

EXPLORING NEW ANTI-INFLAMMATORY AGENTS: A PHARMACOLOGICAL APPROACH TO RHEUMATOID ARTHRITIS

Esther Obdulia Franco Soto¹, Jessica Yolanda Huarcaya Rojas², Julio José Peña Galindo³, Milexy Amelia Cusi Escate⁴, Teresa Jesús Ccahuana Gonzales⁵, Jaime David Torres Lévano⁶, Luis Alejandro Calle Vilca⁷

1 Universidad Nacional de Ica (UNICA), Perú

Email: esther.franco@unica.edu.pe

ORCID: [0000-0002-5343-8837](https://orcid.org/0000-0002-5343-8837)

2 Universidad Nacional de Ica (UNICA), Perú

Email: jessica.huarcaya@unica.edu.pe

ORCID: [0000-0002-7483-7239](https://orcid.org/0000-0002-7483-7239)

3 Universidad Nacional de Ica (UNICA), Perú

Email: julio.pena@unica.edu.pe

ORCID: [0000-0001-6475-7609](https://orcid.org/0000-0001-6475-7609)

4 Universidad Nacional de Ica (UNICA), Perú

Email: milexyce23@gmail.com

ORCID: [0000-0001-6051-6429](https://orcid.org/0000-0001-6051-6429)

5 Universidad Nacional de Ica (UNICA), Perú

Email: teresa.ccahuana@unica.edu.pe

ORCID: [0000-0003-2409-5676](https://orcid.org/0000-0003-2409-5676)

6 Universidad Nacional de Ica (UNICA), Perú

Email: jaime.torres@unica.edu.pe

ORCID: [0000-0002-9024-2630](https://orcid.org/0000-0002-9024-2630)

7 Universidad Nacional de Ica (UNICA), Perú

Email: lcalle@unica.edu.pe

ORCID: [0000-0003-0473-3175](https://orcid.org/0000-0003-0473-3175)

Abstract

A documentary review was carried out on the production and publication of research papers related to the study of the variables Anti-inflammatory Agents, Rheumatoid Arthritis and Pharmacology. The purpose of the bibliometric analysis proposed in this document was to know the main characteristics of the volume of publications registered in the Scopus database during the period 2018-2023 with respect to the study of the aforementioned variables, achieving the identification of 126 publications in total. The information provided by this platform was organized through graphs and figures categorizing the information by Year of Publication, Country of Origin, Area of Knowledge and Type of Publication. Once these characteristics have been described, the position of different authors regarding the proposed theme is referenced through a qualitative analysis. Among the main findings made through this research, it is found that China, with 82 publications, was the country with the highest scientific production registered in the name of authors affiliated with institutions in that nation. The Area of Knowledge that made the greatest contribution to the construction of bibliographic material related to the study of Anti-inflammatory Agents, Rheumatoid Arthritis and Pharmacology was Pharmacology, Toxicology and Pharmaceuticals with 101 published documents, and the Type of Publication that was most used during the period indicated above was the Journal Article, which represents 58% of the total scientific production.

Key words: Anti-inflammatory agents, Rheumatoid arthritis, Pharmacology.

1. Introduction

Rheumatoid arthritis is one of the most common diseases presented in the adult population which affects about 2% of the world population, this type of arthritis predominates mainly more in women than in men, this type of autoimmune disease generally occurs in the ages of 35 and 50 years, which leads to an attack on the immune system that attacks the joints and this leads to a disability for patients who suffer from it. This chronic disease is characterized by its long duration in patients and in turn these invade and erode the cartilage and bones of the joints. . One of the main treatments to alleviate this disease is based on the use of analgesic and anti-inflammatory methods, as well as the use of male steroids, which helps to reduce symptoms. (Puig, Ferreiro, Castaño, & Clara, 2011)

The approach to the treatment of rheumatoid arthritis is not based on curing the disease, but this branch aims to reduce the health problems that this pathology brings with it such as serious, reduction of pain, control of joints, early prevention and improvement of the quality of life of patients, this series of factors includes pharmacological or non-pharmacological means, which must be attended by a rheumatologist doctor.

In the first instance, it is understood that the problems of this disease are of a multifactorial order, since there are a series of factors that must be taken into account, such as the genetic disposition of people, the immune system, the environmental environment such as viruses, and bacteria, among others. In this series of factors that can aggravate the disease, the pharmacology sector has been responsible for developing pharmacological alternatives that improve the quality of life of people with this disease and also observe how they evolve in the long term (Table 1). Therefore, despite the intervention of pharmacology in this chronic disease, it is expected that pharmacological treatments can contribute to lowering the numbers of adhesions and improve therapeutic use for better management and control.

	Examples	Mechanism of Action
glucocorticoids	Naproxen, Paracetamol, Prednisone	Reduction of pain and inflammation, acts in the inhibition of cyclo-oxygenases (COX-1 and 2)
Disease-modifying antirheumatic drugs (DMARDs)	Sulfazalacine, Lefluonamide, Methotrexate, Hydroxychloroquine	It inhibits the secretion of pro-inflammatory cytokines or decreases the interaction of T cells. These are involved in metabolism and block cell proliferation and provide an inflammatory response.
Biological agents	Infliximab, Tocilizumab	It intervenes in response to the action of cytokines and pro-inflammatory regulators.

Board 1: Pharmacological Alternatives for the Treatment of Rheumatoid Arthritis

This table details the mechanisms of action by pharmacology in alternative treatments for Rheumatoid Arthritis (RA).

