- Manufacturing Technology and Effectiveness of Corona Vaccines: A Bibliometric Review
- ٣

۲

٤

# • Abstract:

٦ Covid-19, a respiratory disease, first emerged in late 2019 as the causative agent of the coronavirus. ٧ The end of this pandemic was announced in 2023, and during this period, various vaccines with ٨ different strategies were made. The effectiveness and other immunological characteristics of these ٩ vaccines have been tested. The publication of documents related to the Covid-19 vaccines has ۱. continued until after the pandemic has ended. This study was conducted to investigate the research 11 process and published documents related to the manufacturing technology and effectiveness of ۱۲ Covid-19 vaccines. The documents published in the Scopus database in early 2024 were collected ۱٣ using restrictions in 4 subject areas and the English language. The bibliographic analysis was done ١٤ using Bibliometrix-package in Rstudio and VOSviewer. A total of 2810 documents were reviewed. Most of the documents are articles and reviews, 2320 and 394 respectively. Peptides and capillary 10 ١٦ electrophoresis are trending topics in 2024. Additionally, elasomeran, covilo, and tozinameran are ۱۷ more recent than other keywords based on time. This study examines the documents published in ۱۸ one of the most reliable databases of Covid-19 vaccines from a bibliometric perspective. The ۱٩ obtained results help other researchers and scientists in future research, opportunities, and ۲. challenges.

۲۱

# Keywords: Vaccine, COVID-19, 2019-nCov, SARS-CoV-2, Bibliometric.

۲۳

# ۲٤ **1. Context**

Zoonotic diseases are common between humans and various species of animals that are caused 20 ۲٦ by a pathogen. The cause of the Covid-19 pandemic is a virus from the *Coronaviridae* family that can cause respiratory disease in humans (1-4). The end of this pandemic was announced in 2023. ۲۷ From the beginning to the end of the coronavirus pandemic, research was conducted in some ۲۸ ۲۹ countries and the results were published. These investigations have been continued until now. One ۳. of the trending topics in the field of Covid-19 is the topic based on disease prevention such as 31 vaccines. Nucleic acid-based, inactivated, virus-like particles, and live attenuated virus vaccines ٣٢ were candidates for Covid-19 (5, 6).

- Some RNA-based vaccines include Tozinameran, Elasomeran, and Gemcovac. ZyCoV-D vaccine
- ri is based on DNA. Nuvaxovid, Covovax, Zifivax, Corbevax, and Razi Cov Pars vaccines are of
- ro protein subunit type. Covaxin, Covilo, VLA2001, and CoronaVac can be mentioned among the
- types of inactivated coronavirus vaccines. Covifenz vaccine is a type of virus-like particles (7).
- TV Documents are published in various types such as research articles, review articles, conferences,
- books, etc., related to Covid-19. These documents can be found in search databases such as Scopus,

Web of Science Core Collection Database, and PubMed. In bibliometric analysis, a large number
 of documents are analyzed with mathematical methods. This type of document study analyzes
 keywords, authors, countries, and organizational affiliations. The obtained results can be classified
 from the most to the least and from the newest to the oldest mentioned items. A very interesting
 and practical analysis is to identify the most cited document, author, organizational affiliation, and
 country. By studying the research process in a bibliographic analysis, researchers are provided
 with the conditions to identify opportunities, challenges, and hot spots (8-10).

A The present study is a bibliometric review article that examines the publication process of documents in the Scopus database. The manufacturing technology and effectiveness of corona vaccines are the aim of this study. This study takes a general look at the state of research and published documents in the investigated area and presents the results by categories of keywords, authors, sources, and trend topics.

