Information

Publication activity in the field of medicinal chemistry in 2008—2017: Russian research in the global flow

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The bibliometric analysis of scientific works on medicinal chemistry published over the last ten years is performed. The data obtained from the Web of Science Core Collection citation database suggest a decrease in the number of studies in the European developed countries and the United States, while this number increased in China, India, and the Latin American countries. There is a growing number of open-access articles on medicinal chemistry among which the portion of review papers increases. In Russia, this field is extensively progressing: the publication activity from 2008 to 2017 increased 2.5-fold.

Key words: bibliometric analysis, medicinal chemistry, impact factor, scientific publications.

Medicinal chemistry is one of the most extensively developing and economically significant fields of chemistry. The special glossary of IUPAC terms defines medicinal chemistry as a "chemical discipline which includes aspects of biological, medical, and pharmaceutical sciences".[1] It involves the search, design, identification, and synthesis of bioactive compounds, the study of their metabolism and action mechanism at the molecular level, as well as determination of the quantitative relationship between the structure, properties, and bioactivity of substances. In these studies, organic chemistry is of fundamental significance. Modern medicinal chemists work in the cross-disciplinary medium and actively cooperate with scientists in the field of molecular biology, structural biology, pharmacology, physical chemistry, biochemistry, pharmacokinetics, pharmaceutical technology, and toxicology, as well as with experts in translational medicine. Discoveries in these fields have a considerable effect on medicinal chemistry and challenges for the search of new medicines.

As an individual scientific field, the medicinal chemistry originated in the late 1900s — early 2000s and truly formed by 1970s. The works in these chemical field were initiated by pharmaceutical industry research teams first in the United States and then in European countries. Later, state institutions, including academic ones, joined developments in this field. The term "medicinal chemistry" came to be used when the American Chemical Society renamed the Division of Pharmaceutical Chemistry established in 1909 initially for the Division of Chemistry of Medicinal Products in 1920 and then for the Division of Medicinal Chemistry in 1928.[2] In 1966, this department began to pu

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blish their annual reports covering the most important events in medicinal chemistry in the *Annual Reports in Medicinal Chemistry* book series. In 2017, the milestone 50th volume of this series was published. Another successful project of this department was *Journal of Medicinal Chemistry* appeared in 1959. At the present time, it is the leading journal in its subject area.

In Europe, the discipline developed slower due to a conventionally strong position of the organic chemistry in universities. It took long time before the medicinal chemistry became a generally recognized fundamental field of chemistry. The success of the ACS Division for Medicinal Chemistry of the American Chemical Society attracted attention of European scientists and new scientific societies were created in some countries (for example, independent organizations in France, Italy, and the United Kingdom, or departments as a part of chemical societies in Belgium, Germany, Sweden, Netherlands, and other countries). In 1970, the European communities united into the European Federation for Medicinal Chemistry (EFMC) which currently includes 25 scientific organizations from 23 European countries.[3—5] The Asian Federation of Medicinal Chemistry (AFMC) was established in 1992.[6]

In 1970, IUPAC created the Section on Medicinal Chemistry as a committee at the Division for Organic Chemistry which upon restructuring of divisions in 1996 was combined with the Division of Clinical Chemistry into the Division VII Chemistry and Human Health. Today, the medicinal chemistry problems are put by the Subcommittee on Drug Discovery and Development. Its mission is to support the activity of medicinal chemists and to facilitate progress in the pharmaceutical industry.[6]

In Russia, fundamental studies in chemistry and biology performed at institutes of the Russian Academy of Sciences, the Russian Academy of Medical Sciences, and corporate research institutes laid the groundwork for the tailor-made synthesis of drug substances. In 1997, the Moscow State University introduced a new discipline, the medicinal chemistry, at the Department of Organic Chemistry which is taught to students specialized in organic synthesis.[7] In 2011, the specialty "02.00.16 — medicinal chemistry" was registered by the Higher Attestation Commission and approved for the defense of doctoral theses. The students of chemistry faculties of many Russian universities majoring in "Fundamental and applied chemistry" study medicinal chemistry.[8] The Medicinal Chemistry and Bioinformatics Laboratory at the Moscow Institute of Physics and Technology was founded at the end of 2015 as a part of the 5-100 Project.[9]

The Russian government set a task in 2012 to bring up by 2018 the production of domestic strategically significant drugs to a rate of 90%, for which purpose several federal target programs were adopted.[10,11]

Intensification of researches in a natural manner entails an increase in the number of scientific papers. There are studies on the dynamics of publication activity in medicinal chemistry for Latin American countries, China, and India, industry-academia collaborations, and particular scientific journals[12—14] which demonstrate development trends of this discipline.

