

## Pharmacological Effects of Curcumin in Chronic Inflammatory Therapy

**Muntasir<sup>1</sup>, Anggia Faradina<sup>2</sup>, Tutik Wuryandari<sup>3</sup>, Khrisna Agung Cendekiawan<sup>4</sup>**

Universitas Nusa Cendana, Kupang, NTT, Indonesia<sup>1</sup>, Universitas Jambi, Indonesia<sup>2</sup>, Universitas Muhammadiyah Tegal, Indonesia<sup>3</sup>, Universitas dr. Soebandi Jember, Indonesia<sup>4</sup>

E-mail: [muntasir@staf.undana.ac.id](mailto:muntasir@staf.undana.ac.id)

### INFO ARTICLE

**Accepted : February 10, 2025**

**Revised : February 20, 2025**

**Approved : March 19, 2025**

**Published : March 21, 2025**

**Keywords:** Curcumin, Chronic Inflammation, Pharmacological Effects



Creative Commons Attribution-ShareAlike 4.0 International License:

<https://creativecommons.org/licenses/by-sa/4.0/>

### ABSTRACT

*Herbal plants in Indonesia have an important role in traditional medicine and public health. The study aims to evaluate the effectiveness and mechanism of action of curcumin in chronic inflammatory therapy. This study uses the Systematic Literature Review (SLR) method. This study uses a database from Scopus of 9 Scopus articles from the range of 2020 to 2025. There are three stages carried out in mapping the effectiveness and mechanism of action of curcumin in chronic inflammatory therapy, namely data harvesting, screening data and Data Analysis and Visualization. The results obtained are that curcumin is effective in chronic inflammatory therapy by inhibiting the main inflammatory pathways (NF- $\kappa$ B and JAK/STAT), has antioxidant effects, accelerates tissue regeneration, and functions as an immunomodulator. However, the low bioavailability of curcumin is a major challenge in its application. Nanoformulation technology and its combination with other compounds such as CMPs can improve its effectiveness in clinical therapy. The implications of this research are directed to researchers, the community and the government.*

### INTRODUCTION

Herbal plants in Indonesia have an important role in traditional medicine and public health. One of them is turmeric, which contains curcumin content. Curcumin is a polyphenol compound found in turmeric (*Curcuma longa*), which has been used for centuries in traditional medicine and as a cooking spice. This compound is known for its various biological activities, including antioxidant, anti-inflammatory, and anticancer properties, which makes it a promising ingredient in the development of functional products for health (Kunnumakkara et al., 2017; Prasad et al., 2014; Xu et al., 2018). Curcumin has the ability to suppress cellular signaling pathways involved in inflammation, such as NF- $\kappa$ B and COX-2, as well as reduce oxidative stress by

eliminating free radicals (Kunnumakkara et al., 2017; Patel et al., 2020; Xu et al., 2018). Curcumin can induce growth capture and apoptosis in premalignant and malignant cells, making it a potential agent for cancer chemoprevention and chemotherapy. (Fu et al., 2021; Sharma et al., 2005). Curcumin also shows protective effects against a variety of chronic diseases, including diabetes, cardiovascular disease, neurological disease, and autoimmune diseases. (Kocaadam & Sanlier, 2017; Kunnumakkara et al., 2017; Xu et al., 2018). The mechanism of action of curcumin is that curcumin works by modulating various cellular signaling pathways and transcription factors, such as PI3K, Akt, mTOR, and Nrf2, which play a role in the regulation of inflammation, apoptosis, and cellular defense. (Fu et al., 2021; Patel et al., 2020). In addition, curcumin can interact with various target proteins through molecular docking, which amplifies its pharmacological effects (Fu et al., 2021). Based on some of the sources above, it can be concluded that curcumin is a highly biologically active compound with great potential in the prevention and treatment of various diseases.

Curcumin, the main component of turmeric (*Curcuma longa*), has long been used in traditional medicine for its antioxidant, anti-inflammatory, and antimicrobial properties. Research shows that curcumin has significant therapeutic potential in addressing a variety of health conditions. Curcumin has Antioxidant and Anti-inflammatory properties by showing anti-inflammatory effects by reducing the number of white blood cells and inflammatory mediators such as phospholipase A2 (Memarzia et al., 2021). It also inhibits enzymes involved in inflammatory processes such as COX-2 and iNOS. (Menon & Sudheer, 2007). As an antioxidant, curcumin decreases levels of malondialdehyde and nitric oxide, as well as increases levels of thiol, superoxide dismutase, and catalase (Memarzia et al., 2021; Menon & Sudheer, 2007). In addition, curcumin also has antimicrobial properties. Curcumin has strong antimicrobial activity, although its effectiveness varies depending on the type and strain of microorganism. Gram-positive is more sensitive to curcumin than Gram-negative (Adamczak et al., 2020).

Curcumin has been used in the treatment of various inflammatory conditions such as inflammatory bowel disease, pancreatitis, and arthritis (Jurenka, 2009). However, its low bioavailability is a challenge, so research continues to be conducted to improve its effectiveness through strategies such as the use of curcumin analogues and exosome vesicles (Hsu et al., 2023). Based on some of these sources, curcumin from turmeric has great potential as a therapeutic agent thanks to its antioxidant, anti-inflammatory, and antimicrobial properties. Although bioavailability challenges still exist, research continues to optimize their use in the treatment of various inflammatory and infectious diseases.

Chronic inflammation is a key factor in the development of various degenerative diseases such as arthritis, diabetes, cancer, and cardiovascular diseases. The condition is characterized by a persistent inflammatory response and tissue destruction, which can accelerate the aging process and increase the risk of degenerative diseases. Chronic inflammation can be triggered by a variety of factors such as infection, physical inactivity, poor diet, environmental toxicity, and psychological stress. (Furman et al., 2019; Prasad et al., 2012). Chronic inflammation involves activation of inflammasomes and a decrease in endogenous anti-inflammatory mechanisms, which can accelerate vascular aging and atherosclerosis (Falzone et al., 2023; Liberale et al., 2020). This process can also lead to oxidative stress and DNA damage, potentially triggering cancer and other age-related disorders (Khansari et al., 2009; Manabe, 2011). Chronic inflammation plays

a central role in the development of various degenerative diseases. Understanding the mechanisms and risk factors for chronic inflammation can aid in the development of effective prevention and treatment strategies, including dietary and lifestyle interventions.

