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Scientometric analysis: Identification of research trends in the field of ‘herb drug interactions’ between 2011-2019.

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Abstract

Due to the advent of allopathy and concomitant usage of the medicinal drugs with herbal medicines, many herb drug interactions are increasingly reported in the scientific literature. In this study, we have collected the scientific literature in the field of herb drug interactions published between 2011 to 2019 and analyzed it for the scientometric trends to understand the research direction in the last decade. We analyzed for the most prolific authors and their affiliations, top ten countries, funding agencies that sponsored the most publications and journals with most articles published in the field of herb drug interactions. We also identified three top articles of the field, two out of which made it to the list of top articles (based on citation count) of all time. We have identified upcoming research trend of network analysis and systems biology approach in the broad field of herbal medicines and application into the field of herb drug interactions. Our study demonstrated a dominant role of China and authors working in Chinese institutions (research output measured through analysis of publications, author contributions and grant fundings) in the field of herb drug interactions. As use of allopathy and herbal medicines together is on the rise worldwide, we predict that herb drug interactions will become an important concern in the future and precise regulatory guidelines must be developed worldwide as soon as possible.

Keywords: Herb-drug interaction, Scientometry, Publications

Introduction

In today's world, traditional medicines are used by over sixty percent of the world's population. Interestingly, a huge proportion of their consumers are present in developed countries even though out of developing countries, China and India are still the leaders for traditional medicinal systems. Nearly 40 percent of Chinese and approximately seventy percent of Indian population uses traditional medicinal systems for treatment and about, 11,146 and 20,000 medicinal plants have been recorded with curative potential in China and India, respectively. Currently, 8000 traditional Chinese herbal medicines and more than 10,000 Indian herbal preparations (including Ayurvedic, Siddha, Unani, Homeopathic, Tibetan and folk preparations) are available (1-3). Owing to the arrival of allopathy, people are using these herbal treatments in conjunction with allopathic drugs resulting in herb-drug interactions. The occurrence of herb-drug interactions is due to absence of awareness in general public as well as limited reported scientific evidence available with the regulatory authorities. Many herb drug interactions have recently become available in the literature (4-6). A retrospective population-based study on adults that were given *Ginkgo biloba* alone or in combination with anti-coagulant drugs displayed increased risk of haemorrhage in male patients aged 65 and above (7). An Indian herb, *Momordica charantia* (popularly known as karela) has synergistic interactions with four oral hypoglycaemic agents (Rosiglitazone, Metformin, Glibenclamide, and Chlorpropamide) and administration of the herb and the drug together results in excessive lowering of body blood glucose levels (8, 9).

Still, many herb-drug interactions are either under-reported or not yet known because they are largely confused with drug side-effects. As a large portion of world population is using herbs for treatment or symptomatic cure and is thus, at risk, of adverse effects due to reported or not yet reported herb-drug interactions, this field requires considerable attention by the scientific community. To assess if this is the case, we aimed to study the scientometrics about herb drug

interactions in the last nine years i.e. 2011-2019. We collected data from SCOPUS and analyzed it for top authors, top funding agencies, top countries, top journals and top author affiliations in the field of herb drug interactions. We also analyzed the top three articles of this era to identify the upcoming research trend.

Methodology

Data acquisition and scientometry indicators assessment

We selected SCOPUS as a valid source for retrieval of data used for this scientometric analysis. SCOPUS is the main international database for health sciences, and the terminology included in its thesaurus can be used to search for published documents on specific aspects of a given topic. A search with words ‘herb drug interactions’ as descriptor was performed for the years 2011-2019 to retrieve publications that contained these words in publications’ titles, keyword lists, and abstracts (selection setting in the SCOPUS portal). Although it is possible that there may be other terminologies, the search terms were kept broad to ensure that all the right matches would be included. To refine the search results, document type articles or reviews was selected and other document types such as book chapter, data paper, proceedings abstracts were excluded. Once the search was complete, all the documents were selected and data for citation information (author(s), document title, year, source title, volume, issue, pages, citation count, source & document type), bibliographical information (affiliations, serial identifiers (e.g. ISSN), PubMed ID, publisher, editor(s), language of original document, correspondence address, abbreviated source title, DOI), abstract & keywords (abstract, author keywords, index keywords), funding details (number, acronym, sponsor, funding text) was exported as CSV files for subsequent analyses. The electronic search was performed in November, 2019 and record of articles (original and review) with a total of 4,183 was retrieved. No restriction based on language of articles was made although only a small percentage of total articles was non-

English (<8%). The above data was further assessed for identifying the most cited articles, highest published researchers/authors, most influential funding agencies and countries.

