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Pharmacological Properties of Herbal Drugs

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ABSTRACT

Due to a lack of knowledge regarding the underlying mechanisms of action of the herbs, modern medicine frequently disagrees with traditional medicine, such as Indian herbal medicine. An effective systems pharmacology platform representing ideal information convergence of pharmacochemistry, ADME properties, drug-likeness, drug targets, associated diseases, and interaction networks is desperately needed in order to foster integration of both sides and expedite the drug discovery process from herbal medicines

In the US, a quarter of adult's report having used a herb to treat a medical condition in the previous year, demonstrating the widespread usage of herbal remedies in the country. Herbs are complex blends of organic compounds, the concentrations of which can vary greatly based on numerous parameters associated with the development, manufacturing, and preparation of the herbal product. Although standardization is a method used by many producers to deliver products with uniform levels of suspected active components, its implications on the finished product's safety and efficacy are not entirely clear. The foundation of systems pharmacology for herbal medicines served as the foundation for the development of the traditional Chinese medicine systems pharmacology database and analytic platform (TCMSP). It is made up of all 499 Chinese herbs that are listed in the Chinese Pharmacopoeia, together with 3,311 targets, 29,384 constituents, and 837 related disorders. For the purpose of drug screening and evaluation, twelve significant ADME-related features are offered, including human oral bioavailability, half-life, drug-likeness, Caco-2 permeability, blood-brain barrier, and Lipinski's rule of five.

Keywords: Pharmacochemisty, ADME, Pharmacopeia, Bioavaiability, Blood brain Barrier.

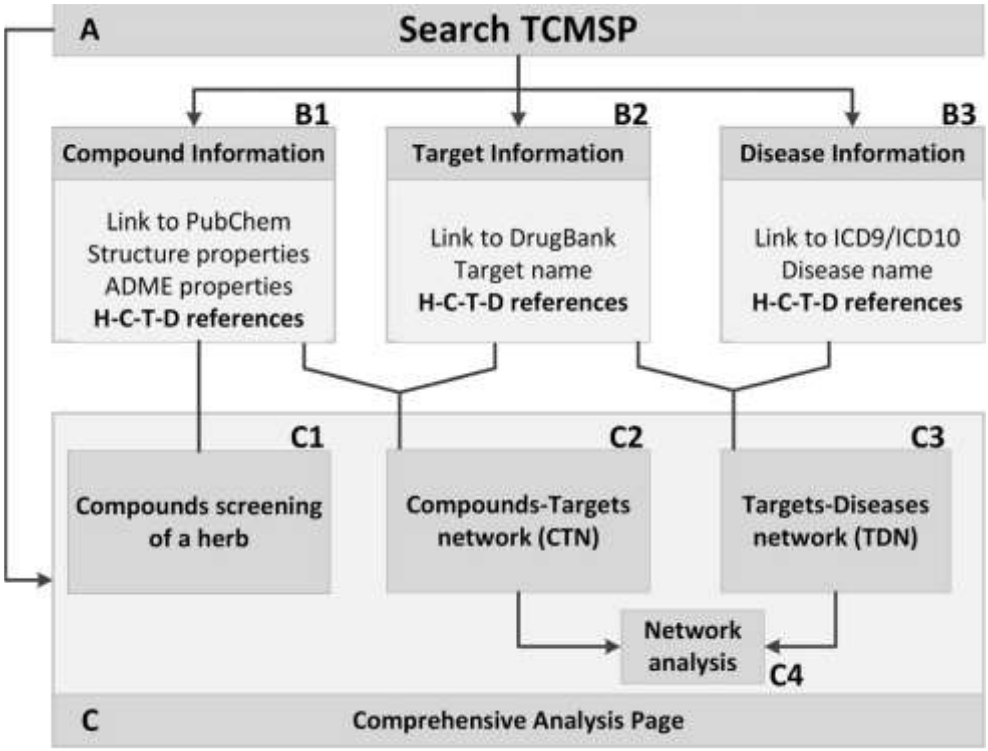
Background

With the longest history in Asia, traditional herbal medicine is an affordable medical practice that differs from contemporary medicine in terms of philosophy, methodology, and content. It is crucial to the maintenance of global health for all peoples [1]. Due to the growing demand for herbal products, the industry's worth has increased to hundreds of millions of dollars annually. As a result, there is a growing need to thoroughly analyze and assess the intricate physiological impacts of herbal products. Herbal medicine formulas frequently incorporate a variety of botanicals, occasionally including as many as 50 species and thousands of chemical components. But only a small percentage of them show promising pharmacokinetics—the drug's absorption, distribution, metabolism, and excretion (ADME) qualities.[1]

