

Research Articles

Knowledge map of artemisinin research in SCI and Medline database

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ABSTRACT

Background & objectives: Artemisinin was first extracted from the herb *Artemisia annua* which has been used for many centuries in Chinese traditional medicine as a treatment for fever and malaria. It has been given the 2011 Lasker-DeBakey clinical medical research award. In this paper, knowledge map of artemisinin research was drawn to provide some information for global researchers interested in artemisinin and its relevant references.

Methods: In this work, bibliometric analysis and knowledge visualization technology were applied to evaluate global scientific production and developing trend of artemisinin research through Science Citation Index (SCI) papers and Medline papers with online version published as following aspects: publication outputs, subject categories, journals, countries, international collaboration, citations, authorship and co-authorship, author key words and co-words analysis. The Thomson Data Analyzer (TDA), Netdraw and Aureka software were employed to analyze the SCI as well as Medline papers data for knowledge mapping.

Results: Global literature of artemisinin research has increased rapidly over the past 30 years and has boosted in recent years. Seen from the statistical study in many aspects, Pharmacology & Pharmacy, and Chemistry are still the main subjects of artemisinin research with parasitology and tropical medicine increasing quickly. *Malaria Journal* and *American Journal of Tropical Medicine* are top productive journals both in SCI and Medline databases. Quantity and quality of papers in US are in a leading position, although papers quantity and active degree in developing countries such as P.R. China, Thailand and India are relatively high, the quality of papers from these countries needs to be improved. New emerging key words and co-words remind us that mechanism of action, pharmacokinetics, artemisinin-based alternatives, etc. are the future trends of artemisinin research.

Conclusion: Through bibliometric analysis the development trends of artemisinin research are predicted. With further development of artemisinin research, it is presumed that scientists might concentrate mainly on the synthesis of new compounds with activity, action mechanism, new artemisinin-based combination therapy regimens, etc.

Key words Artemisinin; bibliometric analysis; co-authorship; co-words; knowledge mapping; research trend

INTRODUCTION

Artemisinin (called QingHaoSu in Chinese, also short for QHS), is an antimalarial drug used as a treatment for fever and malaria from Chinese traditional medicine and used in China for many centuries¹. It was first isolated from the leafy portions of the herb *Artemisia annua* responsible for its reputed medicinal action by Chinese scientist You-you Tu and her team in 1971^{2,3}. In recognition of her invention of “artemisinin for treating malaria in the world, especially for developing countries to save the lives of millions of people”, Professor Tu Won the Lasker-DeBakey clinical medical research award in 2011.

Artemisinin is the most effective antimalarial medicine following chloroquine, pyrimethamine, primaquine

and sulfanilamide⁴, especially in the treatment of cerebral malaria and chloroquine-resistant malaria with the characteristics of promptness and low toxicity⁵. In 2001, the World Health Organization (WHO) recommended that countries where malaria is resistant to conventional treatments such as chloroquine should switch to artemisinin-based combination therapies (ACTs)⁶. Since then ACT has made a significant contribution to malaria control and has reduced disease transmission effect in the world⁷.

In addition to antimalarial properties, many researchers have confirmed that artemisinin has many other important pharmacological effects including antitumor, antibacterial, antifibrosis and immune function regulation in recent years⁸. Among them, antimalaria, antitumor, and immune function regulation were paid more attention^{9,10}.

Because of its special clinical application, artemisinin attracts attentions from several fields, such as its derivatives, pharmacological action, clinical application, extract methods, synthesis route, therapy scheme, etc¹¹. Although artemisinin is a common drug for pharmaceutical researchers, there are many aspects that need to be explored deeply. Especially for its long-term application in the treatment of malaria, artemisinin may have risks of drug resistance, are there some other derivatives or substances can relieve resistance or improve the remedy effect? To benefit for clinical therapy of malaria, tumor and some inflammatory-immune diseases, invention of new action mechanisms and targets of artemisinin are important. Hence, deep research on artemisinin is needed to grasp its previous studies and to develop trends for its more extensive application fields in future.

Up to now, a lot of papers on artemisinin in several languages have been published, and many vital SCI papers and Medline papers have reported new findings. Hence, bibliometric methods were employed to investigate the artemisinin-related literature, expecting to overview all the studies in the world. The bibliometric techniques are already widely used in quantitative evaluation of scientific and technological productivities, journal qualities, research agencies, institutes of science and technology and the research level of the country¹². In this study, SCI papers as well as the Medline papers of artemisinin research productivity with short but uneasy history were investigated using bibliometric methods. Here, the global scientific productions on artemisinin research from the following aspects were discussed: global publication outputs, subject categories, journals, countries, citations, author key words and co-words, authorship and co-authorship, etc. Though information from two databases may not contain all, quantitative analysis of global artemisinin research will be beneficial for understanding its historical development, forecasting its future development trends and directions, and providing references for the scholars or institutions committed to artemisinin research¹³.

MATERIAL & METHODS

Data source

The data were retrieved on 1st July 2012 from Science Citation Index-Expanded (SCI-E) and the Medline database with an online version, which is operated by Thomson Reuters, Philadelphia, PA, USA. The retrieval strategies were arranged as topic="artemisinin or arteannuin or qinghaosu or QHS" with the time span by the end of 2011. In all, 4076 SCI papers and 4065 Medline

papers were available from the databases respectively.

Because SCI or Medline papers are the database with high quality on the subjects, standing the best one in the world of medicine-related research, the results of these papers are believable. SCI database has more papers with high quality, medical articles included largely in Medline database will be more targeted for medicinal and pharmaceutical research. The scientists of artemisinin research will get most of the literature or overviews of publications from the later. Only the papers published in so called core journals were included in the database of Web of Science (WoS, including SCI & Medline database), therefore, most of the articles collected from the core journals in SCI and Medline databases for statical analysis were of typical illustration for analyzing on global artemisinin research trend.

Bibliometric methods

Bibliometric analysis¹⁴, which was a branch of intelligence science was firstly proposed by Alan Pritchard in 1969, has previously been employed as a mathematical and statistical method to describe productivity of science and technology and the development of research¹⁵, evaluating and predicting the relative research with geographic variation in outputs and findings¹⁶. The primary assumption supporting the use of bibliometrics is that the exchange and recognition of research results are one of the key driving forces desired in the advancement of science¹².

Lots of statistical methods and corresponding software were developed to describe the total literature in an overview angle^{17, 18}. The Thomson Data Analyzer (TDA) is one of these softwares which can be used for statistics of thousands of data¹⁹. In this work, the artemisinin related research papers were downloaded from the database in the form of simple text and soon read into TDA. Then the data were conversed into a matrix for some special need, at this stage the production of the data were re-ordered by time or space. In next stage, it was led into the software named Netdraw to perform a net to show cooperations among some countries or institutes to visualize the relationship better and the entire key words matrix was read into the software of Aureka to get a contour map, which called knowledge mapping technology^{20, 21}. The map of key words can forecast the future trend of a science subject well²².

