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ÖZGÜN ARAŞTIRMA/ORIGINAL ARTICLE

Arı Zehri Literatürünün Bütünsel Bir Analizi: 1975- 2017 Yılları Arasındaki Arı Zehri Üzerine Küresel Yayın Verimliliğinin Bibliyometrik Olarak Değerlendirilmesi

A Holistic Analysis of Bee Venom Literature: Bibliometric Evaluation of the Global Publication Productivity on Bee Venom Between 1975 and 2017

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Anahtar Sözcükler:
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Yayın Eğilimi Analizi

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ÖZ

Amaç: Apis mellifera tarafından üretilen arı zehri, biyoaktifpeptitler, enzimler ve biyojenik aminlerin bir karışımıdır. Bibliyometri, akademik literatürün belli bir alandaki değerlendirilmesinde yeni ve popüler bir istatistiksel yöntemdir. Bu çalışmada arı zehri literatürünü analiz etmeyi amaçladık ve Web of Science tarafından sağlanan dört veritabanını kullandık.

Gereç ve Yöntem: 1975-2017 yılları arasında yayınlanan tüm dokümanlar WOS veritabanlarından alınmış ve analiz edilmiştir.

Bulgular: Toplam 4117 makale bulundu. Belgelerin çoğu orijinal makalelerdi (%88,15) ve %87,37'si İngilizce idi. ABD literatürde 884 makale ile birinci sırada yer alırken ardından Güney Kore, İsviçre ve Almanya (sırasıyla %10,42, 6.82 ve %6,46) gelmekteydi. İsviçre en yüksek verimlilik puanına sahip en verimli ülkeydi (33,15), ardından Avusturya, Danimarka ve Slovenya geliyordu (sırasıyla 12,36, 11,51 ve 11,06). Güney Kore'den KyungHee Üniversitesi 112 yayını olan öncü kurum olarak kaydedildi. En çok kullanılan anahtar kelimeler "arı zehri", "alerji", "immünoterapi" ve "melittin" olarak bulundu.

Sonuç: En fazla katkıda bulunan tüm ülkelerin Birleşmiş Milletler sınıflamasında gelişmiş ülkeler olduğunu tespit ettik ve az gelişmiş ve gelişmekte olan ülkelerden araştırmacıların yeni arı zehri çalışmaları için desteklenmelerini önerdik.

ABSTRACT

Objective: Bee venom produced by *Apis mellifera* is a complex mixture of bioactive peptides, enzymes and biogenic amines. Bibliometrics is a novel and popular statistical method of evaluation of academic literature in a certain field. We aimed to analyze bee venom literature in this study and used four databases provided by Web of Science.

Materials and Method: All documents published between 1975 and 2017 were included from WoS databases and analyzed.

Results: A total of 4117 articles was found. The most items were original articles (88.15%) and 87.37% of which were in English. The USA ranked first in the literature with 884 papers followed by South Korea, Switzerland and Germany (10.42, 6.82 and 6.46%, respectively) while Switzerland was found to be the most productive country with the highest productivity score (33.15) followed by Austria, Denmark and Slovenia (12.36, 11.51 and 11.06, respectively). Kyung Hee University from South Korea was noted to be the leading institution with 112 publications. "*Bee venom*", "*allergy*", "*immunotherapy*" and "*melittin*" were found as the most used keywords.

Conclusion: Wedetected that all the most contributor countries were developed in the classification of United Nations and we suggest that researchers from least developed and developing countries should be supported to perform novel bee venom studies.

Introduction

Apitherapy is medicinal use of honey bee products such as honey, propolis, royal jelly and bee venom for both treatment and prevention of diseases (1). Bee venom produced in the glands of *Apis mellifera* includes a complex mixture of small bioactive peptides, enzymes such as phospholipase A2, phospholipase B, acid phosphatase, α-glucosidase and hyaluronidase, and biogenic amines (2). Bee venom exhibits anti-inflammatory, anti-bacterial, anti-nociceptive, anti-mutagenic, anti-cancer and immunity promoting activity. Bee venom has been used as a traditional and complementary therapy in various conditions such as asthma, dermatological disorders, rheumatoid arthritis and neoplastic diseases (3).