Results

To assess the trend in the field of herb-drug interactions, we performed a search in SCOPUS using the terms 'herb drug interactions' limited to original articles and review publication types published between years 2011-2019. The search was performed to include the searched term whenever it appeared in abstract, title of the publication and keywords. The data obtained was assessed for indicators of scientometry such as trends in publications over the years, countries with most prolific authors, funding agencies with most contributions in form of funding for research and so forth.

Our assessment of the publications between years 2011-2019 demonstrated that the number of publications has remained consistent throughout the years studied. No significant rise was observed in the last 10 years with the majority of publications lying between 260 (in 2011) and 330 (in 2018) (Fig 1).

[Fig 1 here]

Although no trend could be identified in the number of publications in Fig 1, an assessment of publications according to countries displayed China as the leader on herb drug interactions with 1208 publication, approximately half of the recorded publications (Fig 2). This is no surprise as China is a world leader in traditional medicine (10). United States closely followed with 916 publications and, interestingly, authors from India, another hub for traditional medicinal systems (Ayurveda, Siddha and Unani), have published comparatively smaller number of publications (257) between 2011 and 2019. The variation in the total number of publications between Fig 1 and Fig 2 arises from collaborations between authors from different countries although only top 10 countries have been analyzed in Fig 2.

[Fig 2 here]

A bar graph analysis of sponsoring agencies funding the grants, associated with recorded publications, demonstrated that six out of the top ten funding agencies were located in China (Fig 3). This may explain the results obtained in Figure 2. NNSF or National Natural Science Foundation of China, affiliated to China's State Council, topped the list with 372 publications, seven times as high as the closest competitor NBRP (973) or National Basic Research Program of China (973 program). Although USA led the publications in the country wise analysis with 916 publications, only one USA funding agency i.e. NIH or National Institutes of Health made it to the top ten. Furthermore, even if India came in third with 257 publications, none of the Indian research funding agencies made it to the top 10 list.

[Fig 3 here]

A similar bar-graph analysis for top 10 journals displayed Journal of Ethnopharmacology surpassed other journals with 176 publications closely followed by Phytotherapy Research with 104 publications and Evidence Based Complementary and Alternative Medicine with 78 publications during 2011-2019 (Fig 4).

[Fig 4 here]

Bar graph for top 10 author affiliations (Fig 5) showed Chinese Academy of Sciences (CAS China; 118 publications) as the leader in the field of herb-drug interactions between 2011-2019, closely followed by Chinese University of Hong Kong (CU Hong Kong; 106 publications) and Ministry of Education China (ME China; 81 publications).

[Fig 5 here]

E. Ernst led the list of top 10 authors with 31 publications in 2011 to 2019-year range while M. Huang (23), Y. C. Hou (22), S.F. Zhou (21) and J.A. Duan (20) published 20-23 articles in the same time-period (Table 1).

[Table 1 here]

In addition, an analysis of the top three articles in our search identified three articles, published during 2013-2014, as the most cited articles (Table 2). These articles were “Structure and dynamics of molecular networks: a novel paradigm of drug discovery: a comprehensive review”, “A review on therapeutic potential of *Nigella sativa*: A miracle herb” and “TCMSP: A database of systems pharmacology for drug discovery from herbal medicines” with citation counts of 445, 339 and 297 respectively. Interestingly, none of these articles could be attributed to the identified top authors in table 1.

[Table 2 here]

Discussion

As a considerable number of people, even westerners, are turning towards herbal medicines, herb-drug interactions are increasingly gaining public interest. As of now, testing of herb drug interactions is not an essential part of allopathic drug development process and therefore, these interactions are easily missed. China and India are important regions for local traditional medicinal systems and the advent of allopathy has resulted in increased probability of herb drug interactions in these countries. Perceiving the need for interaction testing, China have been world leaders in this field as evident from the publication count and funding for research as observed in our collected data. Almost half of the publications (1208) were authored or co-authored by Chinese authors (Fig 2). It was surprising that although India is a hub for traditional medicine too (such as Ayurveda), Indian authors authored or co-authored only 257 publications. As our data is based on SCOPUS search, we cannot rule out the possibility of Indian researchers publishing in non-SCOPUS indexed journals. In addition, India has local journals, many of which are not SCOPUS indexed. We did observe a variation in the publication count between Figure 1 and Figure 2 which could be based on collaborations between authors from different nationalities. This would explain the publication count of 2124 for China (1208) and USA (916) and indicate huge number of China-USA collaborations in

the field of herb-drug interactions. The high amount of Chinese researchers-authored publications also correlates with the six funding agencies being Chinese as shown in figure 3. Interestingly, only one funding agency, NIH, has been involved in funding USA based research in this field and none of the Indian funding agencies made it to the list of top ten funding sponsoring agencies. This may indicate a regional bias for research area and possibility that while China heavily invested in identifying possible drug interactions with herbs used in traditional Chinese medicines and American scientists, therefore, heavily collaborated with them, Indian funding agencies channelized their funds on other areas of biological sciences.

