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Original Article

Mechanism of Curcumin as a Modulator of the SIRT1–NF-κB Pathway in Preventing Inflammation

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ABSTRACT

The aging process is often associated with increased chronic low-grade inflammation known as inflammaging. This phenomenon is caused by an imbalance between the activation of the pro-inflammatory NF-κB pathway and decreased SIRT1 expression, which plays a role in regulating cellular homeostasis and oxidative stress. Curcumin, a polyphenolic compound derived from Curcuma longa, has potent antioxidant and anti-inflammatory effects and is able to modulate the activity of both pathways. This review aims to discuss the mechanism of curcumin in regulating the SIRT1–NF-κB pathway as a potential strategy in preventing inflammaging. The method used is a literature review from various recent scientific sources discussing the relationship between SIRT1, NF-κB, and the molecular effects of curcumin on the aging process. The results of the review indicate that curcumin can increase SIRT1 expression, which functions to suppress NF-κB acetylation, thereby reducing the production of pro-inflammatory cytokines and improving cellular function. Through this mechanism, curcumin has the potential to slow the aging process and reduce the risk of degenerative diseases related to inflammaging. In conclusion, curcumin acts as a natural modulator of the SIRT1–NF-κB pathway which is promising in both preventive and therapeutic efforts against inflammation-based aging.

Keywords: *Inflammaging, Kurkumin, NF-κB, SIRT1*

ABSTRAK

Proses penuaan sering dikaitkan dengan meningkatnya kondisi inflamasi kronik tingkat rendah yang dikenal sebagai inflammaging. Fenomena ini disebabkan oleh ketidakseimbangan antara aktivasi jalur proinflamasi NF-κB dan penurunan ekspresi SIRT1 yang berperan dalam regulasi homeostasis seluler dan stres oksidatif. Kurkumin, senyawa polifenol yang berasal dari Curcuma longa, memiliki efek antioksidan dan antiinflamasi yang kuat serta mampu memodulasi aktivitas kedua jalur tersebut. Tinjauan ini bertujuan untuk membahas mekanisme kurkumin dalam mengatur jalur SIRT1–NF-κB sebagai strategi potensial dalam pencegahan inflammaging. Metode yang digunakan berupa kajian literatur dari berbagai sumber ilmiah terkini yang membahas

hubungan antara SIRT1, NF-κB, dan efek molekuler kurkumin terhadap proses penuaan. Hasil tinjauan menunjukkan bahwa kurkumin dapat meningkatkan ekspresi SIRT1 yang berfungsi menekan asetilasi NF-κB, sehingga menurunkan produksi sitokin proinflamasi dan memperbaiki fungsi seluler. Melalui mekanisme ini, kurkumin berpotensi memperlambat proses penuaan dan menurunkan risiko penyakit degeneratif yang terkait inflammaging. Kesimpulannya, kurkumin berperan sebagai modulator alami jalur SIRT1–NF-κB yang menjanjikan dalam upaya preventif maupun terapeutik terhadap penuaan berbasis inflamasi.

Kata Kunci: *Inflammaging, Kurkumin, NF-κB, SIRT1*

INTRODUCTION

Inflammaging is a term describing a chronic, low-grade inflammatory condition that occurs with aging, characterized by increased levels of proinflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and C-reactive protein (CRP). This process contributes to accelerated cellular aging and an increased risk of various degenerative diseases such as diabetes mellitus, atherosclerosis, and Alzheimer's disease.[1, 2] One of the main mechanisms of inflammation is dysregulation between the sirtuin 1 (SIRT1) and nuclear factor kappa B (NF-κB) pathways, where decreased SIRT1 activity leads to excessive activation of NF-κB, triggering the production of inflammatory mediators[3].

Curcumin is the main polyphenolic compound from Curcuma longa, known to have anti-inflammatory, antioxidant, and anti-aging effects. Several studies have shown that curcumin can activate SIRT1 and suppress NF-κB activity, thereby reducing the expression of inflammatory genes such as cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS)[4,5]. This modulatory effect makes curcumin a potential candidate in preventing inflammation by restoring the balance of the SIRT1 and NF-κB pathways.