The main mechanism of inflammation involves various cellular and molecular components that work together to protect the body and initiate the healing process. Innate and Adaptive Immune Systems: Inflammation begins when innate immune cells detect infection or injury through pattern recognition receptors (PRRs) that respond to pathogen-associated molecular patterns (PAMPs) or damage-associated molecular patterns (DAMPs) (Newton & Dixit, 2012). This triggers the activation of transcription factors such as NF- $\kappa$ B and IRF that induce genes for enzymes, chemokines, and cytokines (Newton & Dixit, 2012).. Inflammatory mediators such as cytokines and chemokines play a central role in cell-to-cell communication, initiation, amplification, and regulation of inflammatory responses (Megha et al., 2021; Turner et al., 2014). They regulate the recruitment and activation of leukocytes that are essential for the removal of foreign particles and tissue debris (Newton & Dixit, 2012). Inflammation is a complex response that involves the interaction between innate and adaptive immune systems, inflammatory mediators, and cellular and microvascular processes. These mechanisms work together to protect the body from infection and injury, as well as initiate the healing process. However, chronic inflammation can contribute to a variety of diseases, emphasizing the importance of proper regulation of the inflammatory response.

Curcumin, the active compound in turmeric, is known to have significant anti-inflammatory effects. Research shows that curcumin can inhibit inflammatory pathways by suppressing the expression of transcription factor NF- $\kappa$ B and pro-inflammatory enzymes such as COX-2 and iNOS. Anti-Inflammatory Mechanism of Curcumin in which Curcumin suppresses the activation of NF- $\kappa$ B, which is an important transcription factor in the regulation of pro-inflammatory genes. This is done by inhibiting the activity of I $\kappa$ B kinase and Akt, which prevents translocation of NF- $\kappa$ B into the nucleus and reduces the expression of genes regulated by NF- $\kappa$ B (Afshari et al., 2023; Aggarwal et al., 2006; Buhrmann et al., 2011). Curcumin significantly decreases the expression of COX-2 and iNOS, which are key enzymes in the inflammatory process. This decrease occurs through inhibition of the MAPK p38 pathway and other signal transductions associated with inflammation (Camacho-Barquero et al., 2007; Paulino et al., 2016; Yu et al., 2018). Studies show that curcumin may enhance anti-inflammatory effects when used in conjunction with other compounds, such as imidazo[1,2-a]pyridine and *Allium hookeri*, by more effectively suppressing the NF- $\kappa$ B/COX-2/iNOS pathway (Afshari et al., 2023; S. Lee et al., 2020). Therefore, the purpose of this study is to evaluate the effectiveness and mechanism of action of curcumin in chronic inflammatory therapy.

## METHODOLOGY

This study uses the Systematic Literature Review (SLR) method. SLR is a synthesis of literature studies that are carried out systematically, clearly, and thoroughly. SLRs are often used to conduct thematic analysis, identify major themes and subthemes in existing literature, and explore recent trends and developments (Oladimeji et al., 2020). The purpose of this method is to help researchers understand more deeply about the research that is the subject of the study, including why and how the results of the study can be used as a reference for new research. In this study, researchers evaluated the effectiveness and mechanism of action of curcumin in chronic inflammatory therapy. This

study uses a database from Scopus. There are three stages carried out in mapping the effectiveness and mechanism of action of curcumin in chronic inflammatory therapy, namely:

1. Harvesting Data. At this stage, the researcher harvests data by collecting articles that have been published and indexed by the Scopus indexing agency. To collect publications from this Scopus indexing institution, researchers directly on the Scopus database. The search for publications was carried out using the keywords in this study, including: "curcumin", "AND chronic", "AND inflammation", and "AND therapy" with a time span from 2020-2025. In this data harvest, it is also based on several countries in Southeast Asia, such as Indonesia, Malaysia, and Singapore.

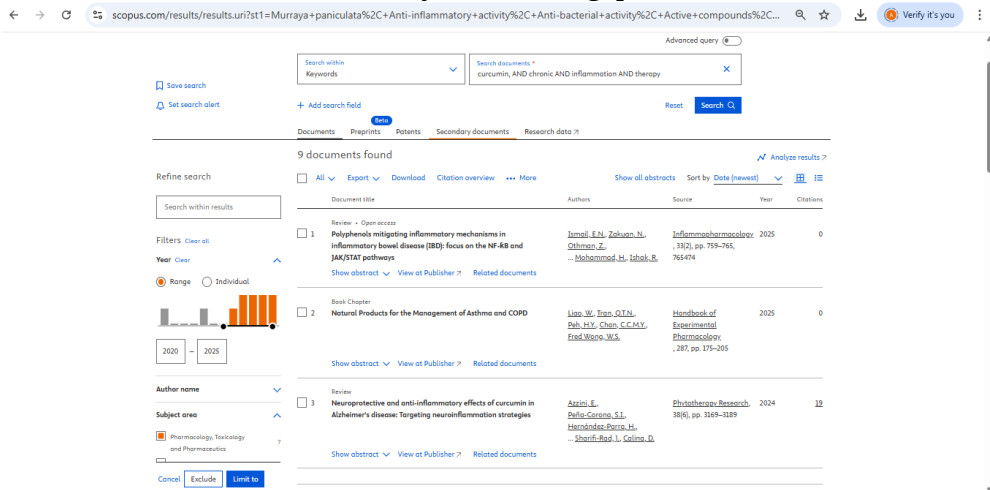


Figure 1. Results of data harvesting on the Scopus website  
*Source: Data Research*

From the results of data harvesting (data harvesting), 9 articles were published. Furthermore, the researcher downloads all scientific papers in the form of RIS. Click "Select All", then click "Export" and select "RIS Format". Then it will go to the page as below