We performed the bibliometric analysis of publications using the Web of Science Core Collection (WoS CC) citation database in the medicinal chemistry thematic category. The main aim of the present work was to trace the history of publication activity worldwide in recent ten years and to analyze how this field developed in Russia compared to other countries. Only journal articles were considered as the statistical material and patents were not taken into account. In the medicinal chemistry subject area, the WoS CC database indexes 60 journals with calculated impact factors (IF) from Science Citation Index Expanded (SCI-EXPANDED) and six journals from Emerging Sources Citation Index (ESCI). It should be noted that many advanced publishing houses publish research data on this subject area. The Wiley, American Chemical Society, and Bentham Science Publishers publishing houses issue the biggest number of publication titles. Five leaders among periodicals by the IF index for 2016 are given in Table 1.

Note all of them belong to different publishing houses and the last one is an open-access journal. The list of most productive journals by the number of articles in the past decade (2008—2017) is given in Table 2. Here, the Elsevier publishing company is, for sure, the leader.

Among Russian-language journals, WoS CC indexes *Khimiko-Farmatsevticheskii Zhurnal* (Pharmaceutical Chemistry Journal, Russia) and *Khimiya Prirodnykh Soedinenii* (Chemistry of Natural Compounds, the Academy

Table 1. Distribution of journals over impact factors in WoS CC

Entry	Journal title	Publishing house	Impact factor
1	*Natural Product Reports*	Royal Society of Chemistry	11.014
2	*Medicinal Research Reviews*	Wiley	8.763
3	*Journal of Medicinal Chemistry*	American Chemical Society	6.259
4	*European Journal of Medicinal Chemistry*	Elsevier	4.519
5	*Journal of Enzyme Inhibition and Medicinal Chemistry*	Taylor & Francis	4.293

Table 2. Distribution of journals over the number of publications in 2008—2017

Journal title	Number of publications	IF (2016)	Quartile
Bioorganic Medicinal Chemistry Letters (Elsevier)	13251	2.454	Q3
Planta Medica (Thieme)	11659	2.342	Q3
Bioorganic Medicinal Chemistry (Elsevier)	8037	2.930	Q2
Journal of Medicinal Chemistry (ACS)	7991	6.259	Q1
European Journal of Medicinal Chemistry (Elsevier)	7017	4.519	Q1

Table 3. Distribution of journals over the number of publications of Russian scientists in 2008—2017

Journal title	Number of publications of Russian scientists	IF (2016)	Quartile
Pharmaceutical Chemistry Journal	1043	0.445	Q4
Chemistry of Natural Compounds	680	0.460	Q4
Natural Product Commuications	118	0.773	Q4
Bioorganic Medicinal Chemistry	100	2.930	Q2
Bioorganic Medicinal Chemistry Letters	95	2.454	Q3

of Sciences of the Republic of Uzbekistan) which have English translated versions. The most of Russian researchers choose these periodicals to present their studies. Among foreign journals, *Natural Product Communications* and *Bioorganic & Medicinal Chemistry* are the most popular ones (Table 3).

Having estimated the global flow of publications in recent ten years, note that 2008—2011 feature a growth in the publication activity and this index became steady from 2011 to 2017 (Fig. 1) with the number of open-access articles increasing from year to year. The average rate of increase in the past decade was 17.7% of the total publication number and it was 21.7% in 2017. This rate is higher than that for chemistry publications (17.8%), but lower than that for medicine (36.3%).

Such an increase can be considered as regularity, since open-access journals are cited more frequently than subscription ones and this publication type is more preferred for scientists. However, it should be noted that the publication of an open-access paper is paid by authors themselves (usually using research grant resources). This approach is still not popular in Russia: the number of open-access journals is low. In the West, this trend progresses more rapidly. For example, open-access journals of MDPI and Hindawi Publishing were published for more than ten years and have become very popular among scientists in the field of medicine and biology. These include also medicinal chemistry periodicals which are included in the Web of Science, Scopus, and PubMed Central scientometric databases having a high impact factor and developed tools for control of citation, social promotion of scientific works, and their public evaluation.[15,16] According to SpringerOpen, many of these studies in this field will benefit from the open access to a wide range of experimental data and open-access journals potentially can provide such information.[17]

