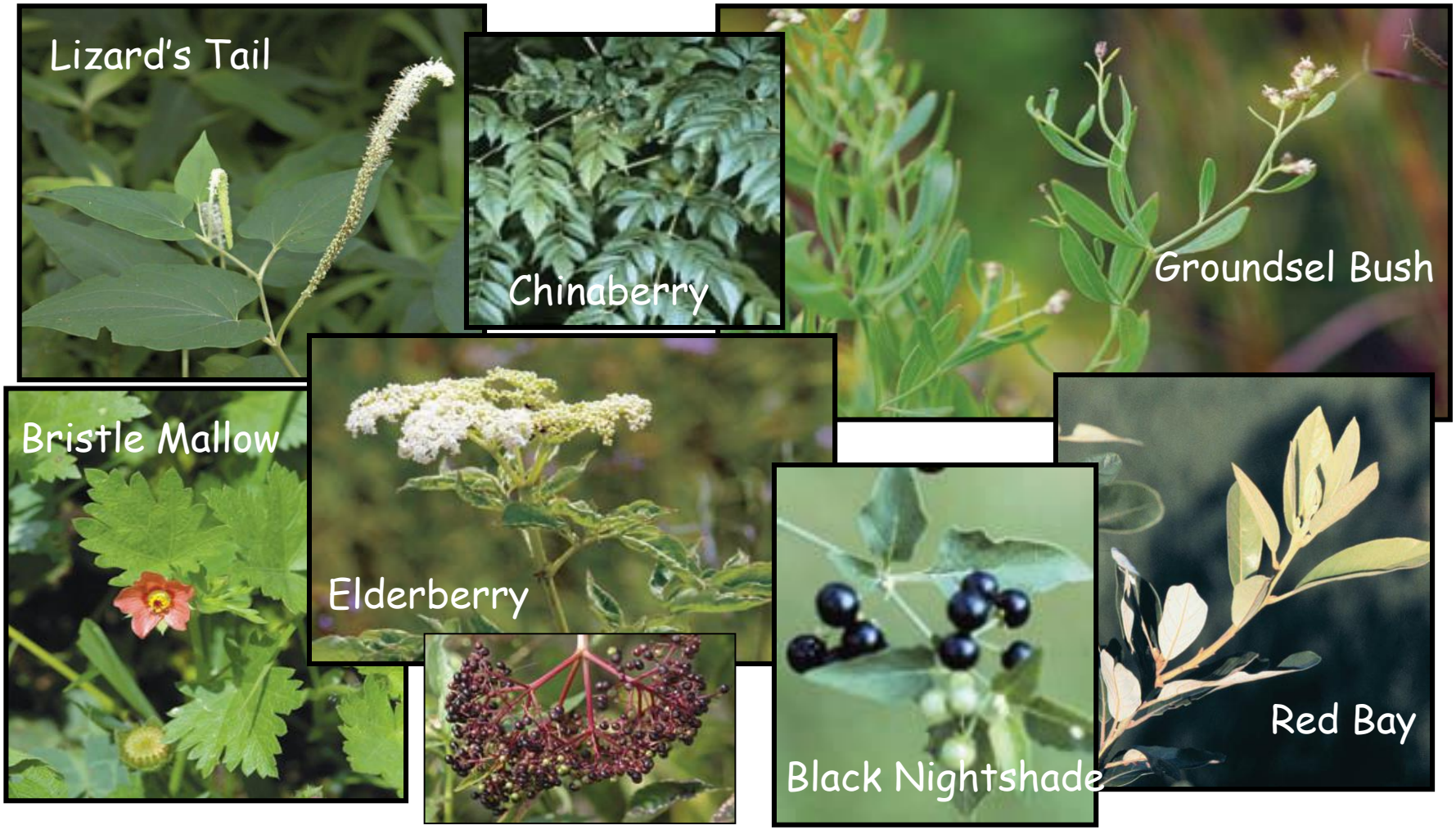
BOTANICAL DIETARY SUPPLEMENTS RESEARCH CENTER

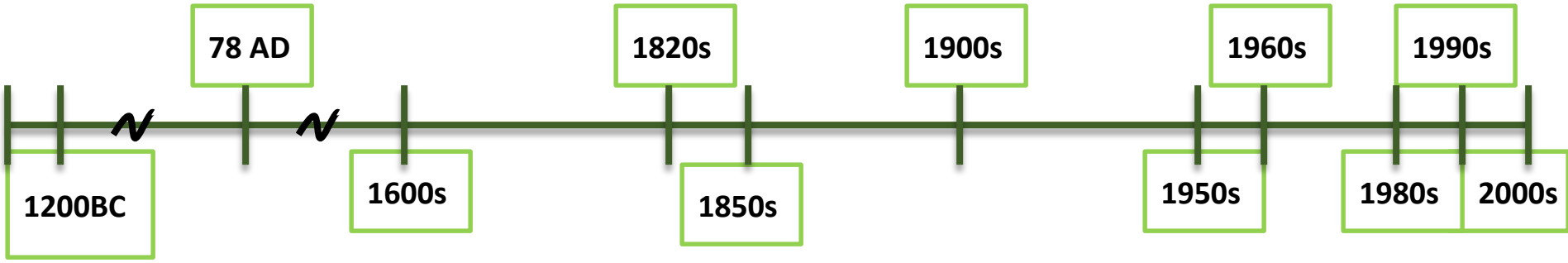
A National Center for the Study of Botanicals and Metabolic Resiliency



Broad Definitions

- A botanical is a plant or plant part valued for its medicinal or therapeutic properties, flavor, and/or scent.
- Herbs are a subset of botanicals.
- Products made from botanicals that are used to maintain or improve health may be called herbal products, botanical products, or phytomedicines.

History of Herbal Medicines

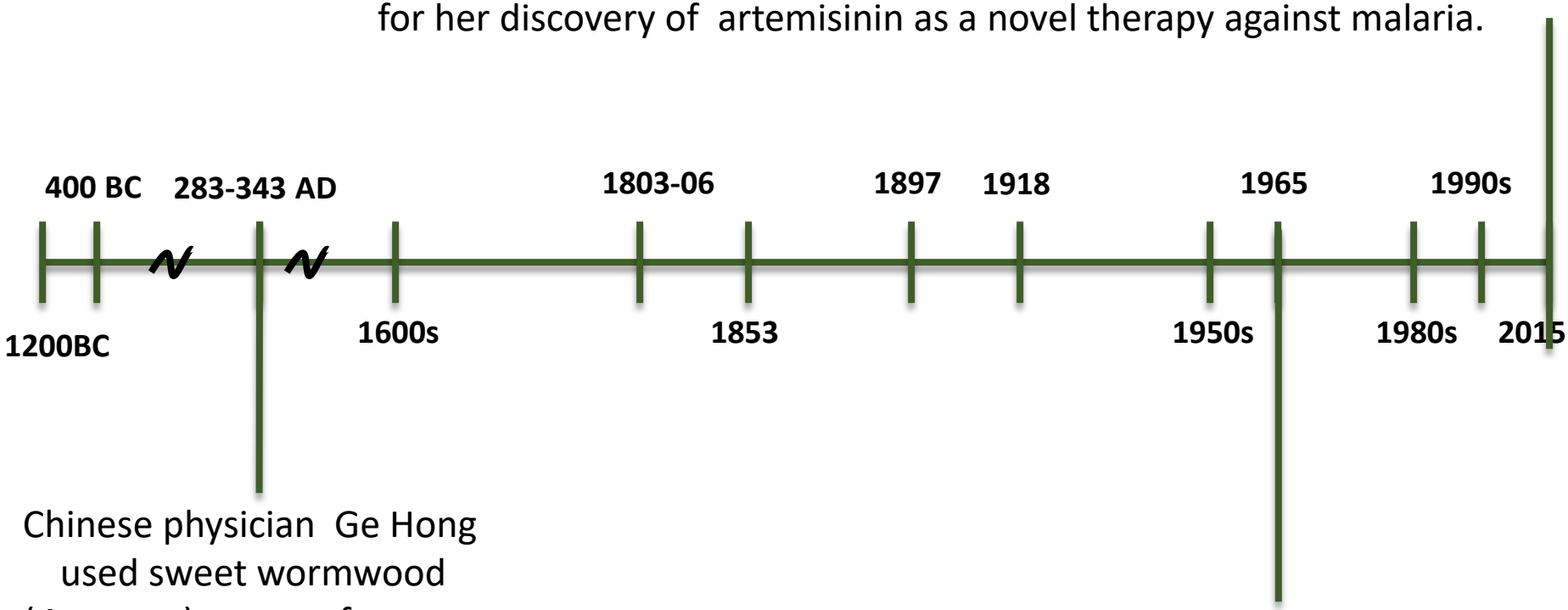


Ancient Ayurveda

Most Ancient Health Care System of India, Sri Lanka, and other Countries. Based on Traditional Herbal Medicines.

History of Herbal Medicines: *Artemisia annua* L.

Nobel Prize in Physiology or Medicine awarded to Youyou Tu
for her discovery of artemisinin as a novel therapy against malaria.



Chinese physician Ge Hong
used sweet wormwood
(*A. annua*) to treat fevers.

He wrote a handbook of
Emergency Formulas.

Youyou Tu, a Chinese scientist,
extracted Artemisinin from *A. annua.*
Used to treat malaria.

Drugs Derived from Plant Sources

Drug	Action	Plant Source
Aspirin	Anti-inflammatory	*Salix alba* L.
Atropin	Anti-cholinergic	*Atropa belladonna* L
Caffeine	CNS stimulant	*Camellia sinensis* (L.)
Camphor	Antiseptic	*Cinnamonum camphora* L.
Camptothecin	Anticancer	*Camptotheca acuminata* D
Codeine	Analgesic	*Papaver somniferum* L.
Curcumin	Choleretic	*Curcuma longa* L.
Digitoxin	Cardiotonic	*Digitalis purpurea* L.
Ephedrine	Sympathomimetic	*Ephedra sinica* Stapf.
Etoposide	Antitumour agent	Podophyllum peltatum L.
Morphine	Analgesic	*Papaver somniferum* L.
Physostigmine	Cholineserase inhibitor	*Physostigma venenosum* L.
Quinine	Antimalarial	*Cinchona ledgeriana* L.
Santonin	Ascaricide	*Artemesia maritima* L.
Taxol	Anticancer	*Taxus brevifolia* Nutt.
Vincristin/vinblastine	Antitumour agent	*Catharanthus roseus* L.