۱۳

#### **2.** Data Acquisition

by collecting information in the 10 The present study was conducted Scopus (https://www.scopus.com/) database 2024-01-30. The term ("Coronavirus disease 2019" OR ١٦ ۱۷ "Coronavirus disease-2019" OR "Severe acute respiratory syndrome coronavirus 2" OR "Severe ۱۸ acute respiratory syndrome coronavirus-2" OR "COVID-19" OR "COVID 19" OR "2019-nCov" ۱٩ OR "2019 nCov" OR "SARS-CoV-2" OR "SARSCoV-2") AND ("Vaccin\*" OR "Autovaccine\*" OR "Autogenous vaccine\*" OR "Active immunization\*" OR "Mass immunization\*" OR "Mass ۲. vaccination\*") AND ("Effectiveness") AND ("Technology" OR "Technology" OR "Procedure\*" ۲١ OR "Method\*" OR "Performance\*" OR "Biotechnology" OR "Technique\*") was searched in the ۲۲ ۲۳ title, abstract and keywords. Then the limitations of the English language and four subject areas ۲٤ were applied: 1) medicine, 2) immunology and microbiology, 3) biochemistry, genetics and 50 molecular biology, and 4) pharmacology, toxicology, and pharmaceutics. No time filters were ۲٦ applied. Finally, 2810 documents were collected from the Scopus database with the mentioned ۲۷ conditions.

Collected documents were bibliometrically reviewed with VOSviewer v.1.6.16
 (<u>http://www.vosviewer.com/</u>) (11) and Bibliometrix-package (<u>http://www.bibliometrix.org/</u>) in
 Rstudio (12). Due to the collection of documents from one database, it was not practical to remove duplicate documents.

٣٢

### **77 3. Results:**

*γ*ε 4. 1. Main information:

ro In total, 2810 documents were analyzed with the conditions mentioned in section 2. Types of

documents including article (n = 2320), book (n = 2), book chapter (n = 7), conference paper (n = (n = 2320))

 $\gamma$  9), editorial (n = 16), erratum (n = 8), letter (n = 19), note (n = 26), retracted (n = 1), review (n = 1)

 $\gamma$  394) and short survey (n = 8) were determined. The most number of types of documents belong to

rq articles and reviews. So the ratio of the article to the review was 5.88.

In the analysis of keywords, the number of keywords plus (ID) and author's keywords (DE) were determined as 10118 and 4715 respectively. Other collection information exported from the Scopus database is shown in Table 1. Since no time limit was applied during data collection, the results obtained according to Table 1 indicated that these documents were published in this database during the years 2020 until the time of data extraction (2024). Therefore, until 2020, no document has been published in the Scopus database that meets the conditions mentioned in

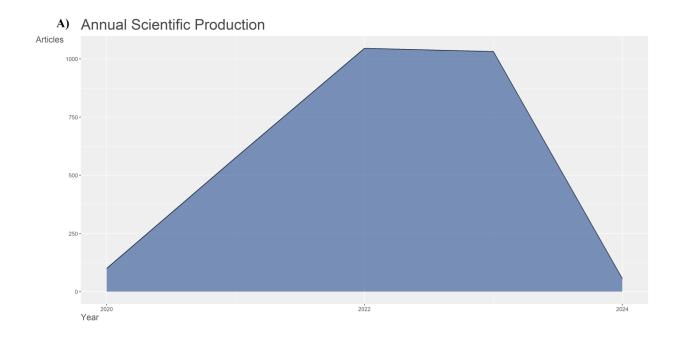
- v Section 2.
- <sup>A</sup> The results of annual scientific production and average article citations per year are shown in

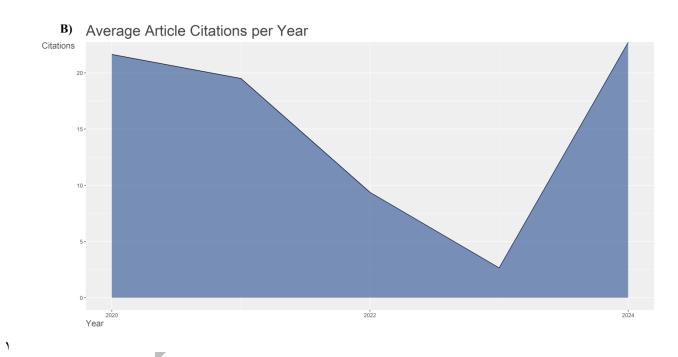
Figure 1. According to this figure, the highest number of documents were published in 2022 (n = 1046). However, a significant decrease is observed in average article citations per year in 2023.