In this study, the publications, subjects, collaborations, time cited, co-words, clusters of SCI papers and Medline papers were thoroughly examined. The TDA, Netdraw and Aureka software were employed to analyze the data of SCI papers as well as Medline papers for knowledge mapping²³.

RESULTS & DISCUSSION

In this part, papers from SCI and Medline databases were analyzed together by using bibliometric method, figures and tables were used to describe the production of artemisinin research and will contribute to give the current status of artemisinin-related research.

Global publication output

The publication outputs of artemisinin research from 1980 to 2011 are shown in Fig. 1. During the past decades both SCI and Medline papers on artemisinin research increased from 1 in 1980 to >400 after 2010. It can be seen from the figures that not many researchers paid their attention to artemisinin research before 1990, and only a few papers were produced in this time span. From 1990 to 2000 some scientists turned their attention to artemisinin research, so progress in the effect, mecha-

nism of action, molecular structure and its determination method, structure modification and synthesis of artemisinin had been reported much more^{22, 24–26}. The annual number of papers on artemisinin research in China has increased steadily after 2000. In 2001, WHO recommended ACTs to malignant malaria prevalence to all the countries and the number of papers rose rapidly to more than two fold. The annual number of publications grew exponentially from 2004, indicating that the research on artemisinin has attracted more and more attention recently.

Subject categories of articles

Based on the classification of subject categories in Journal Citation Reports (JCR) of Thomson Reuters, the publication output data of artemisinin were distributed in >80 subject categories during the past 3 decades. Subject categories containing at least 500 articles are shown in Fig. 2. The five most productive subjects were all branches

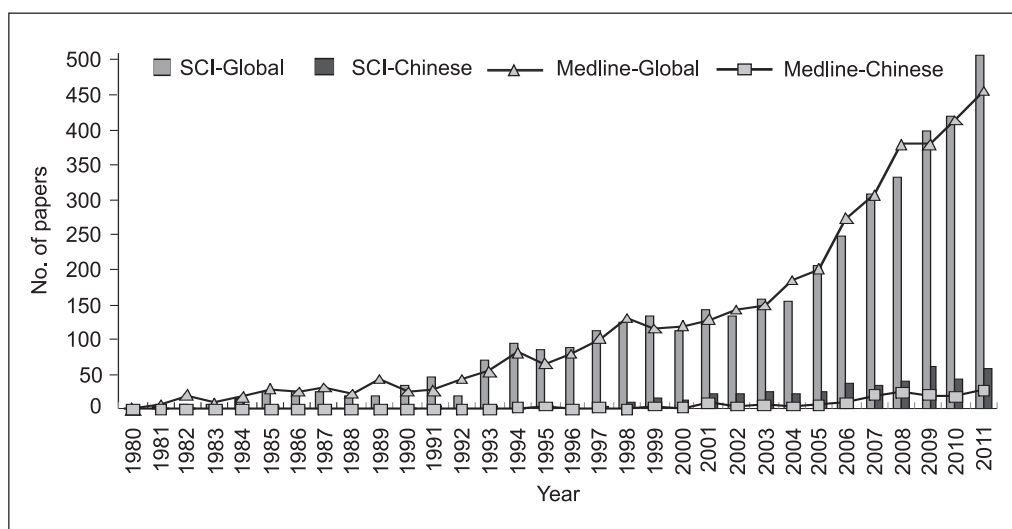


Fig. 1: SCI and Medline papers published from 1980 to 2011.

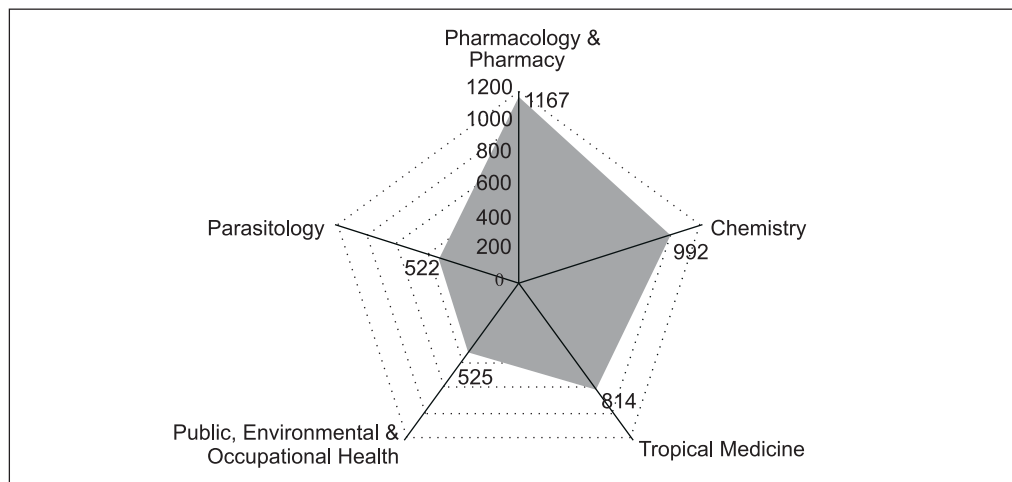


Fig. 2: Main subjects of SCI papers on artemisinin.

of medical science and produced 85% of the artemisinin publications. The artemisinin researches on the subjects of pharmacology & pharmacy and chemistry occupy a dominant position from the outset. Figure 3 shows that artemisinin research is mainly distributed in the fields of pharmacology & pharmacy and chemistry mainly with some research in the areas of tropical medicine, public, environmental & occupational health and parasitology (other top subjects such as biochemistry & molecular biology, plant sciences, microbiology and infectious diseases are also involved).

Since artemisinin was proven to treat malaria well in 1971^{6,20}, scientists tend to focus on the research of chemical composition and pharmacology for drug development, which can benefit malarial patients all over the world. Moreover, present studies use more and more approaches on pharmacology^{27–29}. There was a period of rapid growth after 2004 in all subjects which may be related to WHO's declaration that a surge in demand led to the shortage of artemisinin-based combination therapy for malaria in 2004. In 2009's "World Malaria Report", it was showed that antimalarial drugs have failed in most parts of the world because of parasite resistance³⁰, which would threaten malaria control as shown in Fig. 3. Artemisinin resistance in *Plasmodium falciparum* was found in Kampuchea and Thailand border zone. Therefore, the study in the fields of parasitology and tropical medicine exceed that of chemistry in recent 3 years gradually, which shows that pharmacology & pharmacy associated with parasitology and tropical medicine would be the mainstream of artemisinin research and development in the coming days.