Table adapted from Fabricant, et al., 2001

Botanicals in the Treatment of Diabetes

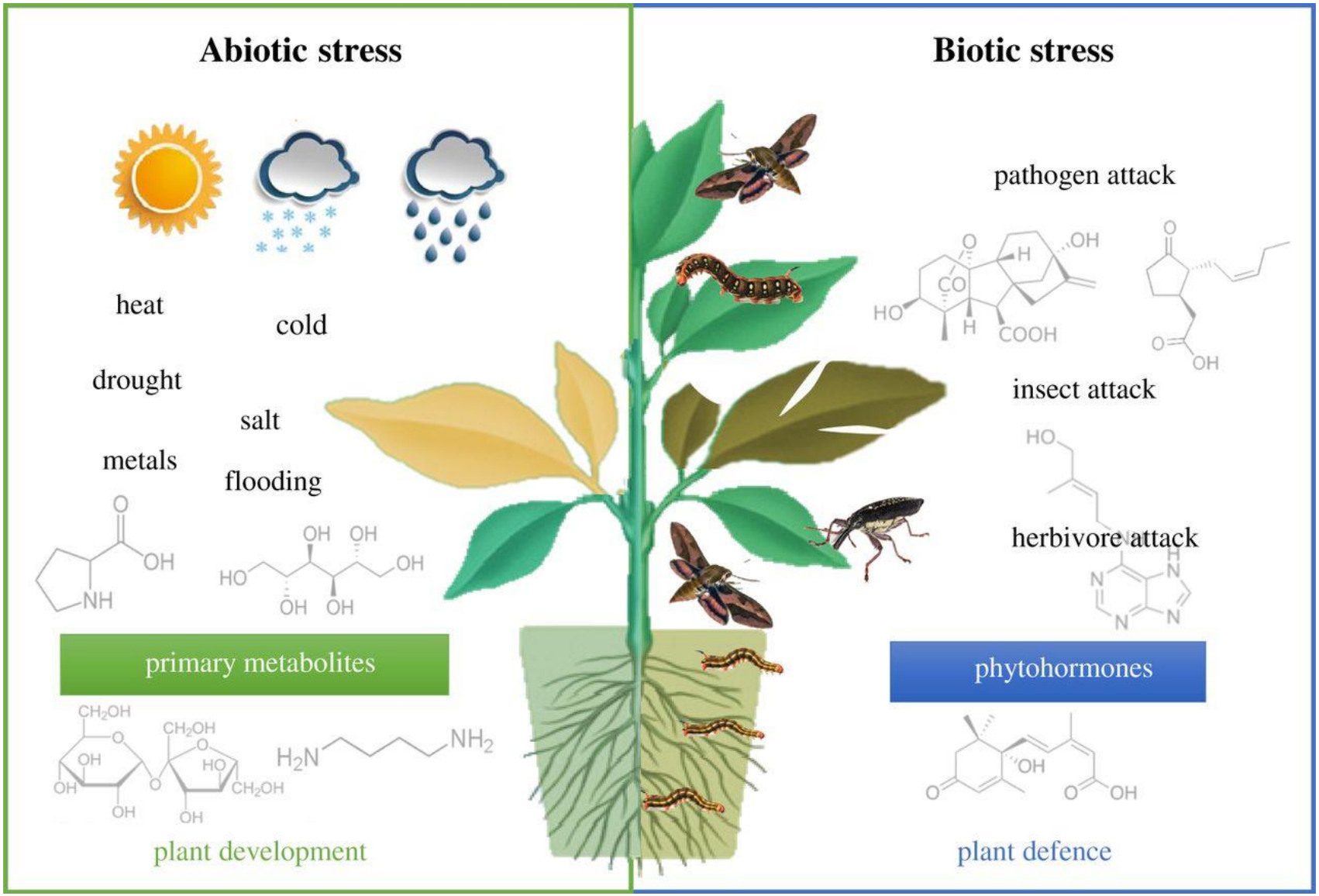
"Goat's Rue" ; French Lilac

Metformin in the Treatment of Diabetes

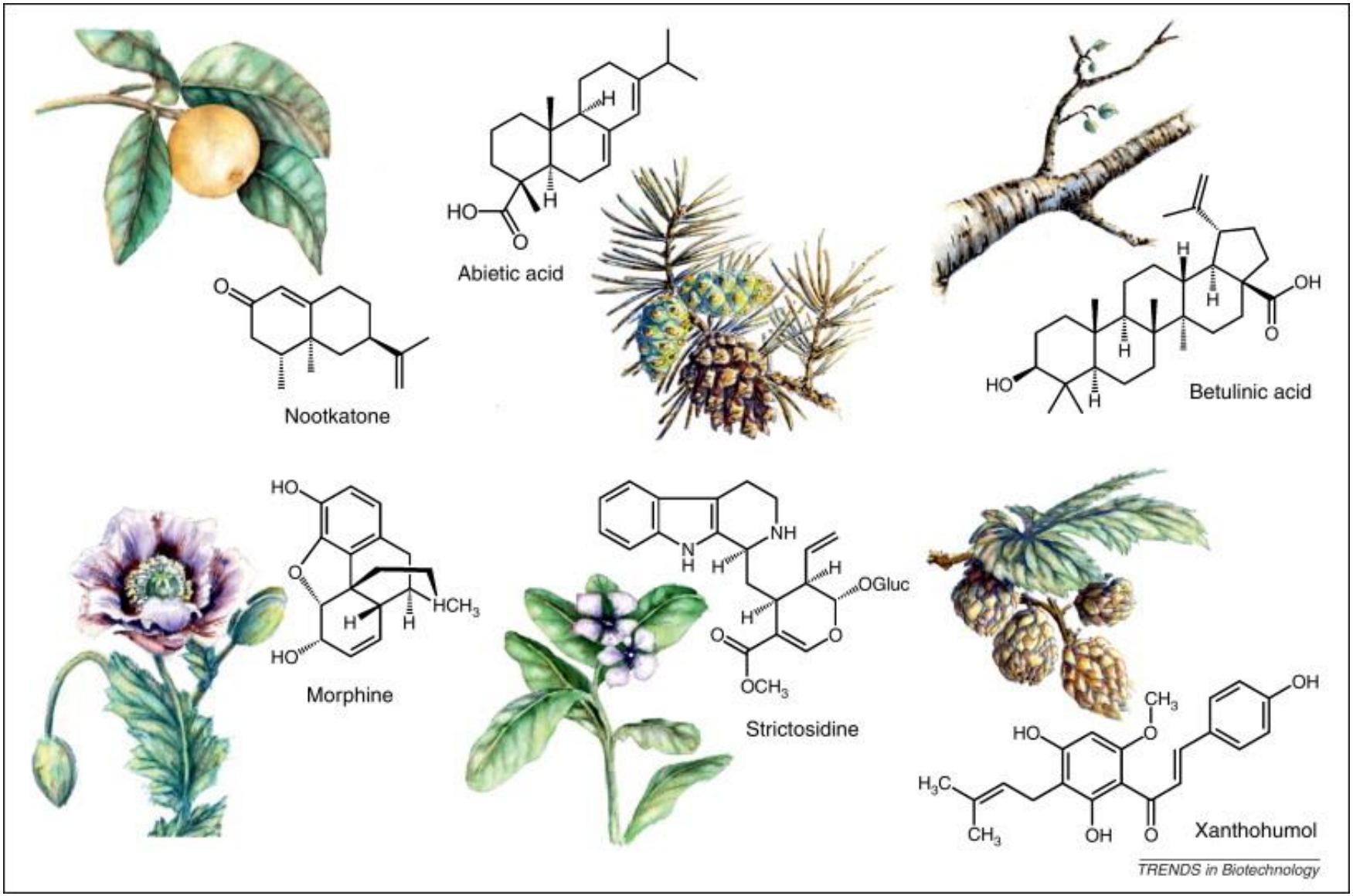
Galega officinalis L.

- Extracts from French Lilac were used in the middle ages (500-1500 AD) to treat symptoms typical of type 2 diabetes.
- Accounts of using “goat’s rue” or French lilac reappeared in the 17 century
- Metformin is based on compounds found in French lilac. It is the most widely prescribed anti-diabetic drug in the world.
- U. S. > 48 million prescriptions filled in 2010.
- Now studied for other uses…cancer prevention, anti-aging…not currently approved for these uses.

Why are Plants a Great Source of Medicinal Compounds?



But is Plant-based/Natural Always Safe or Effective?



Plant-based Dietary Supplements: How Safe are They? Are They Effective?

Dietary Supplement Ads

What are dietary supplements?

Pills, powders, or shakes that include vitamins, minerals, herbs, enzymes, or probiotics.

Ads may say they can help with things like:

- weight loss
- bodybuilding
- energy boosting
- anti-aging
- pain or disease management

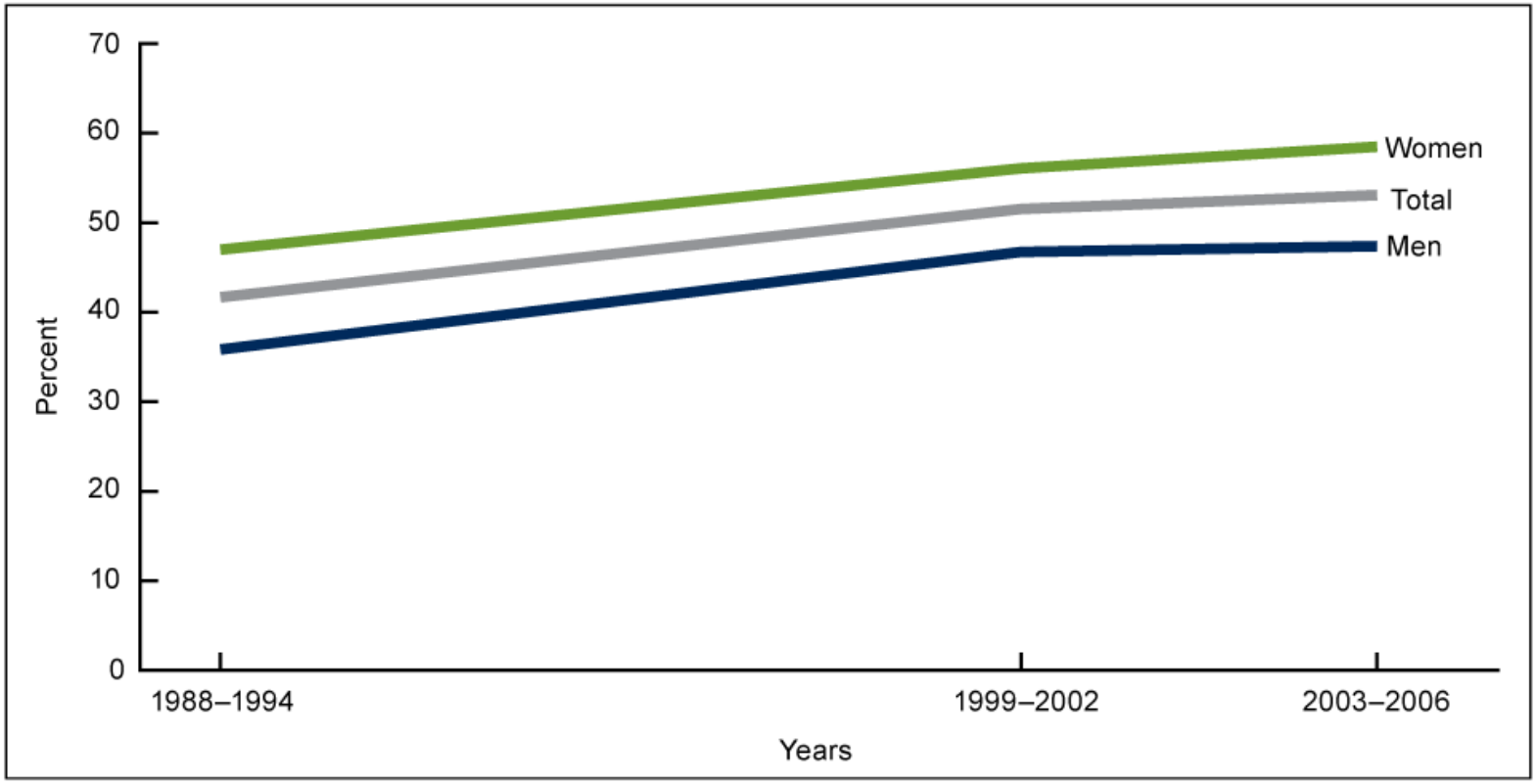
While some dietary supplements have proven benefits, others don't. And some could even be risky for your health.

