

Research on Nonsteroidal Anti-inflammatory Drugs in Malaysia: A Bibliometric Analysis

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ABSTRACT **Background:** Nonsteroidal anti-inflammatory drugs (NSAIDs) are the most common analgesics used for pain relief. Adverse effects of NSAIDs range from gastrointestinal tract disturbances to increased risk of bleeding, renal injury, and myocardial infarction. In Malaysia, the research productivity of NSAIDs is not well explored. **Objective:** This study examined research productivity of NSAIDs in Malaysia. **Materials and Methods:** This bibliometric study included all published research articles on NSAIDs from 1979 to 2018, which were conducted in Malaysia. The search databases such as Google Scholar, PubMed, ScienceDirect, and Scopus were used. Search terms included NSAIDs and specific drug names such as ibuprofen, celecoxib, and naproxen. Growth of publication, authorship pattern, citation analysis, journal index, type of studies, and geographical distribution of institutions publishing articles on NSAIDs were measured. **Results:** Overall, 111 articles were retrieved from 1979 to 2018. The annual productivity of articles throughout the study fluctuated in which the highest productivity was in 2018, 12.61% ($n = 14$). Majority of articles were multiple authored, 99.10% ($n = 109$), and University of Science Malaysia (USM) produced the highest number of articles (30 articles). Most of the articles were International Scientific Indexing-indexed, 52.25% ($n = 58$), and the main issue studied in most of the articles was the drug formulation of NSAIDs. **Conclusion:** The growth of NSAID research in Malaysia was slow, and the majority of research involved laboratory studies. Clinical studies evaluating the clinical outcomes of NSAIDs in patients, particularly using large healthcare databases are still lacking.

KEYWORDS: Analgesics, bibliometric, diclofenac, ibuprofen, Malaysia, nonsteroidal anti-inflammatory drugs


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BACKGROUND

Nonsteroidal anti-inflammatory drugs (NSAIDs) are medicines that provide anti-inflammatory effects and analgesic effects with some antipyretic properties.^[1] NSAIDs are divided into three broad categories based on their selectivity for cyclooxygenase (COX) enzyme. The first category is the selective COX-1 inhibitors such as ketorolac^[2] and aspirin.^[3] The second category includes nonselective COX inhibitors, such as flurbiprofen,^[4]

naproxen,^[5] and indomethacin.^[6] The third category is the selective COX-2 inhibitors such as meloxicam^[7] and celecoxib.^[8] NSAIDs provide pain relief in various pain conditions including osteoarthritis, sprains and strains, lower back pains, gout, and rheumatoid arthritis.^[1]

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The side effects of NSAID include gastrointestinal,^[9] cardiovascular, and renal toxicity.^[10]

To date, the information on the progress of the NSAID research in Malaysia is little known. As such, this study aimed to analyze published literature on NSAIDs conducted in Malaysia, specifically on the growth of publications, citation analysis, type of publications, number of authors, and geographical contribution of the NSAID research. The bibliometric analysis was used to quantitatively and statistically analyze these published articles.^[11]

MATERIALS AND METHODS

This study was exempted from ethical approval as it only involved reviewing the articles and no human subjects were involved in the study.

Search database

In this study, information about NSAID research in Malaysia was retrieved from several databases including Google Scholar, PubMed, ScienceDirect, and Scopus. The databases were sufficient to access all relevant articles because most of the databases were having same articles. Among these databases, only Scopus and ScienceDirect have the analytical function of "source type," which allowed us to analyze the retrieved articles whether they are journal publications, books, or conference proceedings. This study only included original research articles, whereas books and review articles were excluded.

Search strategy

We used search term "NSAIDs in Malaysia" and specific drug names such as ibuprofen, piroxicam, ketoprofen, celecoxib, mefenamic acid, indomethacin, naproxen, meloxicam, and diclofenac. This study included articles published from January 1979 to November 2018.