Journals of research publication

In JCR 2011, 7387 journals were listed in SCI with 402 journals in the field of medicine. Artemisinin research outputs were published in 720 journals while the journals with >50 articles with its Impact Factor (IF) in 2011 are displayed in Fig. 4, where the lighter columns are for SCI papers and darker columns for Medline papers. Approximately 27% of the SCI papers resided in these most productive top 10 journals, which are considered the core journals of artemisinin research area under Bradford Law^{31,32}. Similarly, artemisinin research output in Medline was published in 662 journals and journals with >50 articles with its Impact Factor (IF) in 2011. More than 32% of Medline papers resided in the top 12 most productive journals. In addition, *Malaria Journal* and *American Journal of Tropical Medicine and Hygiene* are top productive journals both in SCI and Medline databases.

From the annual distribution of papers (Fig. 5, and Table 1) of which the frontier columns for SCI papers and backer columns for Medline papers, it can be seen that the published articles from *Malaria Journal* which started in 2004 produced rapidly from 3 to 73 in SCI database while from 5 to 76 in Medline database during 2004 to 2011. The *American Journal of Tropical Medicine and Hygiene* and *Transactions of the Royal Society of Tropical Medicine and Hygiene* published articles with a fluctuant growth during this period. However, publication of other journals increased slowly while steadily in these years. From the above analysis it can be expected that *Malaria Journal* will be the primary journal for artemisinin research publication in future.

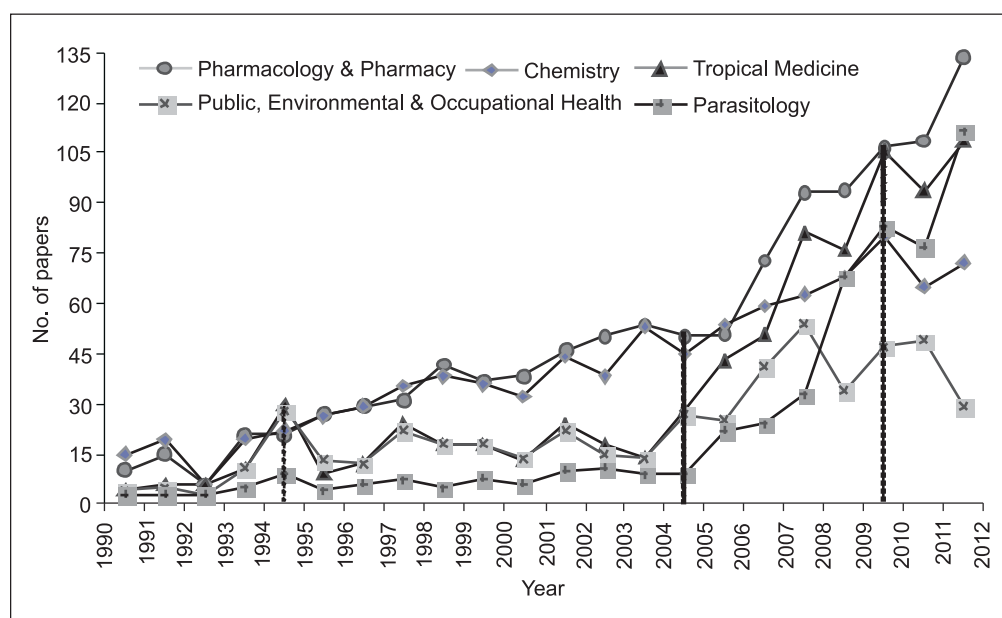


Fig. 3: Annual distribution of SCI papers in different subject categories.

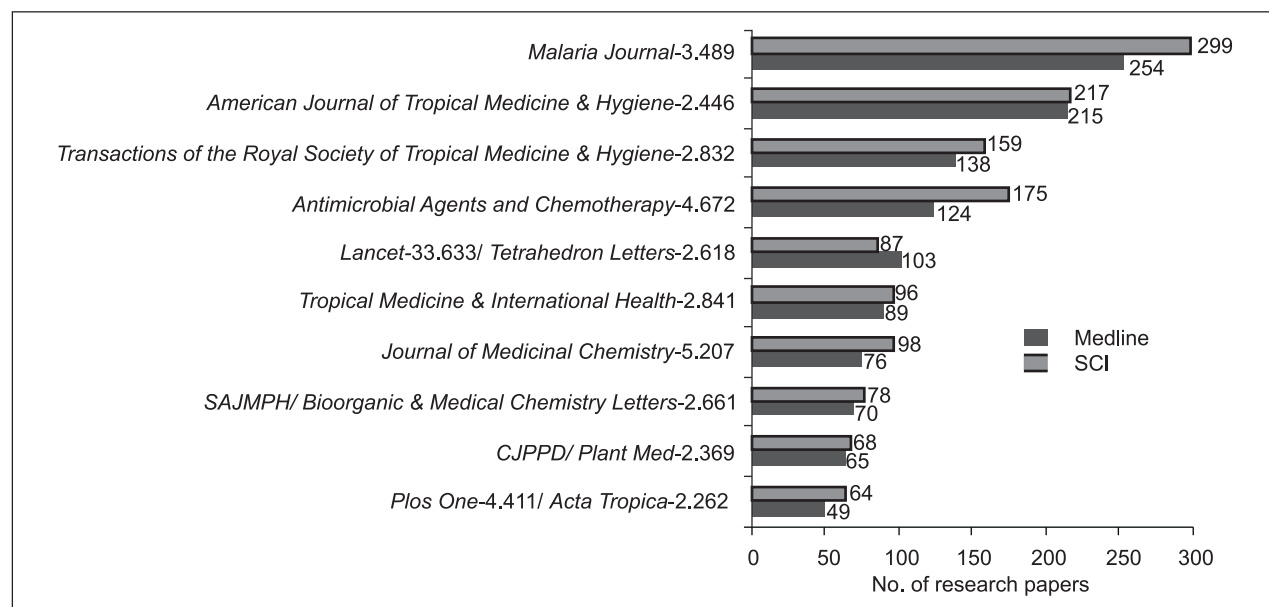


Fig. 4: Top 10 productive journals of SCI and Medline papers on artemisinin.

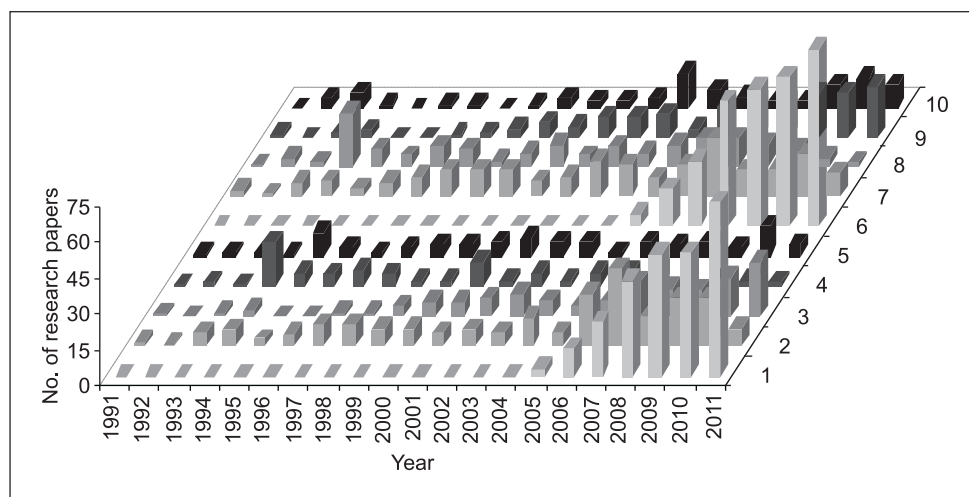


Fig. 5: Annual journals distribution of SCI and Medline papers on artemisinin.