Did you know?

- Unlike drugs, dietary supplements are **not evaluated** by the FDA for safety and effectiveness before they're sold.
- Dietary supplements are **not meant** to prevent, treat, or cure diseases.
- "Natural" doesn't always mean safe.
- Supplements could have hidden ingredients.

FTC.gov/DietarySupplements
Federal Trade Commission
November 2015

Percentage of Adults (20 year of age and older) Using Dietary Supplements in the United States



From the CDC, National Health and Nutrition Examination Survey

In 2012, Americans spent $12.8 billion out-of-pocket on natural products supplements
This is 1/4th of what we spent out-of-pocket on prescription drugs

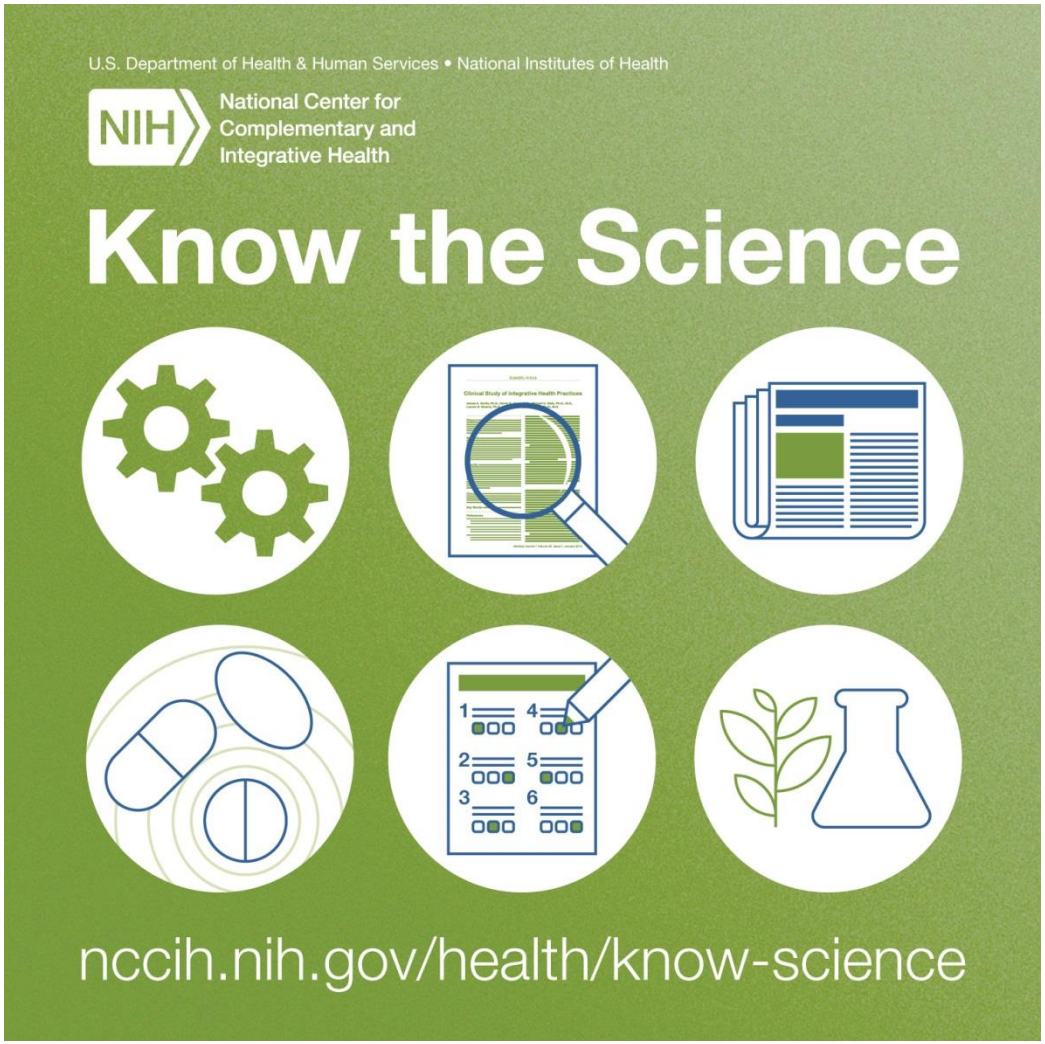
Botanical-based Dietary Supplementation: Who is taking dietary supplements?

Table 1. Prevalence of Dietary Supplement Use by Demographic, Anthropometric, Socioeconomic, and Lifestyle Characteristics Among Adults (≥20 Years) in the United States, 2007-2010[1,2]

Characteristic	No.	% (SE)
Total	**11 956**	48.8 (1.1)
Sex		
Men	5911	43.1 (1.4)[a]
Women	6045	54.4 (1.1)[b]
Age range, y		
20-39	3809	34.2 (1.5)[a]
40-59	3925	50.8 (1.6)[b]
>60	4222	67.4 (1.4)[c]
BMI		
<18.5	730	44.1 (2.2)[a]
18.5-24.9	3074	52.8 (1.6)[b]
25.0-29.9	3897	49.1 (1.6)[c]
≥30	4255	45.9 (1.2)[a]
Current health status (n = 10417)		
Excellent or very good	3670	54.8 (1.2)[a]
Good	4130	47.1 (1.6)[b]
Fair or poor	2617	43.7 (1.4)[b]

Adapted from Bailey *et al* 2013 JAMA Intern Med. 173(5): 355-361

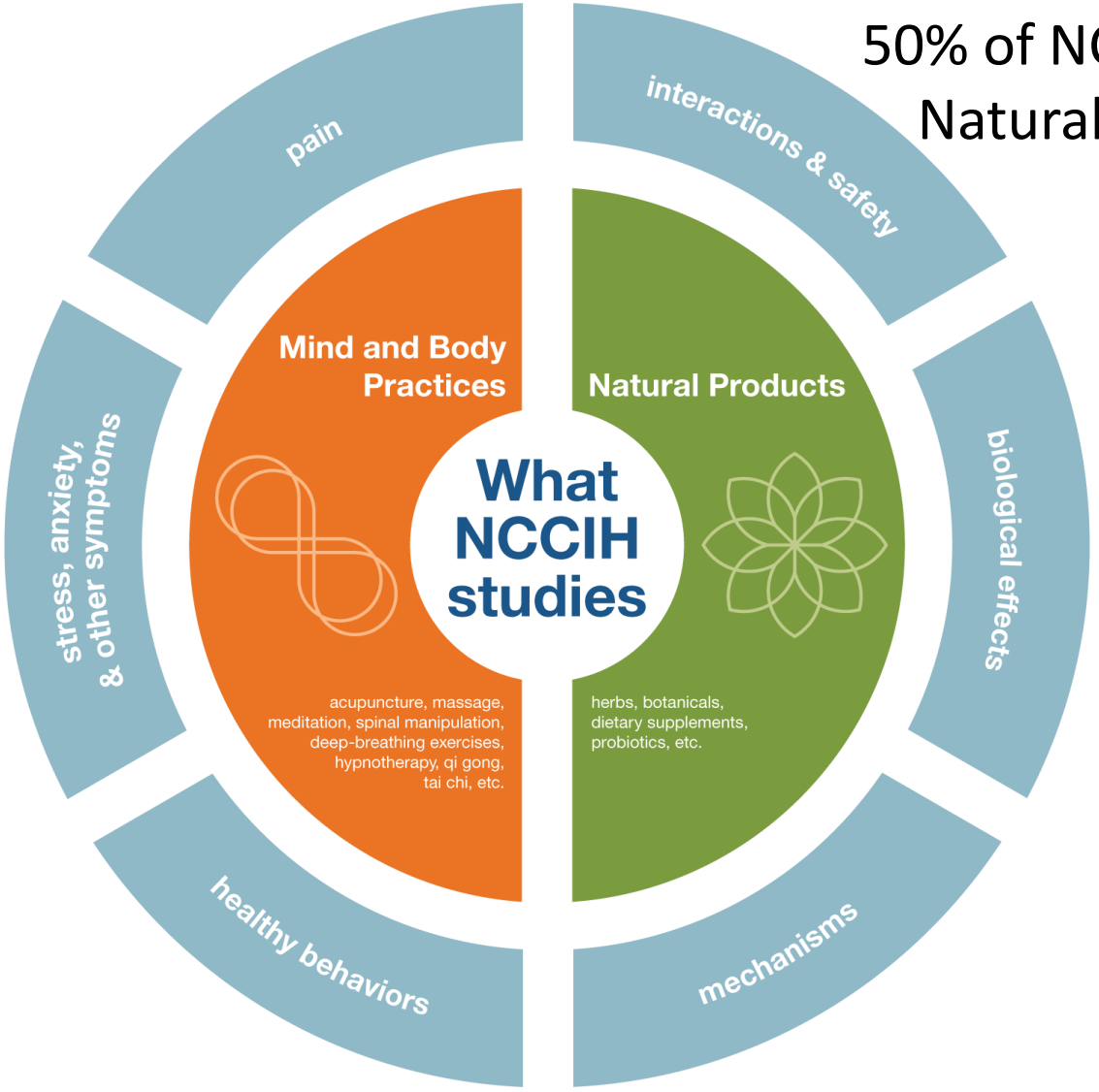
National Center for Complementary and Integrative Health
Formed in 1998 by Congressional Mandate



https://nccih.nih.gov/health/know-science

National Center for Complementary and Integrative Health
NCCIH

50% of NCCIH effort
Natural Products



National Center for Complementary and Integrative Health

U.S. Department of Health and Human Services | National Institutes of Health

NIH National Center for Complementary and Integrative Health

NIH...Turning Discovery Into Health

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Dietary and Herbal Supplements

Share:

A dietary supplement, as defined by the Dietary Supplement Health and Education Act (DSHEA), is a product that:

- Is intended to supplement the diet
- Contains one or more dietary ingredients (including vitamins, minerals, herbs or other botanicals, amino acids, and certain other substances) or their constituents
- Is intended to be taken by mouth, in forms such as tablet, capsule, powder, softgel, gelcap, or liquid
- Is labeled as being a dietary supplement.

