

Future of Botanicals Depends on Authentication, Quality-by-Design, and Regulatory Credibility



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Phase 1: The Pre-regulatory ERA

- **Regulation by Tradition**
- For millennia, Traditional Medicine (TM) was self-regulated. Efficacy and safety were policed by:
 - **Community Trust: Practitioners' reputations were paramount.**
 - **Oral History:** Knowledge was passed down through apprenticeships.
- **Codified Texts:** Early "standards" like the *Ebers Papyrus* (Egypt) or *Shennong Bencao Jing* (China), Charaka Samhita cataloged substances and uses.



Phase 2: Marginalization

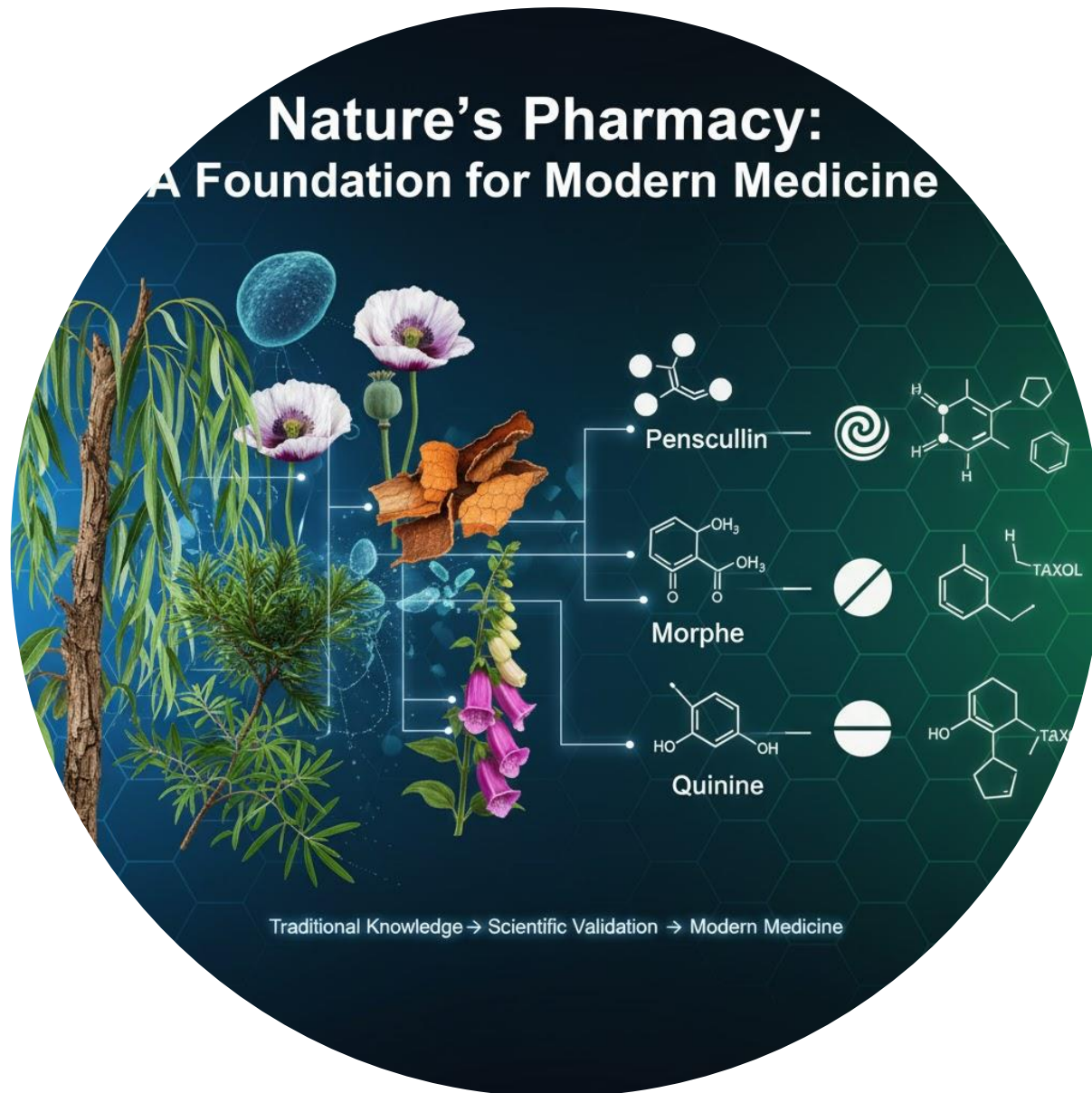
The Rise of Western Medicine

In the 19th and 20th centuries, the rise of pharmaceutical science led to the legal dominance of biomedicine.

TM was often dismissed or suppressed.

Early laws, like the U.S. Pure Food and Drug Act of 1906, had no category for TM. Products were forced into ill-fitting boxes, creating a "fit problem" that still exists today.

