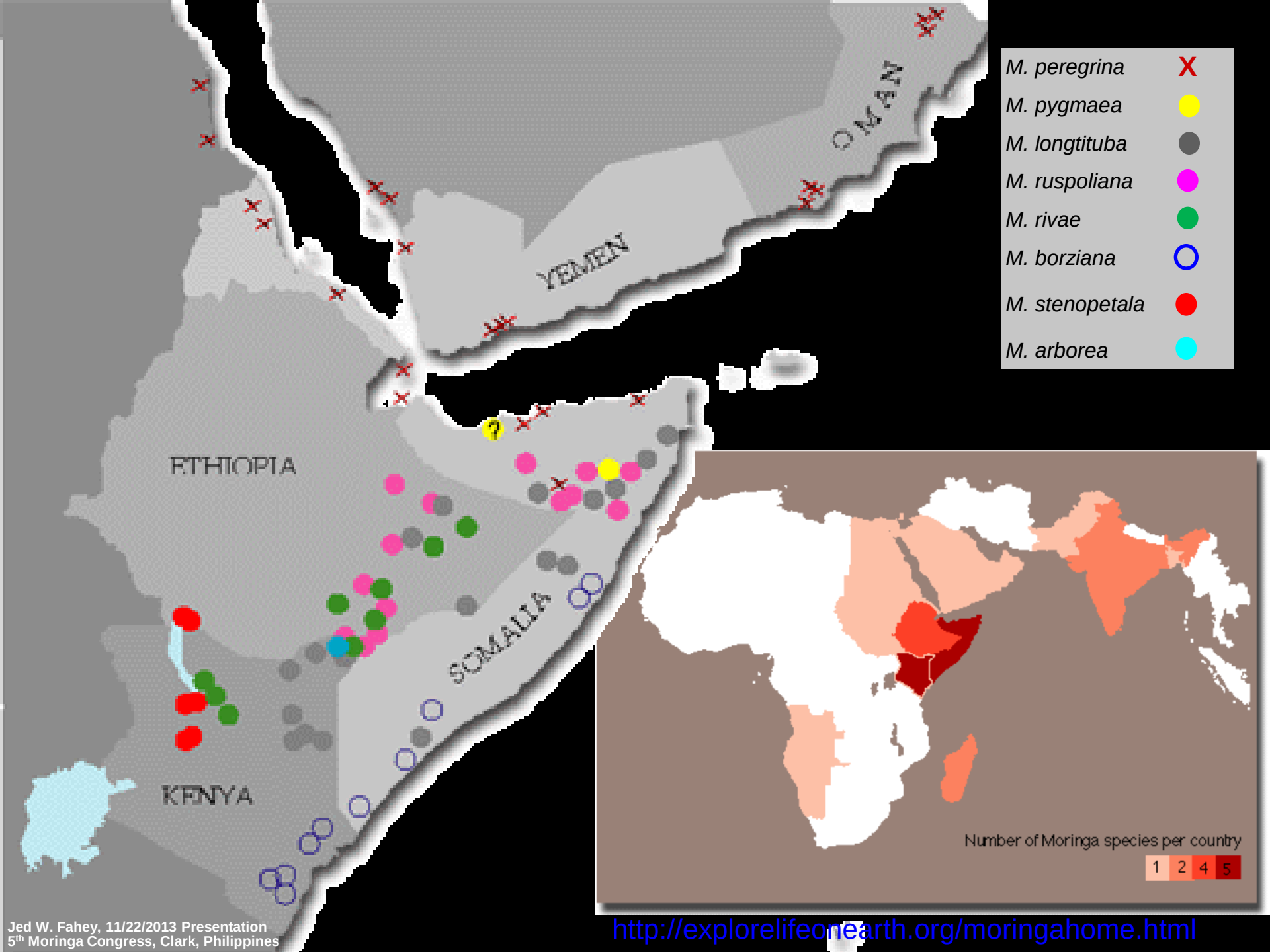
Slender trees

Trees with a tuberous juvenile stage and cream to pink slightly bilaterally symmetrical flowers
M. concanensis; mostly India
M. oleifera; India
M. peregrina; Red Sea, Arabia, Horn of Africa