Bibliometrics is statistical evaluation of the publications or total literature in a certain field (4). Bibliometric analysis can be used to investigate authors, institutions, countries or research areas in the literature. Although in recent years there has been an increasing interest and popularity in bibliometric studies, to the best of our knowledge, only a few reports focusing on apitherapy have been reported and the medical literature lacks a study investigating bibliometric evaluation of the publications on bee venom. In this study we aimed to perform a preliminary and holistic bibliometric assessment of bee venom literature.

Material and Method

All data of this study was obtained by searchingWeb of Science databases provided by Thomson Reuters (WoS, Thomson Reuters, New York, NY, USA).All documents published in bee venom literature between 1975 and 2017 were included and all items produced in 2018 were excluded. Articles from England, Scotland, Wales and Northern Ireland were united under the United Kingdom (UK) title. All documents produced from East Germany, West Germany and Federal Republic of Germany were collected under “Germany” heading. The country classification system of United Nations (UN) was used to classify countries (5). Gross domestic product (GDP) and GDP per capita data of the countries were provided from the World Bank Database (6). We performed statistical analyses by using SPSS (Version 22.0, SPSS Inc., Chicago, IL, USA). Spearman's correlation coefficient analysis was performed for the evaluation of the association between scientific and demographic features of the countries. We created info-maps showing distribution of publication density of the world countries (7). We generated info-graphics revealing bibliometric networks by using a freeware named VOS viewer software (8).

Results

Features of published documents

A total of 4117articles was found in bee venom literature during the period of 1975 to 2017. Most documents were original articles (n=3631, 88.15%) followed by meeting reports and meeting abstracts (10.82% and 9.76%, respectively) (Table 1). Out of all documents, 3597 articles were written in English (87.37%). The second most used language was Korean (10.56%) followed by German (2.36%) and Russian (0.99%).

[a] Total number may exceed 4117 and total percentages may exceed 100% because certain items were included in more than one category.

Document type	Record count [a]	% [a]
Original article	3630	88,17
Meeting report	446	10,83
Abstract	402	9,76
Review	316	7,68
Case report	93	2,26
Letter	90	2,19
Clinical trial	66	1,60
Editorial	45	1,09
News	8	0,19
Correction	4	0,10
Biography	3	0,07
Book	3	0,07
Reference material	3	0,07
Other	1798	43,67
Total	***4117***	***100***

Table 1. Types of publications of bee venom literature[a]

Global productivity

The USA dominated the bee venom literature with 884 articles (21.54%) followed by South Korea, Switzerland and Germany (10.42, 6.82 and 6.46%, respectively) (Figure 1).

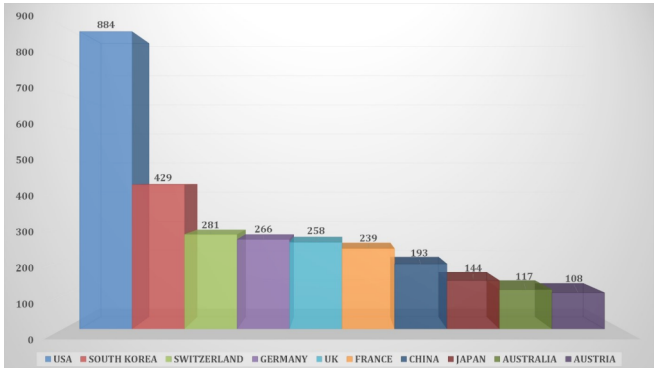

Figure 1. Top ten countries publishing bee venom publications by total number of documents

Bee venom articles were published throughout the world, except from the most countries in Africa (Figure 2). We measured a productivity score for each country by using a correction formula (publication number/population*100) used in previous bibliometric and scientometric studies (9). Switzerland was found to be the most productive country with the highest productivity score (33.15) followed by Austria, Denmark and Slovenia (12.36, 11.51 and 11.06, respectively) (Figure 3).

