Mini Review

A Systematic In Vivo Pharmacology Research to Establish Yupingfeng's Effective Asthma Methodology

Santosh Mishra*

Department of Endocrinology, Federal University of Bahia, Brazil

*Corresponding Author's E-mail: Santoshmishra43@gmail.com

Abstract

Although Yupingfeng's clinical impact on asthmatics has been established, no research has been done to substantiate its pharmacological mechanism. Hypothesis purpose to understand YPF's possible pharmacological mechanism and molecular basis for use in the treatment of asthma. Study methodology and design: Initially, a systems pharmacology-based approach was employed to systematically elucidate the mechanism of YPF in asthma by integrating pharmacokinetic screening, target prediction, network analysis, GO, and KEGG analyses. Second, using the online programme GEO2R, differentially expressed genes between asthma sufferers and healthy controls were discovered. Finally, molecular docking was carried out using the Discovery Studio 2020 Client version to find the ability of compounds to attach to targets based on systems pharmacology and DEGs data. The C57BL/6 mice that had been exposed to ovalbumin received either YPF or its efficient compound to evaluate the forecasts. After target fishing and matching, a total of 35 active compounds were eliminated, leaving 87 prospective targets for additional investigation. The primary components of YPF were determined to be quercetin, kaempferol, and wogonin. The top signalling pathways in KEGG enrichment were found to be phosphatidylinositol 3-kinase protein kinase tumour necrosis factor and IL-17.

Keywords: Traditional Chinese medicine, Systems pharmacology, Molecular docking, Wogonin

INTRODUCTION

Over 334 million people worldwide suffer from asthma, a common respiratory condition characterised by varying respiratory symptoms and airflow restriction. Asthma's primary pathogenic characteristics include airway remodelling, hyper responsiveness, and inflammation. Today, long-acting 2 agonists, long-acting muscarinic antagonists, and inhaled corticosteroids are the main treatment options for asthma (Greenland P., et al 2004). Nevertheless, inhaled corticosteroids have been linked to cataracts, bruising of the skin, osteoporosis, diabetes, respiratory infections, and lung infections (Généreux P., et al 2014). Moreover, only 10% of asthmatics respond favourably to traditional medications. Traditional Chinese medicine has been used in clinical practise in China for thousands of years. It is an old, complete medical system

with a lot of potential value (Madhavan MV., et al 2014). TCM prescriptions, which are based on syndrome-based therapy and have multicomponent, multimarket components, always have extensive and synergistic effects on the human body (Jang IK., et al 2002). the effectiveness and safety of treatments a large number of experimental and clinical trials have consistently demonstrated the effectiveness of TCM prescriptions in asthmatics. is a traditional TCM remedy made out of the roots of three herbs: Astragals membranaceus Bunge, Saposhnikovia divaricata Trucz, and Atractylodes macrocephala Koidz. YPF has been utilised extensively in the treatment of respiratory inflammatory disorders and allergy diseases, with a significant body of prior research attesting to its extraordinary results. In addition to animal models, asthmatic people have also shown significant improvements in lung function and symptoms as a result of YPF, which has a favourable safety profile (Yabushita H., et al 2002). Due