Journal of Ethnopharmacology, Phytotherapy Research and Evidence Based Complementary and Alternative Medicine published the highest number of research and review articles on herb drug interactions between 2011 and 2019 as shown in Figure 4. Majority of the journals in the top ten are natural medicine-based journals. Although any herb drug interaction report is equally important both for readers and scientific community working on herbal medicines as well as allopathy, this may result in unequal distribution of scientific reporting. According to our collected data, few allopathy-based journals publish reports of herb drug interactions. Our data from Figure 5 confirmed the finding that most of the publications were co-authored by Chinese researchers as majority of affiliations were located in China and displayed the highly collaborative attitude of Chinese researchers in the field of herb drug interactions. Interestingly, E. Ernst, an author working in United Kingdom and not working in China, topped the list of authors with 31 publications (Table 1). He is affiliated with Department of Complementary Medicine, School of Postgraduate Medicine and Health Sciences, University of Exeter, Exeter, United Kingdom and all his 31 publications were funded by National Center for Complementary and Alternative Medicine (NCCAM), USA and National Health Service (NHS), U.K. (data through assessment of author's profile from scientific database online). Also, four publications authored by E. Ernst made it to the top 20 publications of all-time list

(Suppl Table 1). Top three authors also include M. Huang, China (23) and Y.C. Hou, Taiwan (22). Five Chinese authors (Table 1) made it to the top 10 list while no Indian authors made it to the list. Other authors, S.F. Zhou, Hong kong (21), B.J Gurley, USA (19) and T.H Tsai, France (19) were also included in the top authors list.

An analysis of top three articles published during 2011-2019, based on citation count, indicated that novelty has gained importance in the last decade. It is surprising that although these articles were published comparatively recently, two of the top articles of the assessed years made it to the list of top 20 articles of all time (Suppl Table 1). Not surprisingly, All the top three articles are review articles. Also, 14 articles in the top publication of all-time list are review articles indicating that review articles are cited more frequently than research articles (Supple Table 1). Two of these articles, namely, “Structure and dynamics of molecular networks: a novel paradigm of drug discovery: a comprehensive review” and “TCMSP: A database of systems pharmacology for drug discovery from herbal medicines” utilized and merged upcoming scientific areas such as molecular networks and database mapping. Both these articles set a precedent in the broader field of biological sciences and demonstrated the application of online databases and network analysis in herb drug interactions. All the three articles (Table 2) have included the term herb drug interactions in that met are search criteria (see methodology section for detailed search parameters).

The review article titled “Structure and dynamics of molecular networks: a novel paradigm of drug discovery: a comprehensive review” published in 2013 in the Journal ‘Pharmacology & Therapeutics’ is a comprehensive review on molecular networks and possible application in drug discovery. The article has been cited by 445 publications till our search. The article performed a comprehensive assessment of the analytical tools of network topology and dynamics. The two basic strategies for network targeting i.e. central hit strategy and network influence strategy have been described and their role in identification of single-target, edgetic,

multi-target and allonetwork drug target candidates have been discussed. This 190-page article describes important tools to study and identify molecular networks and their role in diseases and possible targeting in cancer and diabetes. Although this article is important for drug discovery and development per se, it has acted as a breakthrough for herb-based drug development too. Drug-drug interactions as a measure of network interactions with a direct reference to online databases has been discussed. Interestingly, use of networks to assess herb-drug interactions has resulted through the networks or interaction partners that were identified through this approach. Many interactions such as herb CYP450 interactions (11-13). Although the term herb drug interactions has been vaguely mentioned in the articles that have cited this review article, many articles are too broad to categorize under a specific category. However, as this approach shows promise in identifying herb-drug or herb-CYP (effect on drug metabolism) in the field, its role as a milestone cannot be disputed.

The article titled “TCMSP: A database of systems pharmacology for drug discovery from herbal medicines” describes a free online platform that converges information of pharmacology, ADME properties, drug-likeness, drug targets, associate diseases and interaction networks for traditional Chinese medicine. The database indirectly aims at widening the understanding of mechanism of actions for Chinese herbal medicines and possible herb targets inclusive drug interactions and provides tools for visualization at the network level. This article has acted as a milestone for many research articles published on network pharmacology of Chinese herbal medicines in later years (14-16). Network pharmacology has been further explored for disease specific herbal treatments and targets such as in neurodegenerative diseases (17, 18), hepatoma and hepatoprotective mechanisms (19-21), vitiligo (22), cardiovascular diseases (19, 23), diabetes mellitus (24) and many more. Attempt to identify new herbal drug candidates for cancer therapy (25) and explain herb combinations in a concoction have also been performed (26). All the above approaches have thus identified

herb phytoconstituent targets which may be shared by allopathic drugs as well as herb effects on the body's metabolic enzymes such as CYP450s.