However, for these alternative mechanisms to have a positive impact on the adherence to treatment of people with RA lies in the impact that this disease has on health systems and how they must offer quality of life for patients. Despite this, there are challenges that must be faced since a low level of this correlates with unfavorable therapeutic prognoses and can lead to a progression of the disease, these factors would lead to a collapse in the specialties in charge of this disease and increase in costs for health systems. To mitigate these problems, educational interventions must be carried out between patients and doctors, since patients must be made aware of the importance of the use of drugs for this disease, likewise, with the help of technological resources, it seeks to promote quality information about the disease, negative effects of the lack of therapy and how it is essential that patients are at the forefront of therapeutic schemes. For this reason, this article seeks to describe the main characteristics of the compendium of publications indexed in the Scopus database related to the variables Anti-inflammatory Agents, Rheumatoid Arthritis and Pharmacology, as well. Such as the description of the position of certain authors affiliated with institutions, during the period between 2018 and 2023.

2. General objective

To analyze, from a bibliometric and bibliographic perspective, the production of research papers on the variables Anti-inflammatory Agents, Rheumatoid Arthritis and Pharmacology registered in Scopus during the period 2018-2023.

3. Methodology

Quantitative analysis of the information provided by Scopus is carried out under a bibliometric approach on the scientific production related to the study of Anti-inflammatory Agents, Rheumatoid Arthritis and Pharmacology. Likewise, examples of some research works published in the area of study indicated above are analyzed from a qualitative perspective, from a bibliographic approach to describe the position of different authors regarding the proposed topic.

The search is carried out through the tool provided by Scopus and parameters referenced in Figure 1 are established.

3.1 Methodological design

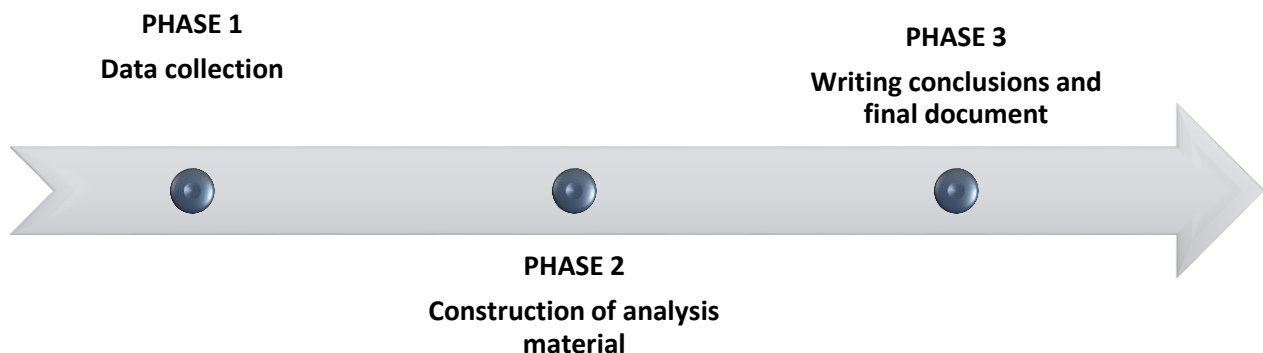


Figure 1. Methodological design
Source: Own elaboration

3.1.1 Phase 1: Data Gathering

Data collection is carried out through the Search tool on the Scopus website, through which a total of 126 publications are identified. To this end, search filters were established that consisted of:

TITLE-ABS-KEY (anti-inflammatory AND agents, AND rheumatoid AND arthritis, AND pharmacology) AND PUBYEAR > 2017 AND PUBYEAR < 2024

- ✓ Published documents whose study variables are related to the study variables Anti-inflammatory Agents, Rheumatoid Arthritis and Pharmacology
- ✓ Without distinction of country of origin.
- ✓ Without distinction of area of knowledge.
- ✓ Without distinction of type of publication.

3.1.2 Phase 2: Construction of analysis material

The information identified in the previous phase is organized. The classification will be made by means of graphs, figures and tables based on data provided by Scopus.

- ✓ Co-occurrence of Words.
- ✓ Year of publication
- ✓ Country of origin of the publication.
- ✓ Area of knowledge.
- ✓ Post Type

3.1.3 Phase 3: Drafting of the conclusions and final document

After the analysis carried out in the previous phase, the conclusions are drafted and the final document is prepared.

4. Results

4.1 Word co-occurrence

Figure 2 shows the co-occurrence of keywords within the publications identified in the Scopus database.

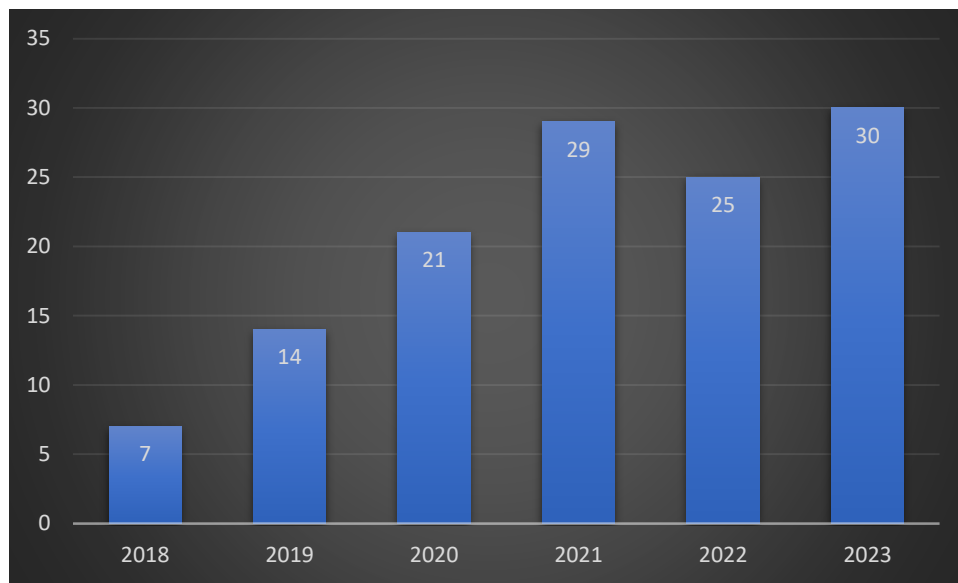


Figure 3. Distribution of scientific production by year of publication.
Source: Authors' elaboration (2024); based on data provided by Scopus.

