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CLINICAL EFFICACY OF COMBINING MEDICINAL PLANTS AND SYNTHETIC PREPARATIONS

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Abstract

This article examines the clinical efficacy, pharmacological rationale, and safety considerations of the simultaneous use of medicinal plant extracts and synthetic drugs that is, phytopharmacological combination therapy on the basis of the scientific literature. The fact that approximately 80 percent of the world's population relies on plant-based preparations for primary healthcare needs (WHO, 2019) underscores the relevance of this topic. The article analyzes synergistic mechanisms of action, pharmacokinetic and pharmacodynamic interactions, and the results of clinical studies conducted for specific nosologies including cardiovascular diseases, diabetes mellitus, oncology, and neuropsychiatric disorders. In addition, the adverse consequences of herb-drug interactions, particularly with regard to phytochemicals that affect the CYP450 enzyme system, are examined separately. In conclusion, the conditions necessary for the development of integrative medicine as a scientifically grounded and safe practice are defined.

Keywords

phytotherapy, combination therapy, herb-drug interaction, synergism, CYP450, pharmacokinetics, integrative medicine, medicinal plants, clinical trials, pharmacognosy, polypharmacy, adaptogens.

Introduction

Humanity has been utilizing medicinal plants for therapeutic purposes for thousands of years. The ancient Egyptian Ebers Papyrus (circa 1550 BCE), Ibn Sina's Canon of Medicine, and the classical sources of Chinese medicine reflect a rich tradition of plant-based treatment methods. Although synthetic drugs came to dominate the pharmaceutical market through the advances of chemistry and pharmacology in the twentieth century, scientific and clinical interest in phytotherapy has intensified sharply over the past three decades. Several factors account for this: the expanding epidemic of chronic diseases, the problems of side effects and resistance associated with synthetic preparations, the growing public confidence in "natural" remedies, and the capacity of modern science to elucidate the mechanisms of action of plant compounds. According to the World Health Organization (WHO), 80 percent of the population in Asian and African countries rely on plant-based preparations at the primary level of medical care. Uzbekistan also possesses a rich tradition in this area: the botanical diversity of the Zarafshan Valley, the Hissar mountain range, and the Fergana Valley has served as the raw

material base of folk medicine for centuries. However, the concurrent use of plant preparations with modern synthetic drugs the bridge between these two worlds remains an insufficiently studied and clinically unsubstantiated field. The present article systematizes the available scientific evidence with the aim of bridging this gap.

Main body

The pharmacological interactions observed in combinations of medicinal plants and synthetic preparations fall into two principal categories: pharmacodynamic and pharmacokinetic interactions. Pharmacodynamic synergism refers to a situation in which the effects of two substances directed at the same biological target a receptor, enzyme, or ion channel mutually potentiate one another. For example, the serotonin reuptake-inhibiting properties of hypericin and hyperforin compounds found in St. John's Wort (Hypericum perforatum) extract have been observed to lead to serotonin syndrome when used in combination with SSRI-class antidepressants. This scenario illustrates the potential hazards of pharmacodynamic synergism. Pharmacokinetic interactions, on the other hand, occur in processes related to the absorption, distribution, metabolism, and elimination of drug substances. The most significant mechanism in this domain operates through the cytochrome P450 (CYP450) enzyme system: plant compounds may induce or inhibit these enzymes, thereby altering the plasma concentration of concurrently administered synthetic drugs.

St. John's Wort (Hypericum perforatum) is the most extensively studied example in this regard. Clinical studies have demonstrated that St. John's Wort extract, a potent inducer of CYP3A4 and P-glycoprotein, can reduce the plasma concentrations of drugs such as cyclosporine (an immunosuppressant used following transplantation), antiretroviral agents (indinavir, nevirapine), oral contraceptives, and warfarin by as much as 50 to 70 percent. In a randomized clinical trial conducted by Bauer et al. (2003), co-administration of St. John's Wort extract with digoxin was found to reduce the AUC of digoxin by 25 percent, a finding that may significantly compromise the therapeutic efficacy of the cardiac glycoside. Conversely, certain plant compounds inhibit CYP enzymes, leading to a potentially dangerous increase in the concentration of synthetic drugs. Furanocoumarins present in grapefruit juice block CYP3A4, sharply elevating the concentrations of statins, calcium channel blockers, and a number of immunosuppressants.