to the variety of active substances and potential targets, it is difficult to clarify the holistic action mechanisms of TCM (Sugiyama T., et al 2019). The complicated pharmacological mechanisms of TCM have been extensively studied using systems pharmacology, a thorough approach founded on the idea of "disease-gene target-medicine (Nakajima A., et al 2021)." The pharmacological mechanism of Yupingfeng's has been studied in relation to a number of disorders, including chronic obstructive pulmonary disease, immunosuppression, coronavirus disease, and asthma, thanks to the widespread use of systems pharmacology (Afolabi A., et al 2021). The main working pathways for treating asthma are defined as the signalling pathways of tumour necrosis factor phosphatidylinositol-3-kinase protein kinase B interleukin and phosphorylated nuclear factor-kappa B nucleotide-binding oligomerization domain like receptor, among others. Quercetin, Kaempferol, and Wogonin are screened out as the key active ingredients for the treatment of asthma (Kitabata H., et al 2010). Only the NOD-like receptor signalling pathway has been demonstrated using an in vivo investigation from them (Chan JA., et al 2012). To confirm the primary hypotheses, experimental studies are yet insufficient. active components and YPF's modes of action. In this study, the putative mechanism of YPF in asthma was clarified using systems pharmacology analysis, molecular docking, and experimental verification. Building a database of chemical compounds The chemicals for YPF were gathered through extensive data mining. First, expert pharmaceutical databases including the Traditional Chinese Medicine System Pharmacology Database were obtained. Evaluation of oral bioavailability OB is the percentage of a pharmacological dosage that ultimately enters the systemic circulation. Screening the active components is important. OBioavail, a statistical model that predicts the P-glycoproteins and cytochrome P450s based on 805 structurally different pharmaceuticals and drug-like compounds, was used to determine the OB value of a herbal constituent. First, a systems pharmacology-based approach was employed to systematically elucidate the mechanism of YPF in asthma by integrating pharmacokinetic screening, target prediction, network analysis, GO, and KEGG analyses. Second, using the online programme GEO2R, differentially expressed genes between asthma sufferers and healthy controls were discovered. Third, molecular docking was carried out using the Discovery Studio 2020 Client version to find the ability of compounds to attach to targets based on systems pharmacology and DEGs data. Finally, YPF or its active component was administered to C57BL/6 mice challenged with ovalbumin in order to test the predictions. Although Yupingfeng's clinical impact on asthmatics has been established, no research has been done to substantiate its pharmacological mechanism. To identify the underlying molecular mechanisms and potential therapeutic effects of YPF with asthma. After target fishing and matching, a total of 35 active compounds were eliminated, leaving 87 prospective targets for additional investigation. The primary

components of YPF were determined to be quercetin, kaempferol, and wogonin.

DISCUSSION

The main signalling pathways in the KEGG enrichment analysis were found to be those of phosphatidylinositol 3-kinase protein kinase B, tumour necrosis factor, and IL-17. Five DEGs were found by NCBI's GEO2R tools to be overlapping with YPF's therapeutic targets. The outcomes of molecular docking demonstrated that wogonin is the most active substance in YPF. YPF and wogonin dramatically reduced airway resistance and lung inflammation, according to in vivo tests, by lowering levels of inflammatory cytokines and essential components of TNF signalling pathways. & YPF Wogonin, its primary active ingredient, may reduce asthma inflammation through a variety of biological targets and signalling pathways, including Protein kinase AKT Analysis of Variance (BANOVA)Androgen receptor, AP-1activator protein-1BALfluid used in bronchoalveolar lavageCASP3caspase-3CASP8caspase-8Ccompliance with chordstasisCdyndynamic conformitySpecific cyclin-D1c for CCND1G1/SDeoxyribonucleic acid complementary to DNAmuscarinic cholinergic receptor number fourCOVID-192019C-Tcompound-targetDEGsdifferentially expressed genes in coronavirus illnessDrug-likeness of DIO1Iodothyronine deiodinase 1DLDNADna, a kind of DNAEnzyme-linked immunosorbent test (ELISA)Ecdysone growth factorEGFRreceptor for epidermal growth factorTyrosine-protein kinase, ERBB2 erbB-2oestrogen receptorESR1andreceptorESR2,respectively,FCfoldchangeF-C-T-Dformula-compound-target-diseasec-FosFRCfunctional residual capacity of the FOS proto-oncogeneSubunit of the gamma-aminobutyric acid receptor Ontology for GOGenethe HTR3A5-hydroxytryptamine receptor in hematoxylin and eosin Intercellular adhesion molecule 3aICAM1 1IgEIKK, an immunoglobulinantagonist of kappa Kinase BThe Kyoto Encyclopaedia of Genes and Genomes' entry for ILinterleukinhomogenate of lung tissue (LTH)Mitogen-activated protein kinase 8 (MAPK8) 8mMessenger RNA for RNAproto-oncogene protein MycNuclear factor kappa (NOCOA2nuclear receptor coactivator 2) BNIHNational Institutes of HealthNOS3nitric oxide synthaseNODnucleotide-binding oligomerization domain Bioavailability of 3OBoralMendelian Inheritance in ManOVA at OMIMOnlineovalbuminp-AKTkinase for phosphorylated protein BPBS saline buffered phosphate PI3Kphosphatidylinositol-3-kinasep-IKKphosphorylated kappa inhibitor Kinase B nuclear factor kappa with phosphorylation Peroxisome proliferator-activated receptor, or BPPARGProtein–protein interaction (PPI) PRKCAAlpha protein kinase Cquantitative polymerase chain reaction PRSS1trypsin-1PTGS1prostaglandin G/H synthase 1PTGS2prostaglandin G/H synthase 2Traditional terms include: RUNX1T1RUNX1 partner transcriptional corepressor

1TCM, RELA, transcription factor p65, RNA, and Eastern medicineChinese Medicine System Pharmacology Database, or TCMSPT-Dtarget-diseaseTLCtotal lung volumeToxic necrosis factorVEGFABlood vessel endothelial growth factor AYPFYupingfeng Traditional Chinese medicine has been used in clinical practise in China for thousands of years. It is an old, complete medicinal system with a lot of potential value.

