



New Drug Research Hotspots and Frontier Visualization Analysis in China

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Abstract. Objective To explore the status, hot spots and frontiers of new drug research in China through visual maps. Methods Using CNKI as the literature source and using CiteSpace software, the quantitative tool CiteSpace software was used to visually analyze the literature related Chinese to new drugs in China published by CNKI from 2010 to 2021. Results: The literature volume of new drug research in China shows a fluctuating upward trend, and the closeness of cooperation between researchers and research institutions was low; keyword clustering formed a total of 9 categories, mainly for new drug research and development, innovative drugs, pharmacology, clinical trials, adverse reactions, clinical studies, new Chinese medicine drugs, drug registration, and new drug clinical trials. Conclusion: The research hotspots in the field of new drug research in China are mainly concentrated in three aspects: preclinical research, clinical research and new drug marketing research. Innovative drugs and policy trends and legal and regulatory systems and major disease prevention and treatment of drug research and development is an important direction of future research.

Keywords: New Drugs · Visualization · CiteSpace · Hotspots · Frontier

1 Introduction

New drugs refer to drugs whose chemical structure, drug composition, and pharmacological effects differ from existing drugs [1]. New drug research refers to the whole process from laboratory discovery to market application of new drugs, including two major stages of new drug discovery research and new drug development research [2]. Traditional new drug research is faced with the double dilemma of high cost and low efficiency. The development of modern science and technology has brought new technical means for new drug research. Enabling preclinical research links such as drug target discovery and compound screening through machine learning (ML), computer drug design and other methods can save costs, improve the efficiency of new drug research and development, and attract extensive attention from scholars. Exploring the hot spots and frontiers of new drug research in China will help scholars build a modern research system for new drugs. Through literature review, it is found that the literature on new drug research tends to deeply analyze drug technology content, patents, clinical needs, etc., and lacks comprehensive research in the whole research field. In view of this, we

take CNKI (China National Knowledge Infrastructure) as the representative, and from the aspects of time distribution, spatial distribution, keyword clustering and keyword emergence, we use the metrological tool CiteSpace software to visually analyze the Chinese literature related to “new drugs” from 2010 to 2021, and sort out the hot spots and frontiers of new drug research in China in the past 12 years. Provide reference and reference for further research of new drugs in the future.

2 Data and Methods

2.1 Data Source

The Chinese literature on “new drugs” retrieved by CNKI was taken as the object. Advanced search is selected in CNKI. The search conditions are periodical search, the subject is “new drugs”, the journal source is Chinese literature of CNKI journals, and the time span is “2010–2021”. After manually removing the conference notice, recruitment, report and other documents irrelevant to the research, 2498 literature data were obtained, and finally the data were exported and saved in CNKI’s Refworks format.

2.2 Methods

Use the visualization tool CiteSpace to conduct visual analysis of literature, draw a map of cooperative knowledge based on authors, institutions and countries and a map of co occurring knowledge based on keywords [3], extract information such as authors and keywords of highly cited literature, and use Excel for auxiliary analysis.

3 Results

3.1 Overview of New Drug Research

3.1.1 Time Distribution

The distribution of the annual number of literature studies in a certain field can reflect the level of research development and overall results in that field to a certain extent [4]. This study counted the articles related to new drug research published in core journals from 2010 to 2021, and obtained the trend chart of annual literature quantity of new drug research, as shown in Fig. 1. From 2010 to 2021, the number of publications related to new drugs in China has shown a fluctuating upward trend, and the number of publications in 2017 reached a peak, with a total of 256 articles.

3.1.2 Distribution of Researchers

Draw the cooperation map through CiteSpace software to understand the cooperation between major researchers and institutions in the field of new drug research in China. The researchers with a large number of articles are as follows: Du Guanhua (52 articles), Chen Benchuan (48 articles), Yang Junyi (33 0 50 100 150 200 250 300 2010, 2012, 2014, 2015, 2016, 2018, 2019, 2020, 2021 articles), Tang Jianyuan (28 articles), Shao