Among the main characteristics evidenced by the distribution of scientific production by year of publication, an increase in the number of publications registered in Scopus during the years 2023 is notorious, reaching a total of 30 documents published in journals indexed on this platform. This can be explained thanks to articles such as the one entitled "Calicosin improves collagen-induced arthritis by suppressing the inflammatory response in macrophages through the JNK and NF- κ B pathway" The anti-inflammatory role and mechanism of calicosin were validated in this study by using mouse models of collagen-induced arthritis and bone marrow-derived macrophages stimulated by lipopolysaccharides/interferon gamma. By applying RNA sequencing technology and the networked pharmacological method, the findings demonstrate that calicosin treatment produces significant relief of arthritis symptoms, mitigation of synovial proliferation, impediment of bone and cartilage devastation, and suppression of activated synovial macrophages in collagen-induced arthritis. Mechanistically, activation of the JNK and NF- κ B pathways is inhibited by calicosin in bone marrow-derived macrophages stimulated by lipopolysaccharides/interferon gamma. These results confirm the potential of calicosin, a naturally occurring compound, to attenuate rheumatoid arthritis by acting as an anti-inflammatory agent through multiple pathways.(Liu, 2023)

4.3 Distribution of scientific production by country of origin.

Figure 4 shows how scientific production is distributed according to the nationality of the authors.

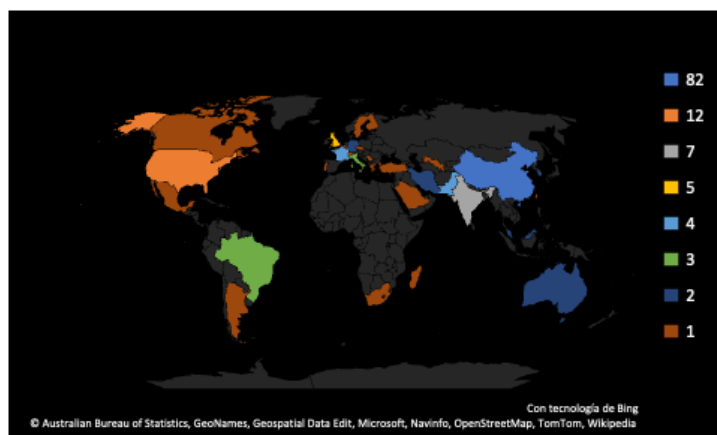


Figure 4. Distribution of scientific production by country of origin.
Source: Authors' elaboration (2024); based on data provided by Scopus.

Within the distribution of scientific production by country of origin, records from institutions were taken into account, establishing China as the country of that community, with the highest number of publications indexed in Scopus during the period 2018-2023, with a total of 82 publications in total. In second place, the United States with 12 scientific papers, and India occupying the third place presenting to the scientific community, with a total of 7 papers among which is the article entitled "Activation of the mitochondrial inflammasome-NLRP3 in macrophages: a novel mechanism of the anti-inflammatory effect of *Notopterygium* in the treatment of rheumatoid arthritis" The mechanism by which *Notopterygium* (NE) regulates nucleotide binding was investigated. the oligomerization domain (NOD)-like receptor family and the pyrin domain-containing inflammasome 3 (NLRP3) to treat rheumatoid arthritis (RA) to reveal the scientific implications of NE in the treatment of RA. Methods: Rats with adjuvant arthritis (AA) were replicated. After the EN intervention, the anti-inflammatory efficacy of EN in vivo was determined. The mechanism of EN in the treatment of RA was predicted by network pharmacology, and the key target for future experiments was found by analysis from the Kyoto Encyclopedia of Genes and Genomes (KEGG). The effect of EN on the NLRP3 inflammasome was verified in AA rats. In addition, with the induction of inflammation in RAW264.7 cells by lipopolysaccharide (LPS), several techniques, such as the Griess assay, enzyme-linked immunosorbent assays, electron microscopy, and fluorescence probe technology, were used to investigate anti-inflammatory and related mechanisms. of EN in the treatment of RA. Results: EN could inhibit inflammation in AA rats.(Liu X. C., 2023)

4.4 Distribution of scientific production by area of knowledge

Figure 5 shows how the production of scientific publications is distributed according to the area of knowledge through which the different research methodologies are executed.