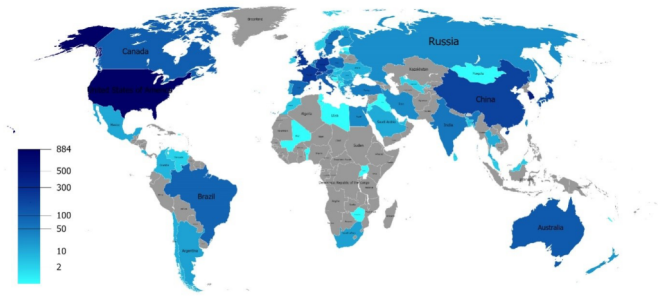

Figure 2. Global publication density on bee venom

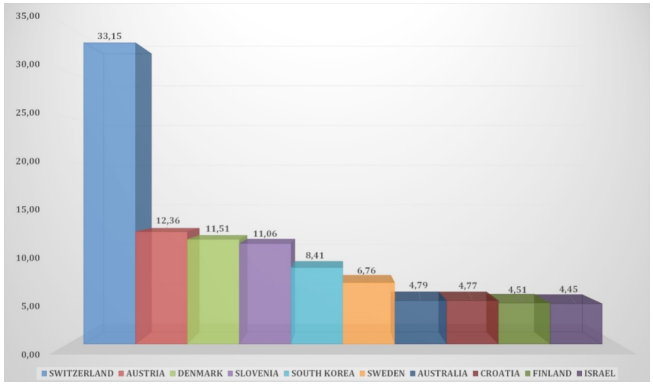

Figure 3. The most productive ten countries on bee venom research

Research areas, top authors, journals and institutions

We detected that biochemistry was the most studied research area covering 59.73% of the bee venom literature (n=2459 documents) followed by toxicology, pharmacology and immunology (59.12, 45.06 and 41.39%, respectively) (Table 2). Chen J from The Fourth Military Medical University, China was noted to be the most prolific author with 63 documents (Table 3). Kyung Hee University from South Korea was found to be the leading institution with 112 publications (2.72%) (Table 4). *Allergy*dominatedbee venom literature and covered 5.08% of all publications followed by the*Journal of Allergy and Clinical Immunology*and*the Acupuncture* (4.57 and 3.84 %, respectively) (Table 5).

Research Areas	Number of Publications	%
Biochemistry	2459	59.73
Toxicology	2434	59.12
Pharmacology pharmacy	1855	45.06
Immunology	1704	41.39
Entomology	1227	29.80
Cell biology	1175	28.54
Allergy	1114	27.06
Physiology	976	23.71
Zoology	796	19.33
Agriculture	774	18.80

Table 2. The first 10 research areas by publications in bee venom literature

*of total documents published in bee venom literature

Author	Institution	Country	Record Count	%*
Chen J	The Fourth Military Medical University	China	63	1.53
Akdis CA	University of Zurich	Switzerland	61	1.48
Blaser K	University of Zurich	Switzerland	60	1.46
Lazdunski M	Institute of Molecular and Cellular Pharmacology	France	51	1.24
Lee JH	Seoul National University	South Korea	51	1.24
Park KK	Hanyang University	South Korea	51	1.24
Akdis M	University of Zurich	Switzerland	49	1.19
Han SM	National Institute of Agricultural Science	South Korea	48	1.17
Müller U	Spital Ziegler	Switzerland	46	1.12
Bae H	Kyung Hee University	South Korea	37	0.90

Table 3. Top ten authors producing publications in bee venom literature by record count

Senel E. A Holistic Analysis Of Bee Venom Literature: Bibliometric Evaluation Of The Global Publication Productivity On Bee Venom Between 1975 And 2017. Hitit Med J 2019;1(1):6-11.

Organizations	Document number	%
Kyung Hee University (South Korea)	112	2.72
Centre National De La Recherche Scientifique (France)	107	2.6
Swiss Institute of Allergy Asthma Research (Switzerland)	99	2.40
University of California System (USA)	86	2.09
Fourth Military Medical University (China)	76	1.85
University of London (UK)	74	1.8
Catholic University of Daegu (South Korea)	56	1.36
Seoul National University (South Korea)	56	1.36
Imperial College London (UK)	54	1.31
Institut National De La Sante Et De La Recherche Medicale (France)	53	1.29

Table 4. The first ten institutions by number of publications in bee venom literature

Journal Name	Number of Publications	%
Allergy	209	5.08
Journal of Allergy and Clinical Immunology	188	4.57
The Acupuncture	158	3.84
Journal of Pharmacopuncture	133	3.23
Biochimica Et Biophysica Acta	124	3.01
Biochemistry	106	2.57
Toxicon	92	2.23
Clinical and Experimental Allergy	90	2.19
Biophysical Journal	60	1.46
Allergologie	59	1.43

