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Original Article

The Expanding Complexity of Medicine–Herb–Food Combinations

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ABSTRACT: *Modern pharmacology usually tests one drug at a time. However, in the real world, patients take pharmaceuticals alongside herbal supplements and bioactive food components.This article looks at the massive complexity of these combinations and what they mean for patient safety. Using data from DrugBank and botanical databases, we estimate that humans regularly encounter about 33,987 bioactive substances. This leads to more than 570 million potential pairwise interactions a scale that makes it impossible for doctors to memorize or for labs to test. Adverse drug reactions should be seen as a result of a complex system rather than just a "bad drug." We argue for a shift toward systems pharmacology and the use of computer tools to manage the unpredictability of modern medicine.*

KEYWORDS: *Medicine–Herb–Food Interactions, Herb–Drug Interactions, Nutraceuticals, Pharmacokinetics, Food–Drug Interactions, Phytochemicals, Safety Assessment, Complementary and Alternative Medicine (CAM), Adverse Effects, Polypharmacy.*

1. INTRODUCTION

It is very rare for a person to consume just one bioactive substance. Most patients navigate a landscape of prescriptions, over-the-counter products, and herbal supplements, all mixed with food chemicals and environmental pollutants [21, 27]. Once swallowed, these compounds all hit the same metabolic enzymes and signalling pathways [24, 31]. Figure 1 provides a visual overview.

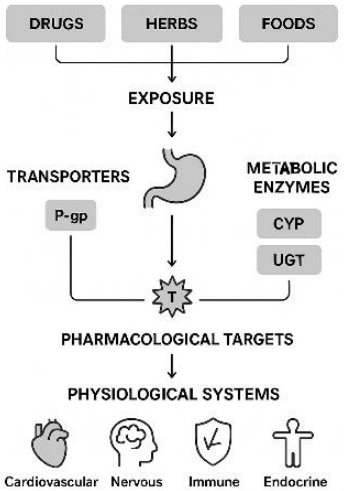

FIGURE 1 Unified Pharmacological Interaction Model.

The human body does not care whether a molecule comes from a synthetic pill, a plant extract, or a meal; it is processed the same way. Despite this, drug testing still focuses on single agents in controlled settings. This creates a huge gap between lab results and the "polysubstance" reality of modern life. Medicines, herbs, and foods share the same biological pathways like Cytochrome P450 enzymes meaning they can easily boost, block, or cancel each other out [29, 32,36].

1.1. THE HUMAN BODY AS AN EXCHANGE SYSTEM

This paper focuses on substances taken by mouth. The body acts as a continuous exchange engine: It takes in matter and energy through the gut, lungs, and skin, transforms them, and releases by-products through breath, sweat, and urine. The gut is the primary interface through which nutrients are absorbed and toxins are filtered. All this is embodied in Figure 2.

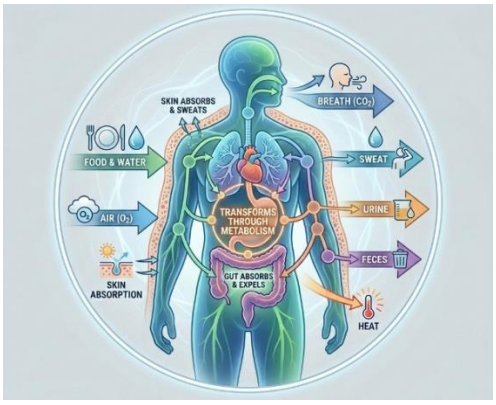

FIGURE 2 **The human body as an open exchange system.**

2. THE BIOMEDICAL MICROCOSM

Our chemical exposure goes far beyond medicine. The modern "exposome" includes alcohol, tobacco, pollution, and food additives. These substances put a constant load on the same metabolic pathways used by drugs. Common food packaging chemicals, like Bisphenol A (BPA) and phthalates [1, 5], act as metabolic disruptors that interfere with how our enzymes are expressed [35,38].

FIGURE 3 **The Biomedical Microcosm of Human Exposure.**

This "biomedical microcosm", where thousands of substances circulate at once, explains why drug efficacy varies so much from one person to another [23, 33].

TABLE 1 **Clinically relevant xenobiotics in the food supply chain**

Chemical / Additive	Common Sources	Pathophysiological Risk & Metabolic Impact	Key References
Bisphenol A (BPA)	Plastics, can linings	Endocrine disruption; metabolic dysregulation	[1, 2,37]
PFAS	Non-stick cookware	Immunotoxicity; thyroid hormone interference	[3,4]
Phthalates	Plastic containers	Androgen interference; developmental toxicity	[5, 6]
Artificial Sweeteners	Diet sodas, snacks	Gut microbiota alteration; metabolic disorder	[7, 8]
Synthetic Colorants	Processed foods	Neurobehavioral effects: hypersensitivity	[9, 10]
Preservatives	Packaged snacks	Potential carcinogenicity; hepatic induction	[11, 12]
Pesticide Residues	Fruits, vegetables	Chronic neurotoxicity; hormone disruption	[13,14]

3. QUANTIFICATION OF BIOACTIVE DIVERSITY

The sheer number of substances is staggering. DrugBank identifies about 4,784 approved drugs [19]. However, the Royal Botanic Gardens, Kew, lists at least 28,187 medicinal plant species [20]. When you add in bioactive compounds from common

foods, we reach a conservative estimate of 33,987 distinct substances. Clinical models that assume a patient is only "on one thing" are clearly inadequate.