Construction and content

Database scheme

TCMSP is divided into three major categories: (1) Compounds, targets and diseases information (Figure 1 B1, B2 and B3); (2) Herbal ingredients with their ADME-related properties (Figure 1 C1); (3) Compounds-Targets



Herbal ingredients

We conducted a thorough literature search for each herbal remedy to compile all the information currently accessible regarding its constituents. Molecule structure files were generated using ISIS Draw 2.5 (MDL Information Systems, Inc.) or downloaded from PubChem [2], the Compound database, ChEMBL [3], and Chem Spider [4]. Sybyl 6.9 (Tripos, Inc.) further optimized the structure using the Sybyl force field and default parameters [5]. Open Babel transformed several chemical file formats into the SDF format [6]. In ChIKey, the duplicates were eliminated.

ADME-related properties

The database was designed to include multiple key ADME-related attributes, including human oral bioavailability (OB), in order to conduct a molecular analysis of the druggability of herbs [7]

MECHANISMS OF HERB–DRUG INTERACTIONS

The primary cause of drug-drug, food-drug, and HDI is thought to be the overlapping substrate specificity in the bio transformative pathway of the physiologic systems (Marchettietal.,2007). Pharmacodynamic drug interactions can be explained by the ability of various chemical moieties to interact with receptor sites and modify the physiological environment, whereas pharmacokinetic drug interactions result from altered absorption, interference with the distribution pattern, and modifications and competition in the metabolic and excretory pathways. Similar to drug-drug interaction, the main underlying mechanism of pharmacokinetic HDI is either the activation or inhibition of hepatic and intestinal metabolic enzymes, especially those in the CYP enzyme family. Furthermore, the majority of other cases are caused by a similar effect on drug transporters and efflux proteins, specifically the p-glycoproteins in the intestines (Meijerman et al., 2006; Nowack, 2008; Farkas et al., 2010).

Drug interactions that may occur in vivo are frequently deduced from in vitro research involving liver enzymes. Although the degree of clinical significance is difficult to deduce, the link between in vitro and in vivo behavior has produced trustworthy results in some situations in terms of in vivo predictability (Rostami Hodjeganand Tucker,2007; Iwamotoetal.,2008; Xuetal.,2009; Umeharaand Camenisch,2011). Therefore, as the following sections will show, the majority of the well-established HDIs were first shown through in vitro research.

Drug discovery and drug combination

Drug ADME evaluations are essential steps in the drug development and discovery process [8]. Costly late-stage drug development failures were primarily caused by unfavorable pharmacokinetic properties [9]. The TCMSP Database Contains A Number Of Important ADME-Related Properties, Such As Compound OB, DL, FASA-, Caco-2 Permeability, BBB, HL, And Lipinski's Rule Of Five, To Asses The Potential Of Turning A Compound Into A Drug. The Molecules That Disobey These Rules Or Other Customized Thresholds Can Be Easily Removed From This Database. For instance, 69 bioactive compounds of licorice were obtained by ADME screening using the criteria OB $\geq$ 40% and DL $\geq$ 0.18 in our case study on the herb.[10]

Section Snippets

Prevalence/epidemiology

Many surveys have revealed that a sizable portion of Americans utilize herbs to treat illnesses or enhance their overall health. According to Eisenberg et al.'s well publicized national survey on the use of complementary and alternative medicine, the proportion of individuals treating medical illnesses with herbs increased from 3% in 1990 to 12% in 1997 [11]. In 1997, a separate nationwide telephone poll of 1500 adults revealed that 17% of them used herbal products.

The complexity of herbal products

Any sort of plant or plant product, including leaves, stems, flowers, roots, and seeds, is commonly referred to as a herb (12). Herbal products might include a single herb or mixtures of several different herbs that are thought to work in concert with one another. Certain herbal products, such as those formulas used in traditional Chinese medicine, also contain minerals and animal products (13).