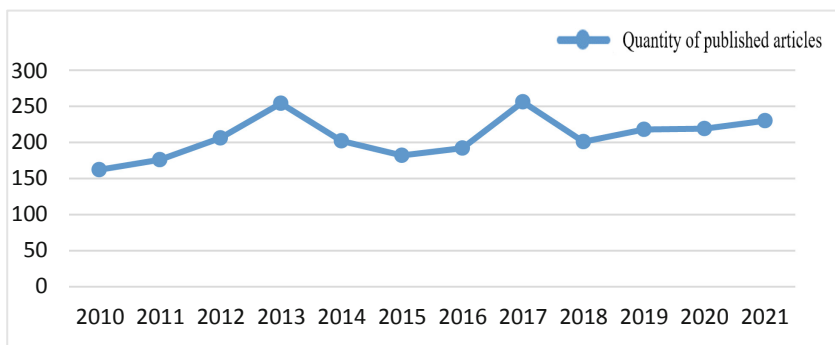


Fig. 1. Literature Statistics of New Drug Research In China

Rong (23 articles). In the cooperation map, the network structure dominated by Chen Benchuan, Du Guanhua and Yang Junyi is more prominent. See Fig. 2. There are 437 nodes, 549 lines and 0.0058 tightness of network structure in the author cooperation network map of new drug research.

3.2 Organization Distribution

In order to understand the current high-yield academic groups and institutions researching new drugs in China, this study counted the number of papers issued by various research institutions in the field of new drug research. The top five institutions with the highest number of documents issued from 2010 to 2021 and their number are shown in Fig. 3: Drug Evaluation Center of the State Drug Administration (228), China Pharmaceutical University (104), Shenyang Pharmaceutical University (81), Department of Pharmacy of Linyi Central Hospital (32), and Institute of Pharmacy of Peking Union Medical College, Chinese Academy of Medical Sciences (26). In the CiteSpace cooperation map, the node is the name of the organization, the size of the node represents the amount of documents issued, the font size of the label represents the level of centrality, and the line segment connects the cooperative organization [5]. There are 387 nodes, 241 lines and 0.0032 tightness of network structure in the institutional cooperation network map of new drug research.

3.3 Cited Literature

CNKI extracts documents with a large number of citations, and the main research directions are as follows: (1) New research and development ideas: big data + new traditional Chinese medicine, such as Liu Zhihua [6], Jie Jing [7], Liu Ailin [8] and Zhou Wenxia [9], using network pharmacology to provide new conceptual support for new drug research and development, Lu Peng [10] and Xu Haiyu [11] respectively proposed software development and computer platform development related to traditional Chinese medicine (2) new drug research and development, For example, You Liangzhen [12] made research progress on astragaloside IV in the treatment of diabetes and its complications, Shi Qingwen [13] made analysis on the research and development of

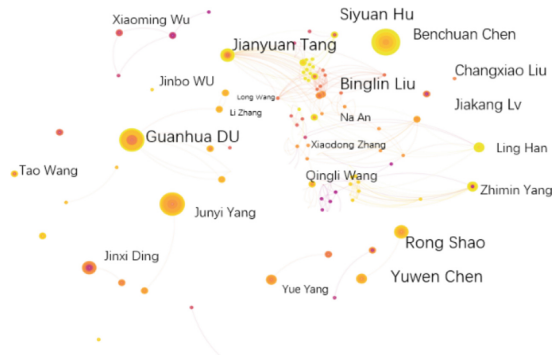


Fig. 2. Author Cooperation Map

natural drugs, and Zhou Bei [14] summarized and analyzed the guiding principle system of clinical research technology for new drugs (3) pharmaceutical enterprises, and Wang Wentao [15] explored the relationship between innovation, value chain expansion and profitability of manufacturing enterprises.

3.4 Hotspot and Frontier of New Drug Research

3.4.1 Keyword Co-occurrence Analysis

High frequency and high centrality keywords can reflect the core content that experts and scholars in this research field generally pay attention to for a period of time from a certain point of view. High frequency keywords can represent the hot topics in a research field. Keyword analysis using CiteSpace shows the results shown in Table 2 and Fig. 4. The keyword network for new drug research has a total of 325 nodes and 490 connections, and the network density is 0.0095. In the new drug related research literature, the key words with high frequency are “new drug research and development”, “clinical trials”, “new traditional Chinese medicine”, “innovative drugs”, “clinical research”, etc. The changes of high-frequency keywords, to some extent, reflect the changes in the focus of the field in the process of in-depth promotion and development. Among all high-frequency keywords, the top 10 keywords account for 60%, which indicates that the research and development of new drugs is the main content of research in the field of new drug research.

3.4.2 Keyword Cluster Analysis

We use “Clusters” of CiteSpace software to cluster keywords. See Fig. 5. These clusters reflect the research status of new drugs in China. There are nine clusters, including # 0 new drug research and development, # 1 innovative drugs, # 2 pharmacology, # 3 clinical trials, # 4 adverse reactions, # 5 clinical studies, # 6 new traditional Chinese drugs, # 7 drug registration, and # 8 new drug clinical trials. See Table 3.