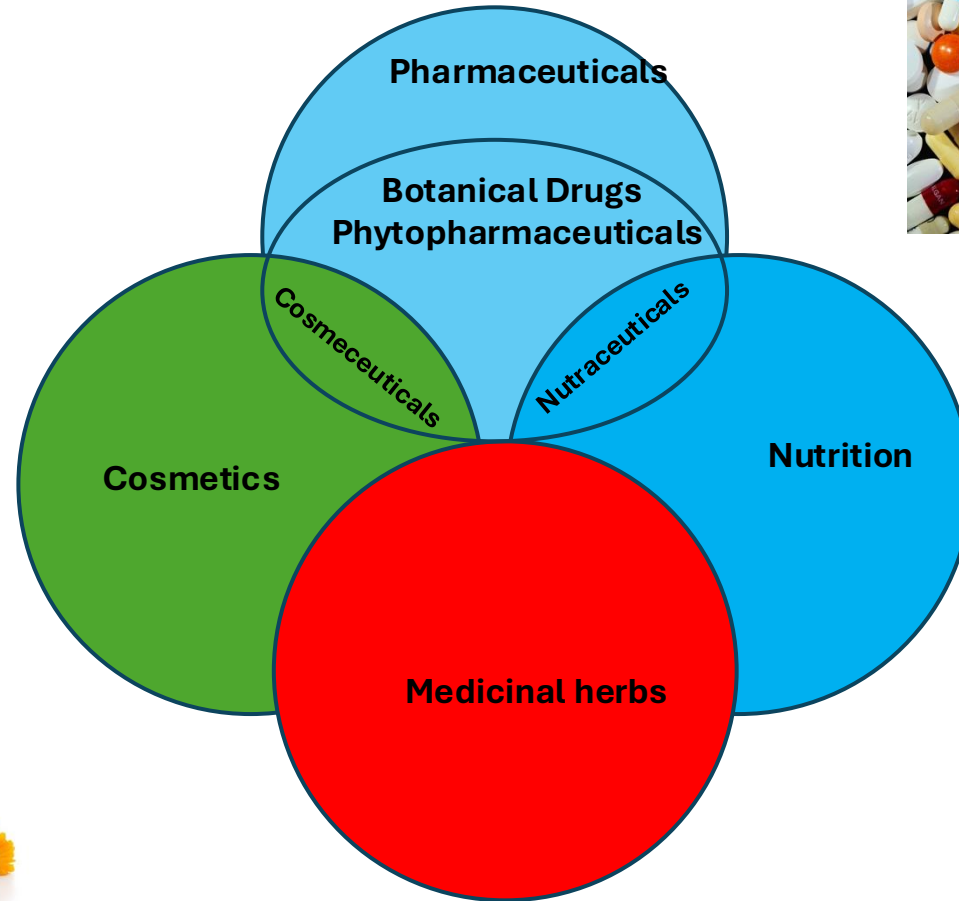




Outcome of Modern Medicine

- Merck, began as a small apothecary shop in Darmstadt, Germany, in 1668, only beginning wholesale production of drugs in the 1840s. Likewise, Schering in Germany; Hoffmann-La Roche in Switzerland; Burroughs Wellcome in England; Etienne Poulenc in France; and Abbott, Smith Kline, Parke-Davis, Eli Lilly, Squibb, and Upjohn in the U.S. all started as apothecaries and drug suppliers between the early 1830s and late 1890s.

Indispensable Role of Natural Products for Human Health and Well-being





Scale-Up Without Scandal

Why the Future of Botanicals Depends on Authentication, Quality-by-Design, and Regulatory
Credibility



Anatomy of a Scandal: NYAG 2015

In 2015, the New York Attorney General used **DNA barcoding** to test store-brand supplements at GNC, Walmart, and Target.

- **Finding:** 79% of samples allegedly contained no DNA from the labeled plant.
- **Impact:** Massive reputational damage and industry-wide litigation.
- **The Lesson:** Misapplying scientific methods (extracts vs. powders) can be as dangerous as the fraud itself.

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Analysis of Crocetins and Safranal Variations in Saffron (*Crocus sativus*) Stigma Samples and Dietary Supplements Using HPLC/UHPLC-PDA-MS: Chemical Profiling and Chemometric Analysis Using LC-QToF

[Bharathi Avula](#) , [Kumar Katragunta](#), [Yan-Hong Wang](#), [Roy Upton](#) & [Ikhlas A. Khan](#)

[Food Analytical Methods](#) **15**, 2238–2259 (2022) | [Cite this article](#)

480 Accesses | **2** Citations | **1** Altmetric | [Metrics](#)

Analysis of Select Dietary Supplement Products Marketed to Support or Boost the Immune System

Cindy Crawford, BA^{1,2}; Bharathi Avula, PhD³; Andrea T. Lindsey, MS^{1,2}; et al

[» Author Affiliations](#) | [Article Information](#)

JAMA Netw Open. 2022;5(8):e2226040. doi:10.1001/jamanetworkopen.2022.26040

Key Points

Question Are select dietary supplement products advertised and sold to support or boost the immune system accurately labeled according to the Supplement Facts listed ingredients on product labels?