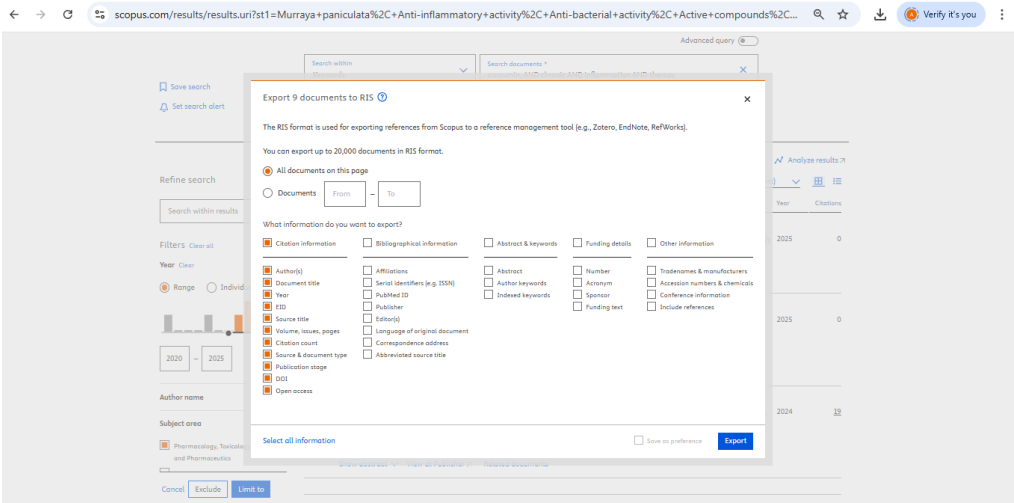
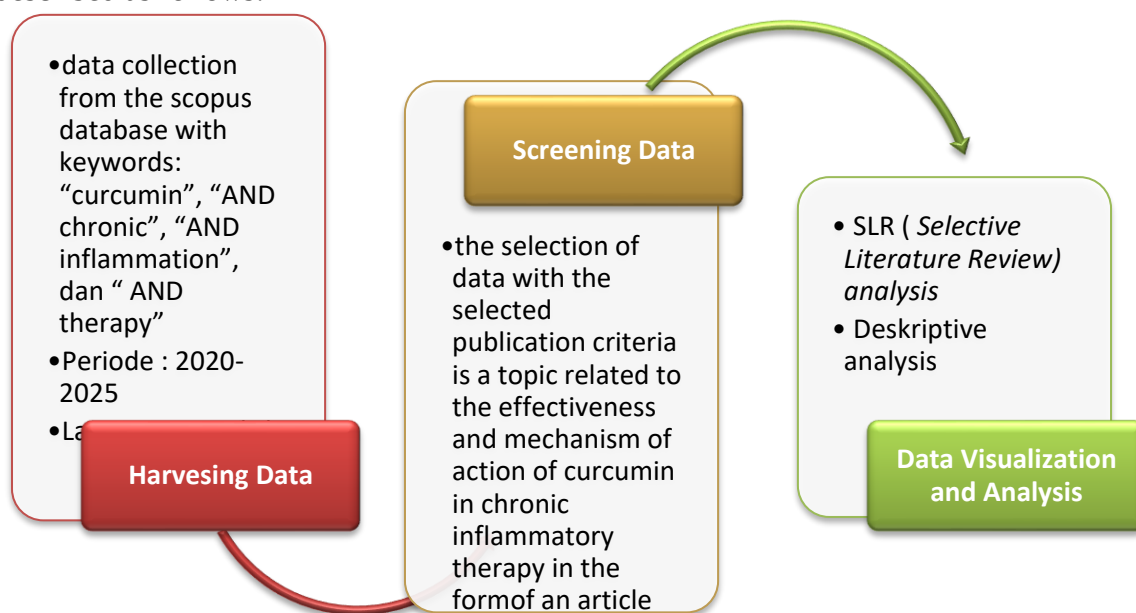


Figure 2. How to download RIS on 9 scopus articles  
*Source: Data Research*

2. Data Screening. Based on the results of data collection obtained from the Scopus indexing agency, there are 9 publications related to the effectiveness and mechanism of action of curcumin in chronic inflammatory therapy during the period of 2020-2025.

3. Data Analysis and Visualization. In this stage of data analysis, the researcher analyzed the publications obtained from Scopus at the time of data harvesting (data harvesting). There are several data related to the published analyzed, such as the development of publications per year during the 2020-2025 range. Of the three stages, namely the stages of data harvesting, data filtering and data analysis and visualization, it can be described as follows:



Picture 3. Design of SLR Methodology on Research related to the effectiveness and mechanism of action of curcumin in chronic inflammatory therapy  
Source: Data Research

## RESULTS AND DISCUSSION

### 1. Publication Development

The development of publications in Scopus journals related to the effectiveness and mechanism of action of curcumin in chronic inflammatory therapy during the period of 2020-2025 has increased in 2021, the number of available documents is only 1. In 2022, there was an increase in the number of documents to 2. From 2022 to 2025, the number of documents will remain constant at 2 per year. After the initial increase from 2021 to 2022, the number of documents produced each year remains stable at 2 documents per year until 2025. There has been no significant spike or decrease in the number of documents after 2022.



Figure 4. Publication Development Based on Scopus Data for the 2020-2025 Period Data

Source: Scopus 2025

The graph above illustrates the list that after an increase in 2022, document production has remained consistent. It could be that this reflects stability in research or document production in that time frame. When linked to the context of research or analysis of documents in a particular field, there may be policy factors, resources, or research trends that keep the number of documents at the same number for several years.

## 2. Afiliation of the country producing acientific Journal

The affiliation of countries producing scientific works is within the scope of countries in Southeast Asia, such as Indonesia, Malaysia, and Singapore. Based on the resulting graph, it shows the distribution of documents based on affiliation. Each institution in the graph has the same number of documents, which is 1 document. No institution dominates in the number of publications, so the distribution of documents is relatively even among various institutions.

Various institutions from different countries are involved in this publication, including Universidad de Concepción, Universiti Putra Malaysia, Indian Council of Agriculture, UCSI University, and others. This indicates that the research related to the analyzed documents involves international collaboration or has a global scope.

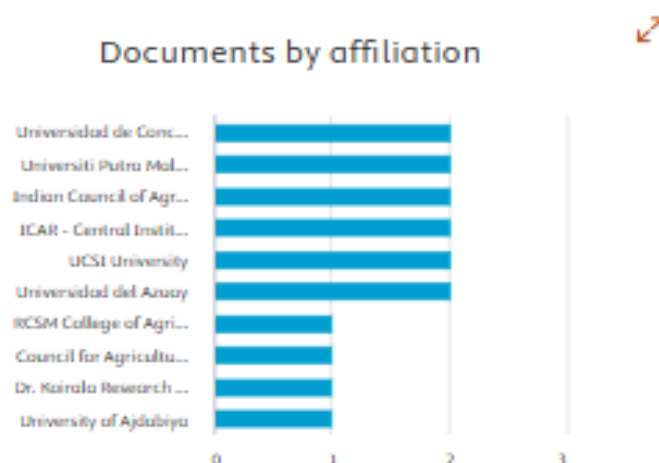


Figure 5. Affiliation of Scientific Producing Countries Based on Scopus Data

Source: Data Scopus 2025

No one institution has had more publications than the other, suggesting that this research may be scattered and not concentrated in a single university or research institution. It could also indicate that each institution has only a limited contribution in the number of publications analyzed. Based on the graphic image above, it can be concluded that this graph shows an even distribution in research contributions from various institutions. International collaborations seem to be quite extensive, but no single institution dominates in the number of publications. If you want to see the specific impact or role of each institution, it is necessary to conduct further analysis of the content of the document and the quality of its contribution.