This literature review was conducted to systematically examine the molecular mechanisms of curcumin in modulating the SIRT1 and NF-κB pathways as an effort to prevent inflammation. A literature search was conducted through PubMed, ScienceDirect, and Google Scholar using the keywords "curcumin," "SIRT1," "NF-κB," and "inflammaging," covering 30 articles from 2015–2025. Through this analysis, it is hoped that a comprehensive understanding of curcumin's potential as a nutraceutical agent that can inhibit inflammation-based aging processes will be obtained.

METHODS

The method used was a literature review with a Boolean logic approach in keyword searches in scientific databases such as PubMed, Science Direct, Elsevier, and Google Scholar. The total number of literature used was 29. Inclusion criteria included articles relevant to inflammatory mechanisms, SIRT1, NF-κB, and curcumin biological pathways. Exclusion criteria included non-SIRT1 biological pathways.

RESULT AND DISCUSSION

Definition and Characteristics of Inflammaging

Inflammaging is a process of increasing levels of chronic, systemic, and “low-grade” inflammation that occurs during the aging process without any triggers such as clear infections.[6] The characteristics of inflammaging are low-scale inflammation but chronic and systemic, the process occurs in a sterile manner without intervention from acute pathogens/infections, an increase in pro-inflammatory mediators such as IL-6, TNF-a, CRP, and the occurrence of immunosenescence, namely a decrease in immune system function[7]. The biological mechanisms involved in inflammaging are oxidative stress, mitochondrial dysfunction, and senescence-associated secretory phenotype (SASP)[8].

Oxidative stress is a reaction when there are reactive oxygen species (ROS) that cause damage to DNA, lipids, and proteins. Activation of inflammatory signal transduction pathways such as NF-κB and mitogen-activated protein kinase (MAPK) will increase pro-inflammatory cytokines such as IL-6, TNF-α, IL-1β[8]. Mitochondrial dysfunction occurs when mtROS increases due to a decrease in the electron transport chain and decreased mitophagy, causing the accumulation of damaged mitochondria, triggering ROS production[8]. Mitochondrial damage produces damage-associated molecular patterns (DAMPs) such as mtDNA fragments, peptides, and cardiolipin, which are then recognized by pattern recognition receptors (PRRs) that will produce interferon/inflammation[9]. Mitochondrial dysfunction can disrupt immune metabolism by changing the phenotype of macrophages/T cells to become more pro-inflammatory and reducing the clearance function of senescent cells[9].

Senescent cells are living cells that have stopped dividing with a characteristic secretory profile, namely SASP containing pro-inflammatory cytokines (IL-6, IL-1β, IL-8), chemokines, growth factors, and matrix

metalloproteinases.[10] SASP works with paracrine signals that will induce local tissue inflammation and reorganize immune components. However, with the aging process, the SASP burden increases due to the increase in senescent cells that modulate pro-inflammatory cytokines.[10] The accumulation of senescent cells is self-amplifying, the number of which will increase over time, thus strengthening the occurrence of tissue inflammation.[11] In addition, the accumulation of senescent cells can also reduce stem cell proliferation, slow the wound healing process, and organ degeneration.[12]

SIRT1 Pathway in the Regulation of Aging and Inflammation

The biological pathways involved in inflammation include the NF-κB pathway, the NOD-like receptor pyrin domain-containing 3 (NLRP3 Inflammasome) pathway, the AMP-activated protein kinase (AMPK) pathway, and the SIRT1 pathway. The SIRT1 pathway was chosen for this literature review because it is the primary control center in inflammation, modulating NF-κB, Nrf2, mTOR, and SASP[13]. The primary transcription factor controlling pro-inflammatory gene expression is NF-κB[14]. Suppression of the NF-κB transcription factor will suppress the entire inflammatory pathway, thus increasing its effectiveness[15].

SIRT1 is an NAD+-dependent deacetylase containing a large Rossmann-fold to bind NAD+ and has a small subdomain that includes a helical module and a Zn^{2+} module. The large Rossmann-fold that binds NAD^+ and a small subdomain + Zn^{2+} motif will create a stable structure and lysine substrate interaction[16]. SIRT1 removes the acetyl group (acetyl-lysine) from the lysine residue (ε-acetyl-lysine) on the target protein using NAD^+ as a cofactor, resulting in the general reaction of acetyl–lysine + NAD^+ to produce deacetylated lysine + nicotinamide + 2′-O-acetyl-ADP-ribose (OAADPr)[17].