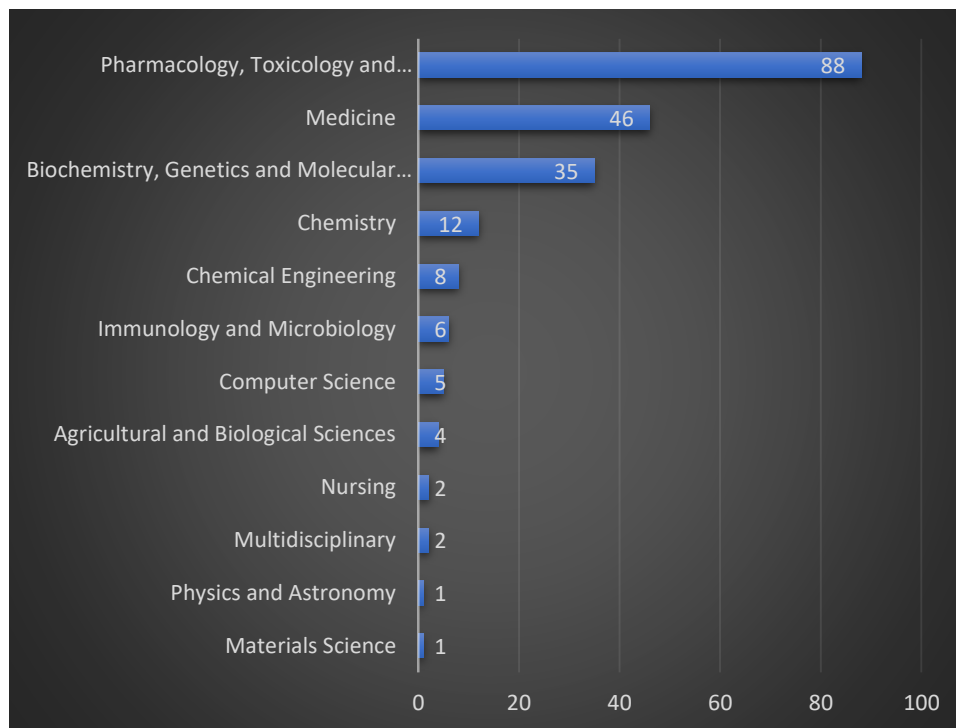


Figure 5. Distribution of scientific production by area of knowledge.
Source: Authors' elaboration (2024); based on data provided by Scopus.

Pharmacology, Toxicology and Pharmacy was the area of knowledge with the highest number of publications registered in Scopus with a total of 88 documents that have based their methodologies on Nursing, Mental Health and Patient Care. In second place, Medicine with 46 articles and Biochemistry, Genetics and Molecular Biology in third place with 35. The above can be explained thanks to the contribution and study of different branches, the article with the greatest impact was registered by Pharmacology, Toxicology and Pharmacy entitled "An integrated network pharmacology approach reveals that darutigenol reduces inflammation and cartilage degradation in a model of collagen-induced arthritis in mice by inhibiting the JAK-STAT3 pathway" The objectives of this research were to determine the effects and elucidate the modes of action of DL on RA-related joint inflammation. Materials and methods: Network pharmacology and molecular coupling were used to select and validate candidate DL targets for the treatment of RA, respectively. A model of rheumatoid arthritis was induced in DBA/1 mice with type II bovine collagen. Administration of intragastric LBP was followed by calculation of the clinical index of arthritis. A section of the ankle joint was removed and stained, and pathological changes were observed in it. Enzyme-linked immunosorbent assays (ELISAs) and Western blotting (WBs) were used to clarify the mechanisms of LBP in the treatment of RA. Results: LBP effectively attenuated inflammation, mitigated joint cartilage degradation and bone erosion, and relieved inflammatory joints associated with RA. The network's pharmacology examined six key DL targets, while molecular coupling revealed that it coupled well with their protein targets.(Wang, 2023)

4.5 Type of publication

Figure 6 shows how the bibliography production is distributed according to the type of publication chosen by the authors

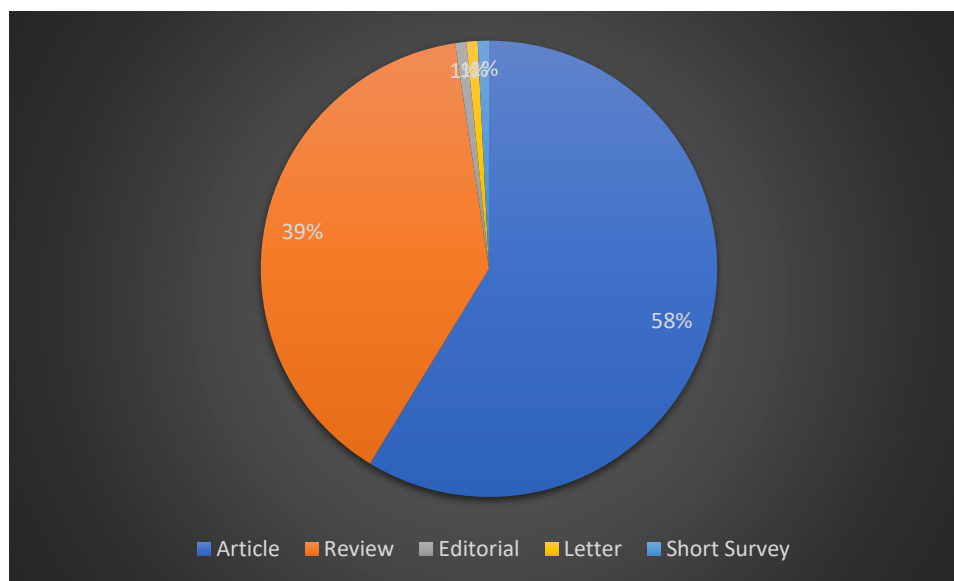


Figure 6. Post Type

Source: Own elaboration (2023); based on data provided by Scopus.