۱۱

				-	
MAIN INFORMATION		AUTHORS		AUTHORS	
ABOUT DATA				COLLABORATION	
Timespan	2020:2024	Authors	23816	Single-authored	76
-				documents	
Sources (Journals,	866	Author	32109	Documents per	0.118
Books, etc)		Appearances		Author	
Documents	2810	Authors of single-	73	Authors per	8.48
		authored documents		Document	
Average years	1.87	Authors of multi-	23743	Co-Authors per	11.4
from publication		authored documents		Documents	
Average citations	23.04			Collaboration	8.71
per documents				Index	
Average citations	6.435				
per year per doc					

**Table 1**: The main information of the documents exported from the Scopus database (n = 2810).





- Figure 1: Analysis of documents and citations by year. A) Annual scientific production, and B)
   average article citations per year
- ٤

# • 4. 2. Analysis of keywords, authors, and sources:

The results of keyword analysis with VOSviewer are shown in Figure 2. The co-occurrence of
 both author keywords and index keywords with a minimum occurrence of 20 times for a keyword

- was considered. In this way, 716 keywords have the mentioned conditions, which were categorized
- <sup>r</sup> into four clusters. As well as, keywords such as interleukin 2, sars-cov-2 delta, elasomeran, covilo,
- <sup> $\tau$ </sup> and tozinameran are more recent than other keywords based on time.
- 5 The top authors and their productions are shown in Figure 3. Based on the results obtained from
- the top dutions and then productions are shown in Figure 3. Dased on the results obtained non this analysis, a small number of authors have continuously published documents from 2020 to the
- <sup>7</sup> time of this review.
- <sup>v</sup> The top document publishing sources and their growth trends by year are shown in Figure 4. Based
- ^ on the results shown in this figure, Vaccines (https://www.mdpi.com/journal/vaccines ) and
- <sup>9</sup> Vaccine (<u>https://www.sciencedirect.com/journal/vaccine</u> ) journals have the highest number of
- documents during the years 2022 until the time of this review.
- ۱۱

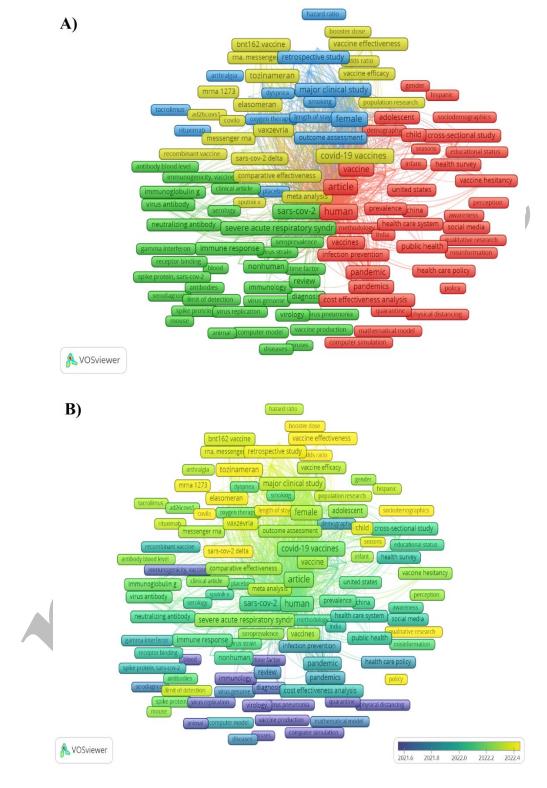
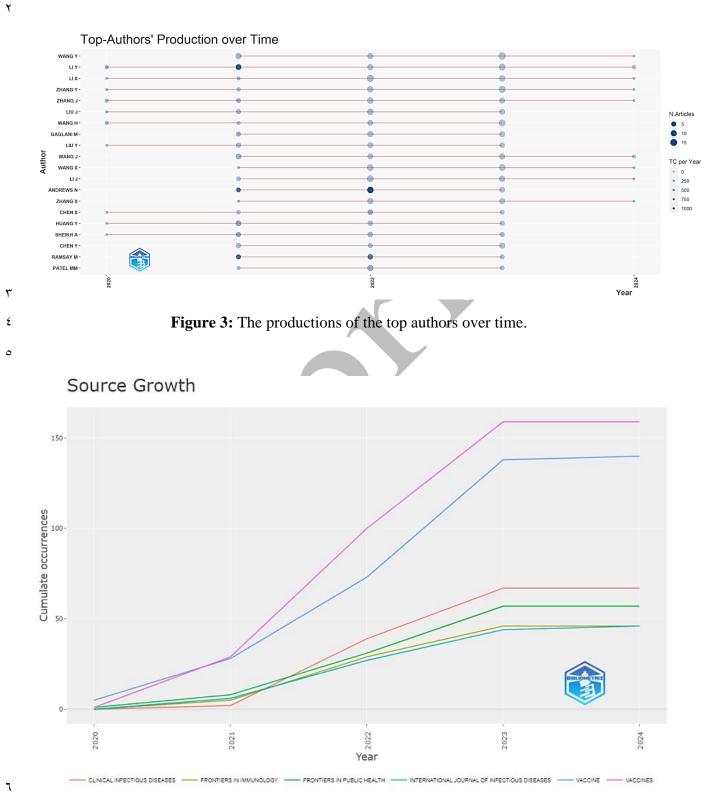