### 3. Most Cited Articles

Based on data harvesting, screening, and processing from the Scopus database on the effectiveness and mechanism of curcumin in chronic inflammatory therapy, nine journal publications were identified during the 2020–2025 period. As shown in Table 1, these publications explore the role of curcumin in managing chronic inflammation and its underlying mechanisms of action.

**Tabel 2.** Summary of the review literature

| N<br>o | Reference             | Heading                                                                      | Study Focus                                                                        | Method and Sample                                                                                               | Result                                                                                                                                                                                   |
|--------|-----------------------|------------------------------------------------------------------------------|------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1      | (Ismail et al., 2025) | Polyphenols mitigating inflammatory mechanisms in inflammatory bowel disease | Polyphenols mitigating inflammatory mechanisms in inflammatory bowel disease (IBD) | The research method used in this study is an experimental method. Processes that polyphenols, such as curcumin, | Polyphenols have potential therapeutic benefits by inhibiting cytokine production and immune cell activation through specific pathways. Preclinical studies suggest they may help reduce |

|    |                       |                                                                                                                          |                                                           |                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                         |
|----|-----------------------|--------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                       | (IBD): focus on the NF- $\kappa$ B and JAK/STAT pathways                                                                 |                                                           | EGCG, resveratrol, and quercetin, perform to reduce inflammation                                                                                                                                                             | intestinal inflammation. However, further clinical research is necessary to assess their effectiveness in treating IBD, particularly concerning their long-term safety and bioavailability.                                                                                                                                                                                                                             |
| 2  | (Liao et al., 2025)   | Natural Products for the Management of Asthma and COPD                                                                   | Management of Asthma and COPD                             | Method type: Experimental in preclinical model and clinical trial<br>sample: natural compounds                                                                                                                               | Many natural products show promise for the treatment of asthma and COPD. Various natural compounds, such as terpenes, polyphenols, alkaloids, fatty acids, polyketides, and vitamin E, have demonstrated effectiveness against asthma and COPD, as well as their exacerbations, in both preclinical models and clinical trials.                                                                                         |
| 3. | (Azzini et al., 2024) | Neuroprotective and anti-inflammatory effects of curcumin in Alzheimer's disease: Targeting neuroinflammation strategies | Neuroprotective and anti-inflammatory effects of curcumin | Metode penelitian : studi literature dalam 10 tahun terakhir . The review methodology included sourcing articles from specialized databases using specific medical subject headings terms to ensure precision and relevance. | Curcumin exhibits strong neuroprotective effects by regulating neuroinflammatory pathways, neutralizing reactive oxygen species, and suppressing pro-inflammatory cytokine production. However, its therapeutic potential is hindered by low bioavailability and a lack of extensive human clinical trials. Nonetheless, curcumin holds promise as a complementary treatment for Alzheimer's disease due to its diverse |

|    |                        |                                                                                                                                                    |                                                         |                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|----|------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                        |                                                                                                                                                    |                                                         |                                                                                                                                                                                                                                                      | neuroprotective properties.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| 4. | (Mustofa et al., 2024) | Combination of curcuminoid and collagen marine peptides for healing diabetic wounds infected by methicillin-resistant <i>Staphylococcus aureus</i> | Combination of curcuminoid and collagen marine peptides | Metode yang digunakan metode eskperimental .<br>Materials and Methods:<br>Hydrolacin-gels were prepared by homogenizing curcuminoid nanoemulsions and CMPs. The evaluation of preparation includes stability tests and antibacterial activity tests. | Hydrolacin-gel was developed by incorporating curcuminoid nanoemulsion (enhancing water solubility) and CMPs in three formulations: formula 1 (1:2 ratio, curcuminoid 43.3 mg and CMPs 5.58 mg), formula 2 (1:1 ratio, curcuminoid 86.8 mg and CMPs 3.72 mg), and formula 3 (2:1 ratio, curcuminoid 130.2 mg and CMPs 1.87 mg), based on the effective doses of curcuminoid (200 mg/kg BW) and CMPs (0.9 g/kg BW). Hydrolacin-gel exhibited potent antibacterial activity against MRSA, promoted wound tissue repair, and mitigated oxidative stress caused by inflammation in MRSA-infected diabetic wounds. Among the formulations, formula 3 (curcuminoid:CMPS = 2:1) showed the highest efficacy in promoting wound healing. |
| 5. | (Wardani et al., 2023) | Treatment of the common cold with herbs used in Ayurveda and Jamu:                                                                                 | Pengobatan flu dengan herbal yang digunakan dalam       | Method: An expert roundtable discussion comprising specialists in                                                                                                                                                                                    | In the absence of specific antiviral treatments, managing the common cold primarily focuses on personal hygiene and                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |

|    |                     |                                                                                |                                                                         |                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|----|---------------------|--------------------------------------------------------------------------------|-------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                     | monograph review and the science of ginger, liquorice, turmeric and peppermint | Ayurveda dan Jamu                                                       | Ayurveda, Jamu, pharmacology and surgery along with a literature review was conducted to evaluate the use of four herbs - ginger, liquorice, turmeric and peppermint | symptom relief. Herbal medicines have long been used across various cultures worldwide. However, despite their increasing acceptance, there is a perception that healthcare providers show limited interest, which may discourage patients from discussing their use. Additionally, insufficient education and training on herbal medicine could further contribute to the communication gap between patients and healthcare providers, potentially affecting effective management. |
| 6. | (Wong et al., 2023) | Senotherapeutics for mesenchymal stem cell senescence and rejuvenation         | mesenchymal stem cell senescence and rejuvenation from Senotherapeutics | Method: literature review                                                                                                                                            | Mesenchymal stem cells (MSCs) are prone to replicative senescence and a decline in function, limiting their effectiveness in regenerative medicine. Senotherapeutics, which include senolytic and senomorphic agents, target cellular senescence by inducing apoptosis and reducing chronic inflammation associated with the senescence-associated secretory phenotype (SASP). As a result, senotherapeutics have the potential to delay aging-related degeneration.                |