Table 1. Top 5 SCI and Medline journals that published research papers on artemisinin

No.	Journals
<i>SCI</i>	
1.	<i>Malaria Journal</i>
2.	<i>American Journal of Tropical Medicine and Hygiene</i>
3.	<i>Antimicrobial Agents and Chemotherapy</i>
4.	<i>Transactions of the Royal Society of Tropical Medicine and Hygiene</i>
5.	<i>Journal of Medicinal Chemistry</i>
<i>Medline</i>	
6.	<i>Malaria Journal</i>
7.	<i>The American Journal of Tropical Medicine and Hygiene</i>
8.	<i>Transactions of the Royal Society of Tropical Medicine and Hygiene</i>
9.	<i>Antimicrobial Agents and Chemotherapy</i>
10.	<i>Lancet</i>

Citation analysis of productions

The total citation count obtained from SCI database shows that the total time that a particular article was cited by other research work listed in this database. The number of citations does not necessarily indicate the quality of a paper, but it is a measure of its impact and/or visibility in this field. The top 10 most frequently cited articles (>320 times) from 1981 to 2011 were selected (Table 2). The most frequently cited article was “Qinghaosu (Artemisinin): An antimalarial drug from China” written in 1985 by Klayman D.L. It has been cited 1140 times since published in the journal *Science*, which vastly exceeds the citation of the other articles. Meanwhile, Meshnick S.R. from Michigan State University contributed the highest contribution (No. 5 and 10) of articles

Table 2. Top 10 cited SCI papers on artemisinin research

No. of citations	Authors	Title	Journal	Institute	Country	Year
1140	Klayman DL	Qinghaosu (Artemisinin): An antimalarial drug from China	Science	Walter Reed Army Inst Res	USA	1985
471	Meunier B, de Visser SP, Shaik S	Mechanism of oxidation reactions catalyzed by cytochrome P450 enzymes	Chemical Reviews	CNRS, Chim Coordinat Lab	France	2004
448	Reed MB, Saliba KJ, Caruana SR, Kirk K, Cowman AF	Pgh1 modulates sensitivity and resistance to multiple antimalarials in <i>Plasmodium falciparum</i>	Nature	Walter & Eliza Hall Inst Med Res, Melbourne	Australia	2000
387	Eckst Medlinen-Ludwig U, Webb RJ, van Goethem IDA, East JM, Lee AG, Kimura M, <i>et al</i>	Artemisinins target the SERCA of <i>Plasmodium falciparum</i>	Nature	St George Hosp	England	2003
383	Meshnick SR, Taylor TE, Kamchonwongpaisan S	Artemisinin and the antimalarial endoperoxides: From herbal remedy to targeted chemotherapy	Microbiological Reviews	Michigan State Univ	USA	1996
380	Hien TT, White NJ	Qinghaosu	Lancet	Cho Quan Hosp	Vietnam	1993
378	Ro DK, Paradise EM, Ouellet M, Fisher KJ, Newman KL, Ndungu JM, Ho KA, Eachus, RA, <i>et al</i>	Production of the antimalarial drug precursor artemisinic acid in engineered yeast	Nature	Univ Calif Berkeley	USA	2006
366	Ridley RG	Medical need, scientific opportunity and the drive for antimalarial drugs	Nature	Med Malaria Venture	Switzerland	2002
345	Francis SE, Sullivan DJ, Goldberg DE	Hemoglobin metabolism in the malaria parasite <i>Plasmodium falciparum</i>	Annual Review of Microbiology	Howard Hughes Med Inst	USA	1997
321	Wongsrichanalai C, Pickard AL, Wernsdorfer WH, Meshnick SR	Epidemiology of drug-resistant malaria	Lancet Infectious Diseases	Armed Forces Res Inst Med Sci	Thailand	2002

among the 10 most frequently cited articles, which exhibited his predominance too. Among the top 10 cited papers, USA contributed four while P.R. China held zero.

Table 2 also shows that, except for the article on artemisinin origins being the most cited one, other articles cited (published after 2000) focused on the action mechanism of artemisinin, preparation process and epidemiological research. In addition, articles published from 1990s on artemisinin-based antimalarial treatment and researches of pathological basis have been cited more because these were produced earlier than the followers.

Countries of publication and their citations

The outputs of SCI articles on artemisinin from different countries are presented in Fig. 6, where the lighter columns are for SCI papers and darker columns are for Medline papers. The most active country is USA, fol-

lowed by England, P.R. China, Thailand and Switzerland in turn. The numbers of publications from other countries are all below 300. Meanwhile, the outputs from the Medline database are presented in Fig. 6, among which the USA (took ratio of 23%) is still the top country in artemisinin publications. The rank of Medline publications from Thailand, P.R. China and India is better than that of SCI publications respectively. However, UK ranks only sixth in Medline publications with 64 papers.

Figure 7 shows top 5 productive countries in SCI (backer) and Medline (frontier) papers publication during the last 21 years in the world, during which the number 1, 6 stand for USA, 3, 8 for P.R. China, 4, 7 for Thailand, 2 for England, 5 for Switzerland, 9 for India and 10 for France. It can be concluded that artemisinin research started in most countries in the 1990s and boosted after 2003. Peoples' Republic of China and England began

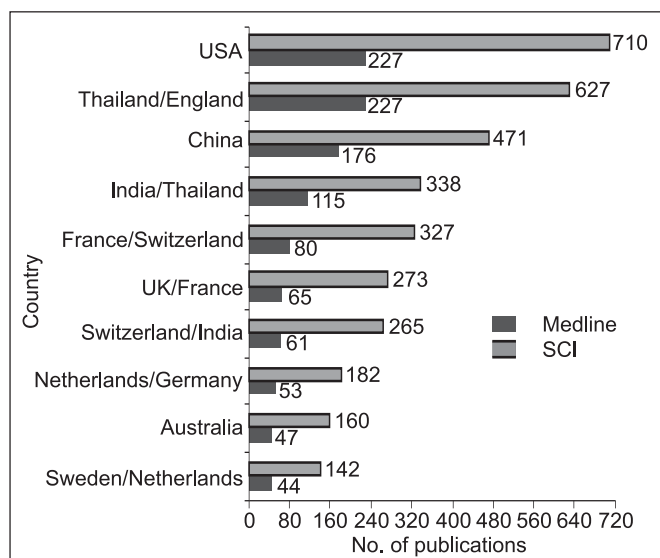


Fig. 6: Top productive countries of SCI and Medline papers published on artemisinin.

