



Literature study: Activity of white turmeric (*Curcuma zedoaria*) as an anti-inflammatory

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ABSTRACT

Inflammation is a response given by the body to protect the body against cellular damage, characterized by swelling, redness accompanied by a sensation of heat and pain. Long term use of *NSAIDs* (*Non Steroid Anti Inflammatory Drugs*) has side effects such as ulcers, stomach upset, bleeding, nausea, disturbances in the kidneys and the cardiovascular system. White turmeric (*Curcuma zedoaria*) is a plant that can be used as an anti-inflammatory. This study aims to determine the anti-inflammatory activity of White Turmeric (*Curcuma zedoaria*) through a literature review in the form of national and international articles or journals. The results of a study of 8 articles that met the inclusion requirements showed that White Turmeric has anti-inflammatory activity. The content of curcumin, essential oils and flavonoids in white turmeric has similarities with NSAIDs, namely by inhibiting the formation of inflammatory mediators.

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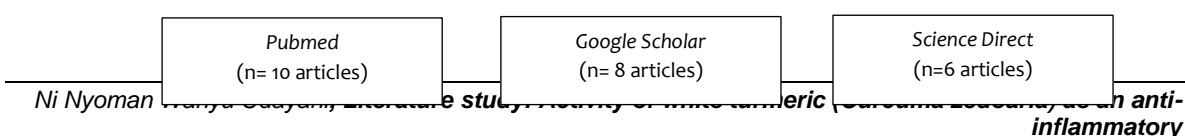
1. Introduction

Inflammation is a response given by the body to protect the body against cellular damage so that the body prepares for the formation of injured tissue (Utami, 2018). Inflammation is characterized by swelling, redness accompanied by a sensation of heat and pain in the part of the body that is experiencing inflammation. Based on several studies, inflammation is the main cause of the pathogenesis mechanism of diseases such as cancer, arthritis, Alzheimer's and depression. Inflammation is caused by triggering factors such as environmental, physical, chemical, emotional and nutritional factors. When tissues in the body are injured physically or chemically, there will be a release of prostaglandins, leukotrienes, histamine, bradykinin and IL-1 which cause inflammation. Inflammation can be divided into 2 types, namely acute and chronic. Acute inflammation is the initial process of the immune system's defense against pathogens that cause damage to cell membranes. Acute inflammation has a shorter duration, may occur in minutes or days, involves a nonspecific immune response and is initiated by macrophages, dendritic cells and mastocytes. Meanwhile, chronic inflammation is inflammation with a longer duration and can last for several months to years. Chronic inflammation can be caused by continuous exposure to certain microbes, viruses and fungi, continuous exposure to chemicals and continuous acute inflammation (Parag Jain, ravindra Pandey, 2015), (Arulselvan, P., 2016). Second-stage inflammation or chronic inflammation can be caused by diseases such as diabetes, obesity, arthritis, cardiovascular disease, metabolism and several types of cancer (He, Y., 2015). The goal of anti-inflammatory therapy is to reduce or control the