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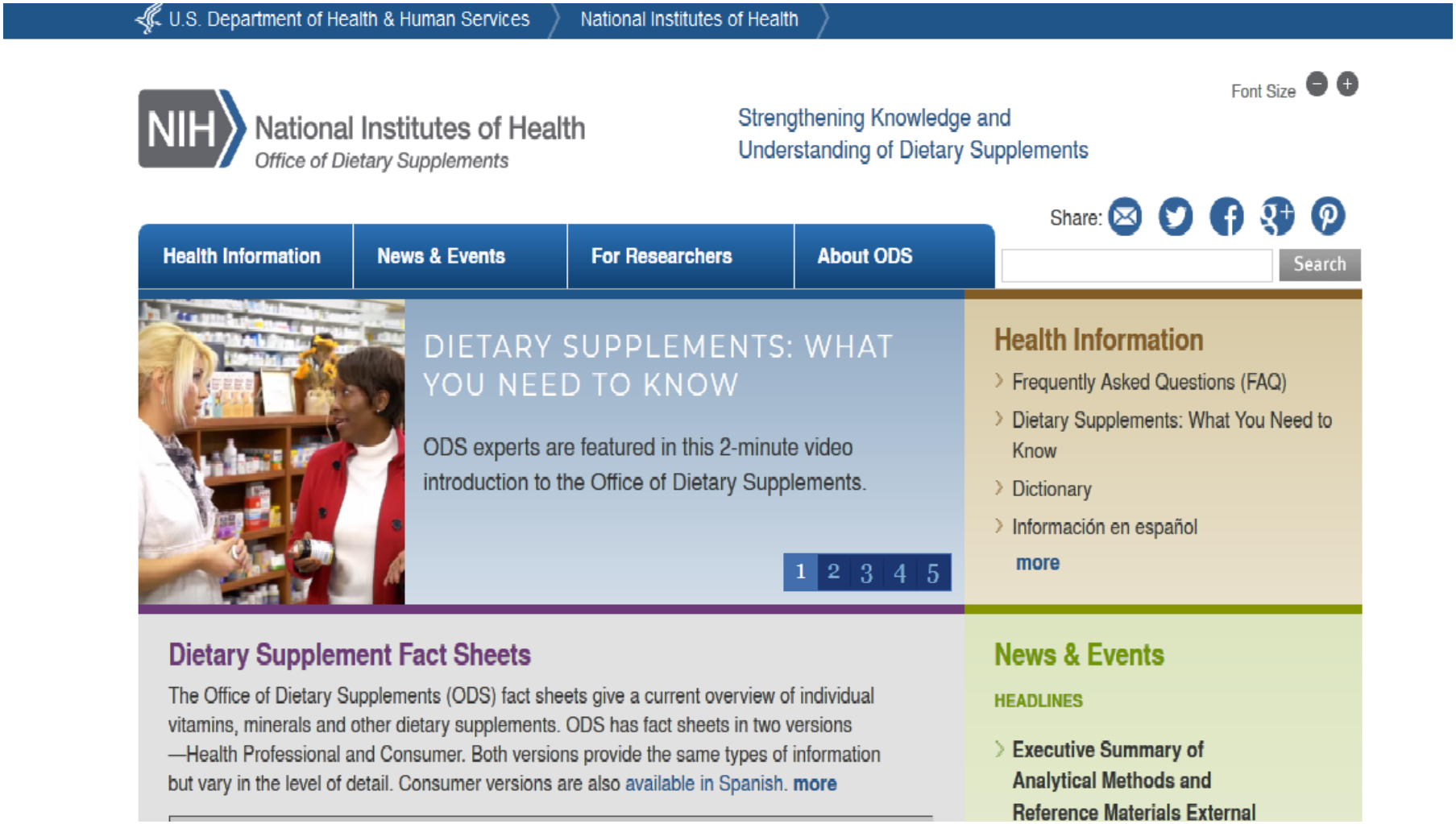
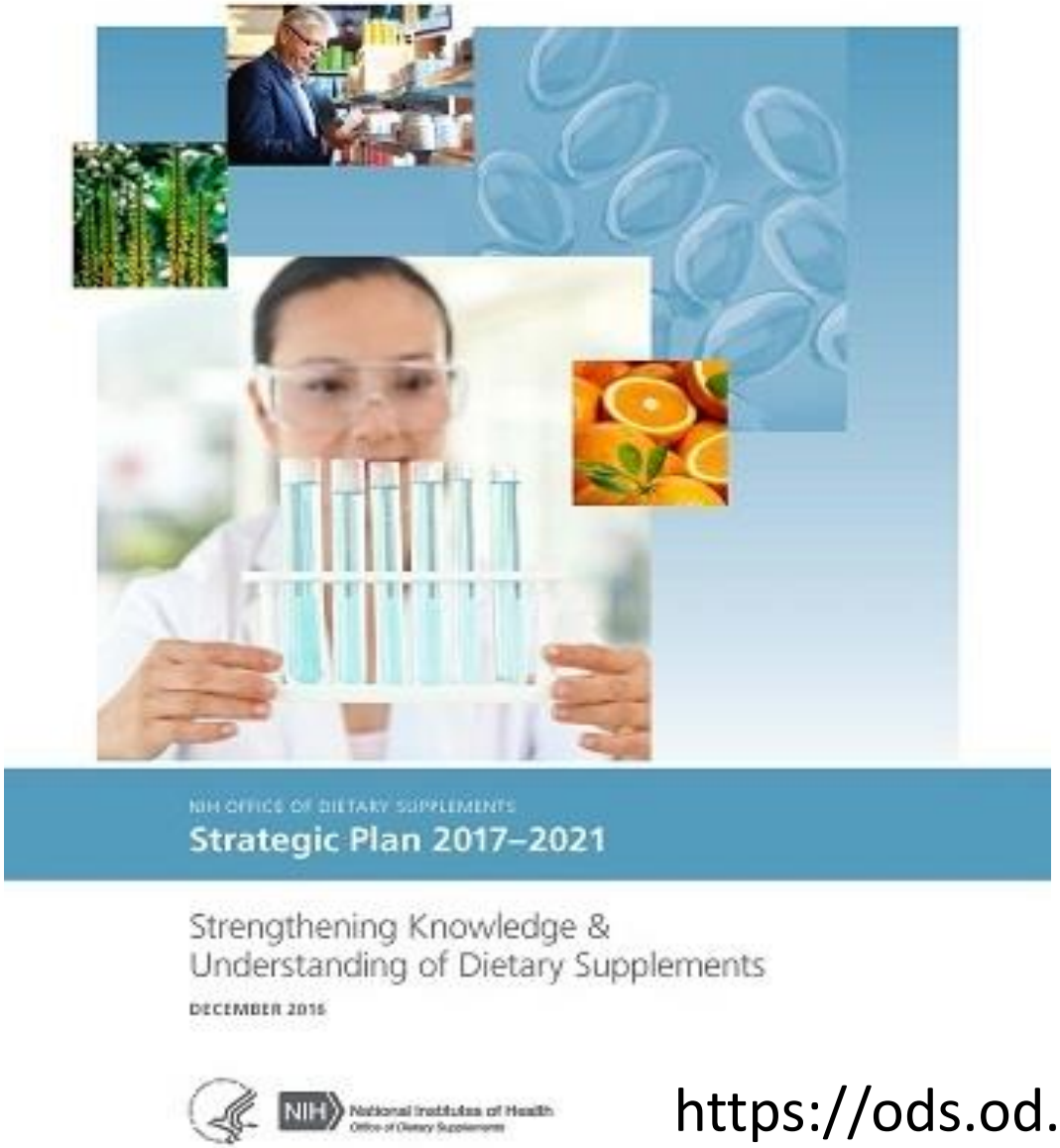
https://nccih.nih.gov/

NIH Office of Dietary Supplements



https://ods.od.nih.gov/

NIH Office of Dietary Supplements



https://ods.od.nih.gov/

The Botanical Dietary Supplements Research Center at Pennington Biomedical Research Center

One of three National Centers for Advancing Research on Botanical and Other Natural Products (CARBON)

National Institutes of Health

Office of Dietary Supplements

and

National Center for Complementary and Integrative Health (NCCIH)

Mount Sinai
Cognitive Function

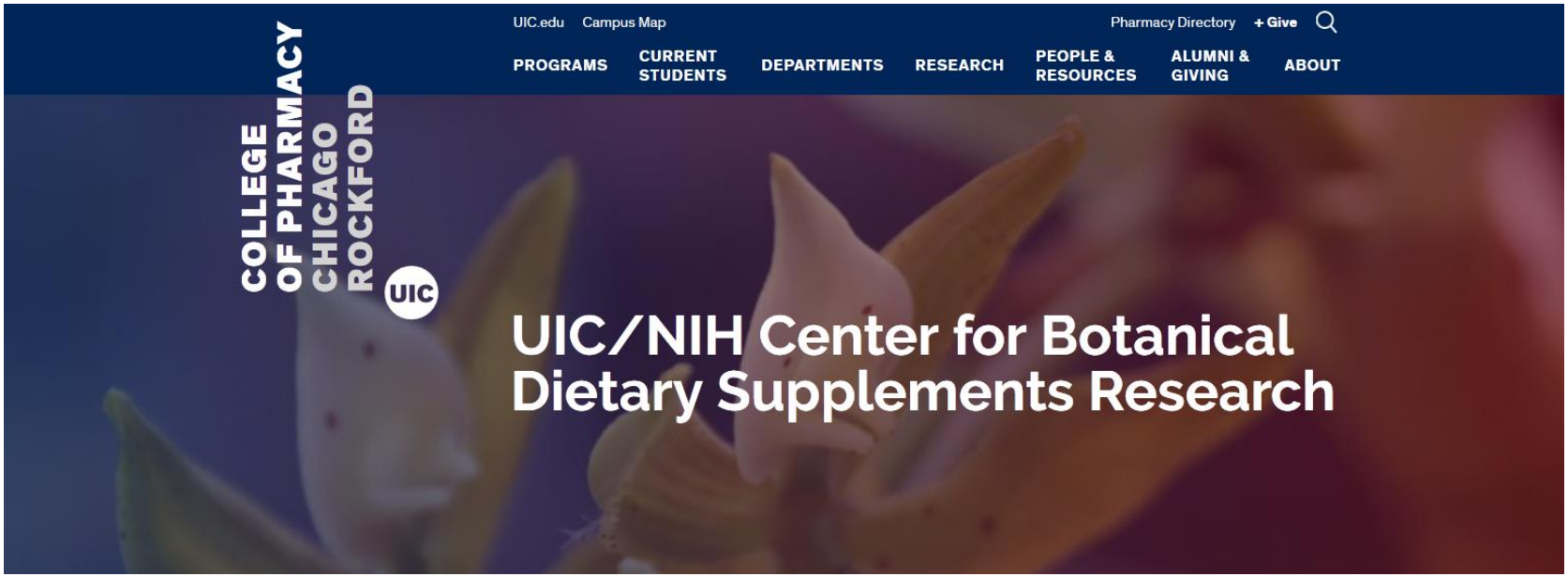
PBRC & Rutgers
Metabolic Resiliency

University of Illinois, Chicago
Women's Health

Botanical Dietary Supplements for Women's Health, University of Illinois, Chicago

Richard van Breemen, PhD

https://pharmacy.uic.edu/research/botanical-dietary-supplements



Botanical Dietary Supplements for Women's Health, University of Illinois, Chicago

UIC Botanical Center Plants (*Latin Name*)	Common Name	Plant Part
Actaea racemosa	Black cohosh	Aerial, root, rhizome
Angelica sinensis	Dang Gui (aka Dong Quai)	Root
Dioscorea villosa	Wild yam	Root
Glycyrrhiza glabra L., *G. uralensis*, *G. inflata*	Licorice	Rhizome
Humulus lupulus	Hops	Strobuli