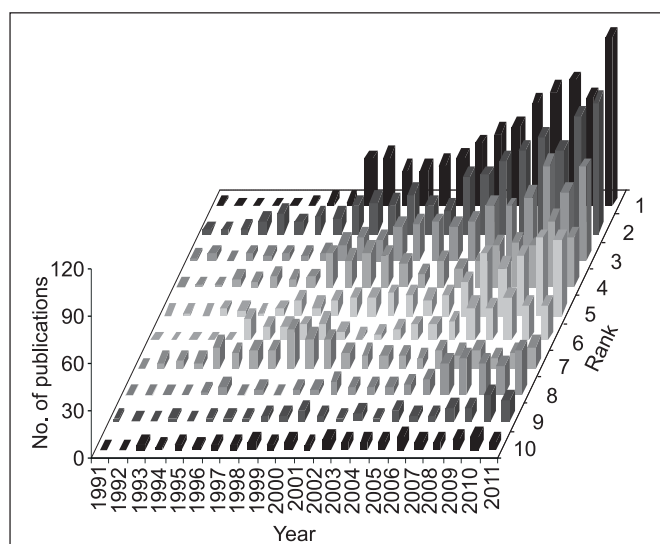


Fig. 7: Annual SCI and Medline publications distribution of top 5 countries.

artemisinin research before 1990s and kept a steady increase during the following years. Compared with USA and England, P.R. China started early but dropped behind in SCI papers publication in the last decade. USA was the leading country during the last decade with a dramatic increase of three times in SCI papers published. In contrast, it also shows that USA, Thailand, P.R. China and Switzerland experienced ups and downs in artemisinin research production before experiencing a great change, during which Thailand's research papers published were unrushed in recent years. However, USA and P.R. China's papers increased quickly with two peaks in the figure while other countries increased slowly during this period.

Figure 8 shows the proportion of paper quantity from countries/regions for the issued volume of the top 5 pro-

ductive countries during 2009–11, during which the darker columns are for SCI papers and lighter columns are for Medline papers. The proportion of the production in recent three years to all the years' publication was called active degree. The most active country was Switzerland with a ratio of 41%. Active degrees of other countries were also >30% for SCI papers. Meanwhile Fig. 8 displays the active degree distribution of the top 7 productive countries of Medline publications. From the distribution view, France is the most active country in the research of artemisinin in the past three years with a high proportion of 39% for Medline papers. The United Kingdom and Thailand also have exceeded 30%. Although USA dispatches the highest quantity, its active degree is only 28% recently. The Thailand, United States and other countries may become the core production countries of artemisinin research in near future. It can also be said that artemisinin research is still a hot field in the world today and is likely to increase constantly.

Figure 9 shows the information of the total and average citation frequencies of the research papers from the top 14 countries in the field of artemisinin research. It can be seen that total citation count in England was highest, followed by the USA, Thailand, P.R. China and Switzerland in turn. The citations per paper sorted in descending order, are the Netherlands, Thailand, England, USA and Australia. England, USA and Thailand are on the front ranks both in the issued number of papers and in total or average citation frequency, showing their superiority in artemisinin research. The Netherlands ranks seventh in issued number of papers and first in article citation frequency, which indicates the high quality of the papers published in the Netherlands. Peoples' Republic of China

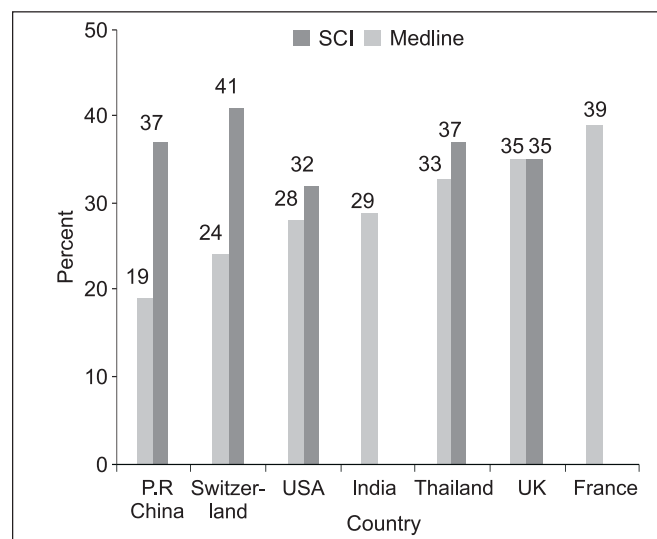


Fig. 8: Active degree for different countries of SCI and Medline publications on artemisinin.

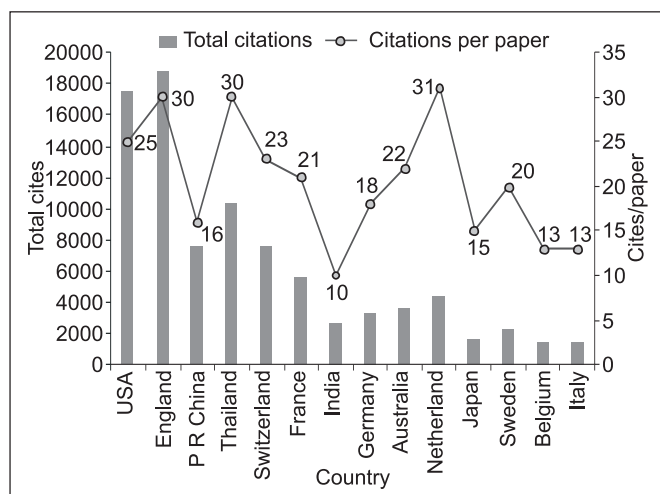


Fig. 9: Top citations of SCI papers for top countries.

ranks fourth in issued volumes with lower article citation frequencies, which from another point of view may show that there is a considerable problem with the quality of Chinese papers issued.