4. THE PRESCRIBING PARADOX

The real difficulty is how these agents interact. With nearly 34,000 potential agents, the number of unique combinations is calculated using the binomial coefficient:

$$\binom{n}{k} = \frac{n!}{k!(n-k)!}$$

TABLE 2 Combinatorial expansion table (*n = 33,987,* Calculations by Gemini.Ai)

Interaction Type	Mathematical Representation	Total Unique Combinations	Approximate Scale
1 + 1 (Pairwise)	$\binom{33,987}{2}$	577,541,091	577.5 million
1 + 2 (3-way)	$\binom{33,987}{3}$	6,542,577,992,545	6.54 trillion
2 + 2 (4-way)	$\binom{33,987}{4}$	55,585,742,624,662,320	55.5 quadrillion

Even at the simplest "1 + 1" level, there are over 577 million potential interactions. By the time a patient takes four substances, the combinations reach the quadrillions. Prescribing in such environments fostered the metaphor in Figure 4.

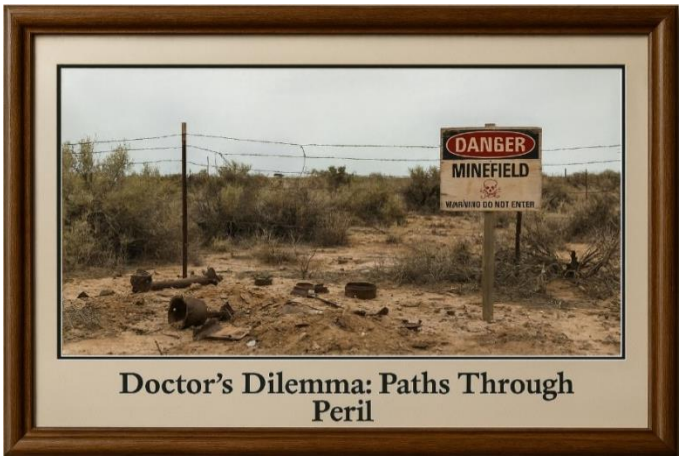

FIGURE 4 The Prescribing Minefield: A Metaphor for Combinatorial Complexity.

This math shows why we need to change how we talk to patients about their results. We often act like a drug's success is guaranteed, however in a body full of other bioactives, that success is actually a moving target. When a patient is taking various supplements and eating processed foods, the "chemical noise" in their system can drown out the "signal" of the prescription. We should help patients understand that their medicine doesn't work in a vacuum; its effectiveness depends on the crowded chemical environment it has to navigate once swallowed.

5. THE "NATURAL" FALLACY AND FOOD CHAIN RISKS

A major risk is the "natural-is-safe" idea. Unlike drugs, herbal supplements are often sold as food, leading to inconsistent doses, contamination, or "silent" interactions that patients forget to report to their doctors [28, 34].

Furthermore, the food supply adds hidden bioactives. Antibiotic residues from livestock create a constant exposure that can change the gut microbiome and alter how we metabolize oral drugs [15]. Environmental excretion means 75–90% of veterinary antibiotics enter our soil and water in active forms [16]. In some regions, meat samples show antibiotic levels much higher than legal limits [39].

5.1. CASE STUDY: NATURAL TOXICITY (THE CASSAVA EXAMPLE)

The risk isn't just from man-made chemicals. Nature produces its own toxins that are just as strong as prescription drugs. For example, common foods like almonds and cassava contain "cyanogenic glycosides" [17]. If not processed correctly, these turn into hydrogen cyanide in the body. In Mozambique, poorly processed cassava has caused "Konzo," a permanent condition where people become paralyzed [18]. This proves that "natural" origin is no guarantee of safety. [25,26]

5.2. CASE STUDY: HIGH-STAKES CARE (ONCOLOGY)

This complexity is most dangerous in cancer wards. Many oncology patients use herbal supplements alongside chemotherapy. These "natural" additions can totally change how the body handles chemo drugs [30], either making the chemo too toxic or washing it out of the system before it can work. In high-stakes care, an unknown herb is just as significant as a drug.

6. TOWARD CLINICAL HUMILITY

The data shows we need to be more humble in our prescribing. In a world of millions of possible interactions, doctors can no longer be expected to know every outcome. Clinical humility means:

- Admitting that simple drug models don't always work for complex conditions.
- Treating a patient's diet and herbal intake with the same seriousness as their prescriptions.
- Investigating "weird" drug reactions as a result of the whole chemical system.

7. CONCLUSION

The massive number of possible combinations between medicines, herbs, and foods shows a big gap between how drugs are tested and how they are actually used. In the real world, we can no longer expect a single drug to behave perfectly every time. Unpredictability is now a normal part of medicine.

Instead of using over-simplified models, the medical community needs to look at the "big picture" of a patient's intake. By practicing clinical humility admitting we can't predict every single interaction we can better protect our patients. We must abandon the idea of "perfect prescribing" and instead focus on navigating the complex chemical environment that every modern patient carries with them.

Declarations and Administrative Statements

Author Contributions

The author was solely responsible for the conceptualization, data synthesis, and mathematical modelling of combinatorial interaction spaces presented in this article. The author drafted the manuscript, performed the critical literature review, and approved the final version for submission to the *International Journal of Medical Science and Technology*.

Conflict of Interest

The author declares that there are no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Disclosure of AI Usage in Scientific Illustration

All figures and graphical models included in this manuscript (Figures 1–4) were generated using **Gemini.ai (Google)** under the specific conceptual direction and iterative refinement of the author. Such usage is asserted to be in compliance with Google's published Terms of Use: https://ai.google.dev/gemini-api/terms

The author has reviewed and verified the scientific accuracy of the underlying biological and systemic concepts depicted in these generated visualizations.

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