|    |                           |                                                                                                                                                         |                                                                         |                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|----|---------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 7. | (Hemrajan i et al., 2022) | Overcoming drug delivery barriers and challenges in topical therapy of atopic dermatitis: A nanotechnological perspective                               | barriers and challenges in topical therapy of atopic dermatitis         | Method : literature review | Atopic dermatitis (AD) is an inflammatory condition characterized by impaired epidermal barrier function and T helper 2 (Th2) immune responses. The complexity and heterogeneity of the disease pose challenges to the optimal use of existing topical and systemic treatments but also drive the development of advanced therapeutic options. Additionally, innovative nanocarrier-based drug delivery systems offer a promising strategy to overcome the limitations of conventional and traditional therapies by enhancing targeted delivery to affected cells. |
| 8. | (Butnariu et al., 2022)   | Bioactive Effects of Curcumin in Human Immunodeficiency Virus Infection Along with the Most Effective Isolation Techniques and Type of Nanoformulations | Bioactive Effects of Curcumin in Human Immunodeficiency Virus Infection | Method : Literature review | Curcumin (CUR), a polyphenol derived from <i>Curcuma longa</i> , has gained significant research interest due to its antimicrobial, anti-inflammatory, antioxidant, immunomodulatory, and antiviral properties. It also exhibits anti-HIV activity by potentially inhibiting gp120 binding, integrase, protease, and topoisomerase II functions, while providing protection against HIV-associated                                                                                                                                                                 |

|    |                     |                                                                                                                                                           |                                                                                        |                            |                                                                                                                                                                                                                                                                                                                                              |
|----|---------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|----------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                     |                                                                                                                                                           |                                                                                        |                            | diseases. However, its therapeutic efficacy is limited by poor water solubility, rapid metabolism, and systemic elimination. Nanoformulations have shown promise in enhancing curcumin's bioavailability and improving its effectiveness as an anti-HIV agent.                                                                               |
| 9. | (Heng et al., 2021) | Understanding lung carcinogenesis from a morphostatic perspective: Prevention and therapeutic potential of phytochemicals for targeting cancer stem cells | Prevention and therapeutic potential of phytochemicals for targeting cancer stem cells | Method : literature review | This study explores the chemopreventive and anticancer properties of nine well-researched phytochemical compounds—curcumin, resveratrol, quercetin, epigallocatechin-3-gallate, luteolin, sulforaphane, berberine, genistein, and capsaicin—focusing on their mechanisms of action in lung cancer and their potential clinical applications. |

Based on Table 2, it shows that curcumin is proven to have high effectiveness in overcoming chronic inflammation, both through inflammatory pathway inhibition (Ismail et al., 2025) mechanisms, antioxidant effects, and increased tissue regeneration. With a wide range of benefits in chronic diseases involving systemic inflammation and oxidative stress. However, from this data, further formulation development is still needed so that it can be widely applied in the medical world.

## DISCUSSION

### Effectiveness and mechanism of action of curcumin in chronic inflammatory therapy

The study examined the efficacy and mechanisms of curcumin in the treatment of chronic inflammatory conditions. The following is a discussion of the table analysis related to the effectiveness and mechanism of action of curcumin in chronic inflammatory therapy from 9 Scopus journals.

#### 1. Effectiveness of curcumin in chronic inflammatory therapy

From several studies in the table, curcumin is proven to have high effectiveness in overcoming chronic inflammation, both through inflammatory pathway inhibition

mechanisms, antioxidant effects, and increased tissue regeneration. Some of the results of the study showed:

- a. (Ismail et al., 2025) : Curcumin can inhibit the synthesis of pro-inflammatory cytokines and reduce immune cell activation through the NF- $\kappa$ B and JAK/STAT pathways, which play an important role in inflammatory diseases such as Inflammatory Bowel Disease (IBD).
- b. (Azzini et al., 2024) : Curcumin has neuroprotective and anti-inflammatory effects on Alzheimer's disease by inhibiting the production of pro-inflammatory cytokines and capturing free radicals that cause oxidative stress in the brain.
- c. (Mustofa et al., 2024) : The combination of curcuminoids with collagen marine peptides (CMPs) in the form of Hydrolacin-gel showed effectiveness in healing diabetic wounds infected with Methicillin-resistant *Staphylococcus aureus* (MRSA) by suppressing inflammation and promoting tissue regeneration.
- d. (Butnariu et al., 2022): Curcumin has immunomodulatory and anti-inflammatory effects in patients with HIV infection, but its effectiveness is limited by its low bioavailability, so nanoformulation technology is needed to improve its effectiveness.

Curcumin intake has been shown to significantly reduce levels of C-reactive protein (CRP), interleukin 6 (IL-6), and tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ), which are key markers of inflammation (Hosseini et al., 2024; Y.-M. Lee & Kim, 2024). It also demonstrates antioxidant properties, reducing oxidative stress markers like malondialdehyde (MDA) and increasing antioxidant defenses such as superoxide dismutase (SOD) (Da Paz Martins et al., 2024; Hosseini et al., 2024; Pourhabibi-Zarandi et al., 2024). Curcumin is a promising natural compound for the treatment of chronic inflammatory conditions due to its anti-inflammatory and antioxidant properties. Its effectiveness is enhanced when combined with piperine, although challenges with bioavailability remain. Further research and development of targeted delivery systems could enhance its therapeutic potential.

## 2. Curcumin's Mechanism of Action in Overcoming Chronic Inflammation

Based on the analysis of various studies, the mechanism of action of curcumin in chronic inflammatory therapy can be explained as follows:

- a. Inhibition of Inflammatory Pathways (NF- $\kappa$ B and JAK/STAT)
  - o Curcumin works by inhibiting the activation of NF- $\kappa$ B, a transcription factor that plays a role in the production of pro-inflammatory cytokines such as TNF- $\alpha$ , IL-1 $\beta$ , and IL-6.
  - o In cases of IBD and neurodegenerative diseases, curcumin also suppresses the JAK/STAT pathway, which is responsible for the differentiation and activation of immune cells.
- b. Antioxidant Effects and Reduction of Oxidative Stress
  - o Curcumin has the ability to capture free radicals and increase antioxidant enzymes such as SOD (superoxide dismutase) and GPx (glutathione peroxidase).
  - o This mechanism is particularly beneficial in neurodegenerative conditions (Alzheimer's) and chronic wounds in diabetes, where oxidative stress plays a role in cell damage and inflammation.
- c. Tissue Regeneration and Wound Healing

- In the case of diabetic wounds infected with MRSA, curcumin combined with CMPs is able to increase fibroblast proliferation and re-epithelialization.
- These compounds help suppress the excessive inflammatory response, which usually inhibits the healing process of chronic wounds.
- d. **Imunomodulasi dan Potensi Antiviral**
  - Curcumin has an immunomodulatory effect by balancing adaptive and innate immune responses.
  - In HIV infection, curcumin inhibits the activity of viral enzymes (integrase, protease, topoisomerase II) and protects against HIV-related diseases by suppressing systemic inflammation.
- e. Curcumin is effective in chronic inflammatory therapy by inhibiting major inflammatory pathways (NF- $\kappa$ B and JAK/STAT), has antioxidant effects, accelerates tissue regeneration, and functions as an immunomodulator.
- f. However, the low bioavailability of curcumin is a major challenge in its application. Nanoformulation technology and its combination with other compounds such as CMPs can improve its effectiveness in clinical therapy.