Figure 2: keyword analysis. A) Keyword clustering: Each color belongs to a cluster. B)
 Classification of keywords by year: Light-colored boxes (yellow) are newer than dark-colored boxes (purple).





**Figure 4:** The source dynamics of research shown regard to year of publication.

## Y 4. 3. Most cited documents and countries:

The most cited global documents based on total citation (TC) per year are listed in Table 2. Based
 on this table, the document of Voysey et al. (2021) has the highest TC and also the highest TC per year (13). More than 50 researchers and authors have collaborated on this document.

The United Kingdom and the USA have the highest total citations with 15377 and 11083
 respectively. Also, the average article citations for the United Kingdom and the USA were
 determined to be 83.119 and 20.833, respectively.

٩

١

۱.

**Table 2:** Most global cited documents based on TC per year.

<u> </u>					
Rank	Title	Total	TC per	Normalized	Ref
		Citations	Year	TC	
1	Safety and efficacy of the	3185	796.25	54.4509	(13)
	ChAdOx1 nCoV-19 vaccine				
	(AZD1222) against SARS-				
	CoV-2: an interim analysis of				
	four randomised controlled				
	trials in Brazil, South Africa,				
	and the UK				
2	Effectiveness of Covid-19	1764	441	30.1574	(14)
	Vaccines against the B.1.617.2				
	(Delta) Variant				
3	BNT162B2 mRNA covid-19	1658	414.5	28.3452	(15)
	vaccine in a nationwide mass				
	vaccination setting				
4	Safety and efficacy of single-	1531	382.75	26.174	(16)
	dose Ad26.CoV2.s vaccine				
	against covid-19				
5	Covid-19 Vaccine Effectiveness	1262	420.667	67.2809	(17)
	against the Omicron (B.1.1.529)				
	Variant				
6	Waning immune humoral	1048	262	17.9167	(18)
	response to BNT162B2				· · ·
	COVID-19 vaccine over 6				
	months				
L					

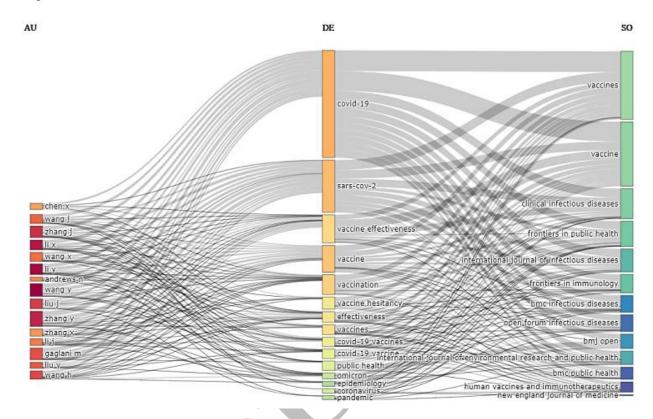
۱۱

17 4. 4. Three-fields plot:

The relationship of the best in the three fields of keyword, author, and source is shown in Figure

5. In each column of this figure, the boxes with higher heights are superior to their counterparts.

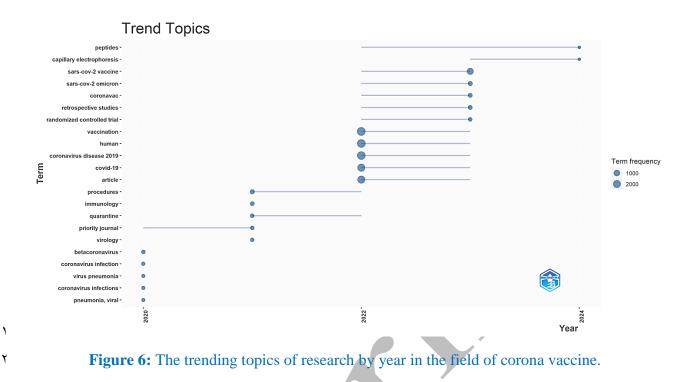
- The keywords Covid-19 and sars-cov-2 are mentioned in the documents of all the authors listed in
- ۲ Figure 5.