Review article titled "A review on therapeutic potential of *Nigella sativa*: A miracle herb" published in 2013 also made it to top articles of all time with 339 citations during our analysis. This article is a collaboration between Indian authors and authors working in the middle east. *Nigella sativa* is a widely used medicinal plant especially in middle eastern and Indian traditional systems. Its pharmacological properties have been explored as an anti-diabetic, anti-cancer, immunomodulator, analgesic, antimicrobial, anti-inflammatory, spasmolytic, bronchodilator, hepatoprotective, renal protective, gastroprotective and anti-oxidant and the review describes a detailed literature survey on *Nigella sativa* pharmacognostical characteristics, chemical composition and pharmacological activities of the seeds of the plant. In our understanding, the topic covered in this review is very broad and thus the chances of the citation increase considerably. Therefore, the review has been extensively cited in research and review articles that discuss the herb directly (27-30) or vaguely mention connected topics (31-34). This review article has discussed the possible Herb drug interactions for *Nigella sativa*. These publications demonstrate an open and collaborative attitude of research scientists working the field of herb drug interactions and a paradigm shift to include new age methods in science. Finally, our study demonstrates a dominant role of China (research output measured through analysis of publications, author contributions and grant fundings). It is unfortunate that a similar trend could not be observed for other countries invested in usage of traditional herbal medicines resulting in a research gap in these medicinal systems.

Conclusion

In this scientometric study, we have identified China as the leader in the field of herb-drug interactions with almost half of publication authored or co-authored by Chinese researchers in SCOPUS indexed journals. Six Chinese researchers made it to the top ten prolific authors list

for the period of 2011 to 2019. We also found that China is leading in the funding provided to researchers with six Chinese funding agencies listed in the top 10. Although important traditional medicinal systems such as Ayurveda and Siddha are localized in India, the publication count and absence of Indian authors and funding agencies in the top ten indicates a regression on identification and implementation of information on herb drug interactions locally. The same scenario is envisaged for other countries with prolific users of traditional medicinal systems (e.g. Brazil). As use of allopathy and herbal medicines together is on the rise worldwide, we predict that herb drug interactions will become an important concern in the future and precise regulatory guidelines must be developed worldwide as soon as possible. Our literature analysis proves a steady output of publications in the field although better research output is observed for Chinese traditional medicines than other systems. A similar attitude must be adopted by other countries that heavily bank on traditional medicines and herb drug interaction testing should be made an important part of any drug development.

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Conflict of Interest: The authors declare no conflict of interest

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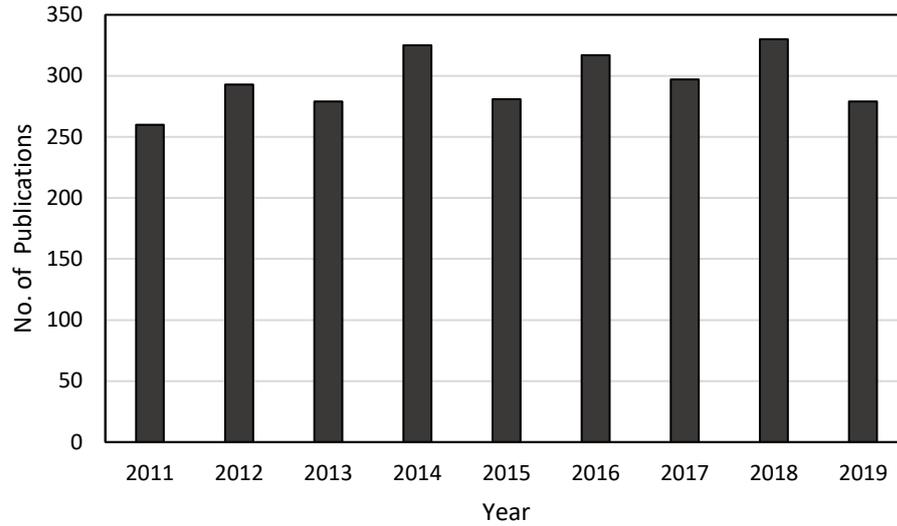


Figure 1 2011-2019 trend in publications on herb drug interactions. SCOPUS search on 'herb drug interactions' for original articles and review articles between 2011 to 2019 were plotted in to a bar-graph and assessed for possible trends in research.