discomfort caused by inflammation. One of the most widely used drug classes as an anti-inflammatory is the steroid class and the NSAID (Non-Steroid Anti-Inflammatory Drug) class. NSAIDs work by inhibiting the synthesis of prostaglandins and enzymes that act like COX-1 and COX-2 (Meltyza, E., 2015). There are 2 cyclo-oxygenation isoenzymes, namely COX-1 and COX-2, COX-1 plays a role in maintaining the mucosal lining of the GI tract, kidney function and platelet aggregation. Whereas COX-2 expresses an inflammatory response. Nonselective NSAIDs will inhibit COX-1 and COX-2, but COX-2 selective NSAIDs only target COX-2. Long-term use of NSAIDs has side effects such as disturbances in the digestive tract (GI) including ulcers, stomach upset and bleeding, nausea, disturbances in the kidneys and the cardiovascular system (Yuda, P.E.S.K., Sasmita, G.A.P.Y. & Cahyaningsih, 2022). Free radicals are molecules that have unpaired electrons. Free radicals will take electrons from other molecules to balance them. Based on this, other molecules whose electrons are taken can cause damage to living cells (Arulselvan et al. 2016). In people who have good body conditions, free radicals and antioxidants have balanced levels. When the body is under pressure which causes stress it can cause the production of free radicals to increase and antioxidants cannot overcome the excess free radicals which cause an imbalance in the body. This can cause cell damage and other health problems such as inflammation. Antioxidants will clean free radicals in the body by inhibiting the enzymes responsible for the formation of free radicals (Hussain, T., 2016). Treatment using herbal plants has been carried out for generations, as an alternative treatment using modern medicine. White turmeric (*Curcuma zedoaria*) is a plant that is used as an anti-inflammatory. Derived from the Zingiberaceae family, it has brown and orange rhizomes. White turmeric (*Curcuma zedoaria*) has a spicy taste, is warm and can also be used as aromatherapy. Various secondary metabolites contained in white turmeric are used as stimulants to treat flatulence, diarrhea, nausea, vomiting and antipyretics. White turmeric has also been used as an anti-inflammatory therapy in ayurvedic medicine and traditional herbs. The content of curcumin, essential oils and flavonoids in white turmeric has similarities to NSAIDs. Curcumin inhibits the production of prostaglandins and curcumin can ward off free radicals that can cause inflammation. Flavonoids can inhibit the inflammatory mediator phospholipase A2 so that arachidonic acid metabolism becomes inhibited. Therefore seeing the potential of white turmeric to be used as an anti-inflammatory, the purpose of this literature review is to find out the profile of the use of white turmeric so that it provides benefits as an anti-inflammatory.

2. Research methods

This study used a descriptive design, namely article review through literature review by collecting and reviewing information obtained from several articles related to the effectiveness of white turmeric (*Curcuma zedoaria*) as an anti-inflammatory, both in the form of national and international articles or journals. This article was reviewed using databases such as PubMed, Google Scholar and Science Direct using the keywords “(((Effectiveness) AND (anti inflammation) AND (“curcuma zedoaria”))). The literature search used the last 10 years and met the inclusion and exclusion criteria. The inclusion criteria in this study were articles obtained using predetermined keywords, all articles spanning the last 10 years and literature obtained from the PubMed, Google Scholar and Science Direct databases. This review article will provide an overview of the effectiveness of white turmeric (*Curcuma zedoaria*) as an anti-inflammatory. We found eight articles that met the inclusion requirements, namely national and international literature related to the activity of white turmeric as an anti-inflammatory, published in the last 10 years, namely in the 2013-2023 range and Free Full Text. Exclusion criteria were national or international articles in the 2013-2023 period which discussed the effectiveness of white turmeric as an anti-inflammatory but were not available in Free Full Text.