- <sup>2</sup> **Figure 5:** Three-field plot of top keywords (middle), top authors (left), and top sources (right).
- 0

**4**. 5. Trend topics:

Figure 6 shows the trending topics based on the minimum frequency of the word 5 times. Based on the results shown in this figure, terms such as peptides and capillary electrophoresis are trending topics in 2024. According to the time of collecting information from the Scopus database, the frequency of these terms is less than 1000. Also, the most frequent terms belong to vaccination, human, coronavirus disease 2019, Covid-19, and article in 2022. The frequency of each of these terms was determined around 2000.



<sup>2</sup> The analysis of documents published in databases or scientific search databases determines the

trend of topics from the past to the present. These results can be useful for researchers by
 illuminating hot spots and scientific gaps (19). Bibliometric analyses are of interest in various

Maintaining not spots and scientific gaps (17)
 A aspects of microbiology (20).

In the past, bibliometric reviews similar to the present study have been carried out by some researchers on the topic of Covid-19 (21-24). Analysis using VOS viewer was used in most of these

• studies. However, the current research is one of the most recent studies in terms of database, time

period, and limitations applied in data extraction and analysis using R software.

Because this review was conducted at the beginning of 2024, the number of published documents is the lowest (n = 56) compared to previous years. This point should be taken into consideration in

is the lowest (n = 56) compared to previous years. This point should be taken into consideration in the review of 2024 trend topics. According to the number of articles and reviews, the number of

published books seems to be low. The smaller number of published books may be justified considering the short time that has passed

considering the short time that has passed.

Elasomeran, Covilo, and Tozinameran are all three Covid-19 vaccines that are shown in the
 keyword analysis. Elasomeran is manufactured by Moderna and Tozinameran is manufactured by
 Pfizer-BioNTech. Both of these vaccines are based on mRNA. Covilo is an inactivated virus

vaccine produced by Sinopharm. Other names of Elasomeran, Tozinameran, and Covilo are

mRNA-1273, BNT162b2, and BBIBP-CorV respectively (7).

The trend topics of 2024 with the terms peptides and capillary electrophoresis are shown in the

research article by Mohammadi et al (25) and the review by Stefanik et al (26). In these documents,

- viral peptides are considered vaccine candidates due to some favorable characteristics such as
- <sup>vo</sup> hydrophilicity, flexibility, antigenicity, and charging characteristics (25). Also, the capillary

electrophoresis technique is introduced as an alternative and cost-effective method for the investigation of peptides (26-30).

٣

٤

### 4. Conclusion:

In this study, no time limit was applied to document collection. However, documents related to the manufacturing technology and effectiveness of the Corona vaccine were found in the four subject areas 1) medicine, 2) immunology and microbiology, 3) biochemistry, genetics and molecular biology, and 4) pharmacology, toxicology, and pharmaceutics in the Scopus database from 2020 onwards. Since there was no need to make and test the vaccines for Covid-19 before the pandemic started. This matter will be taken into consideration in the mentioned areas after the coronavirus

n pandemic.

### **Ethics Declarations**

- **Competing Interests:** There are not any conflicts of interest among the authors.
- **Funding:** Funding information: Not applicable
- **No** Author contributions:
- **Data Availability:** Data will be available after publication
- **Ethics Approval:** All authors approve the ethics in this study
- 14 Acknowledgment: Not applicable.
- ۱۹
- ۲.