Findings This case series study analyzed 30 dietary supplement products purchased from Amazon.com with claims related to immune health. Seventeen of 30 products had inaccurate labels; 13 were misbranded, and 9 had additional components detected but not claimed on the label.

Meaning Quality control measures seem insufficient for most select dietary supplement products. The public has a right to know that they are buying what is stated on the label.

**HEPATOLOGY
COMMUNICATIONS**
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The Contents of Herbal and Dietary Supplements Implicated in Liver Injury in the United States Are Frequently Mislabeled

[Victor Navarro](#) , [Bharathi Avula](#), [Ikhlas Khan](#), [Manisha Verma](#), [Leonard Seeff](#), [Jose Serrano](#), [Andrew Stolz](#), [Robert Fontana](#), [Jawad Ahmad](#)

First published: 03 April 2019 | <https://doi.org/10.1002/hep4.1346> | Citations: 22

The Adulteration Epidemic



Spiking

Adding synthetic pharmaceutical compounds (e.g., Sildenafil in "natural" tonics) to boost performance illicitly.



Dilution

Cutting expensive extracts with undisclosed spent biomass or cheaper solvents to increase volume.



Substitution

Replacing high-cost species (e.g., Ginseng) with cheaper "look-alikes" that lack therapeutic efficacy.

The Cost of Non-Compliance

10k+

Scientific Papers Retracted

Fraud is Not Just in Products

In 2023, over 10,000 scientific publications were retracted globally. Many involved fabricated botanical benefits. Regulatory credibility now requires independent, third-party validation of clinical data, not just lab tests.

The Botanical Boom vs. Trust Deficit

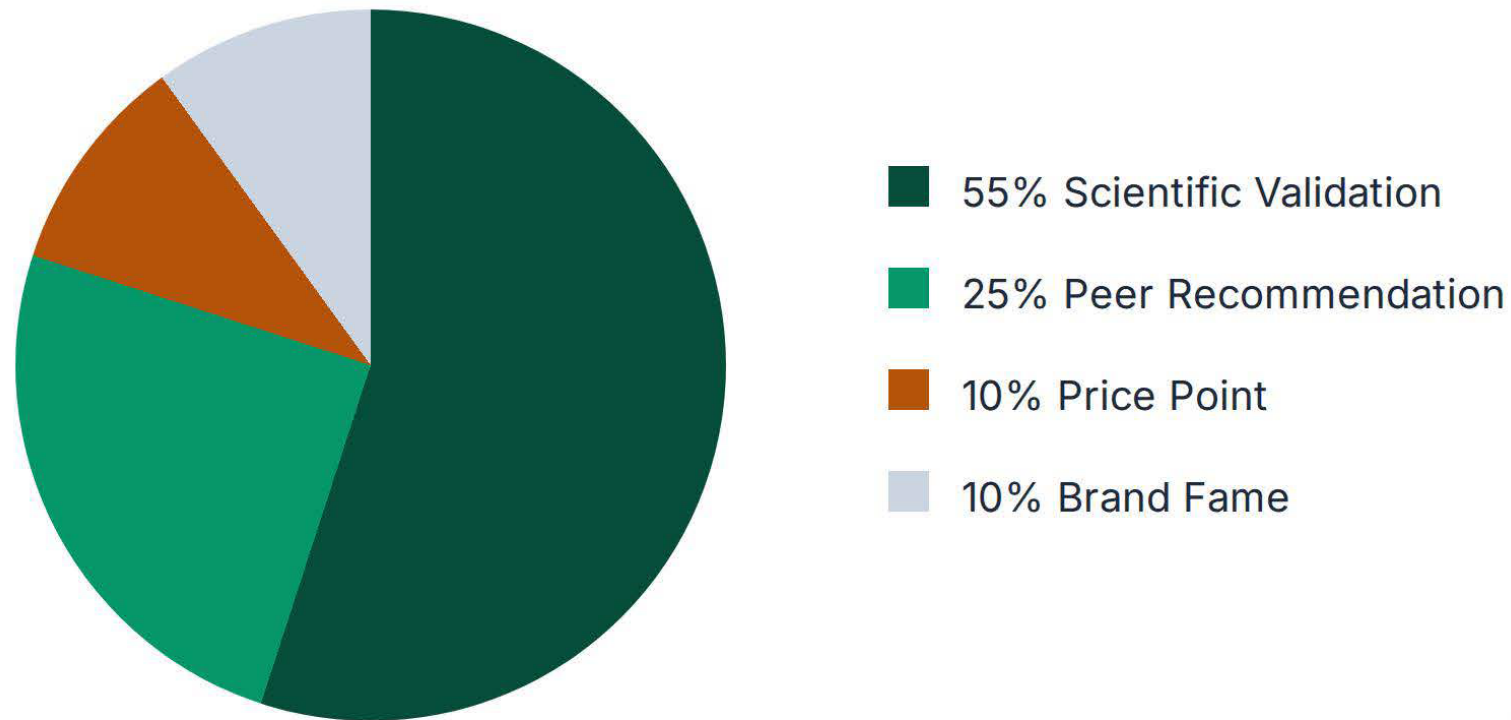
\$164.4 Billion Opportunity

The global botanical market is experiencing unprecedented growth, driven by consumer demand for natural wellness and preventative healthcare.