Fig. 3. Organization Cooperation Map

Table 1. CNKI's Top Ten Citations

Numbering	Title	Author	Periodical	Time(year)	Citation frequency
1	Development and application of TCM inheritance assistance system software	Peng Lu; Jian Li; Shihuan Tang; Jianxin Chen etc.	Chinese Journal of Experimental Medical Formulae	2012	690
2	Network Pharmacology: New Opportunities for the Modernization of Traditional Chinese Medicine	Zhihua Liu; Xiaobo Sun	Acta Pharmaceutica Sinica	2012	374
3	Research progress and application strategy of network pharmacology in the field of traditional Chinese medicine	Jing Xie; Bin Gao; Lin Li; Yilan Xu; Shuming Gao	Chinese herbal medicine	2019	278

(continued)

Table 1. (continued)

Numbering	Title	Author	Periodical	Time(year)	Citation frequency
4	An overview of the technical guiding principles system for clinical research of new traditional Chinese medicines in China was released	Bei Zhou; Yalin Liu; Jianyuan Tang	Chinese Journal of Clinical Pharmacology	2017	183
5	Network pharmacology: new ideas for drug discovery	Ailin Liu; Guanhua Du	Acta Pharmaceutica Sinica	2010	169
6	Network pharmacology: new ideas for understanding drugs and discovering them	Wenxia Zhou; XiaoruiCheng Yongxiang Zhang	Chinese Journal of Pharmacology and Toxicology	2012	161
7	Research progress in pharmacological effects of astragaloside IV on diabetes and its complications	Liangzhen You; Yixuan Lin; Zhaohui Fang; Guoming Shen etc.	Chinese Journal of Traditional Chinese Materia Medica	2017	160
8	Corporate Innovation, Value Chain Expansion and Manufacturing Profitability: A Case Study of Chinese Pharmaceutical Manufacturing Enterprises	Wentao Wang; Jianfeng Fu; Yi Zhu	China's industrial economy	2012	140

(continued)

Table 1. (continued)

Numbering	Title	Author	Periodical	Time(year)	Citation frequency
9	Development and application of integrated pharmacology computing platform for traditional Chinese medicine	Haiyu Xu; Zhenming LIU; YanFu; Yanqiong Zhang, etc.	Chinese Journal of Traditional Chinese Materia Medica	2017	140
10	Natural medicinal chemistry research and new drug development	Qingwen Shi; Ligeng Li; Changhong Huo; Manli Zhang etc.	Chinese herbal medicine	2010	123

Note: CNKI - China Academic Network Publishing Library

Table 2. Keyword Distribution Table in China's New Drug Research Field (partial)

Frequency	Centrality	Time	Keyword
236	0.44	2010	New drug development
124	0.20	2010	clinical trial
111	0.09	2010	New Chinese medicine
87	0.24	2010	Innovative medicine
83	0.17	2010	Clinical research
45	0.08	2010	security
37	0.09	2010	Adverse reactions
35	0.06	2010	Pharmacokinetics
32	0.03	2010	Drug registration
29	0.07	2010	New molecular entity

3.4.3 Keyword Mergence Analysis

Research frontier refers to “a group of emerging dynamic concepts and potential research problems” [16], while emerging words refer to words frequently cited or frequently appeared in relevant literature in a short time. In a certain period of time, the scientific problems or topics discussed by a group of documents based on the knowledge of emergent words can be used as one of the judgment and prediction standards of the



Fig. 4. Keyword Co-occurrence Figure

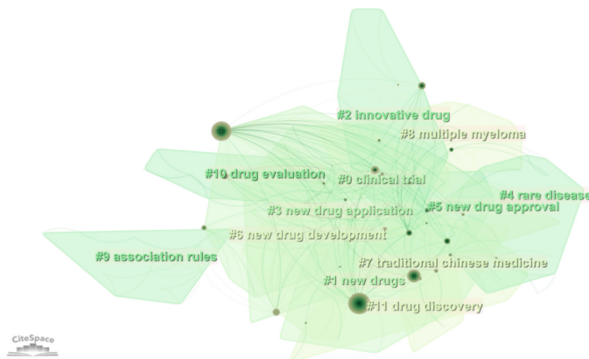


Fig. 5. Co-existing Clustering Map of Keywords in Domestic New Drug Research

research frontier [17]. In this study, CiteSpace ace was used to analyze and explore the salient words of relevant sample data in the field of new drug research, and 17 salient words were obtained (as shown in Fig. 7), namely, “clinical evaluation”, “incompatibility”, “diabetes”, “pharmacokinetics”, “pharmacology”, “new drug approval”, “precision medicine”, “rare diseases”, etc.