#### **References:**

- Contini C, Di Nuzzo M, Barp N, Bonazza A, De Giorgio R, Tognon M, et al. The novel zoonotic COVID-19 pandemic: An expected global health concern. The Journal of Infection in Developing Countries. 2020;14(03):254-64. doi:10.3855/jidc.12671
- Yo
   2. Badasyan I, Nushikyan RV. Investigation of Salmonellosis during and after the COVID-19 Pandemic (2020-2023). Research in Biotechnology and Environmental Science. 2023 Jun 16;2(2):30-4.
- Salehinasab A, Sichani AR, Mousavi M, Bayat Z, Pezhhan A, Hussien BM, Ahmed M, Hassanshahian M. Investigation of Microbial Biofilms during COVID-19 Pandemic: A Bibliometric Analysis. IRANIAN RED CRESCENT MEDICAL JOURNAL. 2023 Jan 1:25(9).
- 4. Qasemi, A., Lagzian, M. and Bayat, Z., Cancer and COVID-19: a double burden on the healthcare system. 2023;25(2):2662.

١ 5. Jevanathan M, Afkhami S, Smaill F, Miller MS, Lichty BD, Xing Z. Immunological considerations ۲ for COVID-19 vaccine strategies. Nat Rev Immunol. 2020;20(10):615-32. doi:10.1038/s41577-٣ 020-00434-6 ٤ 6. Angaji SG, Salim MA, Azizi A, Amiri N, Rastakhiz S, Jahani N, Akhlaghi B, Tirtashi PE. The ٥ Power of Nanovaccines in Immunotherapy of Melanoma, Lung, Breast, and Colon Cancers: A ٦ Comprehensive Review. Research in Biotechnology and Environmental Science. 2023 Dec ٧ 25;2(4):55-64. ٨ 7. Zasada AA, Darlińska A, Wiatrzyk A, Woźnica K, Formińska K, Czajka U, et al. COVID-19 ٩ Vaccines over Three Years after the Outbreak of the COVID-19 Epidemic. Viruses. 2023;15(9). ۱. doi:10.3390/v15091786 8. Donthu N, Kumar S, Mukherjee D, Pandey N, Lim WM. How to conduct a bibliometric analysis: 11 ۱۲ guidelines. An overview and Journal of Business Research. 2021;133:285-96. ۱۳ doi:https://doi.org/10.1016/j.jbusres.2021.04.070 ١٤ 9. Abdalfatah MF, Hjazi A, Saravani K, Hassanshahian M, Bayat Z, Soheil Beigie G. Screening of 10 biofilm-producing genes from Acinetobacter isolates obtained Covid-19 patients in ICU hospital ١٦ section. Archives of Razi Institute. 2024 Jun 15. 10. Past V, Naderi M, Saremi G, Azizi P, Javadzadeh M, Shahveh S, Hosseini P, Sokhanvaran S, ۱۷ ۱۸ Shahveh S, Moghimi S, Hedeshi S. The Application of Ozone Gas in Inactivation of Surface and ۱٩ Airborne SARS-CoV-2 in Hospitals: A Systematic Review. Ozone: Science & Engineering. 2024 ۲. Jun 9:1-21. ۲١ 11. van Eck N, Waltman L. Software survey: VOSviewer, a computer program for bibliometric ۲۲ mapping. Scientometrics. 2010;84(2):523-38. doi:https://doi.org/10.1007/s11192-009-0146-3 ۲٣ 12. Aria M, Cuccurullo C. bibliometrix: An R-tool for comprehensive science mapping analysis. ۲٤ Journal of Informetrics. 2017;11(4):959-75. doi:https://doi.org/10.1016/j.joi.2017.08.007 ۲0 13. Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Safety and efficacy ۲٦ of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four ۲۷ randomised controlled trials in Brazil, South Africa, and the UK. Lancet. 2021;397(10269):99-111. ۲۸ doi:10.1016/S0140-6736(20)32661-1 ۲٩ 14. Bernal JL, Andrews N, Gower C, Gallagher E, Simmons R, Thelwall S, et al. Effectiveness of ۳. Covid-19 Vaccines against the B.1.617.2 (Delta) Variant. New Engl J Med. 2021;385(7):585-94. 31 doi:10.1056/NEJMoa2108891 ٣٢ 15. Dagan N, Barda N, Kepten E, Miron O, Perchik S, Katz MA, et al. BNT162B2 mRNA covid-19 ٣٣ vaccine in a nationwide mass vaccination setting. New Engl J Med. 2021;384(15):1412-23. ٣٤ doi:10.1056/NEJMoa2101765 30 16. Sadoff J, Gray G, Vandebosch A, Cárdenas V, Shukarev G, Grinsztejn B, et al. Safety and efficacy 37 of single-dose Ad26.CoV2.s vaccine against covid-19. New Engl J Med. 2021;384(23):2187-201. ۳۷ doi:10.1056/NEJMoa2101544 ۳٨ 17. Andrews N, Stowe J, Kirsebom F, Toffa S, Rickeard T, Gallagher E, et al. Covid-19 Vaccine ٣٩ Effectiveness against the Omicron (B.1.1.529) Variant. New Engl J Med. 2022;386(16):1532-46. ٤. doi:10.1056/NEJMoa2119451 ٤١ 18. Levin EG, Lustig Y, Cohen C, Fluss R, Indenbaum V, Amit S, et al. Waning immune humoral ٤٢ response to BNT162B2 COVID-19 vaccine over 6 months. New Engl J Med. 2021;385(24). ٤٣ doi:10.1056/NEJMoa2114583 ٤٤ 19. Aliasghari Veshareh A, hamayeli H, Rabbani khorasgani M. Anti-microbial properties of Rosa 20 damascene: A Bibliometric Study. Plant Biotechnology Persa. 2023;5(2):86-99. ٤٦ 20. Vosoughian N, Mohammadi A, Hamayeli H. Bacteria as an Efficient Bacteriosystem for the ٤٧ Synthesis of Nanoparticles: A Bibliometric Analysis. Nano. 2021;16(14):2130014. ٤A doi:10.1142/s1793292021300140 ٤٩ 21. Yaacob A, Gan JL. Bibliometric analysis OF global research developments ON the role OF ٥. technology during COVID-19: current trends and future prospect. Journal of Content, Community 01 and Communication. 2021;13(7):166-80.