Trees, shrubs, and herbs of NE Africa

The eight *Moringa* species found in northeast Africa span the whole range of life form variation found in *Moringa*. All but *M. peregrina* are endemic to northeast Africa, that is, found nowhere else on earth. These species are tuberous adults or tuberous juveniles maturing to fleshy-rooted adults; colorful, bilaterally symmetrical flowers
M. arborea; NE Kenya
M. borziana; Kenya and Somalia
M. longituba; Kenya, Ethiopia, Somalia
M. pygmaea; N Somalia
M. rivae; Kenya and Ethiopia
M. ruspoliana; Kenya, Ethiopia, Somalia

MARK OLSON: http://explorelifeonearth.org/moringahome.html



Jed W. Fahey, 11/22/2013 Presentation
5th Moringa Congress, Clark, Philippines

http://explorelifeonearth.org/moringahome.html

BOTTLE TREES

Moringa drouhardii

from southern Madagascar

the bark of this massive bottle tree is used medicinally

BOTTLE TREES

Moringa stenopetala

BOTTLE TREES

Moringa stenopetala

BOTTLE TREES

Moringa ovalifolia

from Namibia

a very large, very drought-resistant tree

water storage in trunk

Moringa concanensis

from India, Pakistan, and Bangladesh

the closest relative of the "miracle tree" *M. oleifera*

SLENDER TREES

Moringa peregrina

throughout the Red Sea region

edible tubers

oil prized since antiquity

TUBEROUS TREES

Moringa ruspoliana

found only in NE Kenya and S Ethiopia

the larges leaflets of the family

very long, tuberous roots

Moringa borziana

from E Kenya and S coastal Somalia

a pygmy species about 1 m tall

very tender leaves and large fruits

Moringa pygmaea

Moringa rivae

TUBEROUS TREES

Moringa longituba

from NE Kenya, SE Ethiopia, and SW Somalia

a pygmy species

tuber usually grows <u>below</u> ground

Moringa Rescue and Living Repository Effort

The collection hosts a total of over 200 live plants plus some 1800 seeds.

(funding courtesy of Trees for Life International, Wichita, KS)


Cramped collection includes the only *M. arborea* and *M. ruspoliana* plants in cultivation

Jed W. Fahey, 11/22/2013 Presentation
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Seed collection (partial). Many seeds remain in storage at the Institute of Biology of the National University of Mexico. They include many accessions of *M. oleifera*, including abundant material from cultivated and putatively wild plants in easter Pakistan and northern India (upper left), as well as samples from various parts of the Americas, Africa, and Asia. Also shown are *M. rivae, M. stenopetala, M. longituba,* and *M. peregrina.*

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Understanding Moringa Germplasm Diversity

- **We are currently seeking funding for a comprehensive project to better:**
  - **understand this issue,**
  - **produce global maps of *M. oleifera* potential distribution and areas of cultivation,**
  - **detailed genetics analysis (genomics),**
  - **enhanced germplasm collections and**
  - **quantitative genetics of selected attributes including nutritional quality and medicinal properties.**
- **This should lead to:**
  - **the long term improvement of Moringa via breeding,**
  - **clinical trials that establish firmly, by rigorous biomedical standards, its efficacy in various indications**

Grateful Acknowledgement for Primary Funding

American Institute for Cancer Research

National Institutes of Health

Lewis B. and Dorothy Cullman Foundation

Prevent Cancer Foundation

Murakami Noen

Kagome Co. Ltd.

Trees for Life International

National Geographic Society

National Science Foundation

Andrew Mellon Foundation

THANK YOU THANK YOU THANK YOU THANK YOU THANK YOU THANK