The Role of the NF-κB Pathway in Inflammation

NF-κB is a transcription factor that plays a central role as a regulator of inflammatory pathway responses and chronic cellular aging[15]. NF-κB activation can be triggered by various stress signals that increase with aging, including the accumulation of free radicals, DNA damage, glycation end products (AGEs), and PAMP/DAMP ligands that interact with surface receptors such as TLRs[14]. Activation initiates the MyD88 adaptor cascade that activates the IKK complex, resulting in the phosphorylation and degradation of IκBα. This process causes the p65/p50 NF-κB subunit to translocate to the nucleus and activate the transcription of proinflammatory genes[14]. NF-κB target gene expression includes proinflammatory cytokines (IL-1β, IL-6, TNF-α), chemokines, proinflammatory enzymes (COX-2, iNOS), and other components that reinforce the chronic pro-inflammatory environment in tissues[18]. Persistent NF-κB activation is associated with an increased cellular senescence phenotype and SASP production. SASP produces factors that exacerbate tissue damage and disrupt microenvironmental homeostasis[15].

Accumulating evidence from animal models and systems studies suggests that chronic inhibition of the NF-κB pathway can slow some hallmarks of aging and reduce the incidence of age-related diseases, such as cardiovascular dysfunction, cognitive decline, and metabolic disorders, although these effects depend on the target tissue and the temporal context of NF-κB activation[19]. In addition to its role in parenchymal cells, NF-κB dysfunction also affects immune cells, disrupting the balance between effector and regulatory immune responses, contributing to immunosenescence, a decline in adaptive responses accompanied by chronic low-grade inflammation[15].

Curcumin as an Anti-inflammatory and Anti-aging Bioactive Compound

Curcumin is the main polyphenol from Curcuma longa with potent anti-inflammatory, antioxidant, and anti-aging activities. This compound suppresses inflammatory, chronic low-grade inflammation associated with aging through SIRT1 activation and NF-κB inhibition.[20,21] Activation of SIRT1 by curcumin inhibits proinflammatory gene transcription and increases antioxidant gene expression.[22] These effects contribute to reduced oxidative stress, increased mitochondrial stability, and slowed cellular aging.[23]

In vitro and in vivo studies have shown that curcumin can normalize SIRT1–NF-κB regulation, suppress systemic inflammation, and improve biomarkers of aging.[23] Despite its low bioavailability, the formulation of nanocurcumin and phospholipid complexes enhances absorption and biological effectiveness.[23] Based on these explanations, it can be said that curcumin has potential as a natural agent in modulating the SIRT1–NF-κB axis to prevent inflammation.[23]

Mechanism of Curcumin on the SIRT1 Pathway

Curcumin has been reported to increase the expression and/or activity of the NAD^+-dependent deacetylase SIRT1 and plays a key role in the regulation of cellular lifespan, DNA repair, and metabolic homeostasis[24].

In vitro and in vivo studies have shown that curcumin induces activation of the AMPK pathway, which interacts with SIRT1[25]. Activation of SIRT1 by curcumin results in deacetylation of targets including p53 and the p65 subunit of NF-κB. This deacetylation mechanism decreases the transcriptional activity of proinflammatory factors and inhibits the SASP-inducing pathway. [19,24]

Mechanism of Curcumin on the NF-κB Pathway

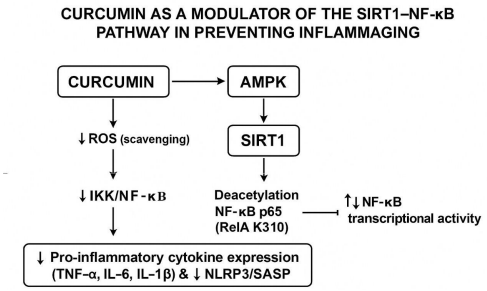
Curcumin inhibits NF-κB activation through several molecular mechanisms, namely by inhibiting IKKβ phosphorylation, preventing IκBα degradation,

decreasing phosphorylation, and translocation of p65 to the nucleus, thereby reducing the transcription of pro-inflammatory genes such as IL-6, IL-1β, and TNF-α[26,27]. In addition to directly interfering with the components of the IKK/IκBα pathway, curcumin reduces upstream pro-inflammatory signals by inhibiting the activation of surface receptors (TLRs), other supporting pathways such as MAPK and JAK/STAT, all of which can contribute to reducing the burden of NF-κB activation in chronic conditions[25,28].