The "Trust Paradox"

As sourcing scales, supply chains fracture. 2023 saw record reports of botanical fraud, creating a systemic risk for global brands.

Drivers of Consumer Trust



Consumers are increasingly looking for "White Paper" proof over marketing fluff.



Botanical Adulterants Prevention Program

- Pharmacognosy embraces a **knowledge of the history, distribution, cultivation, collection, selection, preparation, commerce, identification, evaluation, preservation, and use of drugs and economic substances affecting the health of man and other animals**. Such economic substances extend beyond the category of crude drugs and their derivatives and include a variety of commercial products: allergens, allergenic extracts, antibiotics, immunizing biologicals, flavoring agents, condiments, beverages, insecticides, rodenticides, and herbicides. In a restricted sense, **the definition of pharmacognosy implies a particular knowledge of methods of identification and evaluation of drugs**.



| The Science of Phytochemistry



Bioactive Identification

Isolating key secondary metabolites like alkaloids, flavonoids, and terpenoids to understand their mechanisms.



Biosynthetic Pathways

Mapping how plants produce complex molecules to optimize cultivation and extraction techniques.



Synergy Discovery

Researching the 'Entourage Effect' where multiple compounds work together for better therapeutic outcomes.

Therapeutic Consistency

Ensuring that every batch provides the same therapeutic effect is a primary challenge addressed by ongoing research.

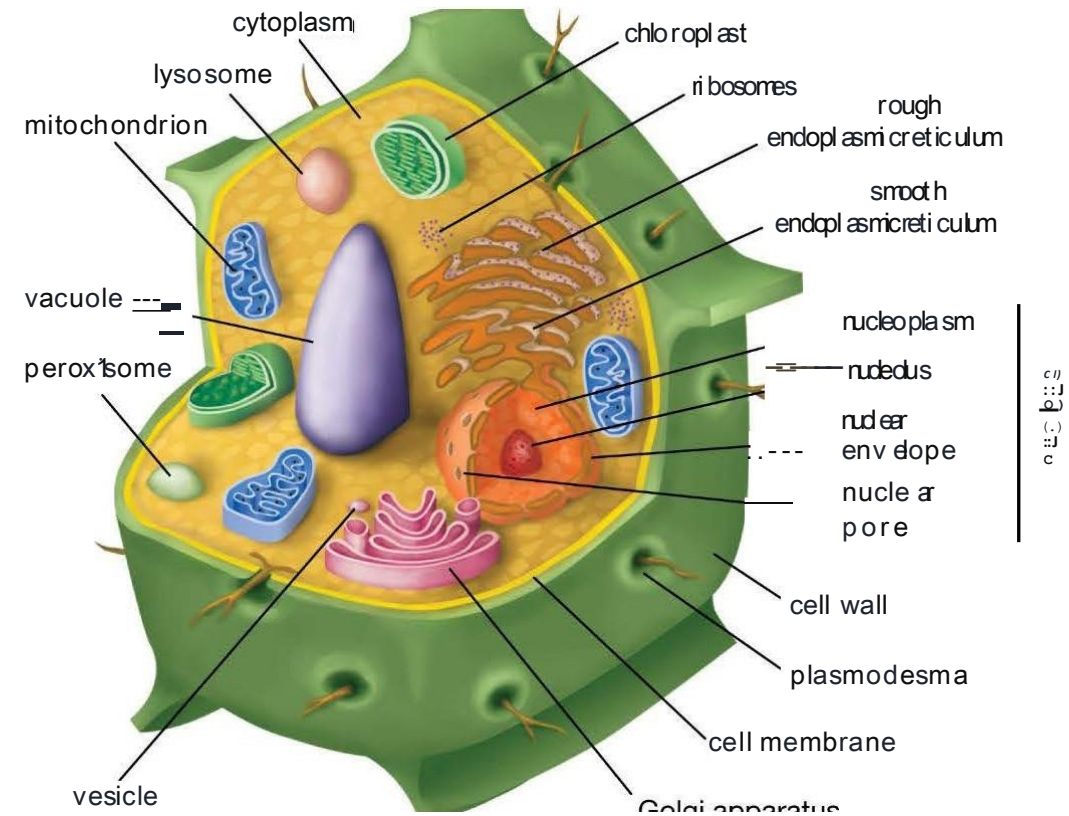
Control Aspect	Research Methodology	Goal for Development
Identity	DNA Barcoding & Microscopy	Preventing Adulteration
Purity	HPLC & Heavy Metal Testing	Eliminating Contaminants
Potency	Standardized Marker Analysis	Dose Reproducibility
Bioavailability	Pharmacokinetic Modeling	Optimizing Absorption

Marketing vs. Mechanism

The Current Status-Quo

Most botanical products rely on **Traditional Use** data or **Borrowing Science** from other studies without validating their own specific extracts.