However, not all herb-drug combinations produce adverse outcomes on the contrary, numerous studies have also documented cases of therapeutically beneficial synergism. This direction is being particularly actively investigated in the context of cardiovascular diseases. The allicin and other organosulfide compounds in garlic (Allium sativum) extract have been demonstrated to reduce platelet aggregation, lower arterial blood pressure, and inhibit LDL oxidation. Several randomized clinical trials showed that the co-administration of garlic extract with

low-dose aspirin produced a combined effect on blood coagulation with a slightly increased risk of bleeding but delivered a synergistic antithrombotic effect, reducing platelet aggregation by 20 to 30 percent more than either agent alone. Ginger (Zingiber officinale) rhizome also possesses antiplatelet properties, and clinical reports have noted that its concurrent use with warfarin elevates the INR value, making it necessary for patients receiving anticoagulant therapy to exercise caution when taking ginger.

Large-scale studies on the efficacy of herb-drug combinations in the treatment of type 2 diabetes mellitus have been conducted by clinics in China, India, and Iran. The hypoglycemic properties of bitter melon (Momordica charantia) fruit are associated with charantins, vicine, and polypeptide-p compounds, which enhance insulin receptor signaling. According to one meta-analysis (Fuangchan et al., 2011), M. charantia preparations in combination with metformin reduced blood glucose levels significantly more than either agent used alone; however, it was noted that larger-scale randomized controlled trials (RCTs) would be required for this effect to be considered clinically significant. The amino acid 4-hydroxyisoleucine derived from fenugreek (Trigonella foenum-graecum) seeds has attracted particular interest due to its insulinotropic effects: this compound stimulates GLP-1 (glucagon-like peptide-1) secretion and, when combined with sulfonylurea agents, supports beta-cell function.

In the field of oncology, promising directions exist for the combination of phytochemicals with synthetic chemotherapeutic agents. Curcumin the principal active constituent of turmeric is being widely investigated in clinical settings due to its ability to inhibit NF-κB signaling, cyclooxygenase-2, and numerous proto-oncogenes. Phase II clinical trials of curcumin in combination with gemcitabine the standard chemotherapeutic agent used in the treatment of pancreatic cancer were conducted by Dhillon et al. (2008): a nine-month follow-up revealed that the combination group demonstrated improved disease control rates compared to the gemcitabine monotherapy group. However, the extremely low bioavailability of curcumin with less than one percent absorbed following oral administration remains the primary obstacle to making this compound clinically practical. Nanoencapsulation, phosphatidylcholine complexes, and formulations combined with piperine are partially addressing this challenge.

In the field of neuropsychiatric disorders, valerian acid (valerenic acid) found in valerian (Valeriana officinalis) root has been shown to modulate GABA-A receptors, producing a sedative effect similar to that of benzodiazepine preparations but with less potential for dependence. In a comparative study of low-dose diazepam combined with valerian for sleep disorders conducted by Ziegler et al. (2002), both groups showed similar improvements in sleep quality; however, the valerian group exhibited less daytime drowsiness the following day. The withanolide compounds present in ashwagandha (Withania somnifera) root, which affect the pathogenesis of Alzheimer's disease, have been shown in vitro and in

animal models to inhibit the formation of beta-amyloid plaques, and Phase I/II clinical trials are currently ongoing.

In the context of Uzbekistan's national medicine, a number of plants that grow wild and are widely used in folk medicine including harmal (Peganum harmala), licorice (Glycyrrhiza glabra), and numerous mountain plants have not been sufficiently studied according to international scientific criteria. Harmine and harmaline compounds present in harmal seeds inhibit monoamine oxidase (MAO) and may exhibit potentially dangerous interactions with antidepressants or antiparkinson agents. The glycyrrhizin component of licorice root is known to disrupt cortisol metabolism, leading to hypokalemia and arterial hypertension a consideration of particular importance for patients receiving antihypertensive therapy. It is therefore essential that in integrative medical practice, Uzbek physicians inquire of patients not only about synthetic medications but also about herbal teas, tablet-form plant preparations, and folk medicine remedies they may be taking.

Conclusion

Combination therapy involving medicinal plants and synthetic preparations constitutes an important and increasingly developing area of integrative medicine. Available clinical evidence indicates that correctly selected combinations can enhance therapeutic efficacy, mitigate the side effects of synthetic preparations, and improve patients' quality of life. However, it is equally true that herb-drug interactions particularly those mediated through the CYP450 enzyme system can give rise to serious safety concerns. For this reason, an integrative treatment approach must be grounded in a rigorous clinical rationale, a complete patient history, and collaboration with a clinical pharmacologist and phytotherapist. In the future, conducting modern scientific and clinical research on Uzbekistan's endemic medicinal plants, training clinicians in herb-drug interactions, and developing integrative medicine protocols within the framework of clinical pharmacology services should be regarded as priority objectives.

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