- 22. Ahmad T, Murad MA, Baig M, Hui J. Research trends in COVID-19 vaccine: a bibliometric analysis. Human Vaccines & Immunotherapeutics. 2021;17(8):2367-72.
  - 23. Xu Z, Qu H, Ren Y, Gong Z, Ri HJ, Zhang F, et al. Update on the COVID-19 vaccine research trends: a bibliometric analysis. Infect Drug Resist. 2021:4237-47.
- 24. Chen Y, Cheng L, Lian R, Song Z, Tian J. COVID-19 vaccine research focusses on safety, efficacy, immunoinformatics, and vaccine production and delivery: a bibliometric analysis based on VOSviewer. Bioscience trends. 2021;15(2):64-73.
- 25. Mohammadi S, Pour SK, Jalili S, Barazesh M. Designing of a Novel Candidate Multi-epitope Vaccine to boost Immune Responses against SARS-COV-2 using Immunoinformatics and Machine Learning based Approach. Lett Drug Des Discov. 2024;21(2):356-75. doi:10.2174/1570180819666220912105856
  - 26. Stefanik O, Majerova P, Kovac A, Mikus P, Piestansky J. Capillary electrophoresis in the analysis of therapeutic peptides—A review. Electrophoresis. 2024;45(1-2):120-64. doi:10.1002/elps.202300141
- 27. Hamayeli, H., Hassanshahian, M., Askari, M. 2019. The antibacterial and antibiofilm activity of sea anemone (Stichodactyla haddoni) against antibiotic-resistant bacteria and characterization of bioactive metabolites. Int Aquat Res. 11:85–97.
- 28. Hamayeli, H., Shoshtari, A., Hassanshahian, M., Askari, M. 2016. Study the antimicrobial activity of six marine sponges and three parts of sea anemone on *Candida albicans*, J Coastal Life Med 4 (2016) 122–129, https://doi.org/10.12980/jclm.4.2016J6-76.
  - 29. Hassanshahian, M., Bayat, Z., Saeidi, S., Shiri, Y. 2014. Antimicrobial activity of *Trachyspermum ammi* essential oil against human bacterial, Int. J. Adv. Biol. Biomed.
- 30. Khoddami M, Sheikh Hosseini M, Hassanshahian M (2018) Antibacterial activity of Semenovia suffruticosa (essential oil) against pathogenic bacteria and determination of chemical composition of essential oils by gas chromatography–mass spectrometry analysis in four regions of Kerman. J Diet Suppl 29:1–11. https://doi.org/10.1080/19390211.2018.147216.

۱.

۲.