- Inconsistent Efficacy
- Regulatory Vulnerability
- Low Consumer Trust



High-Tech Synergy



AI & Big Data

AI models predict molecular interactions between plant compounds and human receptors, accelerating drug discovery by years.



Multi-Omics

Integrating metabolomics, proteomics, and genomics to see the holistic impact of botanicals on human biology.



Precision Farming

IoT-enabled cultivation research ensures optimal light, water, and soil conditions for maximal phytochemical yield.

Defining the Botanical Frontier

Scientific Necessity

As the global demand for natural therapeutics surges, research acts as the bridge between traditional wisdom and clinical validation, ensuring safety and efficacy in modern healthcare.

Innovation Catalyst

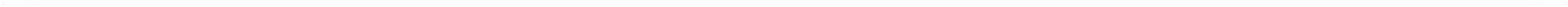
Advanced phytochemical analysis and genomic research are transforming how we discover, standardize, and utilize plant-derived compounds for complex diseases.

• Green tea	EGCG
• Ephedra	Ephedrine
• Citrus	Synephrine
• Geranium	DMAA
• Hoodia	P57
• Garcinia	Hydroxycitric acid
• Aegle	Aegeline
• Caffeine	



Quality-by-Design (QbD)

Engineering consistency into nature's variability.



QbD Matrix: From Seed to Shelf

Process Step	Critical Attribute (CQA)	Process Parameter (CPP)
Cultivation	Genotypic Identity	Soil composition, climate, harvest time
Extraction	Bioactive Concentration	Solvent ratio, temperature, duration
Purification	Impurity Removal	Ethanol precipitation, filtration speed
Formulation	Stability & Bioavailability	Excipient compatibility, humidity control

Persistent Regulatory Challenges

-  **Standardization:** How to ensure consistent quality and potency from variable raw materials (plant to product)?
-  **Intellectual Property:** Protecting collective traditional knowledge from "biopiracy" under patent laws that require "novelty."
-  **The Evidence Gap:** Balancing the value of "traditional use" evidence with the demand for modern, randomized clinical trials.
-  **Practitioner Licensing:** A lack of uniform, international standards for the training and licensing of TM practitioners.