Menopause/estrogenic properties of the botanicals
Hops, licorice have phytoestrogens

Botanical-drug interactions and safety

Identification of compounds and pharmacology of the botanical compounds

Botanical Dietary Supplements for Women's Health, University of Illinois, Chicago

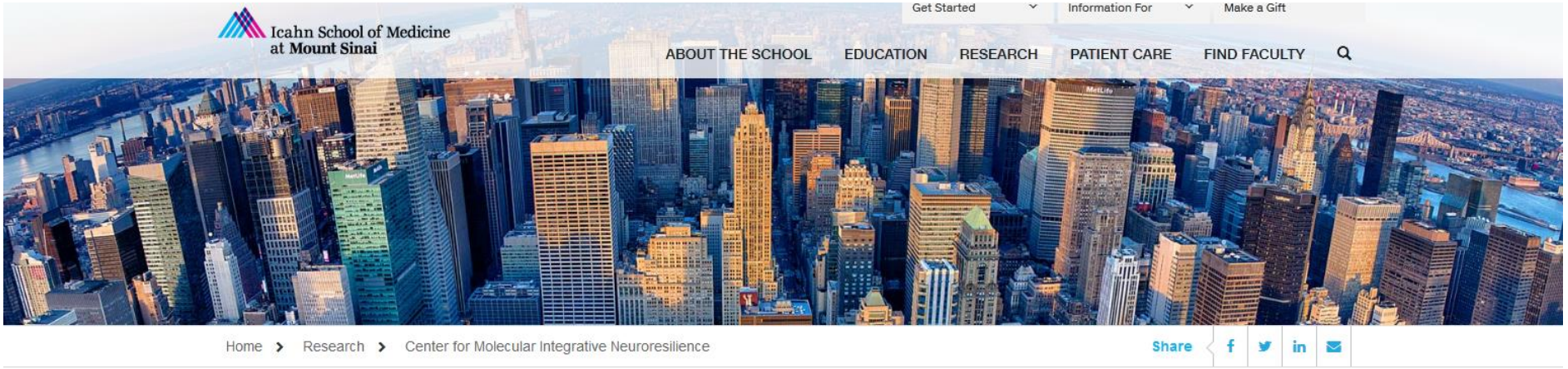
Atkins Medicinal Garden

The Dorothy Bradley Atkins Medicinal Plant Garden offers a unique venue for trainees and visitors to learn about medicinal plants and their historic and current uses.

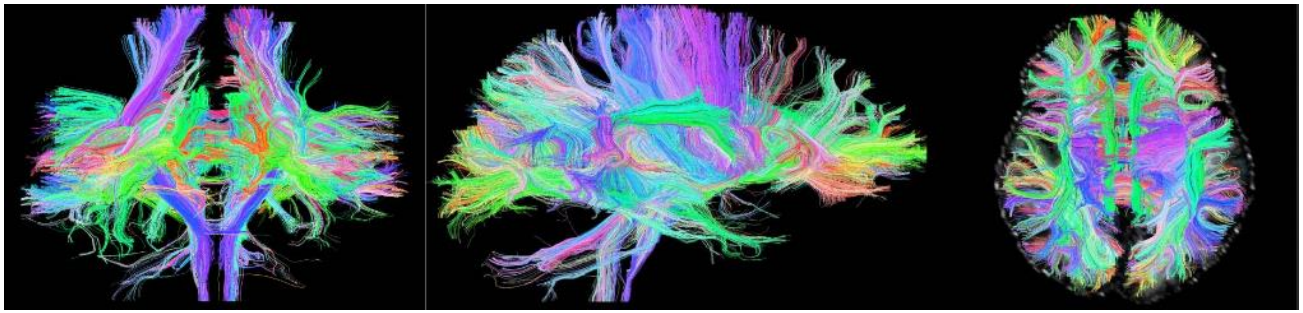
Center for Molecular Integrative Neuroresilience at Mount Sinai School of Medicine

Giulio Pasinetti, MD, PhD

http://icahn.mssm.edu/research/molecular-neuroresilience

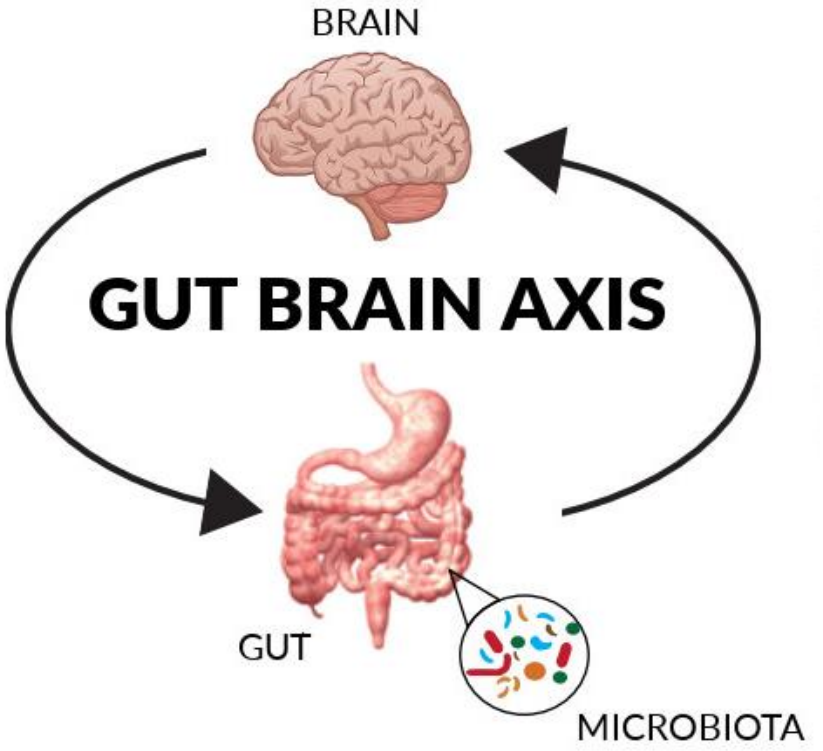


Center for Molecular Integrative Neuroresilience



Center for Molecular Integrative Neuroresilience at Mount Sinai School of Medicine

Grape polyphenols



Cognitive Function

Dementia
Depression
Anxiety
Psychological stressors:
Sleep deprivation

BOTANICAL DIETARY SUPPLEMENTS RESEARCH CENTER
A National Center for the Study of Botanicals and Metabolic Resiliency

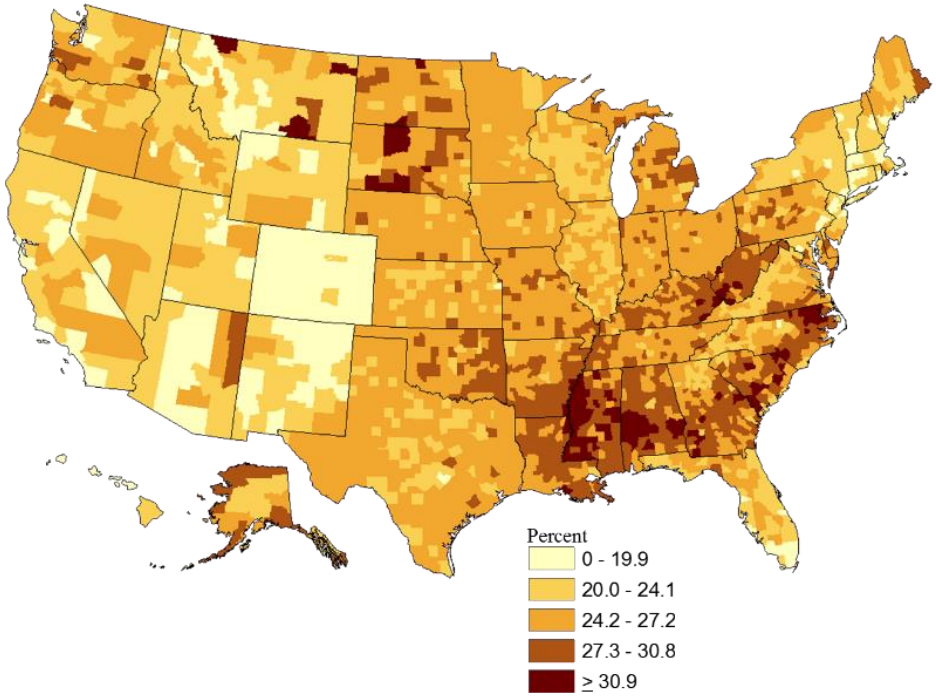
Botanicals and Metabolic Resiliency: Obesity-related Metabolic Syndrome

PENNINGTON BIOMEDICAL RESEARCH CENTER LSU
30 YEARS OF DISCOVERY

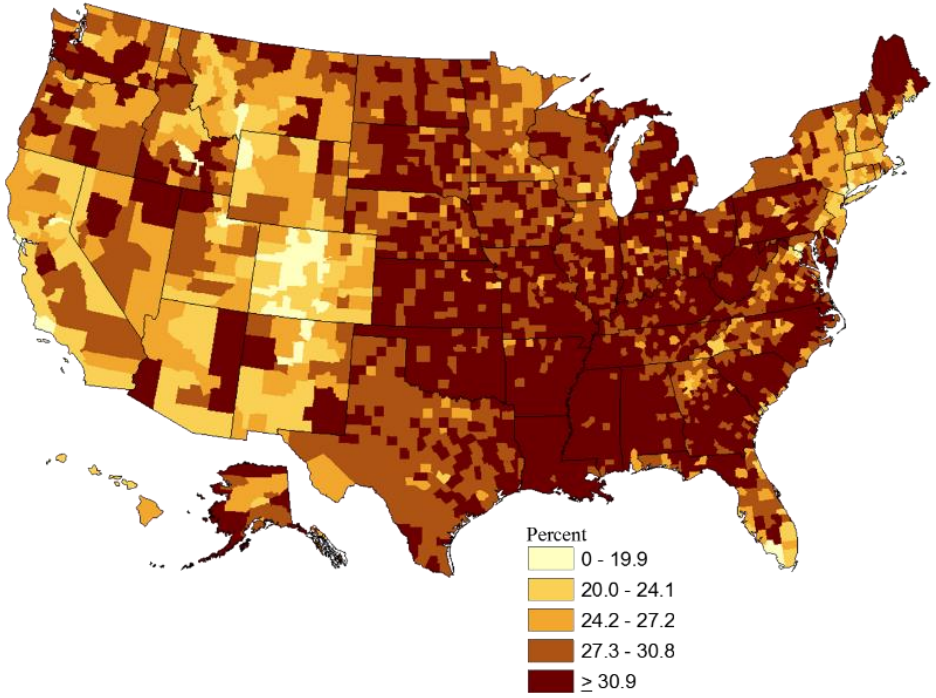
RUTGERS
School of Environmental and Biological Sciences