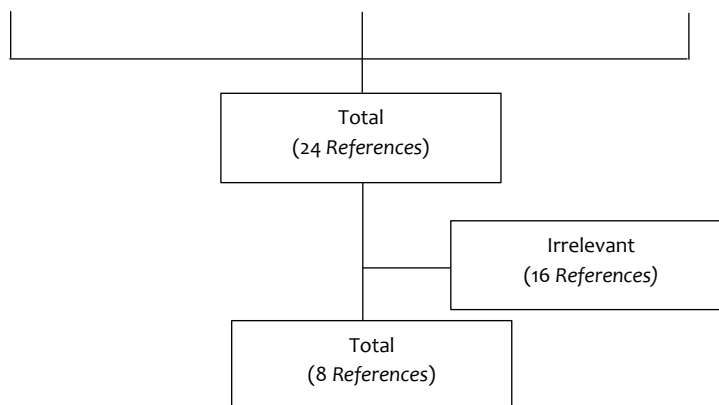


Figure 1. Literature search diagram

3. Results and Discussion

Table 1. List of literature search results that meet the inclusion criteria

No.	Reference	Objective	That part used	Effectiveness
1	(Meltyza et al., 2015)	Knowing the comparison of the anti-inflammatory effect of white turmeric ethanol extract with diclofenac sodium.	Rhizome	<ul style="list-style-type: none"> In the test group doses of white turmeric ethanol extract at doses 1, 2 and 3 there was a decrease in the volume of edema of the soles of the rats' feet. Curcumin, demethoxycurcumin and bisdemethoxycurcumin The 1st dose of white turmeric ethanol extract is 300mg/kgBW, the second dose is 600mg/kgBW and the third dose is 900mg/kgBW. The dose with the lowest effectiveness in reducing edema on the soles of rats' feet was dose 1. The ethanol extract of white turmeric at a dose of 900 mg/kgBB had the same anti-inflammatory effect as a dose of 25 mg sodium diclofenac in inhibiting edema on the soles of rats' feet. The terpenoid compounds in white turmeric have effectiveness as an anti-inflammatory which will reduce prostaglandins. In addition, white turmeric can also reduce fever caused by the presence of flavonoids and terpenoid compounds. Each group of rats was made to experience a febrile reaction in the presence of an inflammatory
2	(Putra et al., 2015)	Knowing the comparison of the antipyretic effectiveness of white turmeric extract and paracetamol in rats.	Rhizome	<ul style="list-style-type: none"> Each group of rats was made to experience a febrile reaction in the presence of an inflammatory

3	(Gozali et al., 2022)	To know the toxicity of white turmeric rhizome extract in terms of LD50 and blood cell components.	Rhizome	<p>response. Arachidonic acid and lysosomal enzyme secretion will be inhibited by flavonoids and blocking of the COX pathway occurs which causes a decrease in prostaglandin levels which act as inflammatory mediators.</p> <ul style="list-style-type: none"> • Giving white turmeric extract to rats affects the value of blood cell components. The increase in the value of erythrocytes is due to the content of flavonoids as antioxidants. • There were no rats that experienced symptoms of toxicity and died at an LD50 above 2000mg/kgBW • White turmeric rhizome has anti-inflammatory effectiveness and is used to treat internal and external swelling. In addition, white turmeric is used to treat digestive tract problems and is recommended as an antitachycardia.
4	(Ayati et al., 2019)	Exploring the therapeutic potential of turmeric (<i>C.longa</i> and <i>C.zedoaria</i>)	-	<ul style="list-style-type: none"> • Administering white turmeric ethanol extract can inhibit the inflammatory response in rats induced by karegano. The resulting inhibition was 92.02% at 250mg/kg and 94.67% at 500mg/kg. White turmeric ethanol extract showed anti-inflammatory activity with a maximum inhibition of $77.15 \pm 2.93\%$ observed at 500 $\mu\text{g}/\text{mL}$ and anti-inflammatory activity using aspirin showed a maximum inhibition of $88.06 \pm 2.07\%$ observed at 500 $\mu\text{g}/\text{mL}$. • Extract of white turmeric rhizome has secondary metabolites such as tannins, saponins, steroids, alkaloids, terpenoids and flavonoids. Flavonoids can significantly inhibit inflammatory mediators, terpenoids can be used as analgesics and anti-inflammatories. Alkaloids can also inhibit inflammation through inhibition of arachidonic acid.
5	(Ullah et al., 2014)	Researching secondary metabolites of white turmeric as analgesic and anti-inflammatory	Rhizome	<ul style="list-style-type: none"> • UV irradiation causes inflammation of the skin and photoaging by inducing the transcription factor AP-1 by regulating the expression of COX-2 and MMP-1 and -13.
6	(Jeong Ha et al., 2018)	Researched the anti-inflammatory effect on skin and UVB-induced photoaging of	-	