3.4.4 Keyword Path Analysis

Based on the keyword clustering analysis, this study analyzes the topic path evolution of keywords, and obtains the keyword path map, as shown in Fig. 6. It can be seen from the figure that the research of new drugs in China can be roughly divided into three stages: the first stage is the basic development period (2010–2013), which is mainly based on the pre clinical research of new drugs; The second stage is the reform and promotion period (2014–2018), mainly studying the laws and regulations related to the listing of new drugs; The third stage is the critical period of development (2019 to date). Epidemics such as the COVID-19 have received extensive attention from scholars.

Table 3. Co-occurrence Clustering of Keywords

Cluster number	Time (year)	Keyword
0	2014	New drug development, Novel coronavirus pneumonia, Drug development
1	2015	Innovative medicine, Phase I clinical trial, Pharmaceutical industry
2	2013	pharmacology, Pharmacokinetics, security
3	2014	clinical trial, Non-alcoholic fatty liver disease, New Drug Registration
4	2014	Adverse reactions, New drug approval, Mechanism of action
5	2013	Clinical research, Multiple myeloma, Small cell lung cancer
6	2015	New Chinese medicine, Human experience, R&D strategy
7	2013	Drug registration, Chinese herbal medicine, Drug approval
8	2016	Clinical trials of new drugs, Anti-tumor new drugs, Antineoplastic drugs

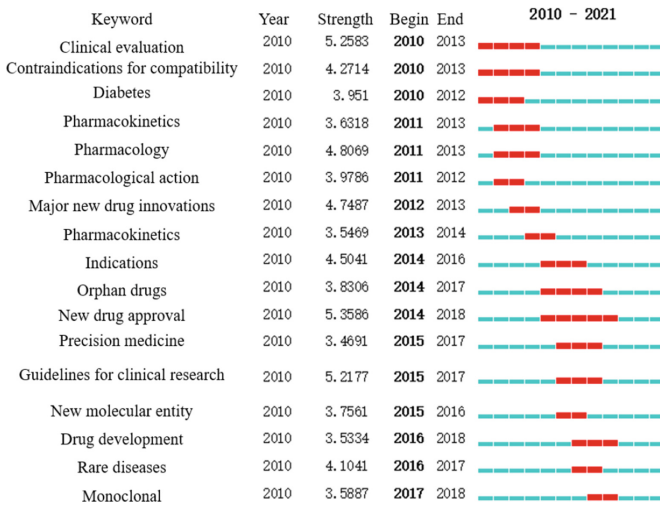


Fig. 6. Keyword Protrusion Figure

4 Discussion

4.1 Overview of New Drug Research

From the perspective of the issuing trend, the research literature of new drugs shows a fluctuating upward trend, and the attention to the research field of new drugs is gradually increasing. The cooperation map of researchers and research institutions shows that the close degree of communication and cooperation between scholars and institutions in the

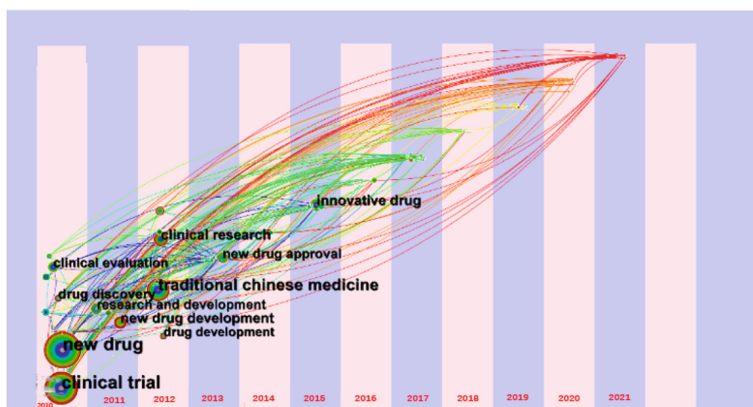


Fig. 7. Keyword Path Map of New Drug Research In China

field of new drug research in China is low, the academic groups of domestic new drug research are relatively scattered, there is less cooperation between different researchers and institutions, and research institutions with strong cohesion have not yet formed. The frequently cited literatures mainly focus on big data + new drug research and development, as well as the analysis of the relationship between innovation, value chain and profitability of pharmaceutical enterprises.

4.2 Keyword Co-occurrence and Cluster Analysis

According to the results of keyword clustering of CiteSpace software and the analysis of literature reading, such as the articles in Table 1, the main research contents in the field of new drug research in China at this stage are roughly summarized into three aspects.