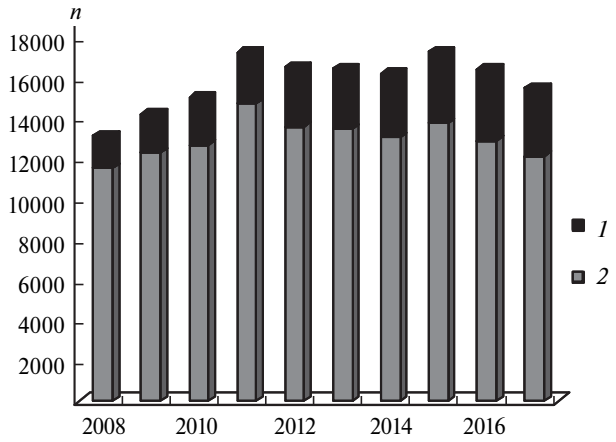

Fig. 1. Number of open-access (*1*) and subscription (*2*) publications in 2008—2017 worldwide (according to WoS CC).

The number of most cited articles varies from 40 to 80 publications per annum (Fig. 2). The most highly cited articles in medicinal chemistry in recent ten years are:

1. D. J. Newman, G. M. Cragg, Natural products as sources of new drugs over the last 25 years, *Journal of Natural Products*, 2007, **70**, No. 3, 461—477.

2. D. J. Newman, G. M. Cragg, Natural Products As Sources of New Drugs over the 30 Years from 1981 to 2010, *Journal of Natural Products*, 2012, **75**, No. 3, 311—335.

3. K. L. Schuchardt, B. T. Didier, T. Elsethagen, L. S. Sun, V. Gurumoorthi, J. Chase, J. Li, T. L. Windus, Basis set exchange: A community database for computational sciences, *Journal of Chemical Information and Modeling*, 2007, **47**, No. 3, 1045—1052.

4. J. B. Baell, G. A. Holloway, New Substructure Filters for Removal of Pan Assay Interference Compounds

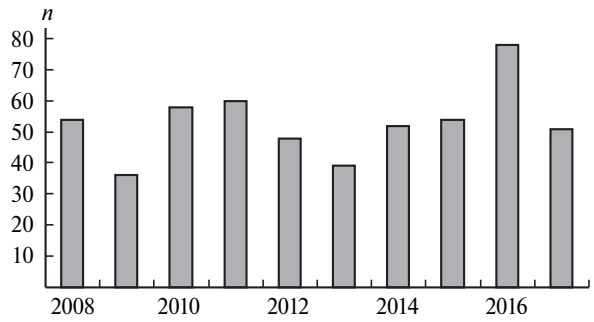

Fig. 2. Number of highly cited papers on medicinal chemistry in 2008—2017.

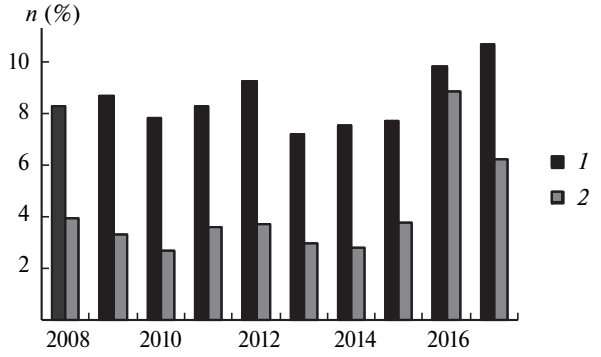

Fig. 3. Portion of reviews in the total number of medicinal chemistry articles (*n*, %) published worldwide (*1*) and in Russia (*2*).

(PAINS) from Screening Libraries and for Their Exclusion in Bioassays, *Journal of Medicinal Chemistry*, 2010, **53**, No. 7, 2719—2740.

5. P. Gramatica, Principles of QSAR models validation: internal and external, *QSAR & Combinatorial Science*, 2007, **26**, No. 5, 694—701.

As it is seen from the titles, the first two reviews are dedicated to new drugs based on natural compounds. Almost all of these articles were published by the American Chemical Society.

Among the most highly cited articles with Russian co-authors, the list is headed by:

1. A. Cherkasov, E. N. Muratov, D. Fourches, A. Varnek, I. I. Baskin, M. Cronin, J. Dearden, P. Gramatica, Y. C. Martin, R. Todeschini, V. Consonni, V. E. Kuz´min, R. Cramer, R. Benigni, C. H. Yang, J. Rathman, L. Terfloth, J. Gasteiger, A. Richard, A. Tropsha, QSAR Modeling: Where Have You Been? Where Are You Going To? *Journal of Medicinal Chemistry*, 2014, **57**, No. 12, 4977—5010.