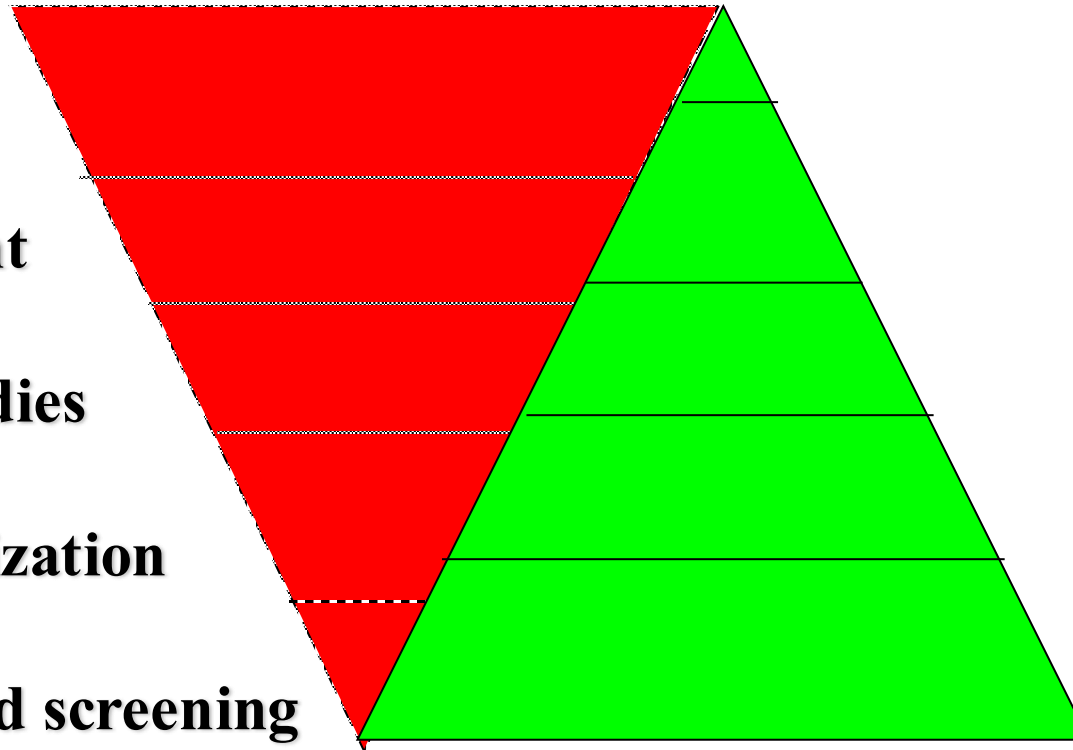
Clinical

Development

Animal Studies

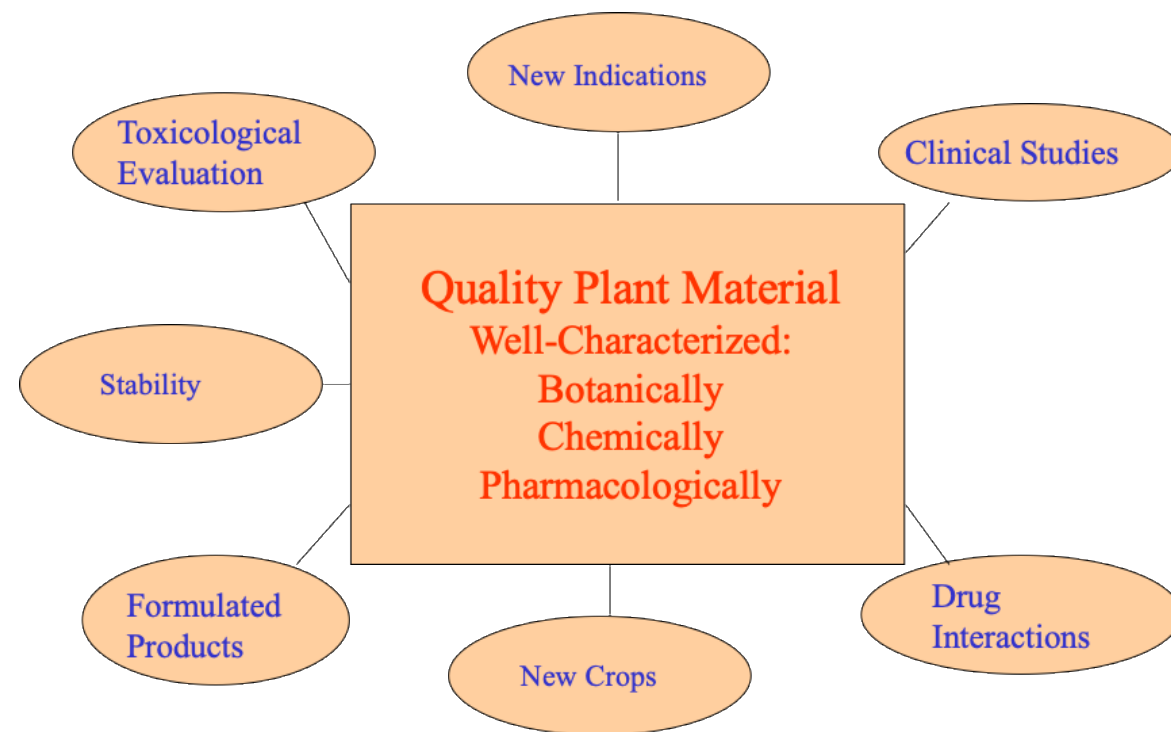
Lead optimization

Isolation and screening





Quality By Design



Medicinal Plant Research

- BOTANY
- HORTICULTURE
- AGRONOMICS
- PLANT GENOMICS
- PLANT TISSUE CULTURE
- NATURAL PROD. CHEMISTRY
- CHEMOTAXONOMY

- ETHNOMEDICINE/BOTANY
- ANALYTICAL CHEMISTRY
- REFERENCE STANDARDS
- BIOLOGICAL ASSAY
- INFORMATICS
- TOXICOLOGY
- ADME



NEW or IMPROVED CROPS
NEW COMPOUND SOURCES
SAFER, MORE EFFECTIVE HERBAL PRODUCTS

National Center for Natural Products Research

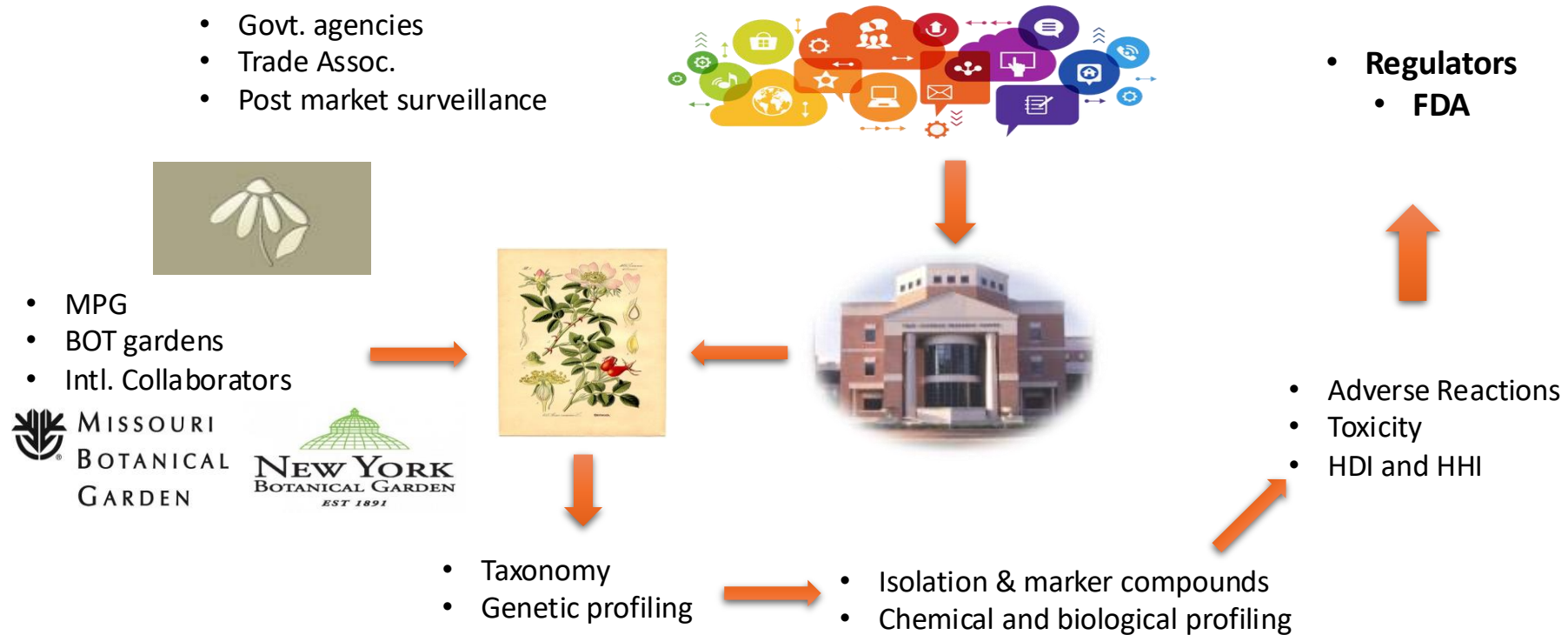