The type of publication most frequently used by the researchers referenced in the body of this document was the one entitled Journal Article with 58% of the total production identified for analysis, followed by Journal with 39%. Editorial are part of this classification, representing 11% of the research papers published during the period 2018-2023, in journals indexed in Scopus. In this last category, the one entitled "Exploration of the chondroprotective effect of *Chaenomeles speciosa* in mice model of glucose-6-phosphate isomerase using an integrated approach of network pharmacology and experimental validation" stands out. In this study, we performed an integrated approach of network pharmacology, molecular coupling and experimental studies to explore the possible mechanism of action of CSP in the treatment of cartilage damage in RA. Results: Studies have shown that quercetin, ent-epicatechin and mairin may be the main active compounds of CSP in the treatment of RA, while AKT1, VEGFA, IL-1 β , IL-6, MMP9, etc., are considered central target proteins for which the main active compounds of CSP bind, as confirmed by molecular coupling. In addition, in vivo experiments validated the potential molecular mechanism of CSP for the treatment of cartilage damage in RA predicted by network pharmacology analysis. CSP was found to downregulate the expression of AKT1, VEGFA, IL-1 β , IL-6, MMP9, ICAM1, VCAM1, MMP3, MMP13, and TNF- α and increase the expression of COL-2 in Glucose-6- joint tissue. Phosphate isomerase (G6PI) model mice. Thus, CSP contributes to the treatment of the cartilage destruction of rheumatoid arthritis.(Duan, 2023)

5. Conclusions

Through the bibliometric analysis carried out in this research work, it was possible to establish that China was the country with the highest number of published records for the variables Anti-inflammatory Agents, Rheumatoid Arthritis and Pharmacology. With a total of 82 publications in the Scopus database. In the same way, it was possible to establish that the application of theories framed in the area of Pharmacology, Toxicology and Pharmacy, As mentioned above, RA is a chronic disease that mainly affects adults, which is characterized by having a great impact on the health of people who suffer from it. since this series of diseases requires continuous treatment that is long-term and

that in turn decreases the activity of this disease. The results obtained from the bibliometric analysis demonstrate the importance of alternative sources by pharmacology for adherence to this disease seeking to improve its quality of life. Despite the interventions of health personnel for the success of these treatments, the drugs reflect multiple adverse effects and dosage schedules that tend to make them complex for patients. This series of challenges shows low rates of treatment adherence, which can trigger negative treatments. To mitigate these problems and the lack of communication about the disease and its causes due to the administration of its treatment, it is important to have an intervention scheme, emphasizing educational activity, this with the objective that patients have greater knowledge about their disease and how their treatments, despite being extended, can generate a higher quality of life. It should also be noted that constant adherence to inflammatory drugs brings with it more and more positive effects. Therefore, these molecules play a critical role in diapedesis which is useful in the treatment of rheumatoid arthritis, which is why it is essential that this series of interventions be carried out on patients, an educational patient about their disease and their situation is essential to achieve positive therapeutic goals and generate an impact on health worldwide.

Bibliographic references

- Duan, Z. J. (2023). *Exploration of the chondroprotective effect of Chaenomeles speciosa in glucose-6-phosphate isomerase model mice using an integrated approach of network pharmacology and experimental validation*. CHINA.
- Liu, X. C. (2023). *Mitochondrial inflammasome-NLRP3 activation in macrophages: a novel mechanism of the anti-inflammatory effect of Notopterygium in the treatment of rheumatoid arthritis*. CHINA.
- Liu, Y. F. (2023). *Calicosin improves collagen-induced arthritis by suppressing the inflammatory response in macrophages via the JNK and NF- κ B pathway*. CHINA.
- Puig, M. N., Ferreiro, R. M., Castaño, S. M., & Clara, M. V. (2011). *Pathophysiology, treatment and experimental models*. Cuba.
- Wang, Y. Y.-L.-R.-G.-D.-C.-Y.-X.-H.-M. (2023). *An integrated network pharmacology approach reveals that darutigenol reduces inflammation and cartilage degradation in a mouse model of collagen-induced arthritis by inhibiting the JAK-STAT3 pathway*. CHINA.
- Alrafiaah, A. S., Alqarny, M. H., Alkubedan, H. Y., AlQueflie, S., & Omair, A. (2017). Are the saudi parents aware of antibiotic role in upper respiratory tract infections in children? *Journal of Infection and Public Health*, 10(5), 579-585. doi:10.1016/j.jiph.2017.01.023
- Alshogran, O. Y., Alzoubi, K. H., Khabour, O. F., & Farah, S. (2018). Patterns of self-medication among medical and nonmedical university students in jordan. *Risk Management and Healthcare Policy*, 11, 169-176. doi:10.2147/RMHP. S170181
- Ambrosy, A. P., Malik, U. I., Thomas, R. C., Parikh, R. V., Tan, T. C., Goh, C. H., . . . Go, A. S. (2021). Rationale and design of the pragmatic randomized trial of icosapent ethyl for high cardiovascular risk adults (MITIGATE). *American Heart Journal*, 235, 54-64. doi:10.1016/j.ahj.2021.01.018
- Angor, M., & Nawasreh, A. O. (2022). Effect of lockdown in the COVID-19 pandemic on dietary habits and self-medication practice in people living in jordan. *International Journal of*

Nutrition, Pharmacology, Neurological Diseases, 12(4), 263-268.