Outcome measures

The original research articles were analyzed for the following:

Growth of publications

The total productivity of articles on NSAIDs was analyzed annually, and the mean number of articles per year was calculated. The growth of publication was presented as the rate of growth for 10 years interval, and the growth rate (GR) was calculated based on the following formula:

$$GR = \frac{(\text{ending value} - \text{beginning value})}{(\text{beginning value})} \times 100\%$$

where ending value = total number of publications in the latter 10 years, and beginning value = total number of publications in the former 10 years

Authorship pattern and citation analysis

The number of the authors was analyzed and stratified according to single or multiauthored articles. The number of citations per article was also analyzed.

Journal index category

The publications were categorized into International Scientific Indexing (ISI), Scopus, or non-indexed, and the information on their impact factor was obtained from Master Journal List Clarivate, Scopus, and JournalGuide websites. Journals with the highest and the lowest impact factor as well as the range of impact factor for majority of journals were presented.

Types of study and issues addressed in NSAID research

The articles were further analyzed according to their types of study whether laboratory, patient, or animal studies. The issues investigated by the researchers, such as formulation, side effect, prevalence, efficacy, or drug interaction, were also recorded.

Geographical distribution of institution publishing articles on NSAIDs

The institution publishing articles were categorized according to the states of the first author affiliation. Second or third authors were considered if the first author was not from Malaysia. The data were presented in a map with color coding, using an online application of "Visme" (Easy WebContent, Inc., Frederick, MD, USA).

Statistical analysis and ethics

The categorical variables were presented as frequency and percentage, whereas continuous data were presented as mean. Microsoft Excel was used to analyze the data.

RESULTS

Growth of publications

A total of 111 articles were retrieved from 1979 to 2018. All articles were published in English. There was a fluctuation in the number of publications during the study period. From 2015 to 2018, there was a gradual increment in the number of publications from 5.41% ($n = 6$) to 12.61% ($n = 14$). The highest productivity was observed in 2018 with a total of 12.61% ($n = 14$) articles, and the lowest productivity was in 1980–1985, 1987–1990, 1992–1999, and in 2001, with a total productivity of 0% ($n = 0$). The GR for every 10 years showed that there was no GR determined for the first 10-year from 1979–1988. In the subsequent period from 1989–1998, 1999–2008, and 2009–2018, the GRs were 0%, 11%, and 2.5%, respectively. The mean number of publications during the study period was 2.78 articles per year.

Authorship patterns and citation analysis

A total of 554 authors had participated in publishing the articles on NSAIDs during the study period with the mean of five authors per article. The average number of authors per article steadily increased over time, from one author in 1979 to six authors in 2018. There were 0.90% ($n = 2$) single-authored articles, whereas 99.10% ($n = 109$) were the multiauthored articles. A total of 1700 citations were recorded in 2018 with a mean of 15.32 citations per article.

Journal index category

Of 111 articles retrieved, 52.25% ($n = 58$) of the articles were published in ISI-indexed, 20.72% ($n = 23$) were in Scopus-indexed, and 27.03% ($n = 30$) were in non-indexed journals. Among the ISI-indexed and Scopus-indexed journals, *Chemical Engineering Journal*, which studied about the production of high purity (S)-ibuprofen acid using innovative enzymatic membrane technology had the highest impact factor of 8.355, whereas *Latin American Journal of Pharmacy* had the lowest impact factor of 0.29. The impact factor for other journals was ranged from 1.00 to 7.00.

Types of study and issues addressed in NSAID research

Majority of NSAID studies in Malaysia were the laboratory studies, 50.5% ($n = 56$), focusing on the formulation of NSAIDs. There were 32.4% ($n = 36$) studies involving patients and 17.1% ($n = 19$) involving animals.

In the laboratory studies, the most common issue explored was on the formulation of NSAIDs with a

total of 40 articles. For research conducted on patients, the issue of effectiveness of NSAIDs was predominately studied with a total of 13 articles published under this category. On the contrary, for the animal study, the issue of side effects of NSAIDs was commonly investigated with a total of 13 articles. The rest of the NSAID articles addressed other issues such as drug interaction, pharmacokinetics, and prevalence of NSAID use in hospital and primary care settings.