Table 5. The first 10 journal source according to the number of published documents

Article	Author	Journal Name	Year	Total Citations	Average Citations per Year
Sequence and Specificity Of 2 Anti-Bacterial Proteins Involved in Insect Immunity	Steiner H *et al.*	Nature	1981	1024	26.95
Role of Interleukin 10 in Specific Immunotherapy	Akdis Ca *et al.*	Journal of Clinical Investigation	1998	724	34.48
Serologic Aspects of IgG4 Antibodies .1. Prolonged Immunization Results in An IgG4-Restricted Response	Aalberse RC, Vandergaag R and Vanleeuwen J	Journal of Immunology	1983	681	18.92
Interfacial Catalysis - The Mechanism of Phospholipase-A2	Scott DL *et al.*	Science	1990	677	23.34
IL-10 And TGF-Beta Cooperate in The Regulatory T Cell Response to Mucosal Allergens in Normal Immunity and Specific Immunotherapy	Jutel M *et al.*	European Journal of Immunology	2003	630	39.38
Barrel-Stave Model or Toroidal Model? A Case Study on Melittin Pores	Yang L *et al.*	Biophysical Journal	2001	613	34.06
Non-Cyclooxygenase-Derived Prostanoids (F2-Isoprostanes) Are Formed Insitu On Phospholipids	Morrow JD *et al.*	Proceedings of The National Academy of Sciences of The United States of America	1992	540	20
Marine Natural Products and Related Compounds in Clinical and Advanced Preclinical Trials	Newman DJ and Cragg GM	Journal of Natural Products	2004	507	33.8
Changes in Membrane Phospholipid Distribution During Platelet Activation	Bevers EM, Comfurius P and Zwaal RFA	Biochimica Et Biophysica Acta	1983	492	13.67
Structure and Functions of Channel-Forming Peptides: Magainins, Cecropins, Melittin And Alamethicin	Bechinger B	Journal of Membrane Biology	1997	486	22.09

Table 6. The 10 most cited manuscripts in bee venom literature

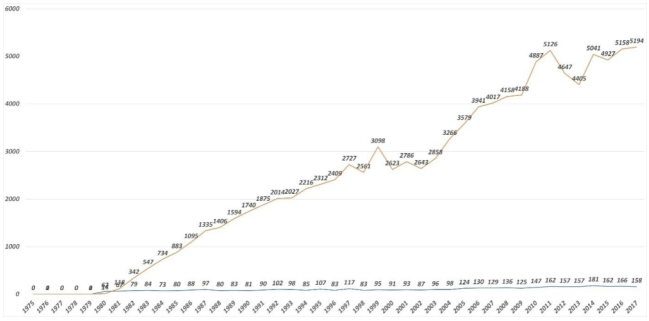

Figure 4. Total publication and citation numbers of bee venom articles by year

Evolution of the literature

H-index of bee venom literature was measured to be 137.Total citations to 4117 articles were calculated to be 1,052,251 times. Average citations per item were 25.56 times. The most cited article was an original article titled *"Sequence and Specificity Of 2 Anti-Bacterial Proteins Involved in Insect Immunity"* published in 1981 by Steiner H *et al.* cited 1024 times (26.95 times, average citations/year) (Table 6). Number of publications and citations increased gradually, and the peak year was 2014 for the publications (n=181) while it was 2017 for the citations (n=5194) (Figure 5). We found a very high correlation between the number of publications and citations by year (p<0.001, r=0.934).