		white turmeric extract		<ul style="list-style-type: none"> • Back skin of mice that had been given UVB radiation was given white turmeric extract topically (20 or 100 mg/kg), significantly inhibiting wrinkle formation and inhibiting UVB-induced expression of COX-2 and MMP-13 in mice skin • Curcumenol reduces the production of nitric oxide (NO), pro-inflammatory cytokines (IL-6 and TNF-α) and the expression of the pro-inflammatory proteins, iNOS and COX-2. • Administering 100mg/kg white turmeric extract significantly helped reduce the formation of atherosclerotic lesions in the aortic sinuses of rats and inhibited the expression of inflammatory mediators TNF-α, IL-6, and HMGB-1, and CX₃CL1 chemokines.
7	(Lo et al., 2015)	Investigated the modulating effect of curcumenol on LPS-induced inflammation in BV-2 microglia	Rhizome	
8	(Kim et al., 2021)	Examining the effectiveness of White Turmeric Extract (Curcuma zedoaria) on atherosclerosis in vivo.	Rhizome	

The use of white turmeric as an herbal plant has been widely used in other countries, such as Bhutan, Nepal, the Philippines, Madagascar, Peru, Colombia, India, Thailand, Bangladesh, Sri Lanka, China, Japan, Brazil and Nepal. White turmeric has many benefits including the rhizome used as an allergy, worm treatment in children, leucorrhoea, vomiting and menstrual haematometra. White turmeric is also recommended as an antidote for various toxic agents and poisons from animals, as a liver tonic and can help overcome digestive tract problems. White turmeric leaves can also be used as a treatment for dropsy and leprosy (Ayati et al. 2019). However, the part of the plant that is utilized the most in this white turmeric plant is the white turmeric rhizome. Based on research conducted by (Meltyza et al. 2015) administration of 900 mg/kg BW white turmeric extract reduced the volume of edema in rats' feet and the volume of edema decreased in the same way as rats given 25 mg of diclofenac sodium. Curcumin in white turmeric decreases the activity of COX-2, lipoxigenase and inhibits the production of TNF- α and interleukin (IL). Administration of white turmeric extract inhibited the inflammatory response by 92.02% at a dose of 250 mg/kg and at a dose of 500 mg/kg the inhibition was 94.67% (Ullah, H.M.A., 2014). Based on this, the higher the dose given, the anti-inflammatory effect will also give a maximum effect.

Based on research (Meltyza et al., 2015), the ingredients in white turmeric are curcumin, demethoxycurcumin and bisdemethoxycurcumin. Other secondary metabolites such as tannins, saponins, steroids, alkaloids, terpenoids and flavonoids (Ullah et al., 2014). Curcumin in turmeric can act as an anti-inflammatory. Curcumin will reduce oxidative stress and inflammation. In addition, curcumin has the ability to inhibit TNF production and TNF-mediated cell signaling in various cell types and suppress pro-inflammatory pathways associated with most chronic diseases (He et al. 2015). Terpenoids can act as analgesics and anti-inflammatories, alkaloids can also inhibit inflammation through inhibition of arachidonic acid, proving the presence of active substances that play a role in inhibiting the release of COX-2 enzymes. Flavonoids contained in white turmeric can inhibit arachidonic acid and release of lysosomal enzymes so that there will be blocking of the COX and lipoxigenase pathways. This will result in a decrease in prostaglandins and result in a decrease in body temperature if fever occurs during inflammation (Putra, M.P., Rahmah, S.B. & Kusmiati, 2015).

According to research (Gozali et al. 2022) white turmeric extract did not have a toxic effect on experimental animals with an LD50 above 2000 mg/kg BW. Flavonoid compounds that act as antioxidants cause a high increase in red blood cells in rats that receive white turmeric ethanol extract at a dose of 2000

mg/kgBB. Flavonoids can regulate lipid peroxidation to decrease so that red blood cells are maintained. Flavonoids can help maintain healthy blood vessels by keeping the heart functioning normally. In addition to red blood cells, hemoglobin levels in test animals also remained within the normal range, this is because flavonoids as antioxidants can prevent the occurrence of free radicals and damage to DNA so that the formation of red blood cells and hemoglobin levels can increase or remain in a stable state.

