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PERSPECTIVES

Interactive Nutrient Process (INP) in a Generative AI of a New Drug—6-Shogaol as a Potential Case

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Abstract: The dynamically evolving science of pharmacology requires AI technology to advance a new path for drug development. The author proposes generative AI for future drugs, identifying suitable drug molecules, uncharacteristically to previous generations of medicines, incorporating the wisdom, experience, and intuit of traditional materia medica and the respective traditional medicine practitioners. This paper describes the guiding principles of the new drug development, springing from the tradition and practice of Tibetan medicine, defined as the Interactive Nutrient Process (INP). The INP provides traditional knowledge and practitioner's experience, contextualizing and teaching the new drug therapy. An illustrative example of the outcome of the INP is a potential small molecule drug, 6-Shogaol and related shogaol derivatives, from ginger roots (Zingiber officinalis fam. Zingiberaceae) evaluated clinically for 12 months for biological markers of iron homeostasis in patients with the myelodysplastic syndromes (MDS). The study's preliminary results indicate that 6-Shogaol and related shogaols may improve iron homeostasis in low-risk/intermediate-1 MDS patients without objective or subjective side effects.

Keywords: Tibetan medicine, interactive nutrient process, 6-shogaol, shogaols, AI, serum ferritin, hepcidin

Contemporary pharma R&D resides in a single molecule with a narrowly defined biological action for a chance to show therapeutic potential. The current generation of prospective drugs exemplifies a single-purpose mechanism of action, limited by drug tolerance development and the side effects of the therapy. Ultimately, the therapeutic purpose of the current drug model is incompatible with the complexity and functionality of the human organism.

The untapped potential of compound herbal and mineral oriental formulae offers a trove of information in the development of a novel model of pharmacologic therapy. The proposed new drug R&D comes from the theory and practice of Tibetan medicine by five generations of physicians in the Badmaev family since 1851.[1] The accumulated experience has led to a concept described as the "Interactive Nutrient Process", or INP, obtaining a safe and effective pharmaceutical product. The INP starts with incorporating the principles of the traditional Tibetan herbal therapy:[1]

- An abrupt insult does not cause the majority of diseases but results from long-standing abuse of the organism,
- The gastrointestinal system is central to the pathogenesis of most diseases,
- Any disease affects all the organs and body systems, despite the apparent manifestation associated with the body organ/system affected most,
- The role of any treatment is to support but not replace the organism's natural defense mechanism against disease.

Each of the compound formulae includes herbal and mineral ingredients arranged into three therapeutic groups:[1]

1. The main acting ingredients,
2. The ingredients that support the main action, and
3. The ingredients that prevent any untoward effects of the first two groups and increase the active principles' gastrointestinal absorption and tissue bioavailability.

This three-group design is unlike the current generation of drugs based on a single molecule and an effective therapeutic dose. The Tibetan formula relies on the structural design and the skillfully followed script of therapy with the gradual, over-time dosing, the intermissions, and the reintroducing of the treatment.[1] Each of the botanicals and

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minerals assigned to the three groups has actives that interact with the target tissues, receptors, and biologics of the body in the process of therapeutic bioavailability.[1] The formula has pluripotential properties, encompassing safety, efficacy, and preventing the tolerance of therapeutic goals.[1] In addition to the three-group assignment, the herbal ingredients encode the stand-alone safety and effectiveness of the therapy—the pluripotential mechanism of the formula and ingredients results in a "smart drug" mechanism. The "smart drug" compares to a pharmacological agent of hormesis: a low dose of a tested compound having opposite biological action to that produced by a higher amount. Yet, the hormesis-like effect of the formula and its ingredients results from the interaction between the pluripotential molecules with the body's biological markers and is not based on the therapeutic dose levels. The total objectives of using the formula are then guided by the traditional knowledge and practitioner's experience, contextualizing and teaching the therapy.[1]

The prospective drug in the INP derives from a sequential extraction process of the target herb, using aqueous and organic solvents or green technologies, eg, the CO2 supercritical extraction process. The therapeutic use of the pluripotential molecules is then proposed based on the AI model developed with an algorithm utilizing multidisciplinary data on the Tibetan herbal drug and the therapy.[1] The INP library of information allows the AI model to calculate safe, effective, and efficient drug use.

The Shogaol molecule obtained from ginger root involves several derivatives with a significant compound of 6-Shogaol, exemplifying the outcome of the Interactive Nutrient Process in a pluripotential, "smart drug" development.[2] Based on the traditional gastrointestinal application of the multicomponent herbal and mineral formula No. 179,[1] the formula's main acting ingredient, 6-Shogaol, derived from ginger, in form of 20 mg/day 6-Shogaol, was evaluated clinically for 12 months with biological markers of iron homeostasis serum ferritin (SF) and the peptide antibiotic hepcidin—in a small sample of patients with iron overload and low-risk/Intermediate-1 myelodysplastic syndromes (MDS). The study showed upregulation of hepcidin with the resultant decrease in SF levels attributable to decreased absorption of dietary iron, with no side effects of the therapy and indications of improved liver function.[2] The liver function deterioration is a common comorbid condition in the MDS patients.

Hepcidin may play a vital role in the first-line defense in the MDS, providing broad protection against bacteria, viruses, fungi, and protozoa by "starving" gut microorganisms from iron availability.[3,4] The go-in-between action of 6-Shogaol with markers of iron homeostasis is partly responsible for the principle of the Interactive Nutrient Process, resulting in the "smart drug" optimal biological and antimicrobial expression of hepcidin and serum ferritin. Although hepcidin can be an exceptionally effective, broad-spectrum antibiotic, the preconditions potentially modified by 6-Shogaol fulfill its safety and efficacy in patients with low/intermediate-1 risk MDS patients, eg, lowering serum ferritin levels when abnormally elevated in the MDS patients.

Conversely, stand-alone hepcidin, especially applied in the MDS in a dose-escalating pattern, may result in untoward mechanisms related, for example, to body iron dysregulation and unfavorable outcomes of the biological action. The Interactive Nutrient Process exemplifies and supports currently trending bioinformatics (AI) using algorithms to predict an effective therapy in specific clinical entities. However, the AI application, which can screen for over 100 million antibiotic molecules in days, can be and often is biased, needing more generative data unforeseen by the current drug AI, such as the knowledgeable input of traditional medicine practitioners. The Interactive Nutrient Process, exemplified by the therapy with 6-Shogaol, may correct this bias.

The 6-Shogaol "smart drug" regulatory action in a specific clinical condition, like MDS, may lead to an optimal biological response of the body, liver-made hepcidin, and the resulting antimicrobial protection of the patient. The Interactive Nutrient Process can help develop and monitor the "smart drug" property of 6-Shogaol and shogaols, eg, by feedback monitoring serum levels of hepcidin and ferritin. The resulting pharmacokinetic information of the markers can lead to an effective, safe, and lasting antibiotic algorithm for the antibiotic use of hepcidin.

In the XIX century, one of the leading causes of mortality was infectious diseases due to the lack of antibiotics. Nowadays, antibiotic-resistant bacteria cause pandemic proportion mortality and determine the unfavorable outcome of myelogenous malignancy like the MDS. The Interactive Nutrient Process can help discover new therapies by providing a practical guide to effective treatments, including new antibiotic development.

Disclosure

Dr Vladimir Badmaev reports a patent (Patent No.: US 10,864,174 B2) issued. The author claims no other conflicts of interest in preparing and writing the manuscript.

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