**NF- $\kappa$ B Signaling Pathway:** Curcumin inhibits the activation of the NF- $\kappa$ B signaling pathway, which plays a crucial role in inflammatory responses. This inhibition is achieved by downregulating sphingosine kinase 1 (SphK1) and binding directly to NF- $\kappa$ B, thereby reducing the expression of inflammatory cytokines such as TNF- $\alpha$ , IL-1 $\beta$ , and IL-8 (Yang et al., 2024; Zhang et al., 2025). Curcumin significantly reduces the production of pro-inflammatory cytokines, including TNF- $\alpha$ , IL-6, and IL-1 $\beta$ , which are critical in chronic inflammatory conditions. This effect is observed across various studies and is enhanced when curcumin is combined with piperine, which increases its bioavailability (Hosseini et al., 2024; Y.-M. Lee & Kim, 2024; Mancillas-Quiroz et al., 2024). Curcumin's ability to modulate key inflammatory pathways and cytokine production underlies its potential as a therapeutic agent for chronic inflammation. Its effects are enhanced by improving bioavailability, such as through co-administration with piperine. These mechanisms highlight curcumin's promise in treating various inflammatory and autoimmune conditions. This analysis shows that curcumin has great potential as a natural anti-inflammatory therapy, but still needs further formulation development to be widely applied in the medical world.

## CONCLUSION

Based on the research with the SLR method that has been carried out, it can be concluded that curcumin is effective in chronic inflammatory therapy by inhibiting the main inflammatory pathways (NF- $\kappa$ B and JAK/STAT), has antioxidant effects, accelerates tissue regeneration, and functions as an immunomodulator. However, the low bioavailability of curcumin is a major challenge in its application. Nanoformulation technology and its combination with other compounds such as CMPs can improve its effectiveness in clinical therapy.

### Research Implication

The implications of this research are;

1. For researchers

Encourage collaboration between researchers, medical personnel, and the herbal medicine industry to develop products based on scientific research.

2. For the public,

Education about the benefits and use of herbal medicines in a safe way and increasing the consumption of natural health products as a preventive step in maintaining health.

3. For the government

Government support in the development of medicinal plant-based medicines to increase public access to natural medicine.

## LITERATURE

- Adamczak, A., Ożarowski, M., & Karpiński, T. (2020). Curcumin, a Natural Antimicrobial Agent with Strain-Specific Activity. *Pharmaceuticals*, 13. <https://doi.org/10.3390/ph13070153>
- Afshari, H., Noori, S., Daraei, A., Movahed, M. A., & Zarghi, A. (2023). A novel imidazo[1,2-a]pyridine derivative and its co-administration with curcumin exert anti-inflammatory effects by modulating the STAT3/NF- $\kappa$ B/iNOS/COX-2 signaling pathway in breast and ovarian cancer cell lines. *BioImpacts : BI*, 14. <https://doi.org/10.34172/bi.2023.27618>
- Aggarwal, S., Ichikawa, H., Takada, Y., Sandur, S., Shishodia, S., & Aggarwal, B. (2006). Curcumin (Diferuloylmethane) Down-Regulates Expression of Cell Proliferation and Antiapoptotic and Metastatic Gene Products through Suppression of I $\kappa$ B $\alpha$  Kinase and Akt Activation. *Molecular Pharmacology*, 69, 195–206. <https://doi.org/10.1124/MOL.105.017400>
- Azzini, E., Peña-Corona, S. I., Hernández-Parra, H., Chandran, D., Saleena, L. A. K., Sawikr, Y., Peluso, I., Dhumal, S., Kumar, M., Leyva-Gómez, G., Martorell, M., Sharifi-Rad, J., & Calina, D. (2024). Neuroprotective and anti-inflammatory effects of curcumin in Alzheimer's disease: Targeting neuroinflammation strategies. *Phytotherapy Research*, 38(6), 3169–3189. <https://doi.org/10.1002/ptr.8200>
- Buhrmann, C., Mobasheri, A., Busch, F., Aldinger, C., Stahlmann, R., Montaseri, A., & Shakibaei, M. (2011). Curcumin modulates nuclear factor kappaB (NF-kappaB)-mediated inflammation in human tenocytes in vitro: role of the phosphatidylinositol 3-kinase/Akt pathway. *The Journal of Biological Chemistry*, 286 32, 28556–28566. <https://doi.org/10.1074/jbc.M111.256180>
- Butnariu, M., Quispe, C., Koirala, N., Khadka, S., Salgado-Castillo, C. M., Akram, M., Anum, R., Yeskaliyeva, B., Cruz-Martins, N., Kumar, M. M. M., Bagiu, R. V., Razis, A. F. A., Sunusi, U., Kamal, R. M., & Sharifi-Rad, J. (2022). Bioactive Effects of Curcumin in Human Immunodeficiency Virus Infection Along with the Most Effective Isolation Techniques and Type of Nanoformulations. *International Journal of Nanomedicine*, 17, 3619–3632. <https://doi.org/10.2147/IJN.S364501>
- Camacho-Barquero, L., Villegas, I., Sánchez-Calvo, J., Talero, E., Sánchez-Fidalgo, S., Motilva, V., & De La Lastra, A. (2007). Curcumin, a Curcuma longa constituent, acts on MAPK p38 pathway modulating COX-2 and iNOS expression in chronic experimental colitis. *International Immunopharmacology*, 7 3, 333–342. <https://doi.org/10.1016/J.INTIMP.2006.11.006>
- Da Paz Martins, A. S., De Araújo, O. R. P., Da Silva Gomes, A., Araújo, F. L. C., Oliveira, J., De Vasconcelos, J. K. G., Rodrigues, J. I., Cerqueira, I. T., De Freitas Lins Neto, M. Á., Bueno, N., Goulart, M., & Moura, F. (2024). Effect of Curcumin