Geographical distribution of institutions publishing articles on NSAID

The research on NSAIDs in Malaysia was conducted in various states in Malaysia; the highest number of published articles was from Wilayah Persekutuan Kuala Lumpur, 37% ($n = 41$), followed by Pulau Pinang, 24% ($n = 27$), and Selangor, 20% ($n = 22$). The overall result of geographical distribution of institutions publishing articles on NSAID is presented in Figure 1. With regard to institution of the first author affiliations, a total of 22 institutions were involved in the publication of articles on NSAIDs, the most active institution being the University of Science Malaysia (USM) with a total of 27.03% ($n = 30$), followed by University of Malaya (UM), 16.22% ($n = 18$), and University Putra Malaysia (UPM), 11.71% ($n = 13$).

DISCUSSION

This study examined the productivity of NSAID research in Malaysia for the past 40 years and found 111 NSAID research articles published within this period. The productivity of NSAID research started to increase in year 2000 onward, the highest being

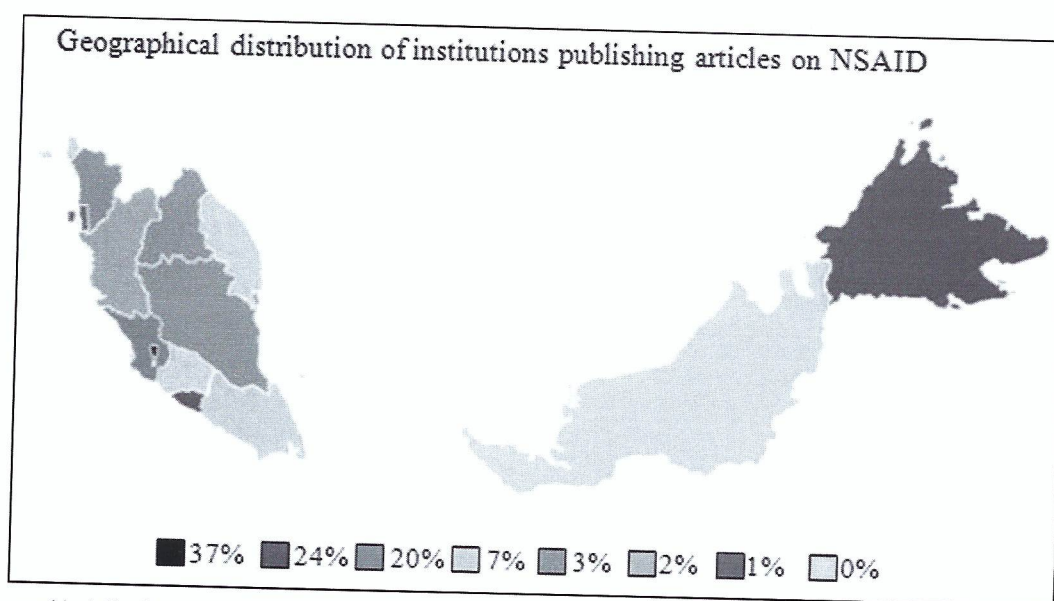


Figure 1: Geographical distribution of articles publishing articles on nonsteroidal anti-inflammatory drug

observed in 2018 with a total of 12.61% ($n = 14$) articles. In the United States, it was reported that approximately 100,000 people were hospitalized as a result of NSAID-related gastrointestinal complications in 1998.^[12] Owing to the various number of reports on side effects of NSAIDs, it had driven the researchers to conduct more research on NSAIDs, particularly on formulations in an effort to minimize the side effects. This study showed that 50% ($n = 7$) of the research done in the year 2018, involved laboratory studies investigating the formulation of NSAIDs. The high number of drug formulation research in Malaysia may reflect the need to explore new and possible generic formulations of NSAIDs in Malaysia. Hence, the new formulations or dosage forms that have more stable and improved pharmacokinetic and pharmacodynamic profiles, such as enhanced solubility and dissolution rate, are required.^[13] As NSAIDs are long-standing analgesic drugs in which most of their patency periods have already lapsed, it is timely for Malaysia to produce its own generic NSAIDs.