CONCLUSION

TCM prescriptions, which are based on syndrome-based therapy and have multicomponent, multistage components, always have extensive and synergistic effects on the human body. Many experimental and clinical research have broadly validated the therapeutic efficacy and safety of TCM prescriptions for asthmatics. Three herbs are used in the traditional TCM recipe known as Yupingfeng's, comprising the roots of Astragalus membranaceus Bunge, Saposhnikovia divaricata Trucz (Fangfeng), and Atractylodes macrocephala Koidz. YPF has been utilised extensively in the treatment of respiratory inflammatory disorders and allergy diseases, with a significant body of prior research attesting to its extraordinary results. cumulative effects of YPF Large-scale improvements in lung functioning and asthma-related symptoms have been reported in both animal models and asthmatic people, with a favourable safety profile. We counted the nodes in networks and assessed their topological characteristics in the interactions using the network analysis plug-in in the software. Betweenness centrality, closeness centrality, and degree were chosen as the three parameters. One of the major parameters of the plug-in to represent the frequency of interactions between one node and the others was "Degree," which refers to the quantity of links to a particular node. The only node that was acknowledged as being essential to the therapeutic impact of YPF against asthma was the one with a "Degree" greater than the median value. Using the ClusterProfiler package of R3.6.1, we performed GO and KEGG pathway enrichment analysis for the target genes in order to investigate the molecular processes of YPF at the pathway level. The relevance of the genes increased with the enrichment score. Based on enrichment analysis for functional items, KEGG analysis was carried out to investigate the biological pathways and probable biological functions. A UPLC equipment with a photo-diode array detector was used to carry out the chromatographic analysis.

REFERENCES

1. Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC, et al (2004). Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. JAMA. 291: 210-215.

2. Généreux P, Madhavan MV, Mintz GS, Maehara A, Palmerini T, et al (2014). Ischemic outcomes after coronary intervention of calcified vessels in acute coronary syndromes. J Am Coll Cardiol. 63: 1845-1854.

3. Madhavan MV, Tarigopula M, Mintz GS, Maehara A, Stone GW, et al (2014). Coronary artery calcification: Pathogenesis and prognostic implications. J Am Coll Cardiol. 63: 1703-1714.

4. Jang IK, Bouma BE, Kang DH, Park SJ, Park SW, et al (2002) Visualization of coronary atherosclerotic plaques in patients using optical coherence tomography. J Am Coll Cardiol. 39: 604-609.

5. Yabushita H, Bouma BE, Houser SL, Aretz HT, Jang IK, et al (2002). Characterization of human atherosclerosis by optical coherence tomography. Circulation. 106: 1640-1645.

6. Sugiyama T, Yamamoto E, Fracassi F, Lee H, Yonetsu T, et al (2019). Calcified Plaques in Patients with Acute Coronary Syndromes. J Am Coll Cardiol Cardiovasc Interv. 12: 531-540.

7. Nakajima A, Araki M, Kurihara O, Minami Y, Soeda T, et al (2021). Comparison of post-stent optical coherence tomography findings among three subtypes of calcified culprit plaques in patients with acute coronary syndrome. Catheter Cardiovasc Interv. 97: 634-645.

8. Afolabi A, Mustafina I, Zhao L, Li L, Sun R, et al (2018). Does spotty calcification attenuate the response of nonculprit plaque to statin therapy?: a serial optical coherence tomography study. Catheter Cardiovasc Interv. 91: 582-590.

9. Kitabata H, Tanaka A, Kubo T, Takarada S, Kashiwagi M, et al (2010). Relation of microchannel structure identified by optical coherence tomography to plaque vulnerability in patients with coronary artery disease. Am J Cardiol.105: 1673-1678.

10. Chan JA, Stuart K, Earle CC, Clark JW, Bhargava P, et al (2012). Prospective study of bevacizumab plus temozolomide in patients with advanced neuroendocrine tumors. J Clin Oncol. 30: 2963-2968.