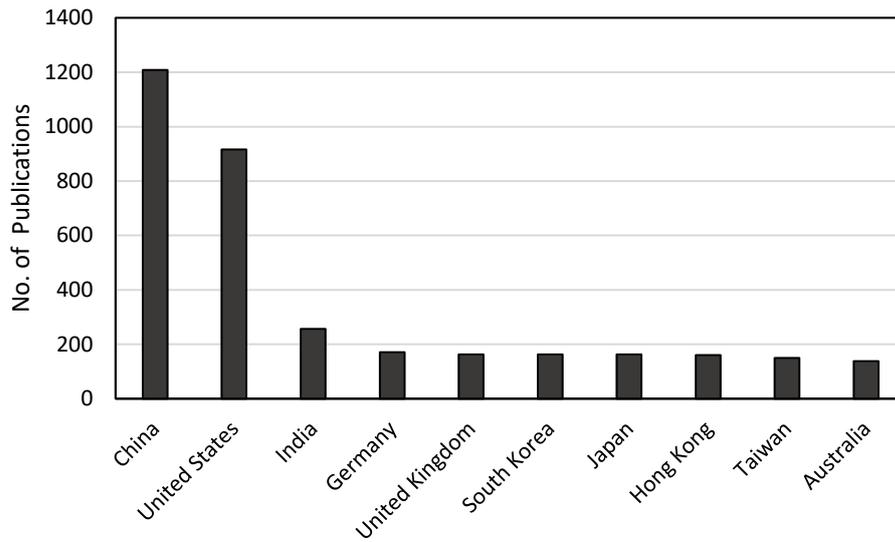
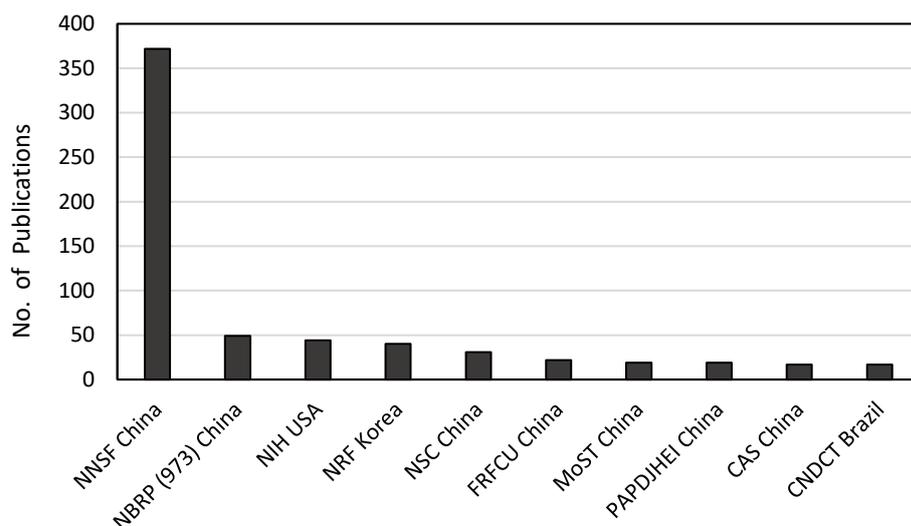
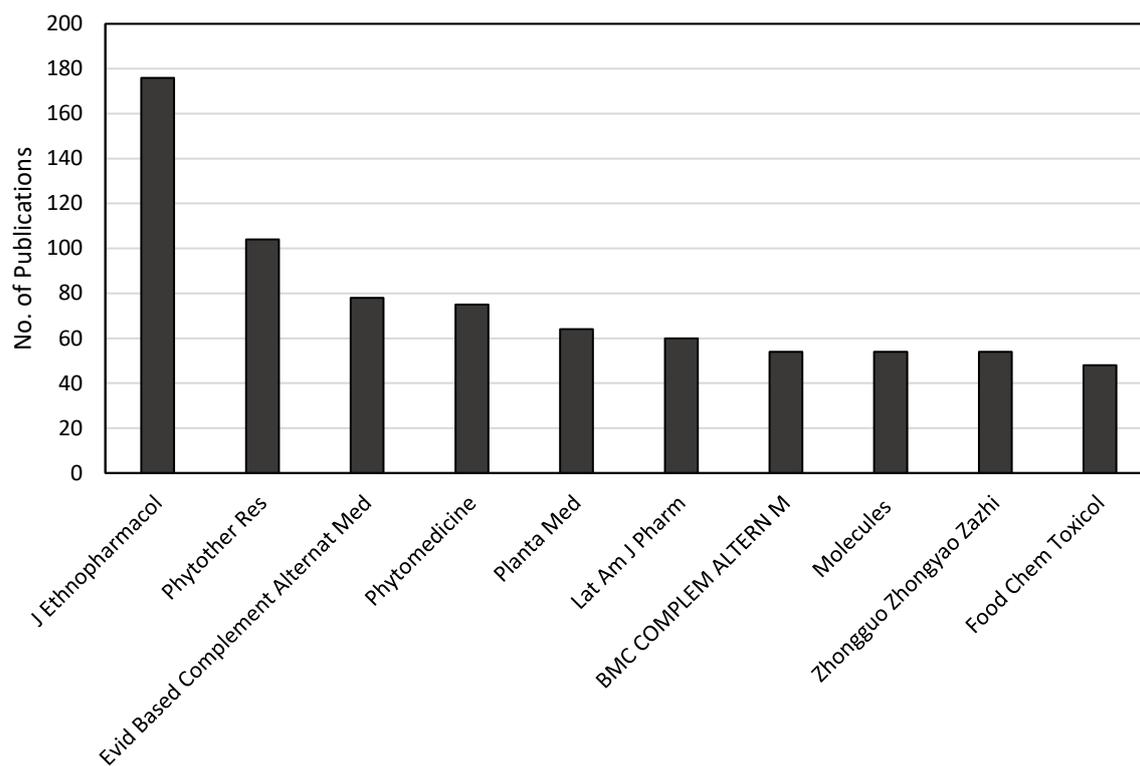