LSU

Prevalence of Obesity in the United States: Adults 20 years of age or older

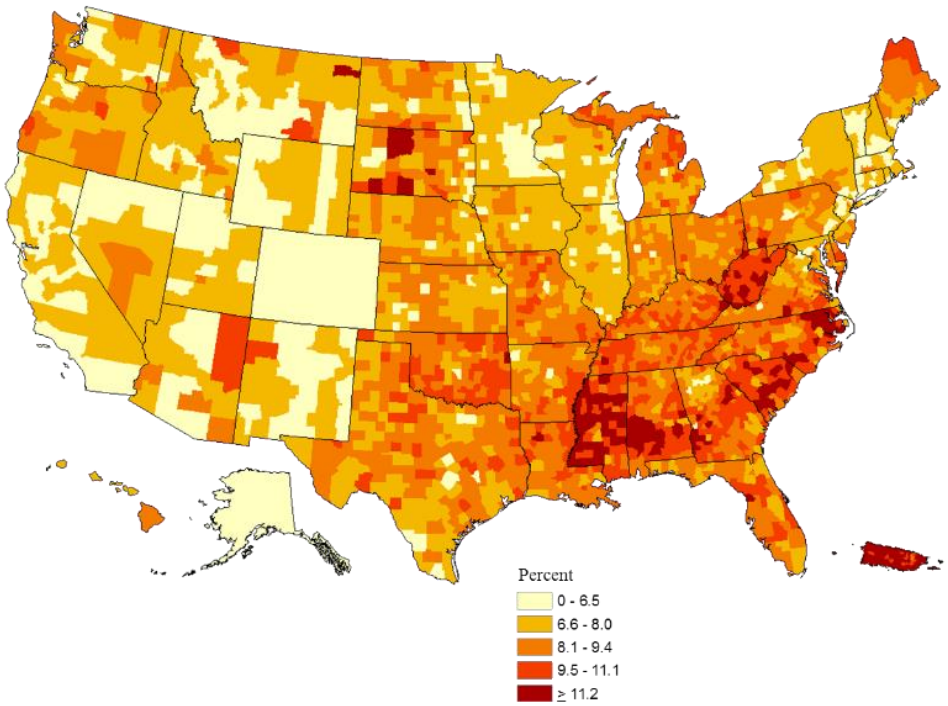


2004

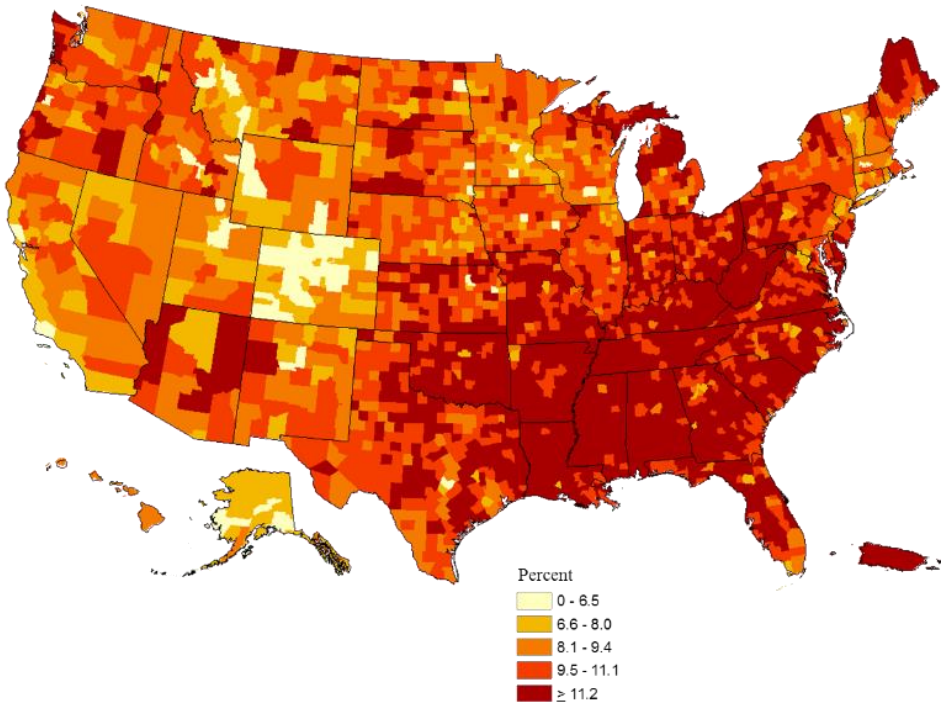


2011

Type 2 Diabetes in Adults over 20 Years of Age

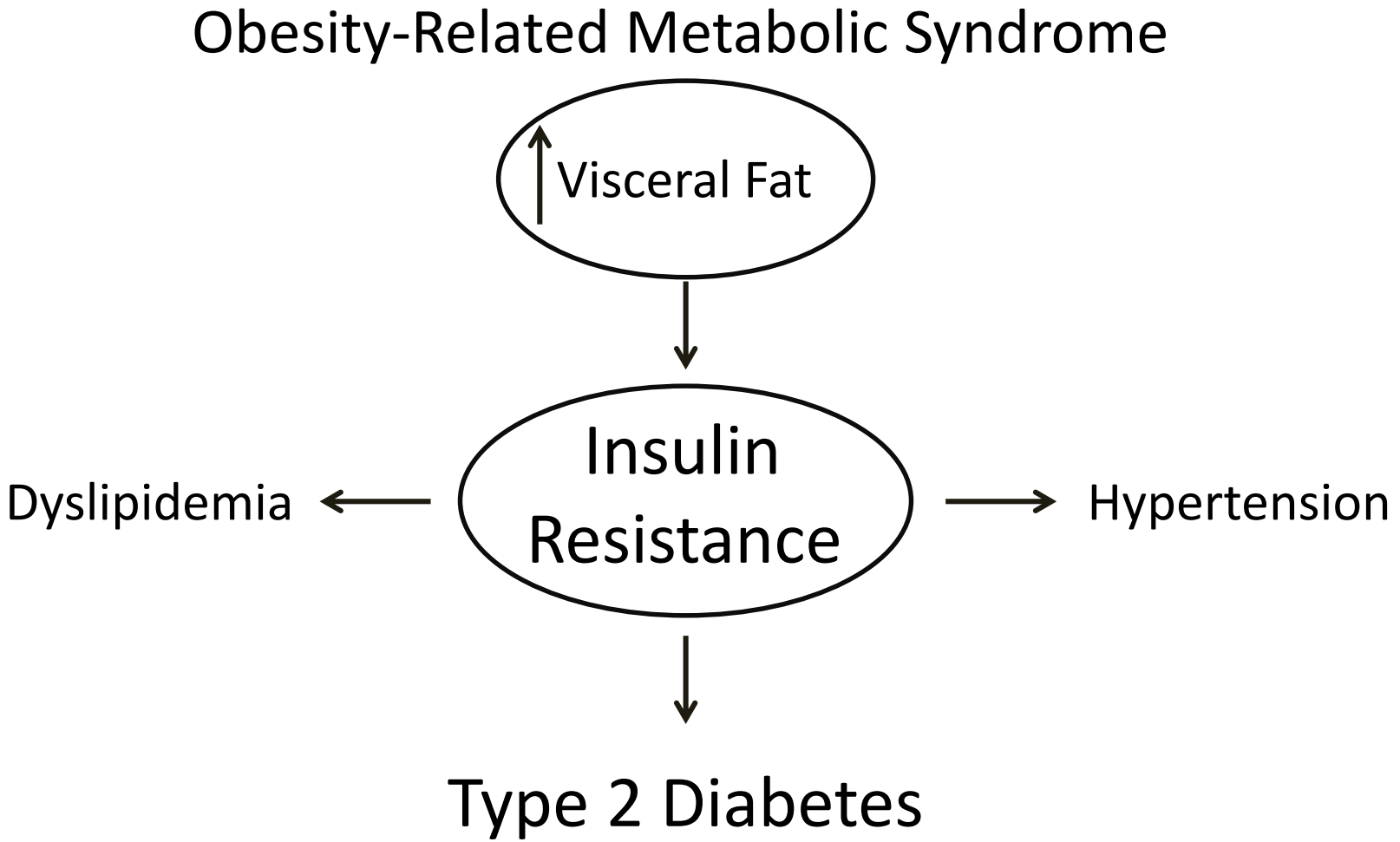


2004



2011

Biological Investigation of a Botanical Extracts in Metabolic Syndrome



Botanicals Currently Being Tested

Artemisia dracunculus

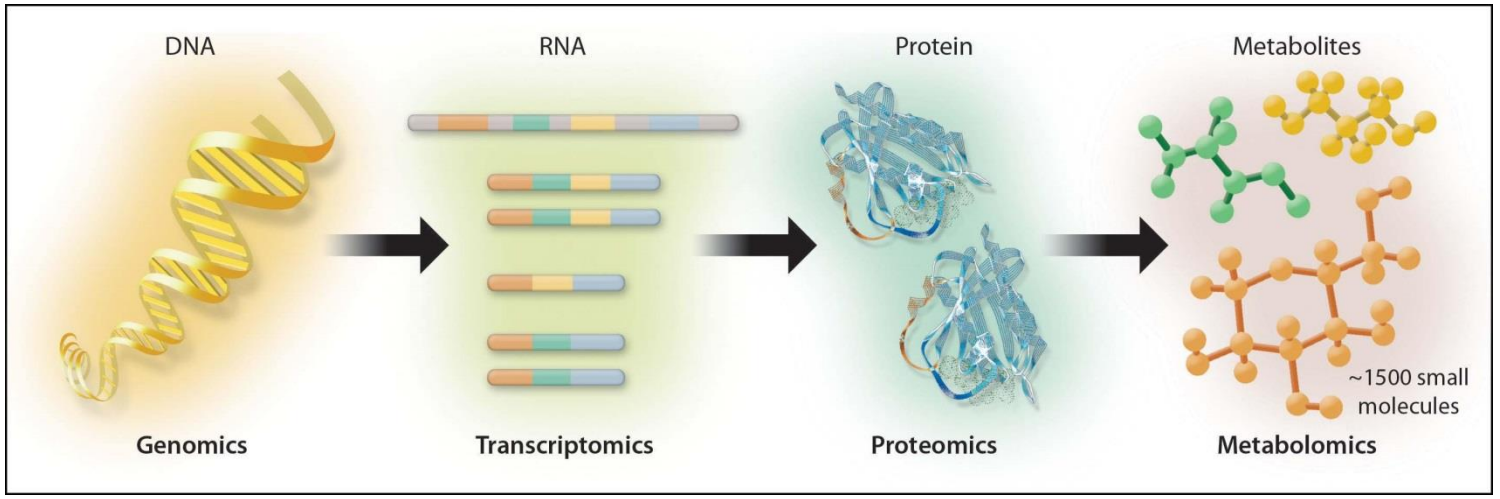
Artemisia scoparia

Bitter Melon

Fenugreek seeds

Moringa

Botanical/Herbal "Traditional" Medicine in the Age of "Omics" Research



Juliette Borda, 2004

- Can apply these tools to understanding the "mechanism of action" of how a botanical extract works in the body.
- Sophisticated tools to study efficacy, toxicity of the extracts
- How safe is the botanical extract to use? What are the adverse effects?
- Determine the best therapeutic use of the botanical extract

CANPIT

Centers for Advancing Natural Products Innovation and Technology

National Institutes of Health

Office of Dietary Supplements

and

National Center for Complementary and Integrative Health (NCCIH)

University of Texas Southwestern Medical Center and Simon Fraser University, BC, Canada

Center for High-throughput Functional Annotation of Natural Products

University of Illinois at Chicago

Center for Natural Products Technologies

Center for High-Throughput Functional Annotation of Natural Products

http://www.hifan.swmed.edu/index.php

UT Southwestern Medical Center

SFU SIMON FRASER UNIVERSITY

UC SANTA CRUZ

HiFAN

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Center for High-Throughput Functional Annotation of Natural Products

Center Overview

Determination of the mechanism of action to botanicals and natural products (mixtures and pure compounds) is often rate limiting for the safe and efficacious use as supplements and therapeutics. Botanicals and dietary supplements are particularly difficult, as these are often complex mixtures that can change in the constituents and concentration of individual compounds. The rapidly growing botanical dietary supplement industry faces a number of challenges regarding the quality, safety and benefit of these products. In order to address these issues, rigorous and sustained efforts are needed to chemically and biologically characterize these products.