Synergy of SIRT1 Activation and NF-κB Inhibition by Curcumin as Anti-Inflammatory

The dual effects of curcumin in stimulating SIRT1 activation and inhibiting NF-κB create a protective loop that suppresses inflammation at multiple levels. Increased SIRT1 leads to deacetylation of p65 NF-κB, thereby reducing pro-inflammatory transcriptional activity. Concurrently, curcumin inhibition of IKK/IκBα reduces the initial signal that activates NF-κB, thus potentiating the reduction in pro-inflammatory cytokine and SASP expression. [24,27]

Reported phenotypic consequences include decreased systemic inflammatory markers (e.g., IL-6, CRP), reduced ROS and oxidative stress, improved mitochondrial function, and decreased expression of senescence markers such as p21 and β-galactosidase in cell and animal models[19,24]. Meta-reviews and systematic reviews confirm the consistent findings that curcumin reduces NF-κB activation and clinical inflammatory parameters across a range of inflammatory conditions, although clinical effects on long-term anti-aging endpoints such as mortality and biological lifespan still require large-scale RCTs and measurement of specific SIRT1/NAD^+ biomarkers for clinical translational verification[29].



Gambar 1. *Diagram of Curcumin as Modulator of The SIRT1–NF-κB Pathway*

CONCLUSION

This review suggests that inflammaging is a chronic, low-grade inflammation caused by decreased SIRT1 activity and increased NF-κB pathway activation, which accelerates aging and susceptibility to degenerative diseases. Curcumin, a natural bioactive compound, is capable of suppressing NF-κB activation while increasing SIRT1 expression, potentially balancing the inflammatory response and protecting cells from oxidative stress.

In practical applications, curcumin's modulation of the SIRT1–NF-κB pathway could provide a basis for developing preventive and therapeutic strategies against inflammation. This potential makes curcumin an attractive candidate for supplement formulations or adjuvant therapies to slow the aging process through molecular control of inflammation.

REFERENCES

1. Franceschi C, Garagnani P, Parini P, Giuliani C, Santoro A. Inflammaging and 'Garb-aging'. Nat Rev Endocrinol. 2018 Jul 25. 14(10):576–590. doi:10.1038/s41574-018-0059-4 https://doi.org/10.1038/s41574-018-0059-4
2. Minciullo PL, Catalano A, Mandraffino G, et al. Inflammaging and anti-inflammaging: The role of cytokines in extreme longevity. Arch Immunol Ther Exp. 2016;64(2):111-126. DOI: 10.1007/s00005-015-0377-3
3. Meng B, Li J, Cao H. Antioxidants and anti-inflammatory activities of curcumin on ageing-related diseases through regulation of SIRT1–NF-κB pathway: A review. Ageing Res Rev. 2021. 69:101362. doi:10.1016/j.arr.2021.101362 https://doi.org/10.1016/j.arr.2021.101362
4. Izadi M, et al. Longevity and anti-aging effects of curcumin supplementation. Aging (Albany NY). 2024. (7):473-490. doi:10.18632/aging.100991. Available from: https://doi.org/10.18632/aging.100991
5. Grabowska W, Suszek M, Wnuk M, Lewińska A, Wasiak E, Sikora E, et al. Curcumin elevates sirtuin level but does not postpone in vitro senescence of human cells building the vasculature. Oncotarget. 2016. 7(15):19201-19213. doi:10.18632/oncotarget.8450. Available from: https://doi.org/10.18632/oncotarget.8450
6. Claudio Franceschi & Judith Campisi. Chronic Inflammation (Inflammaging) and Its Potential Contribution to Age-Associated Diseases. The Journals of Gerontology: Series A. 2014 June. 69;1:4–9, https://doi.org/10.1093/gerona/glu057
7. Tamas Fulop, Anis Larbi, Jacek M. Witkowski. Gerontology. 2019. 65 (5): 495–504.https://doi.org/10.1159/000497375
8. Zuo L, Prather ER, Stetskiv M, Garrison DE, Meade JR, Peace TI, Zhou T. Inflammaging and Oxidative Stress in Human Diseases: From Molecular Mechanisms to Novel Treatments. Int J Mol Sci. 2019 Sep 10;20(18):4472. doi: 10.3390/ijms20184472. PMID: 31510091; PMCID: PMC6769561.
9. Xu X, Wen Z. The Mediating Role of Inflammaging Between Mitochondrial Dysfunction and Sarcopenia in Aging: a Review. Am J Clin Exp Immunol. 2023 Dec 15;12(6):109-126. PMID: 38187366; PMCID: PMC10767199.