Figure 2 Trend in publication count for the top 10 countries. Bar graphs were prepared for the identified top 10 countries leading the 'herb drug interactions' field in 2011-2019 time period.



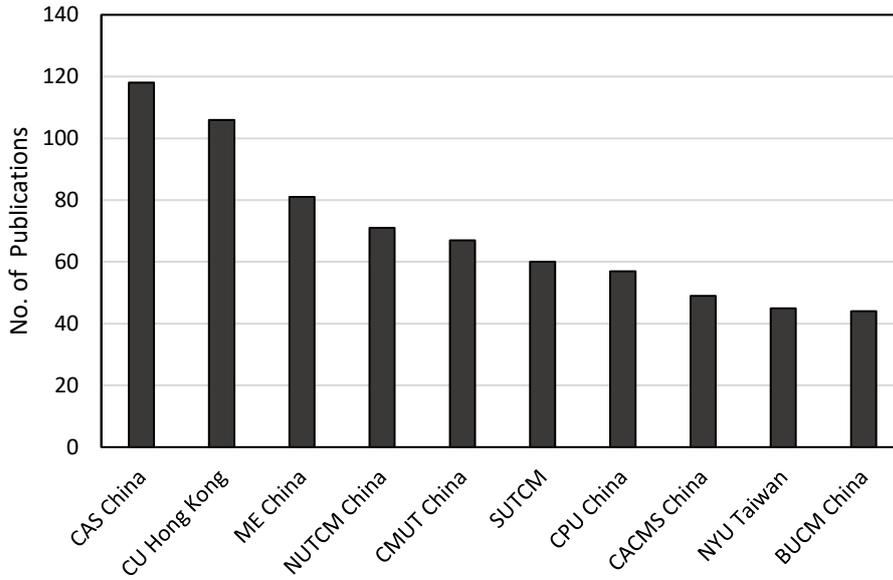
Funding agency	Full name and affiliation
NNSF China	National Natural Science Foundation of China, China's State Council, China
CNDCT Brazil	Conselho Nacional de Desenvolvimento Científico e Tecnológico (National Council for Scientific and Technological Development), Brazil
NBRP (973) China	National Basic Research Program of China (973 program), China
NIH USA	National Institutes of Health, U.S. Department of Health & Human Services. USA
NRF Korea	National Research Foundation of Korea, South Korean Ministry of Culture and Tourism, South Korea
NSC Taiwan	National Science Council, Taiwan
FRFCU China	Fundamental Research Funds for the Central Universities, China
MoST China	Ministry of Science and Technology of the People's Republic of China, China
PAPDJHEI China	Priority Academic Program Development of Jiangsu Higher Education Institutions, China
CAS China	Chinese Academy of Sciences, China

Figure 3 Bar graph analysis of top 10 funding agencies. Top 10 funding agencies that financed the highest number of publications in the field of 'herb drug interactions' were identified and plotted on a bar graph for the years 2011-2019. Full names of funding agencies with abbreviations used in graph are given in the table.