2. E. E. van Faassen, S. Babrami, M. Feelisch, N. Hogg, M. Kelm, D. B. Kim-Shapiro, A. V. Kozlov, H. T. Li, J. O. Lundberg, R. Mason, H. Nohl, T. Rassaf, A. Samouilov, A. Slama-Schwok, S. Shiva, A. F. Vanin, E. Weitzberg, J. Zweier, M. T. Gladwin, Nitrite as Regulator of Hypoxic Signaling in Mammalian Physiology, *Medicinal Research Reviews*, 2009, **29**, No. 5, 683—741.

Note that, among the above-mentioned publications, there are reviews written in the international cooperation with many co-authors.

The portion of review articles of the total article number in the last ten years varies within 7—10% with a trend of its increase (Fig. 3). One of the reasons for this fact is the editorial policy. Journals increase the portion of reviews and publish mini-reviews and review-type articles (account, highlight, perspective, *etc*.) in order to increase their impact factors, since review publications are known to be cited better than narrowly specialized ones.

Considering statistical data for five leading countires publishing materials in this subject area in recent ten years, one can note a rapid increase in the number of Chinese articles (more than three-fold). Currently, this country is the leader which accounts for 22% of the total number of medicinal chemistry publications. An increase in the number of articles on this field in India (about two-fold) should be also mentioned. A slight increase in the number of publications prior to 2012 was observed in the United States, which was followed by its decrease. Japan demonstrates stable results from year to year. In Germany, a slight decrease in the number of medicinal chemistry publications is noted. Unfortunately, Russia is still not in the top ten in this subject area, but demonstrates a stable increase (2.5-fold) in the number of articles (Fig. 4). Our country currently ranks twelfth by the number of publications (2.8% of the total volume).

Figure 5 shows the most productive worldwide organizations publishing work in the subject area under study. All of them are large state research institutions and the Russian Academy of Sciences (RAS) is among them.

The analysis of data on Russian publications revealed a stable increase in both their total number and the number of open-access articles (Fig. 6); the portion of reviews increased in the last two years (see Fig. 3). Since the Russian-language journals are indexed in the WoS CC

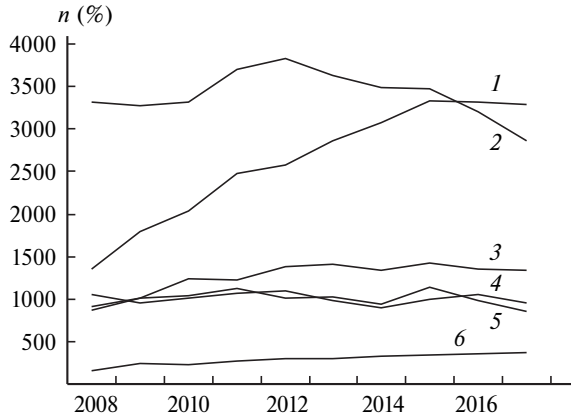

Fig. 4. Distribution of medicinal chemistry publication number over countries: (*1*) China, (*2*) United States, (*3*) India, (*4*) Japan, (*5*) Germany, and (*6*) Russia.

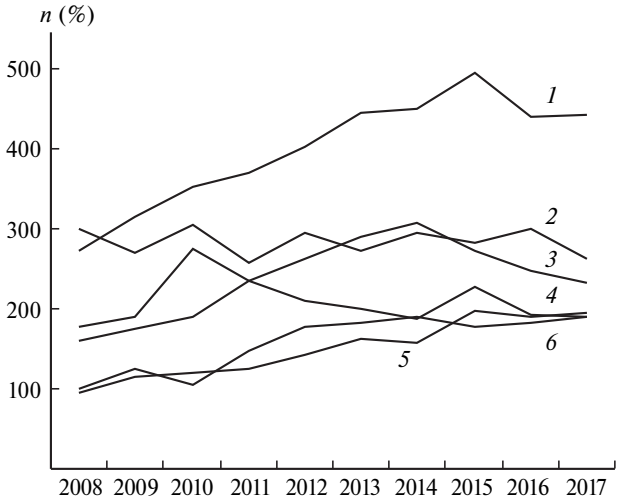

Fig. 5. Distribution of publication number over state organizations worldwide: (*1*) Chinese Academy of Science, (*2*) Centre National de la Recherche Scientifique, (*3*) Council of Scientific and Industrial Research (India), (*4*) University of California System, (*5*) China Pharmaceutical University, and (*6*) Russian Academy of Sciences.