Author affiliation of paper production

As we can see in Fig. 10, there are 14 institutes with paper quantity of more than 20 as the first author's agency. Chinese Academy of Sciences and Thailand Mahidol University performed well as these are the two most powerful institutions in artemisinin research. Chinese Academy of Sciences has published 93 papers, ranking first and is followed by the Thailand Mahidol University with 80 papers. Issuing quantity of other institutions listed are the US University of Mississippi, British University of Liverpool, and French National Center for Scientific Research. United States has four institutes among these productive institutions; UK and Switzerland both have two,

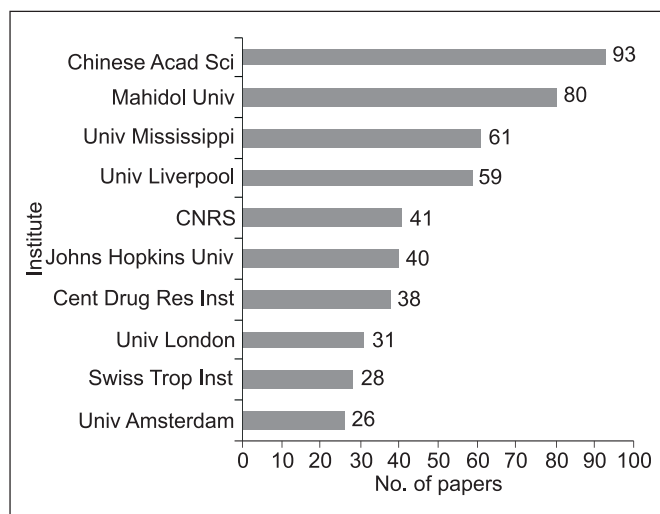


Fig. 10: Top productive institutes of SCI papers.

while P.R. China, Thailand, India, France, Netherlands, Australia and other countries have only one each. This reflects the strong overall strength of the US agencies.

Authorship and co-authorship analysis

According to the national/regional cooperation degree, the national cooperative network map of artemisinin research has been drawn in Fig. 11. As shown in the figure above, a total network of higher density illustrates the cooperation between countries³³. United States of America, England and Thailand cooperate frequently with other countries/regions and stand as the core position of the entire network, which benefit from the knowledge transfer among artemisinin. USA, which has issued the most volumes, and other countries such as Germany, France and Switzerland are in the peripheral layer. Other countries like India, Japan, Italy and Netherlands have less cooperation with other countries/regions, so they are in the outermost layer of the entire cooperation network.

The cooperative network map of organizations in artemisinin research is also drawn according to the cooperation between institutions in Fig. 12. The UK's University of Oxford, London School of Hygiene & Tropical Medicine, the American University of California San Francisco and Mahidol University, the Centers for Disease Control and Prevention are in the core status of the network; these institutions cooperate with other organizations frequently, which play an important role in the process of knowledge transfer in the world. Other high yield institutions such as the Chinese Academy of Sciences and the French National Center for Scientific Research, the Central Drug Research Institute, Swiss Tropical Institute, University of Amsterdam and University of

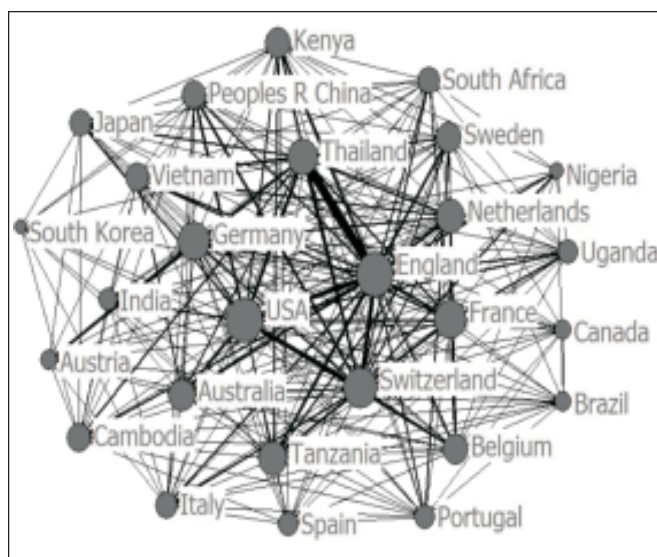


Fig. 11: Co-authorship for SCI publications in different countries.

Table 3. Key words distribution of SCI papers on artemisinin research

Authors' Key words	Artemisinin	Malaria	<i>Plasmodium falciparum</i>	Artesunate	<i>Artemisia annua</i>	Dihydroartemisinin	Antimalarial
Records	688	470	222	159	138	117	112
Rate (%)	36	25	12.4	8.3	7.2	6.2	5.9

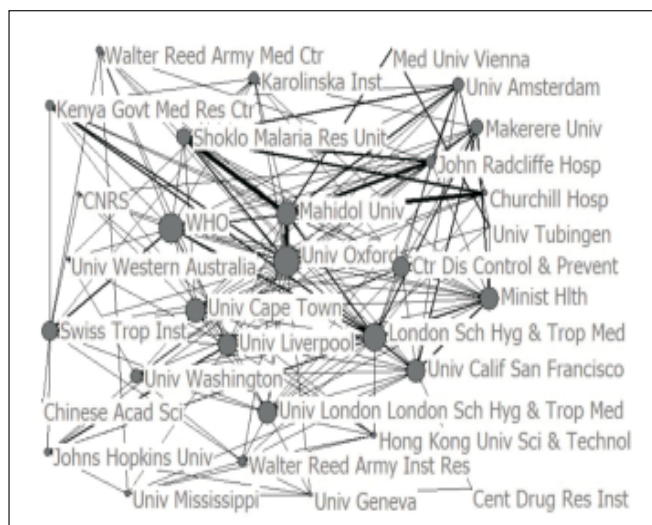


Fig. 12: Co-authorship for SCI publications in different institutes.

Geneva are at the edge of the network due to their less cooperation. It can be concluded that British and American institutions have great advances in the paper production and cooperation, with great strength and good development prospects.

Author key words and co-words study

The technique of statistical analysis of key words

and title-words may indicate directions of research. Especially, authors' key words analysis could offer the information of research trends as view points by researchers³⁴. The examination of authors' key words in this study shows that 1671 authors' key words were used from 1980 to 2011. Table 3 lists the 7 most used authors' key words with their rankings and percentages, other low frequently used words were neglected.

