



The Importance of Testing Natural Compounds for Potential Toxic Effects Before They Are Used in Dietary Supplements or Cosmetics



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Acronym: INNO-SAFE-LIFE



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Introduction



The increasing demand for **natural products** in dietary supplements and cosmetics has led to widespread use of plant-based and bioactive compounds.



Consumers often perceive "**natural**" as synonymous with **safe**; however, many naturally occurring substances have **toxic potential**. Therefore, **rigorous testing** is essential to ensure these compounds are **safe for human use** before incorporation into commercial products.

Key Reasons for Toxicity Testing

Public health safety: Protect consumers from adverse effects

Regulatory compliance: Meet safety standards set by agencies like FDA, EMA, EFSA

Product quality assurance: Ensure consistency and reliability of natural compounds

Scientific validation: Confirm the efficacy and safety of bioactive ingredients



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Why is Toxicity Testing Necessary

- While natural compounds provide many **health benefits**, they can also contain **harmful contaminants or bioactive substances** that may cause **adverse health effects**.
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Potential Risks of Untested Natural Compounds



Toxic secondary metabolites

Some plants produce toxic compounds (e.g., alkaloids, flavonoids, coumarins) that can **cause organ damage or metabolic disruption**.



Heavy metal contamination

Lead, mercury, cadmium, and arsenic can accumulate in plants and pose **neurological, kidney, or liver toxicity risks**.



Pesticides & chemical residues

Agricultural chemicals may **persist** in plant-based ingredients, causing **hormonal disruptions or carcinogenic effects**.





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Potential Risks of Untested Natural Compounds

Microbial contamination

- Bacteria, fungi, or mycotoxins can grow in poorly stored or contaminated raw materials, leading to **infections or toxic effects**.

Allergenic potential

- Botanical ingredients can **trigger allergies** or **hypersensitivity reactions** in some individuals.

Drug interactions

- Some natural compounds may **interfere with medications**, affecting **absorption, metabolism, or potency**.
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Types of Toxic Effects in Natural Compounds

Natural substances can cause a range of **toxic effects** based on their composition and concentration.

Categories of Toxicity:

- **Acute toxicity:** Immediate harmful effects after a **single high-dose exposure**.
 - **Chronic toxicity:** Long-term exposure leading to **organ damage, metabolic disorders, or cancer**.
 - **Genotoxicity:** Damage to DNA, potentially leading to **mutations and carcinogenesis**.
 - **Neurotoxicity:** Adverse effects on the **nervous system**, impacting brain function.
 - **Hepatotoxicity:** Liver damage due to **bioaccumulation of toxic compounds**.
 - **Dermal toxicity & sensitization:** Allergic reactions or **irritation from topical application**.
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Preclinical Toxicity Testing Methods - To assess **safety before human exposure**, natural compounds undergo a **series of preclinical tests**.

In Vitro Testing (Cell-Based Studies)

- **Cytotoxicity assays** (e.g., MTT, LDH assay) to determine cell viability.
 - **Genotoxicity assays** to detect DNA damage.
 - **Reactive oxygen species (ROS) assays** to assess oxidative stress.
 - **3D skin models** for dermal irritation and sensitization tests.
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Preclinical Toxicity Testing Methods - To assess **safety before human exposure**, natural compounds undergo a **series of preclinical tests**.

In Vivo Testing (Animal Studies)

- **Acute and chronic toxicity studies** in animal models (e.g., rats, mice).
 - **Metabolism and pharmacokinetics** studies to determine **absorption, distribution, metabolism, and excretion (ADME)**.
 - **Toxicological endpoints:** Liver/kidney damage, neurological effects, immune response.
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Preclinical Toxicity Testing Methods - To assess **safety before human exposure**, natural compounds undergo a **series of preclinical tests**.

In Silico Toxicology (Computational Methods)

- **AI-based predictive modeling** for toxicity screening.
 - **QSAR (Quantitative Structure-Activity Relationship) analysis** to predict biological effects.
 - **Molecular docking studies** for evaluating potential interactions.
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Regulatory Framework for Safety Assessment

Key Regulatory Agencies:

- **FDA (U.S. Food and Drug Administration)** – Dietary supplement safety and cosmetics regulation.
 - **EFSA (European Food Safety Authority)** – Ensures food safety, including botanical extracts.
 - **EMA (European Medicines Agency)** – Evaluates traditional herbal medicines.
 - **WHO (World Health Organization)** – Provides international guidelines on herbal safety.
 - **ISO & OECD Guidelines** – Establish **toxicity testing standards**.
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Regulatory Framework for Safety Assessment

Regulatory Testing Requirements:

- Toxicological evaluation (LD50, NOAEL, LOAEL)
 - Heavy metal & pesticide residue analysis
 - Microbial contamination testing
 - Clinical trials (for novel supplements or high-risk compounds)
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Case Studies: Toxicity Concerns in Supplements & Cosmetics

Case 1: Liver Damage from Herbal Supplements

- Some weight-loss and detox supplements containing **Garcinia cambogia** or **green tea extract** have been linked to **hepatotoxicity**.
- Studies suggest that **high doses of catechins** can cause **oxidative stress and liver damage**.

Case 2: Allergic Reactions in Botanical Cosmetics

- Certain plant-based skincare products (e.g., containing **lavender oil, citrus extracts**) can cause **contact dermatitis or photosensitivity**.
- Lack of **standardized testing** in the cosmetic industry leads to **hidden allergens** in formulations.

Case 3: Heavy Metal Contamination in Ayurvedic Supplements

- Traditional herbal medicines from **unregulated sources** were found to contain **high levels of lead, mercury, and arsenic**.
 - Regular **quality control and batch testing** are necessary to ensure **consumer safety**.
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Challenges in Testing Natural Compounds

A. Complexity of Plant Extracts

Natural compounds exist in **mixtures**, making it **hard to isolate specific toxic effects**.

B. Variability in Raw Materials

The composition of **plant extracts** can **change based on climate, soil, and processing methods**.

C. Lack of Standardized Testing Protocols

Some **botanical extracts** lack **clear safety guidelines**, leading to **inconsistent results**.

D. Ethical Considerations in Animal Testing

Push for **alternative methods** such as **3D tissue models** and **AI-driven toxicology**.

Future Trends in Toxicity Testing

A. Advanced Non-Animal Testing

"**Organ-on-a-chip**" systems simulate human organ responses to toxic substances.

3D bioprinting for realistic tissue testing.

B. AI-Driven Predictive Toxicology

Machine learning and **Big Data** help predict **potential hazards** before physical testing.

C. Blockchain for Supply Chain Transparency

Ensuring **traceability** of raw materials and **quality control validation**.

D. Personalized Toxicology

Tailoring safety assessments based on **individual genetics and metabolism**.

Conclusion



Natural compounds are not automatically safe and require rigorous preclinical testing.



Advanced toxicological screening ensures **consumer protection and regulatory compliance**.



The **combination of in vitro, in vivo, and in silico methods** provides a **comprehensive risk assessment**.



Future innovations like **AI-driven toxicology and organ-on-a-chip** will **revolutionize safety testing**.