Journal acronym	Journal full name	Location
J Ethnopharmacol	Journal of Ethnopharmacology	Netherlands
Phytother Res	Phytotherapy Research	United States
Evid Based Complement Alternat Med	Evidence Based Complementary and Alternative Medicine	Egypt
Phytomedicine	Phytomedicine	Germany
Planta Med	Planta Medica	Germany
Lat Am J Pharm	Latin American Journal of Pharmacy	Argentina
BMC Complem Altern M	BMC Complementary and Alternative Medicine	United Kingdom
Molecules	Molecules	Switzerland
Food Chem Toxicol	Food and Chemical Toxicology	Netherlands

Figure 4 Top 10 Journals in the field of herb drug interactions during 2011-2019. Journals were classified into top 10 journals on the basis of publication count and plotted in a bar graph. Full journal names with abbreviations used in graph are given in the table.



Abbreviations	Full affiliations
CAS China	Chinese Academy of Sciences, Beijing, China
CU Hong Kong	Chinese University of Hong Kong, Sha Tin, Hong Kong
ME China	Ministry of Education China, Beijing, China
NUTCM China	Nanjing University of Traditional Chinese Medicine, Jiangsu, China
CMUT Taiwan	China Medical University, Taichung, Taiwan
SUTCM China	Shanghai University of Traditional Chinese Medicine, Shanghai, China
CPU China	China Pharmaceutical University, Jiangsu, China
CACMS China	China Academy of Chinese Medical Sciences, Beijing, China
NYU Taiwan	National Yang-Ming University Taipei, Taiwan
BUCM China	Beijing University of Chinese Medicine, Chaoyang, China

Figure 5 Top 10 Affiliations in the field of herb drug interactions during 2011-2019. Author affiliations were ordered according to publication count and plotted in a bar graph. Full affiliations with abbreviations used in graph are given in the table.

Table 1 Top 10 authors in the field of herb drug interactions during 2011-2019. Individual author publications were counted and indexed into the table to produce a list of top 10 authors in the research area during 2011-2019.

Author name	Author affiliation and country	publication count
Ernst, E.	Department of Complementary Medicine, School of Postgraduate Medicine and Health Sciences, University of Exeter, Exeter, United Kingdom	31
Huang, M.	State Key Laboratory of Bioactive Substance and Function of Natural Medicines, Institute of Materia Medica, Chinese Academy of Medical Sciences / Peking Union Medical College, Beijing 100050, China.	23
Hou, Y.C.	Graduate Institute of Pharmaceutical Chemistry, China Medical University, Taichung, 40402, Taiwan.	22
Yang, L.	Laboratory of Pharmaceutical Resource Discovery, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian, China.	22
Zhou, S.F.	Discipline of Chinese Medicine, School of Health Sciences, RMIT University, Victoria, Australia.	21
Duan, J.A.	Jiangsu Key Laboratory for High Technology Research of TCM Formulae, Nanjing University of Chinese Medicine, Nanjing 210046, China	20
Fang, Z.Z	Laboratory of Pharmaceutical Resource Discovery, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian, China.	19
Gurley, B.J	Department of Pharmaceutical Sciences, University of Arkansas for Medical Sciences, College of Pharmacy, Little Rock, AR 72205, USA.	19
Tsai, T.H	Laboratoire de Toxicologie Cellulaire, EA 4267, IFR 133, UFR Pharmacie, Place Saint-Jacques, 25030 Besançon, France.	19
Yeung, J.H.K	School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong, China.	19

Table 2 Top three publications during 2011-2019 based on the citation count as in Nov 2019 authors in the field of herb drug interactions. An extensive analysis of original research and review articles during the time period was performed to identify the three publications with the highest citation count.

Article	Year of publishing	# Citations
Structure and dynamics of molecular networks: a novel paradigm of drug discovery: a comprehensive review. Csermely P, Korcsmáros T, Kiss HJ, London G, Nussinov R. <i>Pharmacol Ther.</i> Jun;138(3):333-408.	2013	445
A review on therapeutic potential of <i>Nigella sativa</i> : A miracle herb. Ahmad A, Husain A, Mujeeb M, Khan SA, Najmi AK, Siddique NA, Damanhoury ZA, Anwar F. <i>Asian Pac J Trop Biomed.</i> 2013 May;3(5):337-52.	2013	339
TCMSP: A database of systems pharmacology for drug discovery from herbal medicines. Ru J, Li P, Wang J, Zhou W, Li B, Huang C, Li P, Guo Z, Tao W, Yang Y, Xu X, Li Y, Wang Y, Yang L. <i>J Cheminform.</i> 2014 Apr 16;6:13.	2014	297

Table 3 Top 20 publications of all time based on the citation count as in Nov 2019 authors in the field of herb drug interactions. Top research and review articles of all time based on citation count on the day of the search with term ‘herb drug interactions’ were collected and indexed in the table.