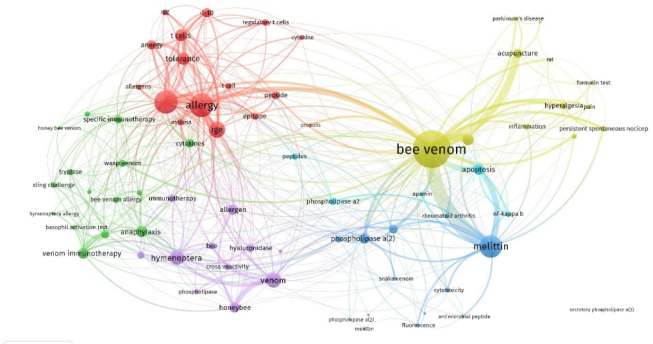

Figure 5. Keyword network of bee venom literature

Bibliometric networks

We generated bibliometric network info-graphics of keywords, institutional cooperation and coauthorship. We noted that the most used keywords were "*bee venom*", "*allergy*", "*immunotherapy*" and "*melittin*" (Table 7). We found five bibliometric network points that keywords "*bee venom*", "*melittin*", "*venom*", "*venom immunotherapy*" and "*allergy*" centered (Figure 5). Seoul National University (South Korea) was detected to be the most cooperative institution in this field with 103 links followed by Kyung Hee University (South Korea, 90 links) and Chonnam National University (South Korea, 81 links). The USA was the most cooperative country with 219 links followed by Germany, the UK, Switzerland and South Korea (n=108, 103, 98 and 88 links, respectively) (Figure 6). Three most cooperative authors were Park KK (South Korea), Han SM (South Korea) and Lee WR (South Korea).

Keyword (Total link strength)	
1. Bee venom (307)	11. Apoptosis (56)
2. Allergy (163)	12. Phospholipase A2 (53)
3. Immunotherapy (160)	13. Honeybee (50)
4. Melittin (152)	14. Anergy (45)
5. IgE (97)	15. IL-10 (45)
6. Hymenoptera (83)	16. Acupuncture (43)
7. Tolerance (65)	17. Apis mellifera (43)
8. T cell(s) (60)	18. Cytokine(s) (39)
9. Inflammation (60)	19. Hyaluronidase (35)
10. Anaphylaxis (57)	20. Apamin (17)

Table 7. Most used 20 keywords in bee venom literature

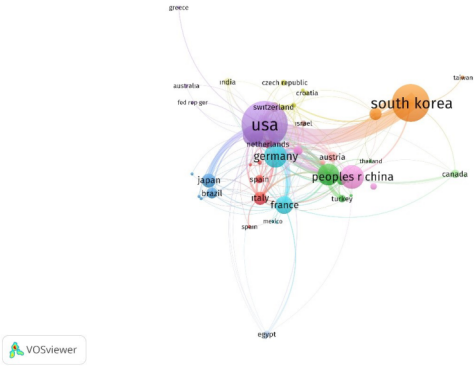

Figure 6. Network of the countries publishing cooperatively in bee venom literature

Discussion

Bee venom which has a primary role of defense of bee colony, is a natural toxin produced by *Apis mellifera* (10).

Bee venom therapy which is one of the most significant treatment modalities of apitherapy has been used for thousands of years (11). Treatment can be performed with application of live bee stings directly into the skin of the patient or injection of bee venom with a hypodermic needle (12). Bibliometrics is a new scientific field providing statistical data of academic literature and describing trends of publications and citations in a certain area. The first

bibliometric study was carried out by Campbell in 1896 and Pritchard coined "bibliometrics" as a novel term instead of "statistical bibliography" in 1969 " (9,13,14). Although there have been numerous studies on the biological and pharmacological activities of bee venom, to the best of our knowledge, the medical literature lacks a holistic assessment investigating bibliometric features of the articles on bee venom.

Fu *et al.* reported a bibliometric evaluation of alternative and complementary medicine literature and the search retrieved 17,002 items in total from WoS database during a period of 1980 to 2009. The authors found that the USA was the most productive country with 4117 items and 70% of documents was original articles (15). Şenel and Demir performed a bibliometric analysis of apitherapy including all articles published between 1980 and 2016 and they found a total of 6917 documents from WoS database. We detected that the USA was the most contributor country in bee venom literature although Brazil previously had been reported to rank first in apitherapy literature. Switzerland was the most productive country and *"bee venom"* and *"melittin"* werein the most used keywords in both studies (16).

Conclusion

Our bibliometric assessment revealed that majority of the world countries published in this field except from Africa continent (Figure 2). In our ten most contributor countries list, we found no developing and least-developed countrieswhereas bibliometric evaluation of apitherapy literature had developing countries in the most contributor countries list (Figure 1) (16). We noted a rising pattern in citations while a stable pattern was detected in publications (Figure 3). Ten most contributor institutions and authors were from developed countries (Table 3 and 4). We suggest that researchers from least-developed and developing countries should be supported to perform novel studies on bee venom.

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