- Plus Piperine on Redox Imbalance, Fecal Calprotectin and Cytokine Levels in Inflammatory Bowel Disease Patients: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial. *Pharmaceuticals*, 17. <https://doi.org/10.3390/ph17070849>
- Falzone, L., Candido, S., Docea, A., & Calina, D. (2023). Editorial: Inflammation and aging in chronic and degenerative diseases: Current and future therapeutic strategies. *Frontiers in Pharmacology*, 13. <https://doi.org/10.3389/fphar.2022.1122786>
- Fu, Y.-S., Chen, T.-H., Weng, L., Huang, L., Lai, D., & Weng, C. (2021). Pharmacological properties and underlying mechanisms of curcumin and prospects in medicinal potential. *Biomedicine & Pharmacotherapy = Biomedecine & Pharmacotherapie*, 141, 111888. <https://doi.org/10.1016/j.biopha.2021.111888>
- Furman, D., Campisi, J., Verdin, E., Carrera-Bastos, P., Targ, S., Franceschi, C., Ferrucci, L., Gilroy, D., Fasano, A., Miller, G., Miller, A., Mantovani, A., Weyand, C., Barzilai, N., Goronzy, J., Rando, T., Effros, R., Lucia, A., Kleinstreuer, N., & Slavich, G. (2019). Chronic inflammation in the etiology of disease across the life span. *Nature Medicine*, 25, 1822–1832. <https://doi.org/10.1038/s41591-019-0675-0>
- Hemrajani, C., Negi, P., Parashar, A., Gupta, G., Jha, N. K., Singh, S. K., Chellappan, D. K., & Dua, K. (2022). Overcoming drug delivery barriers and challenges in topical therapy of atopic dermatitis: A nanotechnological perspective. *Biomedicine and Pharmacotherapy*, 147. <https://doi.org/10.1016/j.biopha.2022.112633>
- Heng, W. S., Kruiyt, F. A. E., & Cheah, S.-C. (2021). Understanding lung carcinogenesis from a morphostatic perspective: Prevention and therapeutic potential of phytochemicals for targeting cancer stem cells. *International Journal of Molecular Sciences*, 22(11). <https://doi.org/10.3390/ijms22115697>
- Hosseini, H., Ghavidel, F., Rajabian, A., Homayouni-Tabrizi, M., Majeed, M., & Sahebkar, A. (2024). The Effects of Curcumin Plus Piperine Co-administration on Inflammation and Oxidative Stress: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Current Medicinal Chemistry*. <https://doi.org/10.2174/0109298673260515240322074849>
- Hsu, K.-Y., Ho, C.-T., & Pan, M. (2023). The therapeutic potential of curcumin and its related substances in turmeric: From raw material selection to application strategies. *Journal of Food and Drug Analysis*, 31, 194–211. <https://doi.org/10.38212/2224-6614.3454>
- Ismail, E. N., Zakuan, N., Othman, Z., Vidyadaran, S., Mohammad, H., & Ishak, R. (2025). Polyphenols mitigating inflammatory mechanisms in inflammatory bowel disease (IBD): focus on the NF- $\kappa$ B and JAK/STAT pathways. *Inflammopharmacology*, 33(2), 759–765. <https://doi.org/10.1007/s10787-024-01607-8>
- Jayanto, I., Gunawan, U., & Yaqya, M. (2024). *Ethics And Responsibility In Pharmaceutical Practice: Facing Moral Dilemmas In The Modern Era*. *Journal Of Pharmacopoeia, Pharmacopeia*, Vol. 2 No.1, March 2025
- Jurenka, J. (2009). Anti-inflammatory properties of curcumin, a major constituent of *Curcuma longa*: a review of preclinical and clinical research. *Alternative Medicine Review: A Journal of Clinical Therapeutic*, 14 2, 141–153.

- <https://consensus.app/papers/antiinflammatory-properties-of-curcumin-a-major-jurenka/b8e66f5ef0385385bd63af912ba028ff/>
- Khansari, N., Shakiba, Y., & Mahmoudi, M. (2009). Chronic inflammation and oxidative stress as a major cause of age-related diseases and cancer. *Recent Patents on Inflammation & Allergy Drug Discovery*, 3(1), 73–80. <https://doi.org/10.2174/187221309787158371>
- Kocaadam, B., & Sanlier, N. (2017). Curcumin, an active component of turmeric (*Curcuma longa*), and its effects on health. *Critical Reviews in Food Science and Nutrition*, 57, 2889–2895. <https://doi.org/10.1080/10408398.2015.1077195>
- Kunnumakkara, A., Bordoloi, D., Padmavathi, G., Monisha, J., Roy, N., Prasad, S., & Aggarwal, B. (2017). Curcumin, the golden nutraceutical: multitargeting for multiple chronic diseases. *British Journal of Pharmacology*, 174, 1325–1348. <https://doi.org/10.1111/bph.13621>
- Lee, S., Cho, S.-S., Li, Y., Bae, C., Park, K., & Park, D.-H. (2020). Anti-inflammatory Effect of *Curcuma longa* and *Allium hookeri* Co-treatment via NF- $\kappa$ B and COX-2 Pathways. *Scientific Reports*, 10. <https://doi.org/10.1038/s41598-020-62749-7>
- Lee, Y.-M., & Kim, Y.-S. (2024). Is Curcumin Intake Really Effective for Chronic Inflammatory Metabolic Disease? A Review of Meta-Analyses of Randomized Controlled Trials. *Nutrients*, 16. <https://doi.org/10.3390/nu16111728>
- Liao, W., Tran, Q. T. N., Peh, H. Y., Chan, C. C. M. Y., & Fred Wong, W. S. (2025). Natural Products for the Management of Asthma and COPD. In *Handbook of Experimental Pharmacology* (Vol. 287, pp. 175–205). [https://doi.org/10.1007/164\\_2024\\_709](https://doi.org/10.1007/164_2024_709)
- Liberale, L., Montecucco, F., Tardif, J., Libby, P., & Camici, G. (2020). Inflamm-ageing: the role of inflammation in age-dependent cardiovascular disease. *European Heart Journal*. <https://doi.org/10.1093/eurheartj/ehz961>
- Manabe, I. (2011). Chronic inflammation links cardiovascular, metabolic and renal diseases. *Circulation Journal: Official Journal of the Japanese Circulation Society*, 75(12), 2739–2748. <https://doi.org/10.1253/CIRCJ.CJ-11-1184>
- Mancillas-Quiroz, J. A., Carrasco-Portugal, M., Mondragón-Vásquez, K., Huerta-Cruz, J., Rodríguez-Silverio, J., Rodríguez-Vera, L., Reyes-García, J. G., Flores-Murrieta, F., Domínguez-Chávez, J., & Rocha-González, H. (2024). Development of a Novel Co-Amorphous Curcumin and L-Arginine (1:2): Structural Characterization, Biological Activity and Pharmacokinetics. *Pharmaceutics*, 17. <https://doi.org/10.3390/pharmaceutics17010011>
- Megha, K., Joseph, X., Akhil, V., & Mohanan, P. (2021). Cascade of immune mechanism and consequences of inflammatory disorders. *Phytomedicine*, 91, 153712. <https://doi.org/10.1016/j.phymed.2021.153712>
- Memarzia, A., Khazdair, M., Behrouz, S., Gholamnezhad, Z., Jafarnejad, M., Saadat, S., & Boskabady, M. (2021). Experimental and clinical reports on anti-inflammatory, antioxidant, and immunomodulatory effects of *Curcuma longa* and curcumin, an updated and comprehensive review. *BioFactors*, 47, 311–350. <https://doi.org/10.1002/biof.1716>
- Menon, V., & Sudheer, A. (2007). Antioxidant and anti-inflammatory properties of curcumin. *Advances in Experimental Medicine and Biology*, 595, 105–125. [https://doi.org/10.1007/978-0-387-46401-5\\_3](https://doi.org/10.1007/978-0-387-46401-5_3)
- Mustofa, D. A. S., Sahari, F. D., Pramudani, S. A., Hidayah, A. B., Tsany, S. F., & Salasia, S. I. O. (2024). Combination of curcuminoid and collagen marine peptides for