The Center will take advantage of technology platforms developed at the University of Texas Southwestern Medical Center and the University of California, Santa Cruz to study the mechanism of action of botanicals and natural products. The end goal is to provide a series of data-driven websites where the scientific community can probe the function of natural product and botanicals.

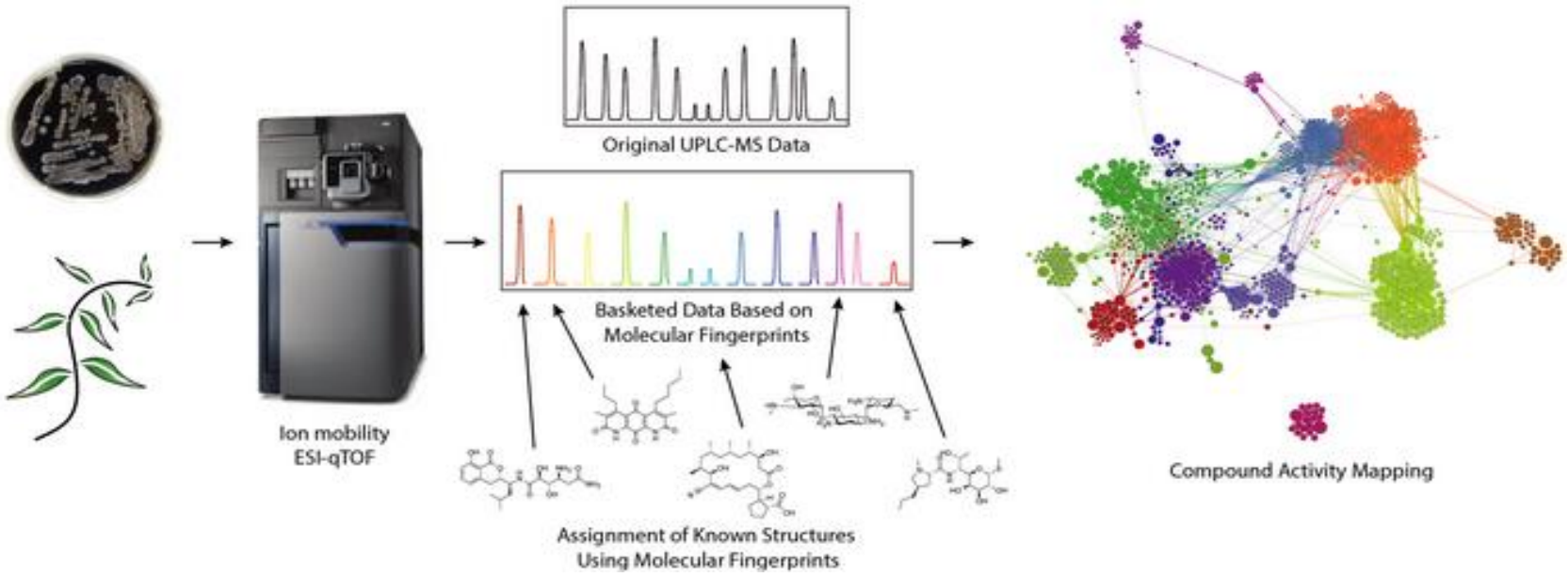
A major goal of this Center is to make the technology platform available to the botanical and natural product community. Use the collaboration link to find out how to initiate a collaboration with the center. We also want this website to be a valuable resource for the botanical and natural product community. As such, we will provide information directly and through links with other resources, such as the other CANPIT funded research at the University of Illinois Chicago.

Center for High-Throughput Functional Annotation of Natural Products/HiFAN

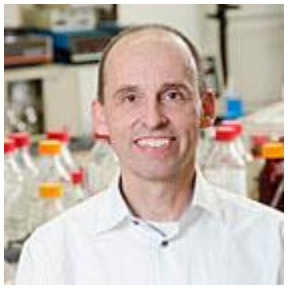
John MacMillan, PhD

Michael White, PhD

Roger Linington, PhD



Center for Natural Product Technologies at UIC



Guido Pauli, PhD

Jonathan Bisson, PhD

Charlotte Simmler, PhD

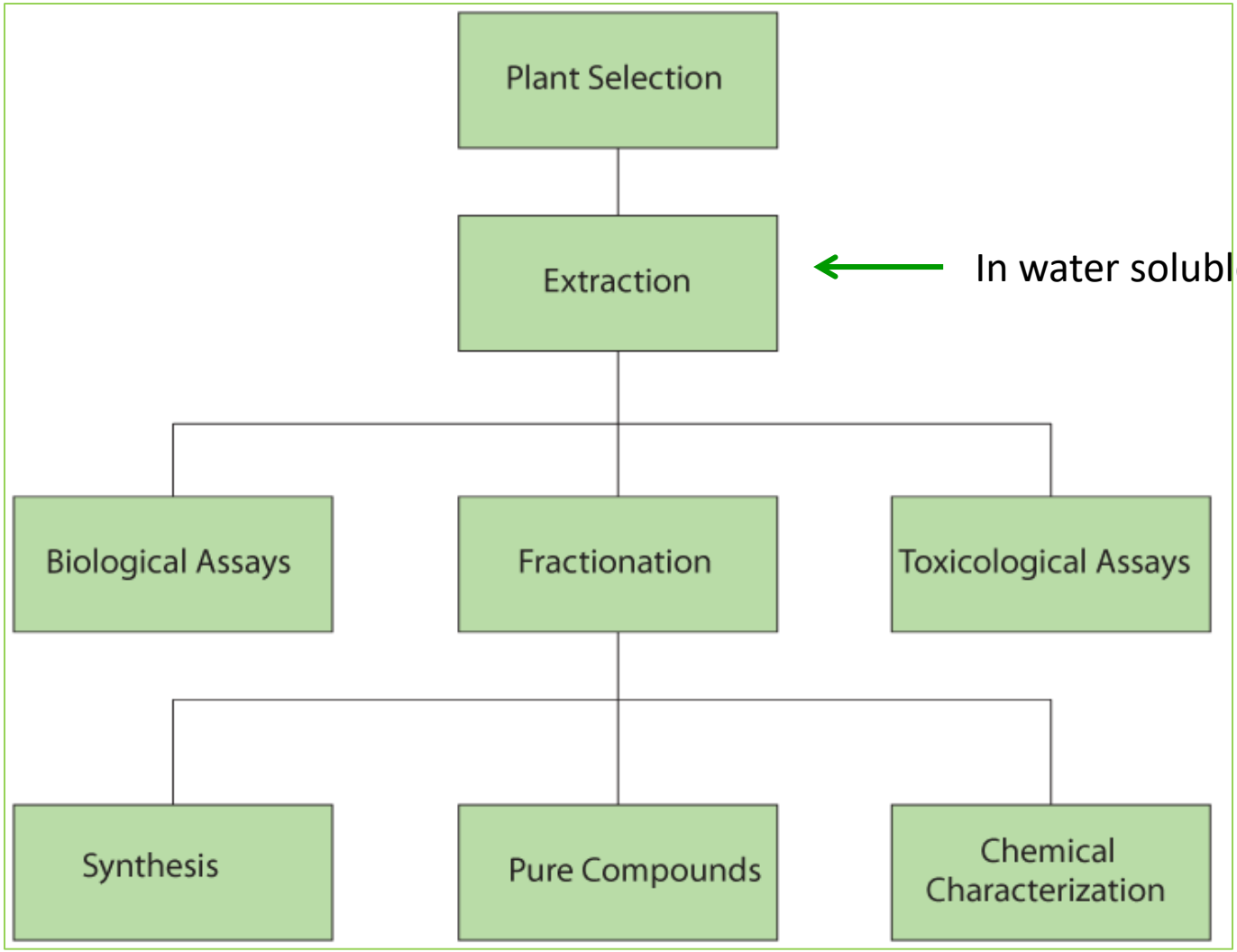
https://cenapt.pharm.uic.edu/

Connecting scientists and technologies

Offering resources for the natural product community

Addressing challenges in natural product research

What is the Process?
Screening Botanical Extracts



Adapted from Rates (2001).

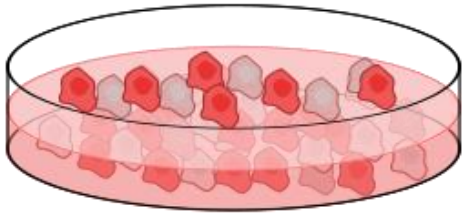
Testing Botanical Extracts: Steps Along the Way