Herbal goods are offered for sale as whole plants or as plant extracts. Boiling is required for extraction.

Regulations

The Dietary Supplement Health and Education Act of 1994 establishes a very different framework for the regulation of herbal products than that of pharmaceutical drugs in terms of establishing efficacy, safety, and postmarketing surveillance. In the United States, herbs are classified as dietary supplements and are therefore subject to regulation. The public's desire for greater access to herbs and the widespread assumption that they are safe led to this congressional action.[15]

Efficacy

Approximately 80% of medical therapies in the developing countries still use herbs, which have been used for generations to cure illness and promote health[16]. Nevertheless, the great majority of herbal products have very little proof of efficacy from randomized controlled trials. Only four of the ten most popular herbs in the US in 2001 (Table 1) have statistically significant evidence of benefit, according to systematic reviews: Ginkgo biloba, and garlic

Safety

Because herbal products are "natural," they are frequently thought to be safe [17]. But herbs have powerful bioactive ingredients; historically, plants were the source of almost one-third of pharmaceutical medications [18]. The usage of herbal products has been linked to numerous fatal and serious side effects. These adverse consequences could result from a number of several pathways, such as the herb's direct toxicity, allergic responses, contaminant effects, interactions with medications

Research and future directions

Based on comprehensive assessments of randomized controlled studies, just four of the top 10 herbs sold in the US—garlic, ginkgo biloba, saw palmetto, and St. John's wort—are likely to be beneficial. The thousands of additional single and multiherb products that are sold in this nation probably have far less evidence supporting their efficacy. The absence of proof of effectiveness is combined with new accounts of severe adverse reactions from herbal products.[19]

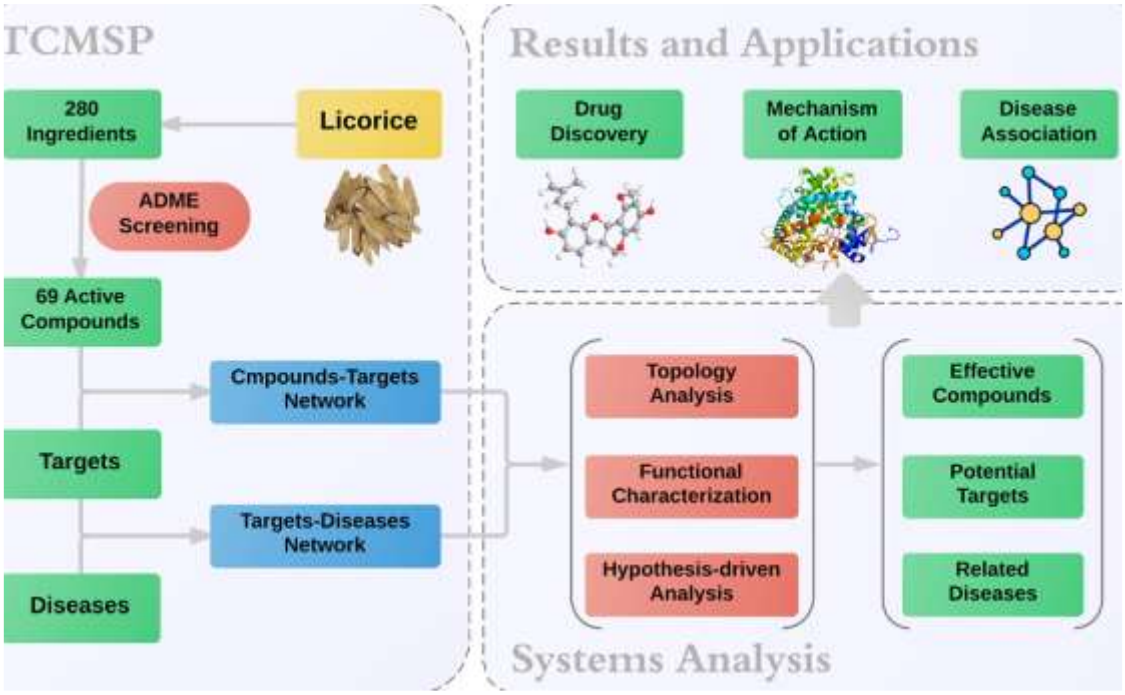
Current situation

For thousands of years, humans have employed traditional remedies and medicinal plants all throughout the world. Regulation and assessment, however, have changed regionally. As such, multiple legal contexts exist today for comparable botanical items. Certain laws concentrate on pharmaceuticals, while others mention goods categorized as food or deal with particular conventional treatments. There is a lack of specific language; examples include "natural health products," "botanical medicines," and "herbal medicinal products."