- healing diabetic wounds infected by methicillin-resistant *Staphylococcus aureus*. *Veterinary World*, 17(4), 933–939. <https://doi.org/10.14202/vetworld.2024.933-939>
- Newton, K., & Dixit, V. (2012). Signaling in innate immunity and inflammation. *Cold Spring Harbor Perspectives in Biology*, 4 3. <https://doi.org/10.1101/cshperspect.a006049>
- Oladimeji, O., Cross, J., & Keathley-Herring, H. (2020). System dynamics applications in performance measurement research: progress and challenges. *Management Decision*. <https://doi.org/10.1108/md-11-2019-1596>
- Patel, S., Acharya, A., Ray, R., Agrawal, R., Raghuwanshi, R., & Jain, P. (2020). Cellular and molecular mechanisms of curcumin in prevention and treatment of disease. *Critical Reviews in Food Science and Nutrition*, 60, 887–939. <https://doi.org/10.1080/10408398.2018.1552244>
- Paulino, N., Paulino, A., Diniz, S., De Mendonça, S., Gonçalves, I., Flores, F. F., Santos, R., Rodrigues, C., Pardi, P., & Suarez, J. A. Q. (2016). Evaluation of the anti-inflammatory action of curcumin analog (DM1): Effect on iNOS and COX-2 gene expression and autophagy pathways. *Bioorganic & Medicinal Chemistry*, 24 8, 1927–1935. <https://doi.org/10.1016/j.bmc.2016.03.024>
- Pourhabibi-Zarandi, F., Rafrat, M., Zayeni, H., Asghari-Jafarabadi, M., & Ebrahimi, A.-A. (2024). The efficacy of curcumin supplementation on serum total antioxidant capacity, malondialdehyde, and disease activity in women with rheumatoid arthritis: A randomized, double-blind, placebo-controlled clinical trial. *Phytotherapy Research : PTR*. <https://doi.org/10.1002/ptr.8225>
- Prasad, S., Gupta, S., Tyagi, A., & Aggarwal, B. (2014). Curcumin, a component of golden spice: from bedside to bench and back. *Biotechnology Advances*, 32 6, 1053–1064. <https://doi.org/10.1016/j.biotechadv.2014.04.004>
- Prasad, S., Sung, B., & Aggarwal, B. (2012). Age-associated chronic diseases require age-old medicine: role of chronic inflammation. *Preventive Medicine*, 54 Suppl. <https://doi.org/10.1016/j.ypmed.2011.11.011>
- Sharma, R., Gescher, A., & Steward, W. (2005). Curcumin: the story so far. *European Journal of Cancer*, 41 13, 1955–1968. <https://doi.org/10.1016/J.EJCA.2005.05.009>
- Turner, M., Nedjai, B., Hurst, T., & Pennington, D. (2014). Cytokines and chemokines: At the crossroads of cell signalling and inflammatory disease. *Biochimica et Biophysica Acta*, 1843 11, 2563–2582. <https://doi.org/10.1016/j.bbamcr.2014.05.014>
- Wardani, R. S., Schellack, N., Govender, T., Dhulap, A. N., Utami, P., Malve, V., & Wong, Y. C. (2023). Treatment of the common cold with herbs used in Ayurveda and Jamu: monograph review and the science of ginger, liquorice, turmeric and peppermint. *Drugs in Context*, 12. <https://doi.org/10.7573/dic.2023-2-12>
- Winata, N., Hasyim, D. M., & Primulyanto, B. A. (2024). *Pharmaceutical Involvement In Infectious Disease Control: Strategies, Challenges, And Solutions. Pharmacopeia*, Vol. 2 No.1, March 2025
- Wong, P.-F., Dharmani, M., & Ramasamy, T. S. (2023). Senotherapeutics for mesenchymal stem cell senescence and rejuvenation. *Drug Discovery Today*, 28(1). <https://doi.org/10.1016/j.drudis.2022.103424>

- Xu, X.-Y., Meng, X., Li, S., Gan, R., Li, Y., & Li, H. (2018). Bioactivity, Health Benefits, and Related Molecular Mechanisms of Curcumin: Current Progress, Challenges, and Perspectives. *Nutrients*, 10. <https://doi.org/10.3390/nu10101553>
- Yang, H., Zhang, H., Tian, L., Guo, P., Liu, S., Chen, H., & Sun, L. (2024). Curcumin attenuates lupus nephritis by inhibiting neutrophil migration via PI3K/AKT/NF- $\kappa$ B signalling pathway. *Lupus Science & Medicine*, 11. <https://doi.org/10.1136/lupus-2024-001220>
- Yu, Y., Shen, Q., Lai, Y., Park, S. Y., Ou, X., Lin, D., Jin, M., & Zhang, W. (2018). Anti-inflammatory Effects of Curcumin in Microglial Cells. *Frontiers in Pharmacology*, 9. <https://doi.org/10.3389/fphar.2018.00386>
- Zhang, X., Zhang, H., Wang, J., Chen, Y., Lin, J., Wang, Q., Wu, C., Chen, H., & Lin, Y. (2025). Curcumin attenuates ulcerative colitis via regulation of Sphingosine kinases 1/NF- $\kappa$ B signaling pathway. *BioFactors*, 51 1. <https://doi.org/10.1002/biof.70001>