DOI:10.4103/ijnpnd.ijnpnd_50_22

- Araluce, E. A. (2021). Pharmaceutical dispensing in bizkaia during the spanish flu pandemic. [Farmazi dispentsazioa Bizkaian espainiar gripearen pandemian] Gaceta Médica de Bilbao, 118, S41-S48. Retrieved from www.scopus.com
- Araújo, M. G., Magalhães, G. M., Garcia, L. C., Vieira, É. C., Carvalho-Leite, M. D. L. R. D., & Guedes, A. C. M. (2021). Update on human papillomavirus – part II: Complementary diagnosis, treatment and prophylaxis. Anais Brasileiros de Dermatologia, 96(2), 125-138. doi:10.1016/j.abd.2020.11.005
- Arvikar, S. L., Crowley, J. T., Sulka, K. B., & Steere, A. C. (2017). Autoimmune arthritides, rheumatoid arthritis, psoriatic arthritis, or peripheral spondyloarthritis following lyme disease. Arthritis and Rheumatology, 69(1), 194-202. doi:10.1002/art.39866
- Ashraf, S., Ashraf, S., Ashraf, M., Imran, M. A., Choudhary, Z. A., Hafsa, H. T., . . . Izhar, M. (2022). Knowledge, attitude, and practice of clinicians about antimicrobial stewardship and resistance among hospitals of pakistan: A multicenter cross-sectional study. Environmental Science and Pollution Research, 29(6), 8382-8392. DOI:10.1007/S11356-021-16178-2
- Aslam, A., Zin, C. S., Jamshed, S., Ab Rahman, N. S., Ahmed, S. I., Pallós, P., & Gajdács, M. (2022). Self-medication with antibiotics: Prevalence, practices and related factors among the pakistani public. Antibiotics, 11(6) doi:10.3390/antibiotics11060795
- Au Yeung, V., Thapa, K., Rawlinson, W., Georgiou, A., Post, J. J., & Overton, K. (2021). Differences in antibiotic and antiviral use in people with confirmed influenza: A retrospective comparison of rapid influenza PCR and multiplex respiratory virus PCR tests. BMC Infectious Diseases, 21(1) doi:10.1186/s12879-021-06030-w
- Azab, M. A., & Azzam, A. Y. (2021). SARS-CoV-2 associated viral encephalitis with mortality outcome. Interdisciplinary Neurosurgery: Advanced Techniques and Case Management, 25 doi:10.1016/j.inat.2021.101132
- Babiarczyk, B., & Sternal, D. (2022). Analysis of self-care strategies among nurses in southern poland - A cross-sectional survey. International Journal of Occupational Medicine and Environmental Health, 35(1), 13-25. doi:10.13075/IJOMEH.1896.01802
- Bach, T. A., & Zaiken, K. (2017). Outcomes of treatment with direct-acting antivirals for infection with hepatitis C virus genotypes 1–4 in an ambulatory care setting. American Journal of Health-System Pharmacy, 74(5), S1-S9. DOI:10.2146/AJHP160567
- Badr, A. F., Humedi, R. A., Alfarsi, N. A., & Alghamdi, H. A. (2021). Rapid antigen detection test (RADT) for pharyngitis diagnosis in children: Public and pharmacist perception. Saudi Pharmaceutical Journal, 29(7), 677-681. doi:10.1016/j.jsps.2021.04.029
- Bak, A. H., Makarewicz-Wujec, M., & Kozłowska-Wojciechowska, M. (2018). Self-medication with otc drugs during the flu or influenza among the residents of warsaw. sources of knowledge and awareness of dangers generated by inappropriate treatment. Acta Poloniae Pharmaceutica - Drug Research, 75(2), 555-562. Retrieved from www.scopus.com

- Bakken, I. J., Wensaas, K. -, Furu, K., Grøneng, G. M., Stoltenberg, C., Øverland, S., & Håberg, S. E. (2017). Legesøkning og legemiddeluttak etter innføring av nye fraværeregler. *Tidsskrift for Den Norske Lægeforening*, 137(16) doi:10.4045/tidsskr.17.0427
- Banakh, I., Lam, A., Turek, M., Htet, T., & Vorlander, C. (2017). Rapid versus standard iron polymaltose infusions: A single centre safety study. *Journal of Pharmacy Practice and Research*, 47(2), 103-109. doi:10.1002/JPPR.1236
- Beechar, V. B., De la Flor, C., & Medford, R. J. (2020). Non-typeable haemophilus influenzae and purpura fulminans. *BMJ Case Reports*, 13(7) doi:10.1136/bcr-2020-234880
- Ben Mabrouk, A., Larbi Ammari, F., Werdani, A., Jemmali, N., Chelli, J., Mrabet, H. E., . . . Mahjoub, B. (2022). Parental self-medication with antibiotics in a tunisian pediatric center. *Therapies*, 77(4), 477-485. doi:10.1016/j.therap.2021.10.007
- Berenson, A. B., Chang, M., Hirth, J. M., & Kanukurthy, M. (2021). Intent to get vaccinated against COVID-19 among reproductive-aged women in texas. *Human Vaccines and Immunotherapeutics*, 17(9), 2914-2918. doi:10.1080/21645515.2021.1918994
- Berlingieri, G., Alvares, C. M. A., Serrano, R. V., Palma, L. F., & Campos, L. (2022). Phototherapies for COVID-19-associated opportunistic oral infections. *Photodiagnosis and Photodynamic Therapy*, 37 doi:10.1016/j.pdpdt.2021.102678
- Bernardo, C. D. O., Gonzalez-Chica, D., & Stocks, N. (2019). Influenza-like illness and antimicrobial prescribing in australian general practice from 2015 to 2017: A national longitudinal study using the medicineinsight dataset. *BMJ Open*, 9(4) doi:10.1136/bmjopen-2018-026396
- Bibby, H. L., de Koning, L., Seiden-Long, I., Zelyas, N., Church, D. L., & Berenger, B. M. (2022). A pragmatic randomized controlled trial of rapid on-site influenza and respiratory syncytial virus PCR testing in paediatric and adult populations. *BMC Infectious Diseases*, 22(1) doi:10.1186/s12879-022-07796-3
- Bouزيد, D., Lucet, J. -, Duval, X., Houhou-Fidouh, N., Casalino, E., Visseaux, B., . . . Ghazali, A. (2020). Multiplex PCR implementation as point-of-care testing in a french emergency department. *Journal of Hospital Infection*, 105(2), 337-338. doi:10.1016/j.jhin.2020.01.021
- Brooten, D., Youngblut, J. M., Caicedo, C., del Moral, T., Cantwell, G. P., & Totapally, B. (2018). Parents' acute illnesses, hospitalizations, and medication changes during the difficult first year after infant or child NICU/PICU death. *American Journal of Hospice and Palliative Medicine*, 35(1), 75-82. doi:10.1177/1049909116678597
- Burns, A., Goodlet, K. J., Chapman, A., & Roberts, E. P. (2020). A case report of self-medication with over-the-counter fish antibiotic: Implications for pharmacists. *Journal of the American Pharmacists Association*, 60(4), e121-e123. doi:10.1016/j.japh.2019.12.020
- Cai, Z. -, Liang, J. -, Lin, Y., & Huang, M. -. (2019). Antimicrobial prescribing for outpatients with laboratory-confirmed influenza in a large children's hospital: A retrospective study. [某大型儿童医院门诊流感患者抗菌药物使用情况回顾性分析] *Chinese Pharmaceutical Journal*, 54(16), 1336-1342. doi:10.11669/CPJ.2019.16.012