Preclinical Studies

Cell Culture

Animal Model of Disease

Clinical Trials

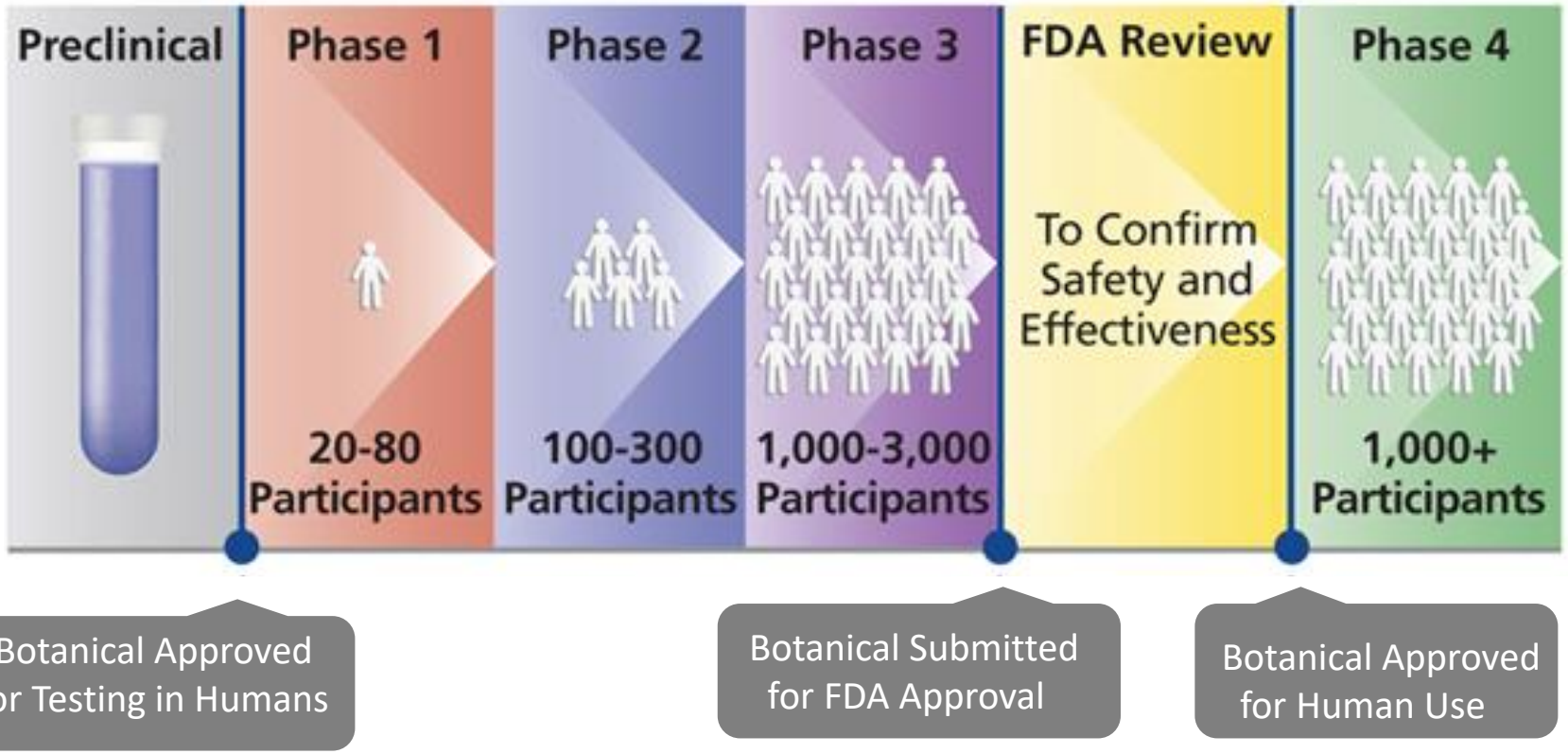


IACUC approval

IRB and FDA approval

Testing Botanical Extracts: Steps Along the Way

How Clinical Trials Work



Include Females in the Preclinical Botanical Studies

HEALTH

Labs Are Told to Start Including a Neglected Variable: Females

May 13, 2014

NIH Takes Steps to Address Sex Differences in Preclinical Research

Policy: NIH to balance sex in cell and animal studies

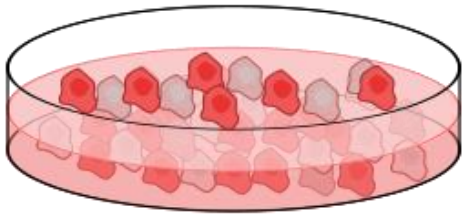
NIH National Institutes of Health
Office of Research on Women's Health

Putting science to work for women's health

Testing Botanical Extracts: Russian Tarragon at PBRC as an Example

Preclinical Studies

Cell Culture → Animal Model of Disease → Clinical Trials



Russian Tarragon
Artemesia dracunculus L

- Perennial Herb
- Asteraceae Family
- Native-Northern Hemisphere
- Genus Artemisia-1500 diverse species
- Rich source of herbal remedies/conventional drugs.
- Ethanolic Extract made when flowering- termed PMI 5011

From Isolating the Extract to Clinical Trial: PMI5011

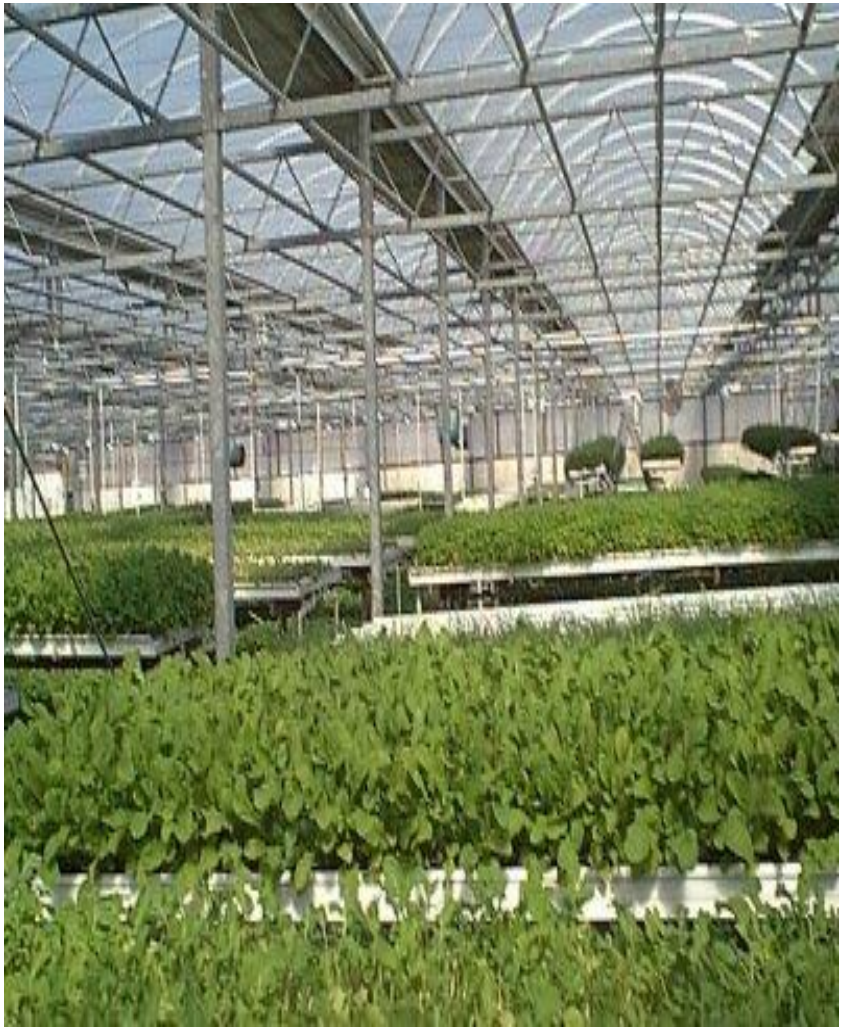
Screen 100s of botanical ethanolic extracts for activity in skeletal muscle in cell culture

Artemisia species selected
dracunculus, scoparia, santolinifolia

Ethanol extract of *A. dracunculus*
Designated PMI5011

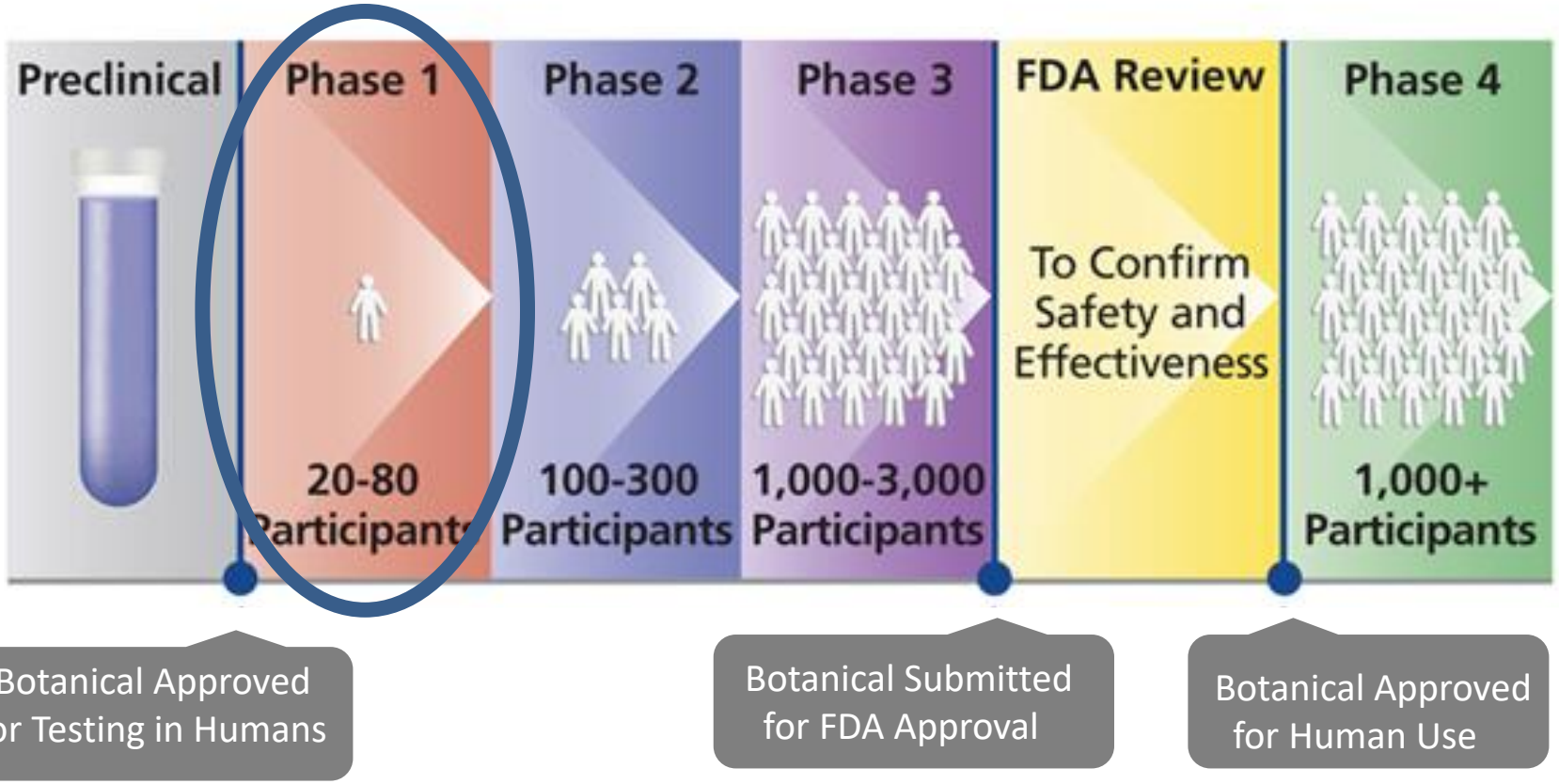
Test biological activity: muscle, fat, liver, pancreas
Bioactivity guided fractionation, toxicology
Testing in cell culture and in rodents

Ongoing Human Trials using Nutrasorb
Testing doses, safety



Testing Russian Tarragon Extracts: First Phase 1 Clinical Trial Completed

Next: Small Clinical Study to test PMI5011 and insulin resistance



Acknowledgements…and Thank You

Botanical and Dietary Supplements Research Center

Jacqueline Stephens and Elizabeth Floyd
Ilya Raskin/Rutgers University
David Ribnicky/Rutgers University
Michael Salbaum
Randall Mynatt
Jennifer Rood
Richard Rogers
William Johnson
Phillip Brantley

Icahn School of Medicine at Mount Sinai Botanical Center

Giulio Pasinetti
Jun Wang

NIH National Center for Complementary and Integrative Health

ODS NIH

Coypu Foundation Trust
John S. McIlhenny Laboratory for Botanical Research