Figure 13 shows the most frequently used authors' key words distributed from 1991 to 2011. During the past decades the key word "artemisinin" was used 80 times thereby becoming the most dominant key word used in the research. "Malaria" was the second most frequently used key word with both of them having high increasing rates. It was also found that combined therapy with artesunate ester and artemether has good curative effect in the treatment of multiple drug resistant falciparum malaria³⁵, so "*Plasmodium falciparum*" and "artesunate" were also the relatively hot key words in the past 20 yr. In addition, with deeper study of artemisinin and its derivatives and further attention to malaria remedy paid by the international society, "dihydroartemisinin", "antimalaria" and "artemether" have become the new emerging key words in artemisinin-related research. The extremely high increasing rate in the ranking of key words shows the importance

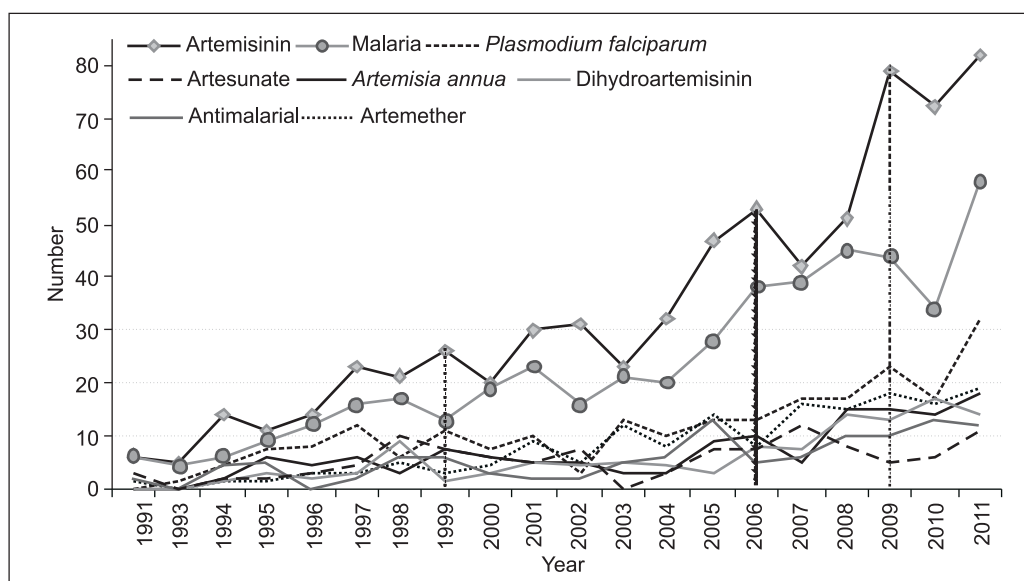


Fig. 13. Annual distribution of key words appeared in the period of 1991–2011.



Fig. 14: Clusters and co-words map of SCI papers on artemisinin.

of these and the new emerging key words might be the next new focus.

The topic of papers can be obtained from the author key words by cluster analysis. Clusters or co-words map of articles could image the core competency of the artemisinin research. Figure 14 was derived from bibliometric analysis on the papers of artemisinin of SCI. It can be seen that these topics listed were hot ones in artemisinin research: clinical research (uncomplicated combination therapy and its efficiency, drug resistance discovery), pharmacokinetic (worm, daily doses and liquid plasma), action mechanism (cells apoptosis induces), and substitution of artemisinin (radical reactions, alkyl radicals, synthesis of arteannuin analogs and *Artemisia*

annua plants). These research fields will be the next potential technology applications and worth more attention.

Figure 15 was derived from bibliometric analysis on the papers of artemisinin in Medline database. It can be seen that topics such as treatment (artemisinin-based combination therapy, other antimalaria drugs like quinine for treating patients fever, schistosoma worms, etc.), pharmacokinetics (by uncomplicated trial of plasma detection), action mechanism (including mutational gene isolates, cancer cell activity) and pharmacy (*Artemisia annua* plants, *in vitro* isolation of mefloquine and preparation of artemisinic acid) were hot topics of artemisinin research. This conclusion is consistent with that by analysis on the cluster and co-words map of SCI papers.

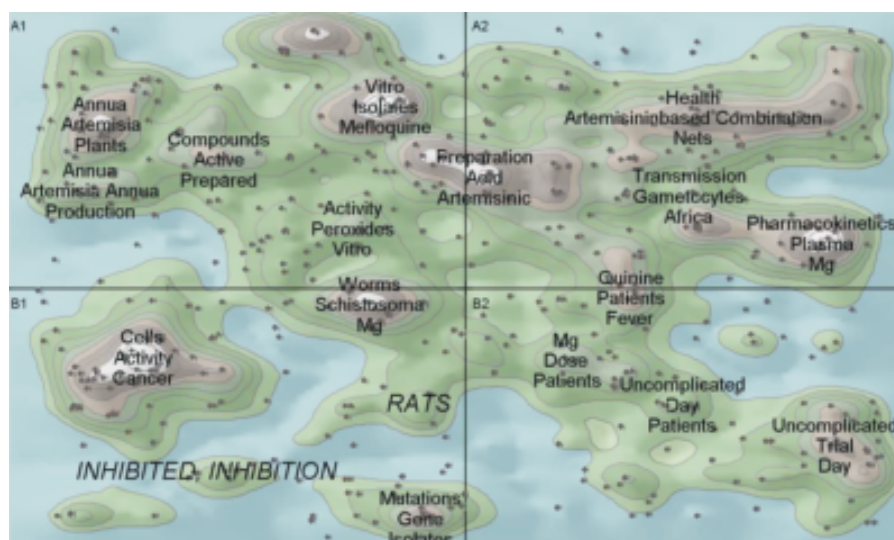


Fig. 15: Clusters and co-words map of Medline papers on artemisinin.

CONCLUSION

A bibliometric analysis on global artemisinin research trend was conducted in this paper to trace artemisinin's extension in the research field of medicine. The research on artemisinin boosted in recent 8 yr from it's been isolated 30 yr ago. This statistical study of the literatures based on SCI and Medline databases illustrated the history and current situation for artemisinin research all over the world. Some countries such as USA, England, P.R. China as well as Thailand, and some institutes such as Chinese Academy of Sciences, Oxford University and Mahidol University produced much in artemisinin research. Quantity and quality of papers in USA are in a leading position, although papers quantity and active degree in developing countries such as P.R. China, Thailand and India are relatively high, their quality of papers needs to be improved.

Meanwhile through this work the development trend of artemisinin research is predicted. New emerging key words and co-words remind us that mechanism of action, pharmacokinetics, artemisinin-based alternatives are the trends of future artemisinin research. The statistical results in many aspects prove that artemisinin research is located on the subjects of pharmacology & pharmacy, chemistry with parasitology and tropical medicine, which in consistent with the results that the *Malaria Journal*, *American Journal of Tropical Medicine and Hygiene*, and *Transactions of the Royal Society of Tropical Medicine and Hygiene* are the top productive journals both in the SCI and Medline database. So the future research of artemisinin will locate on the mechanism and alternatives, researchers should pay more of their attention to these directions and new publications in these top journals.

These results will benefit scientists who study artemisinin or who will publish their research work. However, the artemisinin related publications are so enormous distributing in many databases as to research all. Some kind of high quality papers may not stand for all the publications in artemisinin research. One case is that Chinese chemist You-you Tu's work which was not published on these so-called core journals in WoS for her papers were written in Chinese before. And her research is known of well predominance to all over the world and in the level of state-of-art. If given the chance to collect all the artemisinin literatures in the world, the bibliometrics results may be of more comprehensive and authoritative. But for the limitation of many conditions, the bibliometric analysis of SCI and Medline data were of typical nature.