- Calderón-Parra, J., Muiño-Miguez, A., Bendala-Estrada, A. D., Ramos-Martínez, A., Muñoz-Rubio, E., Carracedo, E. F., . . . Núñez-Cortés, J. M. (2021). Inappropriate antibiotic use in the COVID-19 era: Factors associated with inappropriate prescribing and secondary complications. analysis of the registry SEMI-COVID. PLoS ONE, 16(5 May) doi:10.1371/journal.pone.0251340
- Campos Fernández de Sevilla, M. Á., Gallego Úbeda, M., Heredia Benito, M., García-Cabrera, E., Monje García, B., Tovar Pozo, M., . . . Iglesias-Peinado, I. (2019). Implementation of a pharmaceutical care program for patients with hepatitis C treated with new direct-action antivirals. *International Journal of Clinical Pharmacy*, 41(2), 488-495. DOI:10.1007/S11096-019-00809-3
- Cangini, A., Fortinguerra, F., Di Filippo, A., Pierantozzi, A., Da Cas, R., Villa, F., . . . Gagliotti, C. (2021). Monitoring the community use of antibiotics in Italy within the national action plan on antimicrobial resistance. *British Journal of Clinical Pharmacology*, 87(3), 1033-1042. doi:10.1111/bcp.14461
- Carballo, N., Garcia-Alzórriz, E., Ferrández, O., Navarrete-Rouco, M. E., Durán-Jordà, X., Pérez-García, C., . . . Grau, S. (2021). Impact of non-persistence on healthcare resource utilization and costs in patients with immune-mediated rheumatic diseases initiating subcutaneous TNF-alpha inhibitors: A before-and-after study. *Frontiers in Pharmacology*, 12 doi:10.3389/fphar.2021.752879
- Chae, C., Davies, N. G., Jit, M., & Atkins, K. E. (2020). Effect of pediatric influenza vaccination on antibiotic resistance, England and Wales. *Emerging Infectious Diseases*, 26(1), 138-142. doi:10.3201/eid2601.191110
- Chavoustie, S., Frost, M., Snyder, O., Owen, J., Darwish, M., Dammerman, R., & Sanjurjo, V. (2017). Buprenorphine implants in medical treatment of opioid addiction. *Expert Review of Clinical Pharmacology*, 10(8), 799-807. doi:10.1080/17512433.2017.1336434
- Chen, L., Han, X., Li, Y. L., Zhang, C., & Xing, X. (2020). The impact of early neuraminidase inhibitor therapy on clinical outcomes in patients hospitalised with influenza A-related pneumonia: A multicenter, retrospective study. *BMC Infectious Diseases*, 20(1) doi:10.1186/s12879-020-05322-x
- Chen, Y., Yu, H., Guo, F., Wu, Y., & Li, Y. (2018). Antinociceptive and anti-inflammatory activities of a standardized extract of bis-iridoids from *Pteroccephalus hookeri*. *Journal of Ethnopharmacology*, 216, 233-238. doi:10.1016/j.jep.2018.01.035
- Chiappini, E., Motisi, M. A., Becherucci, P., Pierattelli, M., Galli, L., & Marchisio, P. (2020). Italian primary care paediatricians' adherence to the 2019 national guideline for the management of acute otitis media in children: A cross-sectional study. *International Journal of Pediatric Otorhinolaryngology*, 138 doi:10.1016/j.ijporl.2020.110282
- Chukwu, E. E., Oladele, D. A., Enwuru, C. A., Gogwan, P. L., Abuh, D., Audu, R. A., & Ogunsola, F. T. (2021). Antimicrobial resistance awareness and antibiotic prescribing behavior among healthcare workers in Nigeria: A national survey. *BMC Infectious Diseases*, 21(1) doi:10.1186/s12879-020-05689-x

