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Short communication

Identification of medicinal plants of interest for the development of new drugs

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Introduction

The process of discovery and development of new chemical synthetic drugs is characterized by: expensive and difficult research, capital investments and risky success rate. These factors have sparked growing interest in research into traditional herbal drugs and medicinal plants over the past few decades.

Their long use in the treatment of various diseases in traditional medicine indicates a high success rate in the discovery and development of new drugs. E.g., from the golden grass (*Coptis chinensis* fam. Ranunculaceae), medicinal plant, used in traditional Chinese and Ayurvedic medicine for the treatment of inflammatory symptoms and infectious diseases for more than 3.000 years, has been isolated berberine - a substance that has powerful antibiotic and anti-inflammatory properties. Traditional records of this plant have documented other pharmacological effects with potential implications for clinical conditions - diabetes, hypertension, hypercholesterolemia, depression (Pan et al., 2013).

Discussion

Screening in these processes is determined by: 1. Reductionist approach (single target, single compound - one goal, one compound). The first phase identifies a chemical entity ("hit" - molecule with confirmed structure/activity profile of assays) that will be approved for clinical trials as Investigational New Drug (IND). To define a "hit" requires a primary screening of a number of compounds. E.g., antitumor compounds are analyzed on cell structure, antibiotics on microorganisms, and enzymes on receptors by molecular target analysis. In the case where a molecule communicates with multiple targets, the identification of a "hit" is performed by bioanalytical fractionation methods.

E.g., curcumin, polyphenol extracted from the rhizome of *Curcuma longa* fam. Zingiberaceae, has: anticancer, antiviral, anti-arthritic, antiamyloid, antioxidant and anti-inflammatory properties. The second phase refers to the clinical trials-research on the pharmacological/toxicological effects of "hit" as well as structure/activity relationship (SAR) *in vitro* and *in vivo*. 2. Holistic approach (thorough examination of the: patient, diagnosis, personal therapy, drug that is a mix of several medicinal plants). Practice shows that this is a more comprehensive approach than the reductionist one. Namely, such a holistic evaluation includes the realistic assumption for the occurrence of "prodrug" (formation of an active compound after drug intake). E.g. 1, willow bark (*Salix alba* fam. Salicaceae) used as an analgesic, was the basis for the development of acetylsalicylate (Aspirin®). Neither acetylsalicylate nor salicylate is present in willow bark. The bark contains salicin, a glucoside of salicylic alcohol. In the body, sugar is separated and alcohol is oxidized to salicylate ("prodrug"). E.g. 2, Δ9-tetrahydrocannabinol (THC) as a minor degradation product of THC-acid with low activity is present in the plant *Cannabis sativa* fam. Cannabinaceae. By heating THC-acid (through smoking or brewing tea), and its decarboxylation, the active compound THC ("prodrug") is released (Wilkinson et al., 2003). Modern approaches to the research and development of traditional herbal drugs include revolutionary new technologies (carbon dioxide extraction, membrane separation, semi-bionic extraction, molecular destillation, enzyme extraction), and ADMET

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(Absorption, Distribution, Metabolism, Excretion and Toxicity) studies, and ADME (Absorption, Distribution, Metabolism and Excretion) level interaction profile (Pan et al., 2013). Strategies for the detection of herbal drugs include two other important segments: 1. Environmental ethics (moral principles governing human attitudes towards the environment and rules of conduct for the care and preservation of the environment) - Environmental ethical principles should be respected for time of exploitation of medicinal plants and development of herbal drugs. In many developing countries, traditional herbal drugs are used as the primary source of health care and are much cheaper than new single – component drugs. 2. Sustainable development - In 2004, the World Wildlife Fund released data – 20% of the world's traditional medicinal plants are facing extinction due to overexploitation. E.g., The Chinese Red Book of Plants in the category of "rare and endangered plants" includes: *Ginkgo biloba* fam. Ginkgoaceae, *Magnolia officinalis* fam. Magnoliaceae, *Panax ginseng* fam. Araliaceae (Singh, 2002). Very often biologically active metabolites of medicinal plants that were previously directly applied as a drug, today are produced commercially (synthetic or semi-synthetic). E.g., caffeine, theophylline, theobromine, ephedrine, emetine, papaverine, p-carotene. No less important is the role of these metabolites as a chemical model for the design, synthesis and development of new drugs. The identification and isolation of phytochemical groups (each group contains many individual chemical entities) in plant materials are key to the discovery of new drugs. E.g., over 10.000 alkaloids have been isolated, and only about 80 have clinical use - Belladonna's alkaloids (for the design and synthesis of anticholinergics), physostigmine (for anticholinesterase drugs), quinine (for antimalarial drugs), cocaine (for local anesthetics: benzocaine, procaine, lidocaine), codeine and morphine (for analgesics: pentazocine, propoxyphene, methadone, meperidine), papaverine (for verapamil), Galegine (for metformin as an antidiabetic) (Pan et al., 2013). In recent years, there is a great interest in the so called "hybrid molecule" (composed of different drug entities that are covalently linked). The creation of such a molecule can greatly contribute to the optimization of biological properties, emphasizing affinity and selectivity, as well as to obtain new biological activities different from those of the original drug entities. One of the main sources of components for a "hybrid molecule" are medicinal plants due to the great potential of bioactive substances (Decker, 2011). The multi-herbal formulation as a major feature of herbal drugs in traditional medicine supports research on the "hybrid molecule". In multicomponent herbal formulations (e.g., an Indonesian tea blend known as "jamu", containing 30 different medicinal plants) a "hybrid molecule" is created as a result of the interaction between the present medicinal plants (their active substances) (Pan et al., 2013). The hybrid approach is a promising path for new drug molecules whose effective targets are most often multifactorial diseases and neurodegenerative disorders (Alzheimer's disease and Parkinson's disease). No less important is their applicability in the development of new: anticancer, antimalarial drugs, estrogen hybrids (Decker, 2011).

Conclusion

Ethno-medical studies on the correlation between the ethno-medical use of medicinal plants and modern drugs discovered by those plants (Fabricant and Farnsworth, 2001) confirmed that 88 plant metabolites isolated from 72 medicinal plants introduced into modern therapy have the same or similar therapeutic purpose as their original use. Modern treatment with medicinal plants is in terms of major sources for new active metabolites that need to be technologically defined in standardized pharmaceutical dosage forms. Ethno-pharmacological methodology should essentially link traditional empirical knowledge of ethno-medical preparations with bio-scientific research.

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