ACKNOWLEDGEMENTS

This work was supported by the Natural Science Foundation of China (Grant No. 71173249) and Research project with combination of traditional Chinese and Western medicine in Hubei Province of China (Grant No. 2012Z-Z05). The authors are grateful to Peiyang Xu, Lijun Guo and Kathleen Diane Connors for their helpful discussion and suggestions. The authors would also like to thank anonymous reviewers for their valuable comments.

REFERENCES

1. Cui WY. Ancient Chinese anti-fever cure becomes panacea for malaria. *Bull WHO* 2009; 87(10): 743–4.
2. Butler AR, Wu YL. Artemisinin (Qinghaosu)—A new type of antimalarial drug. *Chem Soc Rev* 1992; 21(2): 85–90.
3. Tu YY. Artesunate and artemisinin drugs. Beijing: Chemical Industry Press 2009; p. 187–204.
4. Ashley EA, White NJ. Artemisinin-based combinations. *Curr Opin Infect Dis* 2005; 18(6): 531–6.
5. Klayman DL. Qinghaosu (Artemisinin): An antimalarial drug from China. *Science* 1985; 228(4703): 1049–55.
6. WHO, surge in demand leads to shortage of artemisinin-based combination therapy for malaria. *J Adv Nurs* 2005; 49(3): 324–5.
7. Kokwaro G. Ongoing challenges in the management of malaria. *Malaria J* 2009; 8(Suppl 1): S2.
8. Lee S. Artemisinin, promising lead natural product for various drug developments. *Mini Rev Medicinal Chem* 2007; 7(4): 411–22.
9. Dhingra V, Rao KV, Narasu ML. Current status of artemisinin and its derivatives as antimalarial drugs. *Life Sci* 2000; 66(4): 279–300.
10. Guo Y, Wang J, Chen ZT. Recent advancement in pharmacological effects of artemisinin and its derivatives. *Chinese J Clin Pharmacol Therapeutics* 2006; 11(6): 615–20.
11. Woodrow CJ, Haynes RK, Krishna S. Artemisinins. *Postgraduate Med J* 2005; 81(952): 71–8.
12. Bornmann L, F de Moya Anegón, Leydesdorff L. Do scientific advancements lean on the shoulders of giants? A bibliometric investigation of the Ortega hypothesis. *PloS One* 2010; 5(10): e13327.
13. Gomez A, Morena A, Pazosa J, Sierra-Alonso A. Knowledge maps: An essential technique for conceptualisation. *Data Knowledge Engineering* 2000; 33(2): 169–90.
14. Rosas SR, Kagan JM, Schouten JT, Slack PA, Trochim WM. Evaluating research and impact: A bibliometric analysis of research by the NIH/NIAID HIV/AIDS clinical trials networks. *PloS One* 2011; 6(3): e17428.
15. Glynn RW, Chin JZ, Kerin MJ, Sweeney KJ. Representation of cancer in the medical literature—A bibliometric analysis. *PloS One* 2010; 5(11): e13902.
16. Hien TT, White NJ. Qinghaosu. *Lancet* 1993; 341(8845): 603–8.
17. Cobo MJ, López-Herrera AG, Herrera-Viedma E, Herrera F. Science mapping software tools: Review, analysis, and cooperative study among tools. *J Amer Soc Information Sci Technol* 2011; 62(7): 1382–402.

18. Van Eck NJ, Waltman L. Software survey: VOS viewer: A computer program for bibliometric mapping. *Scientometrics* 2010; 84(2): 523–38.
19. Wang L, Pan YT. Research frontiers and trends in graphene research. *New Carbon Materials* 2010; 25(6): 401–8.
20. Dang Y, Zhang YL, Hu PJ, Brown SA, Chen HC. Knowledge mapping for rapidly evolving domains: A design science approach. *Decision Support Systems* 2011; 50(2): 415–27.
21. Zhang SL, Wang JP, Zhao YJ. Analysis of international proprietary technology development of solid state lighting material. In: Zhao GM, editor. *Proceedings of the 7th National Conference on Chinese Functional Materials and Applications* 2010; p. 984–92.
22. Tinga N, De N, Vien HV, Chau L, Toan ND, Kager PA, *et al.* Little effect of praziquantel or artemisinin on clonorchiasis in Northern Vietnam: A pilot study. *Trop Med Int Health* 1999; 4(12): 814–8.
23. Van Den Besselaar, P, Heimeriks G. Mapping research topics using word-reference co-occurrences: A method and an exploratory case study. *Scientometrics* 2006; 68(3): 377–93.
24. Cumming JN, Wang D, Park SB, Shapiro TA, Posner GH. Design, synthesis, derivatization, and structure-activity relationships of simplified, tricyclic, 1,2,4-trioxane alcohol analogues of the antimalarial artemisinin. *J Medicinal Chem* 1998; 41(6): 952–64.
25. Misra LN, Ahmad A, Takur RS, Lotter H, Wagner H. Crystal structure of artemisinic acid: A possible biogenetic precursor of antimalarial artemisinin from *Artemisia annua*. *J Nat Prod* 1993; 56(2): 215–9.
26. Pandey AV, Tekwani BL, Singh RL, Chauhan VS. Artemisinin, an endoperoxide antimalarial, disrupts the hemoglobin catabolism and heme detoxification systems in malarial parasite. *J Biol Chem* 1999; 274(27): 19383–8.
27. Efferth T. Molecular pharmacology and pharmacogenomics of artemisinin and its derivatives in cancer cells. *Curr Drug Targets* 2006; 7(4): 407–21.
28. Maude RJ, Pontavornpinyo W, Saralamba S, Aguas R, Yeung S, Dondorp AM *et al.* The last man standing is the most resistant: Eliminating artemisinin-resistant malaria in Cambodia. *Malar J* 2009; 8: 31.
29. O'Neill PM. The therapeutic potential of semi-synthetic artemisinin and synthetic endoperoxide antimalarial agents. *Expert Opin Investig Drugs* 2005; 14(9): 1117–28.
30. *World Malaria Report 2009*. Geneva, Switzerland: World Health Organization 2009; p. 7–15.
31. Lu J, Zhao W, Wang XD. Study on articles distribution in mobile learning documents of China-based on Bradford's law. *International Conference on Future Computers in Education*. In: Zhou M, editor. Sham Shui Po: Int Industrial Electronic Center 2011; p. 67–70.
32. Wang CD, Wang Z. Evaluation of the models for Bradford's law. *Scientometrics* 1998; 42(1): 89–95.
33. Otte E, Rousseau R. Social network analysis: A powerful strategy, also for the information sciences. *J Inform Sci* 2002; 28(6): 441–53.
34. Garfield E. Citation indexing for studying science. *Nature* 1970. 227(5259): 669–71.
35. Shanks GD. Treatment of falciparum malaria in the age of drug resistance. *J Postgraduate Medicine* 2006; 52(4): 277–80.

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Received: 27 August 2012

Accepted in revised form: 6 November 2012