S. No.	Article	Article type	Year of publishing	# Citations
1	Danshen: An overview of its chemistry, pharmacology, pharmacokinetics, and clinical use. Zhou L, Zuo Z, Chow MS. J Clin Pharmacol. 2005 Dec;45(12):1345-59.	Review	2005	931
2	Herb-drug interactions. Fugh-Berman A. Lancet. 2000 Jan 8;355(9198):134-8.	Review	2000	901
3	Complementary/ alternative medicine use in a comprehensive cancer center and the implications for oncology. Richardson MA, Sanders T, Palmer JL, Greisinger A, Singletary SE. J Clin Oncol. 2000 Jul;18(13):2505-14.	Research	2000	778
4	Herbal medicines and perioperative care. Ang-Lee MK, Moss J, Yuan CS. JAMA. 2001 Jul 11;286(2):208-16.	Review	2001	730
5	Herbal medicinals: Selected clinical considerations focusing on known or potential drug-herb interactions. Miller LG. Arch Intern Med. 1998 Nov 9;158(20):2200-11.	Review	1998	692
6	Synergy and other interactions in phytomedicines. Williamson EM. Phytomedicine. 2001 Sep;8(5):401-9.	Review	2001	557
7	Interactions between herbal medicines and prescribed drugs: A systematic review. Izzo AA, Ernst E. Drugs. 2001;61(15):2163-75.	Review	2001	553
8	Pharmacokinetic interaction of digoxin with an herbal extract from St John’s wort (<i>Hypericum perforatum</i>). Johne A, Brockmüller J, Bauer S, Maurer A, Langheinrich M, Roots I. Clin Pharmacol Ther. 1999 Oct;66(4):338-45.	Research	1999	524
9	Free-radical scavenging action of medicinal herbs from Ghana: <i>Thonningia sanguinea</i> on experimentally-induced liver injuries. Gyamfi MA, Yonamine M, Aniya Y. Gen Pharmacol. 1999 Jun;32(6):661-7.	Research	1999	495
10	Harmless herbs? A review of the recent literature. Ernst E. Am J Med. 1998 Feb;104(2):170-8.	Review	1998	490
11	A genetic framework of the control of cell division and differentiation in the root meristem. Dello Ioio R, Nakamura K, Moubayidin L, Perilli S, Taniguchi M, Morita MT, Aoyama T,	Research	2008	486

	Costantino P, Sabatini S. Science. 2008 Nov 28;322(5906):1380-4			
12	Herb-drug interactions: A literature review. Hu Z, Yang X, Ho PC, Chan SY, Heng PW, Chan E, Duan W, Koh HL, Zhou S. Drugs. 2005;65(9):1239-82.	Review	2005	482
13	Structure and dynamics of molecular networks: a novel paradigm of drug discovery: a comprehensive review. Csermely P, Korcsmáros T, Kiss HJ, London G, Nussinov R. Pharmacol Ther. Jun;138(3):333-408.	Review	2013	445
14	The risk-benefit profile of commonly used herbal therapies: Ginkgo, St. John's wort, ginseng, echinacea, saw palmetto, and kava. Ernst E. Ann Intern Med. 2002 Jan 1;136(1):42-53.	Review	2002	407
15	Interactions between herbal medicines and prescribed drugs: an updated systematic review. Izzo AA, Ernst E. Drugs. 2009;69(13):1777-98	Review	2009	396
16	Cardiovascular effects of Danshen. Cheng TO. Int J Cardiol. 2007 Sep 14;121(1):9-22.	Review	2007	369
17	Herbal remedies in the United States: Potential adverse interactions with anticancer agents. Sparreboom A, Cox MC, Acharya MR, Figg WD. J Clin Oncol. 2004 Jun 15;22(12):2489-503.	Review	2004	354
18	A review on therapeutic potential of Nigella sativa: A miracle herb. Ahmad A, Husain A, Mujeeb M, Khan SA, Najmi AK, Siddique NA, Damanhoury ZA, Anwar F. Asian Pac J Trop Biomed. 2013 May;3(5):337-52.	Review	2013	339
19	Degradation of ginsenosides in humans after oral administration. Tawab MA, Bahr U, Karas M, Wurglics M, Schubert-Zsilavecz M. Drug Metab Dispos. 2003 Aug;31(8):1065-71.	Research	2003	337
20	Investigation of the interaction between Berberine and human serum albumin. Hu YJ, Liu Y, Xiao XH. Biomacromolecules. 2009 Mar 9;10(3):517-21.	Research	2009	336