White turmeric extract can also act as an anti-inflammatory due to exposure to UVB rays. UV radiation will regulate AP-1 activity which can induce inflammation in the skin and cause photoaging by increasing the expression of COX-2 and MMPs. White turmeric extract inhibited UVB-induced COX-2 and MMP-13 expression. Compounds in white turmeric that have activity to inhibit inflammation of the skin due to exposure to UVB rays are curcumin and azulene (Jeong Ha et al. 2018). Curcumenol contained in white turmeric shows a safe interaction with drugs and has a mechanism to inhibit BV-2 microglia inflammation stimulated by LPS (Lo et al., 2015). Giving curcumenol can significantly reduce the production of pro-inflammatory mediators, nitric oxide (NO), IL-6 and TNF- α . Treatment using curcumenol content in white turmeric can weaken COX-2 expression on LPS stimulation of BV-2 cells. According to (He, Y., 2015) the content of curcumin in turmeric can also provide protection to the skin. The skin is protected by reducing inflammation and eliminating free radicals, through control of TGF- β , NF-B and mitogen-activated protein kinase pathways. In addition, curcumin controls phase II detoxification enzymes, which are very important components in oxidative stress reactions and detoxification.

White turmeric is able to reduce the formation of atherosclerotic lesions in rats and inhibit the expression of inflammatory mediators. Atherosclerosis is an advanced inflammation that occurs due to narrowing of the arteries due to the buildup of atheromatous plaques. Research conducted by (Kim et al. 2021) states that the content of polyphenols and sesquiterpenes in white turmeric extract are the main components that have anti-atherogenic effects in atherosclerotic rats. Administration of white turmeric extract at a dose of 100 mg/kg reduced blood vessel inflammation and atherosclerosis in rats. This is due to downregulation of TNF- α , IL-6, HMGB-1, and CX3CL1 in atherosclerotic plaques.

4. Conclusion

White turmeric as an herbal plant provides many benefits in the health sector, with the part that is most widely used as an herbal plant, namely the white turmeric rhizome. Secondary metabolites contained in white turmeric include curcumin, demethoxycurcumin and bisdemethoxycurcumin, tannins, saponins, steroids, alkaloids, terpenoids and polyphenol groups such as flavonoids. Based on these ingredients, white turmeric has anti-inflammatory properties with compounds contained in white turmeric that can inhibit the formation of inflammatory mediators. However further anti-inflammatory treatment is not only treated with conventional drugs, but also with herbs, one of which is white turmeric extract. So that white turmeric extract can be better recognized as an anti-inflammatory agent in the future. Further research is needed to determine the right dose to provide maximum effectiveness as an anti-inflammatory.

References

- Arulseivan, P., et. a. (2016). Role of Antioxidants and Natural Products in Inflammation'. *Oxidative Medicine and Cellular Longevity*.
- Ayati, Z., Ramezani, M., Amiri, M. S., Moghadam, A. T., Rahimi, H., Abdollahzade, A., Sahebkar, A., & Emami, S. A. (2019). Ethnobotany, Phytochemistry and Traditional Uses of Curcuma spp. and Pharmacological Profile of Two Important Species (*C. longa* and *C. zedoaria*): A Review. *Current Pharmaceutical Design*, 25(8), 871–935. <https://doi.org/10.2174/1381612825666190402163940>
- Gozali, K., Erny, T., Fiska, W. M., & Rico, S. A. (2022). Acute Toxicity of Extract of White Turmeric Rhizome (*Curcuma Zedoaria*) Review of Ld50 and Blood Cell Components. *Jambura Journal of Health Sciences and Research*, 4(3), 648–655. <https://doi.org/10.35971/jjhsr.v4i3.13309>
- He, Y., et. a. (2015). Curcumin, inflammation, and chronic diseases: How are they linked? *Molecules*, 20(5), 9183–9213.
- Hussain, T., et al. (2016). Oxidative Stress and Inflammation: What Polyphenols Can Do for Us?., *Oxidative*

Medicine and Cellular Longevity.