- Chukwuone, C. A., Onuoha, K. M., & Maxwell, L. C. (2022). Self-medication among undergraduates: A case study of university of nigeria, nsukka. *Journal of Home Economics Research*, 29(2), 76-85. Retrieved from www.scopus.com
- Coppock, K. (2018). Overuse of acetaminophen more common during flu season. *Pharmacy Times*, 2018(September) Retrieved from www.scopus.com
- Cortez, J., Rosário, E., Pires, J. E., Taborda Lopes, J., Francisco, M., Vlieghe, E., & Brito, M. (2017). Antimicrobial storage and antibiotic knowledge in the community: A cross-sectional pilot study in north-western angola. *International Journal of Infectious Diseases*, 60, 83-87. doi:10.1016/j.ijid.2017.05.011
- Creedon, T. B., Zuvekas, S. H., Hill, S. C., Ali, M. M., McClellan, C., & Dey, J. G. (2022). Effects of medicaid expansion on insurance coverage and health services use among adults with disabilities newly eligible for medicaid. *Health Services Research*, 57(S2), 183-194. doi:10.1111/1475-6773.14034
- Crunkhorn, C., van Driel, M., Nguyen, V., & McGuire, T. (2017). Children's medicine: What do consumers really want to know? *Journal of Paediatrics and Child Health*, 53(2), 155-162. doi:10.1111/jpc.13339
- Cuyle, P. -, & Prenen, H. (2018). Practical management of toxicities associated with targeted therapies for advanced gastroenteropancreatic neuroendocrine tumors. *Annals of Gastroenterology*, 31(2), 140-150. doi:10.20524/aog.2018.0224
- Dal Negro, R. W., Zanasi, A., Turco, P., & Povero, M. (2018). Influenza and influenza-like syndromes: The subjects' beliefs, the attitude to prevention and treatment, and the impact in italian general population. *Multidisciplinary Respiratory Medicine*, 13(1) doi:10.1186/s40248-018-0119-6
- Dale, A. P., Ebell, M., McKay, B., Handel, A., Forehand, R., & Dobbin, K. (2019). Impact of a rapid point of care test for influenza on guideline consistent care and antibiotic use. *Journal of the American Board of Family Medicine*, 32(2), 226-233. doi:10.3122/jabfm.2019.02.180183
- Davidson, E. R., Snider, M. J., Bartsch, K., Hirsch, A., Li, J., & Larry, J. (2020). Tolerance of proprotein convertase Subtilisin/Kexin type 9 (PCSK9) inhibitors in patients with self-reported statin intolerance. *Journal of Pharmacy Practice*, 33(3), 276-282. doi:10.1177/0897190018799218
- de Martino, M., Chiarugi, A., Boner, A., Montini, G., & de' Angelis, G. L. (2017). Working towards an appropriate use of ibuprofen in children: An evidence-based appraisal. *Drugs*, 77(12), 1295-1311. DOI:10.1007/S40265-017-0751-Z
- Delyagin, W. M. (2021). Specific therapy and emergency prevention of flu. *Meditinskiy Sovet*, 2021(1), 116-123. doi:10.21518/2079-701X-2021-1-116-123
- Devaraj, N. K., Rashid, A. A., Abdullah, K. H. A., & Manap, A. H. A. (2021). Antidepressant discontinuation syndrome – a case report. *Malta Medical Journal*, 33(1), 116-120. Retrieved from www.scopus.com

- Di Giambenedetto, S., Ciccullo, A., Borghetti, A., Gambassi, G., Landi, F., Visconti, E., . . . Gasbarrini, A. (2020). Off-label use of tocilizumab in patients with SARS-CoV-2 infection. *Journal of Medical Virology*, 92(10), 1787-1788. doi:10.1002/jmv.25897
- Doherty, T. M., Hausdorff, W. P., & Kristinsson, K. G. (2020). Effect of vaccination on the use of antimicrobial agents: A systematic literature review. *Annals of Medicine*, 52(6), 283-299. doi:10.1080/07853890.2020.1782460
- Drury, J. (2018). Sick days because of a cold or a cough: How brown bagging can bring clarity. *Pharmacy Times*, 2018(November) Retrieved from www.scopus.com
- El Guerche-Séblain, C., Moureau, A., Schiffler, C., Dupuy, M., Pepin, S., Samson, S. I., . . . Schellevis, F. (2019). Epidemiology and burden of influenza in healthy children aged 6 to 35 months: Analysis of data from the placebo arm of a phase III efficacy trial. *BMC Infectious Diseases*, 19(1) doi:10.1186/s12879-019-3920-8
- Fahy, E. F., McCarthy, E., Steinhagen-Thiessen, E., & Vaughan, C. J. (2017). A case of autosomal recessive hypercholesterolemia responsive to proprotein convertase subtilisin/kexin 9 inhibition. *Journal of Clinical Lipidology*, 11(1), 287-288. doi:10.1016/j.jacl.2016.10.002
- Fardeau, C., Simon, A., Rodde, B., Viscogliosi, F., Labalette, P., Looten, V., . . . LeHoang, P. (2017). Interferon-alpha2a and systemic corticosteroid in monotherapy in chronic uveitis: Results of the randomized controlled BIRDFERON study. *American Journal of Ophthalmology*, 177, 182-194. doi:10.1016/j.ajo.2017.03.001
- Fjelltveit, E. B., Cox, R. J., Kittang, B. R., Blomberg, B., Buanes, E. A., Langeland, N., . . . Brokstad, K. A. (2022). Lower antibiotic prescription rates in hospitalized COVID-19 patients than influenza patients, a prospective study. *Infectious Diseases*, 54(2), 79-89. doi:10.1080/23744235.2021.1974539
- Flicoteaux, R., Protopopescu, C., Tibi, A., Blanchon, T., Van der Werf, S., Duval, X., . . . Chevret, S. (2017). Factors associated with non-persistence to oral and inhaled antiviral therapies for seasonal influenza: A secondary analysis of a double-blind, multicentre, randomised clinical trial. *BMJ Open*, 7(7) doi:10.1136/bmjopen-2016-014546
- Fu, X., Zhang, Y., Chang, L., Hui, D., Jia, R., Liu, N., . . . Li, Q. (2020). The jpdf has synergistic effect with fluoropyrimidine in the maintenance therapy for metastatic colorectal cancer. *Recent Patents on Anti-Cancer Drug Discovery*, 15(3), 257-269. doi:10.2174/1574892815666200717141205
- Fujibayashi, K., Takahashi, H., Tanei, M., Uehara, Y., Yokokawa, H., & Naito, T. (2018). A new influenza-tracking smartphone app (flu-report) based on a self-administered questionnaire: Cross-sectional study. *JMIR mHealth and uHealth*, 6(6) doi:10.2196/mhealth.9834