Investigate mechanisms of action of herbal medicines and TCM formula

One of the main challenges for current research is understanding how the many chemical components of medicinal herbs contribute to the overall pharmacological impact.

TCMSP offers details on how herbs can get past biological barriers and the corresponding pharmacological objectives. The TCMSP platform's primary methods have been effectively used in earlier research to investigate the ways in which TCM formulas and herbal remedies work to treat viral infections and cardiovascular illnesses [20]. For example, using this model, the pharmacological effects of two typical herbs on influenza, inflammation, and other conditions were examined: Lonicera japonica and Fructus for sythiae.



Because of the extreme complexity of the chemical components and the mechanisms of action, a thorough understanding of liquorice remains elusive. This example will demonstrate how to use Tcmsp to screen active ingredients, find drug targets, and determine disease states. In this section, we will provide a brief overview of the methodology and findings of our study (Figure 2). More in-depth details regarding the biological underpinnings of the pharmacology of liquorice can be found in our earlier research. From Tcmsp, We Obtained 280 Known Licorice Compounds. The criteria for using the Adme screening were Ob ≥ 40% and Dl ≥ 0.18. Ingredients in Licorice Are Determined To Be Active Substances Based On These Criteria.Next, compounds are mapped to the target-disease and compound-target networks. The networks can be imported into Cytoscape software and analyzed using the Networkanalyzer plugin, or they can be downloaded as an Xgmml file via Tcmsp.[21] The significance of a node (a compound or a target) and its influence are indicated by the computation of two essential topological parameters, degree and betweenness. Two nodes communicating with each other. Ultimately, We Found 91 Targets Associated with Various Illnesses, Which Are Essential For Comprehending Licorice's Pharmacological Mechanisms. According to the generated drug-target network, the target proteins Ptpn1, Hrh1, and F2 as well as the glycosperins C, licoagrocarpin, and glycyrrhizic acid are the main players in the drug-target interactions. For Example, Liquiritin and Licochalcone G Are Compounds That Target Metalloelastase to Kill Bacteria and Boost Tissue Macrophages To Protect Against Outside Intruders. Additionally, our previous work provides details on how to use systems pharmacology methods in TCM. [22]

REFERENCE

1. Cheung F: TCM: made in China. Nature. 2011, 480: S82-S83. 10.1038/480S82a.
2. Li Q, Cheng T, Wang Y, Bryant SH: PubChem as a public resource for drug discovery. Drug Discov Today. 2010, 15: 1052-1057. 10.1016/j.drudis.2010.10.003.
3. Gaulton A, Bellis LJ, Bento AP, Chambers J, Davies M, Hersey A, Light Y, McGlinchey S, Michalovich D, Al-Lazikani B, Overington JP: ChEMBL: a large-scale bioactivity database for drug discovery. Nucleic Acids Res. 2011, 40: D1100-D1107.
4. Pence HE, Williams A: ChemSpider: An Online Chemical Information Resource. J Chem Educ. 2010, 87: 1123-1124. 10.1021/ed100697w.
5. Zhang L, Liu T, Wang X, Wang J, Li G, Li Y, Yang L, Wang Y: Insight into the binding mode and the structural features of the pyrimidine derivatives as human A2A adenosine receptor antagonists. Biosystems. 2014, 115: 13-22.
6. O'Boyle NM, Banck M, James CA, Morley C, Vandermeersch T, Hutchison GR: Open Babel: An open chemical toolbox. J Cheminformatics. 2011, 3: 33-10.1186/1758-2946-3-33.
7. Xu X, Zhang W, Huang C, Li Y, Yu H, Wang Y, Duan J, Ling Y: A Novel Chemometric Method for the Prediction of Human Oral Bioavailability. Int J Mol Sci. 2012, 13: 6964-6982. 10.3390/ijms13066964.
8. Su X, Kong L, Lei X, Hu L, Ye M, Zou H: Biological Fingerprinting Analysis of Traditional Chinese Medicines with Targeting ADME/Tox Property for Screening of Bioactive Compounds by Chromatographic and MS Methods. Mini-Rev Med Chem. 2007, 7: 87-98. 10.2174/138955707779317830.
9. Van de Waterbeemd H, Gifford E: ADMET in silico modelling: towards prediction paradise?. Nat Rev Drug Discov. 2003, 2: 192-204. 10.1038/nrd1032.