The first topic is “preclinical research”. “preclinical research” includes keywords such as “new drug research and development”, “research and development strategy” and “pharmacology”. New drug R&D is the power source of pharmaceutical manufacturing industry. With the rapid development of artificial intelligence, big data and artificial intelligence technology have provided important theoretical basis and technical methods for tacit knowledge mining, academic experience inheritance and new drug research and development. Many papers have been published on the research of traditional Chinese medicine by using network pharmacology. The innovative ideas and practical achievements of network pharmacology of traditional Chinese medicine will be used in the research and development of other types of new drugs, helping the cross integration of new drug research and development and artificial intelligence in China, It provides theoretical reference for the innovative development of new drug R&D industry in the new era of China.

The second topic of “clinical research” includes such keywords as “Phase I clinical trial”, “clinical research” and “new drug clinical trial”. Clinical trial management system is the key to ensure the authenticity and reliability of clinical research. The research on clinical trial management system started late in China, but it has developed rapidly in recent years. In July 2021, the National Health Commission issued the Guidelines

for the Administration of Clinical Comprehensive Evaluation of Drugs (Trial Version 2021), which aims to guide relevant subjects to standardize, standardize, scientific and homogeneous clinical comprehensive evaluation of drugs, and promote the standardized development of clinical drug work. The document clarifies the importance of establishing and improving the national drug clinical indicator system and standardized decision-making framework. In order to strengthen data information security and clinical research process compliance, building a scientific clinical trial evaluation index system is an important task for our future research.

The third research topic of “new drug registration regulations” includes keywords such as “new drug registration”, “drug approval” and “drug registration”. During this period, the construction of policies and regulations related to new drug registration attracted the attention of the academic community. In recent years, the State Food and Drug Administration has carried out a series of reforms aimed at the bottleneck of new drug registration, involving new drug review, approval, registration and listing, and constantly promoted the rapid development of China’s new drug industry. As a large country of generic drugs, China has been facing the problem of “low-level duplication”, which restricts the rapid development of the pharmaceutical industry. After the implementation of the Drug Registration Administration Law in July 2020, drug registration and application will gradually become rational, low-level duplication will be significantly reduced, and the new registration method will achieve remarkable results. In order to further improve the threshold of generic drug R&D and promote China’s transformation from a large pharmaceutical country to a powerful pharmaceutical country, the management measures for generic drug registration need to be further studied.

4.3 Keyword Emergence and Path Map Analysis

The key to the analysis and judgment of the research frontier is to grasp the trend of the times on the basis of both prominent literature and prominent words. The higher the degree of prominence, the more representative of the latest research focus and frontier evolution in this period. Based on keyword prominence analysis and path mapping, this study explores the frontier issues in the field of new drug research in China. (1) The early stage was the basic development stage (2010–2013). During this period, the research field of new drugs paid more attention to the research on drug innovation and patent research. With the development of social health environment and the progress of medicine, the depth and breadth of new drug research were expanded, and the focus on drug innovation was relatively high. In the construction of innovative China, innovative drugs have gradually become the main part of the pharmaceutical field and even China’s high-tech industry. (2) The middle stage is the reform and promotion stage (2014–2018). New drug approval and new drug registration are the most prominent words in this field. In 2014–2018, the new drug research and development system and registration regulations were paid attention to by scholars, and quickly became the focus and frontier in the new drug research field. This is greatly related to the low innovation rate, low technological innovation rate, high prevalence and high disease burden of new drugs in China. (3) The latest research frontier. This period is a critical stage of development (2019 to the present). At the end of 2019, the outbreak of COVID-19 quickly became the latest word of the emergence time. Under the normal situation of epidemic prevention and

control, researchers pay more attention to the prevention and control of the epidemic and the health of residents. The in-depth study of major diseases represented by the COVID-19 has become a hot topic in the field of new drugs at present and in the future.

5 Summary

This study visually analyzed the domestic new drug research literature through CiteSpace software, which intuitively showed the current situation and hot trends in the field of new drug research, and has certain reference value and significance for the research in the field of new drug research. Hot keywords include new drug research and development, traditional Chinese medicine, innovative drugs, clinical research, new drug registration, COVID-19, etc. It is predicted that the hot spots of new drug research are artificial intelligence, new drug research and development, construction of clinical trial evaluation index system, and management methods for generic drug registration. The research on innovative drugs for major diseases represented by the COVID-19 is the focus of new drug research at present and in the future.

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