Natural Product Discovery and Development

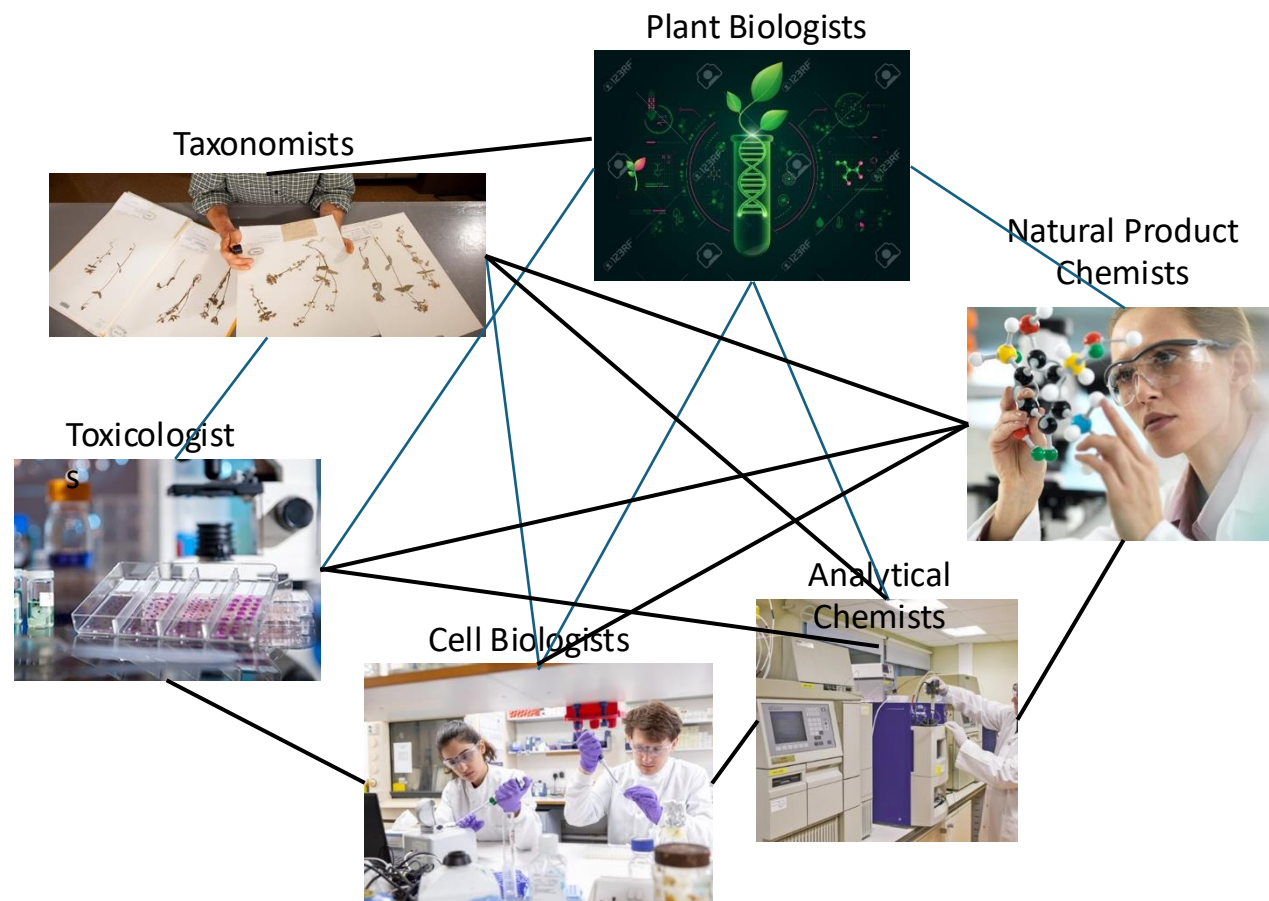
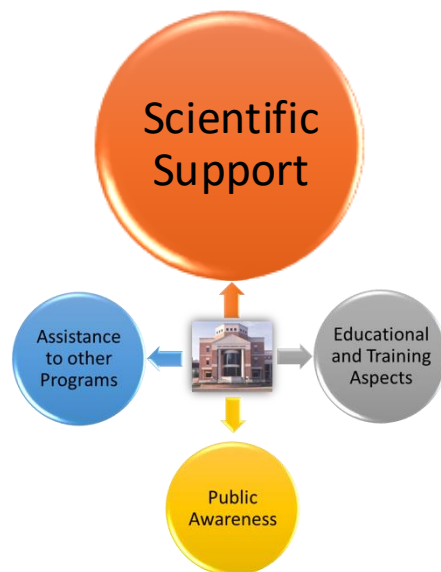
- ***Drug Discovery and Development*** - To discover single entity and multicomponent bioactive natural products that may serve as leads for the development of new pharmaceuticals. Emphasis is on agents that control certain infectious diseases, cancer, inflammatory or immune disorders.
- ***Agrochemical Discovery and Development*** - To identify lead compounds for the development of environmentally benign and toxicologically safe pest management agents. Emphasis is on agents useful in the control of pests affecting small niche crops.