10. Li Y, Han C, Wang J, Xiao W, Wang Z, Zhang J, Yang Y, Zhang S, Ai C: Investigation into the mechanism of Eucommia ulmoides Oliv. based on a systems pharmacology approach. J Ethnopharmacol. 2014, 151: 452-460. 10.1016/j.jep.2013.10.067.

11. Li X, Xu X, Wang J, Yu H, Wang X, Yang H, Xu H, Tang S, Li Y, Yang L, Huang L, Wang Y, Yang S: A System-Level Investigation into the Mechanisms of Chinese Traditional Medicine: compound Danshen Formula for Cardiovascular Disease Treatment. PLoS One. 2012, 7: e43918-10.1371/journal.pone.0043918.

12. Kuruvilla FG, Shamji AF, Sternson SM, Hergenrother PJ, Schreiber SL: Dissecting glucose signalling with diversity-oriented synthesis and small-molecule microarrays. Nature. 2002, 416: 653-657. 10.1038/416653a.

13. Tao W, Xu X, Wang X, Li B, Wang Y, Li Y, Yang L: Network pharmacology-based prediction of the active ingredients and potential targets of Chinese herbal Radix Curcumae formula for application to cardiovascular disease. J Ethnopharmacol. 2013, 145: 1-10. 10.1016/j.jep.2012.09.051.

14. Liu J, Pei M, Zheng C, Li Y, Wang Y, Lu A, Yang L: A Systems-Pharmacology Analysis of Herbal Medicines Used in Health Improvement Treatment: predicting Potential New Drugs and Targets. Evid Based Complement Alternat Med. 2013, 2013: 1-17.

15. Liu H, Wang J, Zhou W, Wang Y, Yang L: Systems approaches and polypharmacology for drug discovery from herbal medicines: an example using licorice. J Ethnopharmacol. 2013, 146: 773-793. 10.1016/j.jep.2013.02.004.

16. Wang X, Xu X, Li Y, Li X, Tao W, Li B, Wang Y, Yang L: Systems pharmacology uncovers Janus functions of botanical drugs: activation of host defense system and inhibition of influenza virus replication. Integr Biol. 2013, 5: 351-10.1039/c2ib20204b.

17. Yao Y, Zhang X, Wang Z, Zheng C, Li P, Huang C, Tao W, Xiao W, Wang Y, Huang L, Yang L: Deciphering the combination principles of Traditional Chinese Medicine from a systems pharmacology perspective based on Ma-huang Decoction. J Ethnopharmacol. 2013, 150: 619-638. 10.1016/j.jep.2013.09.018.

18. Sarasa D, Sridhar S, Prabakaran E. Effect of an antidiabetic extract of Trigonella foenum-graecum on normal and alloxan induced diabetic mice. Int J Pharmacy Pharmaceutical Sci 2012;4(1):63-65

19. Agarwal M, Sharma P, Kushwaha S. Antifertility efficacy of 50% ethanolic extract of Calendula officinalis in male rats. Int J Pharmacy Pharmaceutical Sci 2011;3():192-196.

20. Gupta PC. Withania coagulans Dunal- An Overview. Int J Pharmaceutical Sci Review Research 2012;12(2):68-71.

21. World Health Organization. Summary of WHO guidelines for the assessment of herbal medicines. Herbal Gram 1993;28:13- 14.

22. Naik GH, Priyadarsini KI, Naik DB, Gangabhagirathi R, Mohan H. Studies on the aqueous extract of Terminalia chebula as a potent antioxidant and a probable radioprotector. Phytomedicine 2004;11:530-38.