This study has also shown that most of the articles were commonly published in the indexed journals with the impact factor ranging from 1.00 to 8.00. This may indicate that the research conducted was of good impact, which was accepted by peer-reviewed journal publications. Concerning the geographical distribution, Wilayah Persekutuan Kuala Lumpur ranked first in the NSAID research productivity because of the high number of universities located in Wilayah Persekutuan Kuala Lumpur such as University of Malaya (UM), National University of Malaysia (UKM), and International Medical University (IMU). Pulau Pinang ranked second because there is only one university in this state that publishes research articles about NSAIDs, that is, the University of Science Malaysia (USM), despite being the most productive university. Moreover, the established research groups in this university contributed to the high productivity of NSAID research in Malaysia.

The limitation of this study should be addressed in which some publications did not mention “NSAIDs or specific drug names available in Malaysia” in their titles or abstracts, therefore it is possible that not all publications regarding NSAIDs were included in the study. Despite the limitation, this study provided some insights on the growth of NSAID research in Malaysia of which little was known.

CONCLUSION

In conclusion, the GR of NSAID research in Malaysia was slow and primarily focused on laboratory studies

involving drug formulation. Research on patients using NSAIDs and its relevant clinical outcomes is still lacking, particularly research using large patient dataset. Therefore, the data presented here will guide future researchers on which aspect of NSAID research to focus on and which unexplored issues of NSAIDs in Malaysia to uncover.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Chua SS, Paraidathathu T. Utilisation of non-steroidal anti-inflammatory drugs (NSAIDs) through community pharmacies in Malaysia. *Asia Pac J Public Health* 2005;17:117-23.
2. Waterbury LD, Silliman D, Jolas T. Comparison of cyclooxygenase inhibitory activity and ocular anti-inflammatory effects of ketorolac tromethamine and bromfenac sodium. *Curr Med Res Opin* 2006;22:1133-40.
3. Perrone MG, Scilimati A, Simone L, Vitale P. Selective COX-1 inhibition: a therapeutic target to be reconsidered. *Curr Med Chem* 2010;17:3769-805.
4. Agrawal R, Lee CS, Gonzalez-Lopez JJ, Khan S, Rodrigues V, Pavesio C. Flurbiprofen: a nonselective cyclooxygenase (COX) inhibitor for treatment of noninfectious, non-necrotizing anterior scleritis. *Ocul Immunol Inflamm* 2016;24:35-42.
5. Shah AA, Thjodleifsson B, Murray FE, Kay E, Barry M, Sigthorsson G, *et al.* Selective inhibition of COX-2 in humans is associated with less gastrointestinal injury: a comparison of nimesulide and naproxen. *Gut* 2001;48:339-46.
6. Yamamoto T, Nozaki-Taguchi N. Analysis of the effects of cyclooxygenase (COX)-1 and COX-2 in spinal nociceptive transmission using indomethacin, a non-selective COX inhibitor, and NS-398, a COX-2 selective inhibitor. *Brain Res* 1996;739:104-10.
7. Furst DE. Meloxicam: selective COX-2 inhibition in clinical practice. *Semin Arthritis Rheum* 1997;26:21-7.
8. Goldenberg MM. Celecoxib, a selective cyclooxygenase-2 inhibitor for the treatment of rheumatoid arthritis and osteoarthritis. *Clin Ther* 1999;21:1497-513; discussion 1427-8.
9. Straus WL, Ofman JJ. Gastrointestinal toxicity associated with nonsteroidal anti-inflammatory drugs: epidemiologic and economic issues. *Gastroenterol Clin* 2001;30:895-920.
10. McPherson ML, Cimino NM. Topical NSAID formulations. *Pain Med* 2013;14:S35-9.
11. Sweileh WM, Al-Jabi SW, AbuTaha AS, Zyoud SH, Anayah FMA, Sawalha AF. Bibliometric analysis of worldwide scientific literature in mobile—health: 2006–2016. *BMC Med Inform Decis Mak* 2017;17:72.
12. Conaghan PG. A turbulent decade for NSAIDs: update on current concepts of classification, epidemiology, comparative efficacy, and toxicity. *Rheumatol Int* 2012;32:1491-502.
13. Lyn LY, Sze HW, Rajendran A, Adinarayana G, Dua K, Garg S. Crystal modifications and dissolution rate of piroxicam. *Acta Pharm* 2011;61:391-402.