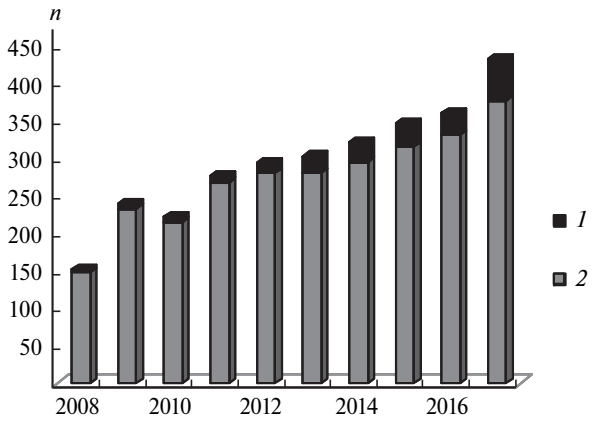

Fig. 6. Number of open-access (*1*) and subscription (*2*) Russian publications in 2008—2017.

database mainly if it has translated version, a considerable portion of Russian scientists is not available within this database, which slightly deteriorates the analysis completeness.

The productivity analysis showed that, among Russian organizations, the leading ones are Moscow and Saint Petersburg State University (Fig. 7), as well as Far Eastern Federal University, Novosibirk State University, and Sechenov University which are included in the 5-100 Project of the Ministry of Education and Science of the Russian Federation aimed to improve the research potential of Russian universities and to strengthen their competitive positions on the global educational market. Among the RAS research institutes, let us mention growing indices

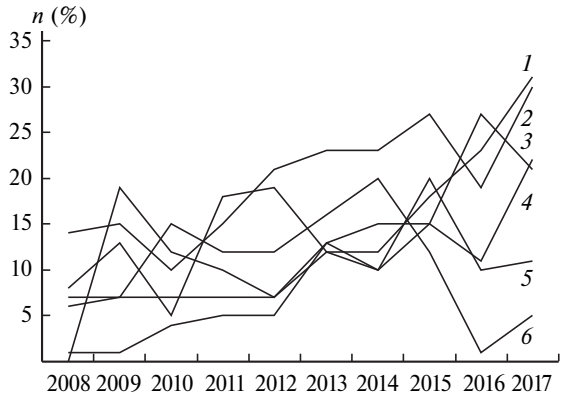

Fig. 7. Distribution of publication number among Russian organizations in 2008—2017: (*1*) Moscow State University, (*2*) Vorozhtsov Novosibirsk Institute of Organic Chemistry, (*3*) Far Eastern Federal University, (*4*) Sechenov University, (*5*) Zelinsky Institute of Organic Chemistry, and (*6*) Institute of Biochemistry and Genetics of Ufa Science Centre of RAS.

of the N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry and a rapid decrease in the number of publications on this topic for the Institute of Biochemistry and Genetics of Ufa Science Centre of the Russian Academy of Sciences which however remains among leaders by the total number of articles published over the last ten years.

The financial support from Russian scientific foundation was declared in 33.5% of publications among which the portion of the Russian Foundation for Basic Research was 21% and the portion of the Russian Science Foundation was 7.5%. The international collaboration was mentioned in 28.5% of papers written in the coauthorship with scientists from near- and far-abroad countries. The priority partners are the United States (7.8%), Germany (4.2%), and France (2.4%). The collaboration is carried out mainly with university researchers. While outside Russia the studies of private companies constitute 20% of the total publications and ~15% is accounted for cooperation of academic institutions with the private sector,[13] in Russia the vast majority of studies are performed in the state sector, research institutes, and universities and the collaboration with private companies, mainly foreign ones, is noted only in ~1.5% of publications. These data correlate with the data from economic studies which note that pharmaceutical drug producers spend only 1—2% of their profit for R&D works.[18]

Summarizing all the aforesaid, note that the medicinal chemistry is a relatively young field of chemical science, but its social and economic significance is very high, since it forms a basis for the design of new drug products.

The global flow of scientific publications in this subject area over the last ten years features stability, which, in turn, results from a decrease in the number of studies in the developed European countries and the United States and its increase in China, India, and Latin American countries

trying to develop their own pharmaceutical industry. The most of frontline publishing houses publish studies in this chemical field; the number of open-access articles increases and a slight increase in the portion of review articles is noted.

In Russia, this field is progressing and demonstrates a 2.5-fold increase in the publication activity, although the portion of our studies is still low and, unfortunately, Russia is not among top ten of the most productive countries. The most of Russian authors publish in domestic journals. The studies are performed predominantly at the laboratories of state universities and research institutes; the portion of studies involving private companies is negligible. Large state universities have opportunities for growth in this field thanks to international cooperation and combination of research and commercial facilities.

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