Medicinal Plant Research

- ***Medicinal Plants as Alternative Crops*** - To examine the biology, chemistry, and agronomics of medicinal plants so they may be developed as alternative crops for US farmers.
- ***Botanicals and Human Health*** - To identify botanicals with potential to improve human health and to enable safe, effective, and proper use of high quality botanical products by informed professionals and consumers.

A snapshot of research at the NCNPR





Annual Oxford International Conference on the Science of Botanicals.

April 19-22, 2027

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The Korean Society of Pharmacognosy

The Vietnam Academy of Science and Technology (VAST)

St Petersburg Institute of Pharmacy

The International Society of Ethnopharmacology

Dr. Panjwani Center for Molecular Medicine and Drug Research (PCMD)



| Sustainability & Ethics

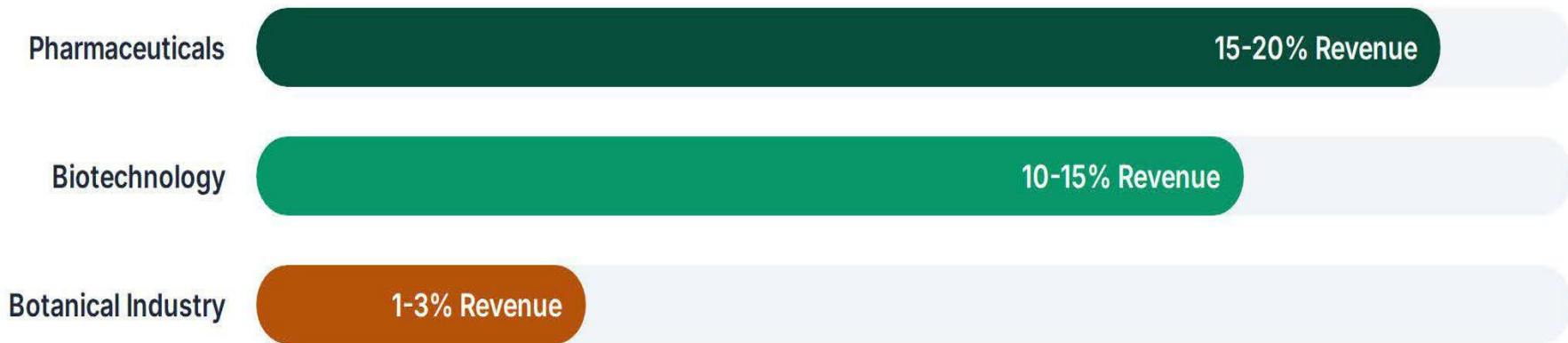


Preserving Biodiversity

Research isn't just about chemistry; it's about ecology. Developing sustainable harvesting practices ensures that high-demand botanicals do not face extinction.

Conservation Research: Identifying endangered species and developing tissue culture or hydroponic alternatives to wildcrafting, ensuring long-term supply chain security.

The R&D Spending Disparity



Basic science remains an under-leveraged asset in the botanical sector, leading to commoditization and thin margins.

“

*The future of the botanical industry
does not lie in the past of traditional
lore, but in the laboratory where
nature's secrets are quantified and
proven.*

— *Leadership in Global Nutritional Science*