- Jeong Ha, S., Song, K. M., Lee, J., Ho Kim, Y., Hyouck Lee, N., Eon Kim, Y., Lee, S., & Keun Jung, S. (2018). Preventive effect of Curcuma zedoaria extract on UVB-induced skin inflammation and photoaging. *Journal of Food Biochemistry*, 42(5), 1–11. <https://doi.org/10.1111/jfbc.12598>
- Kim, K. M., Lee, J. Y., Jeon, B. H., Quan, K. T., Na, M., Nam, K. W., & Chae, S. (2021). Extract of curcuma zedoaria r. Prevents atherosclerosis in apolipoprotein e-deficient mice. *Nutrition Research and Practice*, 15(3), 319–328. <https://doi.org/10.4162/nrp.2021.15.3.319>
- Lo, jia ye, Kamarudin, muhamad noor alfarizal, Hamdi, omer abdalla ahmed, Awang, K., & Kadir, habsah abdul. (2015). Curcumenol isolated from Curcuma zedoaria suppresses Akt-mediated NF- κ B activation and p38 MAPK signaling pathway in LPS-stimulated BV-2 microglial cells. <https://doi.org/10.1039/c5fo00607d>
- Meltyza, E., et al. (2015). Perbandingan efek antiinflamasi ekstrak etanol kunyit putih (Curcuma zedoaria) dengan natrium diklorofenak pada tikus yang diinduksi dengan carragenan'. *Prosiding Pendidikan Dokter*, 112–118.
- Meltyza, E., Indriyanti, R. A., & Rahimah, S. B. (2015). Perbandingan efek antiinflamasi ekstrak etanol kunyit putih (Curcuma zedoaria) dengan natrium diklorofenak pada tikus yang diinduksi dengan carragenan. *Prosiding Pendidikan Dokter*, 112–118.
- Parag Jain, ravindra Pandey, S. S. S. (2015). *Inflammation: Natural Resources and Its Applications*.
- Putra, M.P., Rahmah, S.B. & Kusmiati, M. (2015). Perbandingan Efektifitas Antipiretik antara Ekstrak Etanol Kunyit Putih (Curcuma zedoaria Rosc) dengan Parasetamol pada Tikus Model Demam'. *Prosiding Pendidikan Dokter Universitas Islam Bandung*, 2, 407–415.
- Putra, M. P., Rahmah, S. B., & Kusmiati, M. (2015). Perbandingan Efektifitas Antipiretik antara Ekstrak Etanol Kunyit Putih (Curcuma zedoaria Rosc) dengan Parasetamol pada Tikus Model Demam. *Prosiding Pendidikan Dokter Universitas Islam Bandung*, 2, 407–415.
- Ullah, H.M.A., et al. (2014). Evaluation of antinociceptive, in-vivo & in-vitro anti-inflammatory activity of ethanolic extract of Curcuma zedoaria rhizome'. *BMC Complementary and Alternative Medicine*, 14(1), 1–12.
- Ullah, H. M. A., Zaman, S., Juhara, F., Akter, L., Tareq, S. M., Masum, E. H., & Bhattacharjee, R. (2014). Evaluation of antinociceptive, in-vivo & in-vitro anti-inflammatory activity of ethanolic extract of Curcuma zedoaria rhizome. *BMC Complementary and Alternative Medicine*, 14(1), 1–12. <https://doi.org/10.1186/1472-6882-14-346>
- Utami, et. a. (2018). Uji Aktivitas Antiinflamasi Dan Toksisitas Infus. *Kimia Khatulistiwa*, 7(2), 107–112.
- Yuda, P.E.S.K., Sasmita, G.A.P.Y. & Cahyaningsih, E. (2022). Aktivitas Anti-inflamasi Parem Instant Tradisional dari Bahan Usada Bali pada Mencit Inflamasi yang Diinduksi Karagenan. 20(2), 142–149.