10. Wang, B., Han, J., Elisseeff, J.H. et al. The Senescence-Associated Secretory Phenotype and Its Physiological and Pathological Implications. Nat Rev Mol Cell Biol 25, 2024. 958–978. https://doi.org/10.1038/s41580-024-00727
11. Ohtani, N. The Roles and Mechanisms of Senescence-Associated Secretory Phenotype (SASP): Can it be Controlled by Senolysis?. Inflamm Regener. 2022 Apr 02. https://doi.org/10.1186/s41232-022-00197-8
12. Childs, B., Gluscevic, M., Baker, D. et al. Senescent Cells: an Emerging Target for Diseases of Ageing. Nat Rev Drug Discov 16. 2017 July 21. 718–735. https://doi.org/10.1038/nrd.2017.116
13. Yang Y, Liu Y, Wang Y, Chao Y, Zhang J, Jia Y, Tie J and Hu D. Regulation of SIRT1 and Its Roles in Inflammation. Front. Immunol. 2022. 13:831168. doi: 10.3389/fimmu.2022.831168
14. Masatoshi Haga, Mariko Okada. Systems Approaches to Investigate the Role of NF-κB Signaling in Aging. Biochem J. 2022 January 28. 479 (2): 161–183. doi: https://doi.org/10.1042/BCJ20210547
15. Songkiatisak, P., Rahman, S.M.T., Aqdas, M. et al. NF-κB, a culprit of both inflamm-ageing and declining immunity?. Immun Ageing. 2022 May 17. 19;20 https://doi.org/10.1186/s12979-022-00277-w
16. Sharma, A., Mahur, P., Muthukumaran, J. *et al.* Shedding light on structure, function and regulation of human sirtuins: a comprehensive review. *3 Biotech.* 2023. https://doi.org/10.1007/s13205-022-03455-1
17. Nian-Da Yu, Bing Wang, Xin-Zhu Li, Hao-Zhen Han, and Dongxiang Liu. A Novel Mechanism for SIRT1 Activators That Does Not Rely on the Chemical Moiety Immediately C-Terminal to the Acetyl-Lysine of the Substrate. Molecules. 2022 Apr 22. 27(9), 2714; https://doi.org/10.3390/molecules27092714
18. Li, X., Li, C., Zhang, W. et al. Inflammation and Aging: Signaling Pathways and Intervention Therapies. Sig Transduct Target Ther. 2023. 8, 239. https://doi.org/10.1038/s41392-023-01502-8
19. García-García VA, Alameda JP, Page A, Casanova ML. Role of NF-KB in Ageing and Age-Related Diseases: Lessons from Genetically Modified Mouse Models. Cells. 2021 Jul 27. 10(8):1906. doi:10.3390/cells10081906. PMID:34440675; PMCID: PMC8394846.
20. Hewlings SJ, Kalman DS. Curcumin: A Review of Its Effects on Human Health. Foods. 2017. 6(10):92. https://doi.org/10.3390/foods6100092. Available at: https://www.mdpi.com/2304-8158/6/10/92
21. Fuloria S, et al. A Comprehensive Review on the Therapeutic Potential of Curcumin. Front Pharmacol. 2022. 13:820806. https://doi.org/10.3389/fphar.2022.820806. Available at: https://www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2022.820806/full
22. Prasad S, Tyagi AK, Aggarwal BB. Recent Developments in Delivery, Bioavailability, Absorption and Metabolism of Curcumin: The Golden Pigment from Golden Spice. Cancer Res Treat. 2014;46(1):2-18. https://doi.org/10.4143/crt.2014.46.1.2
23. Kharat M, Zhang G, McClements DJ. Physical and Chemical Stability of Curcumin in Aqueous Solutions and Emulsions: Impact of pH, Temperature, and Molecular Environment. J Agric Food Chem. 2020;68(36):9603–9619. DOI: 10.1021/acs.jafc.6b04815. https://doi.org/10.1021/acs.jafc.6b04815
24. Izadi M, Sadri N, Abdi A, Zadeh MMR, Jalaei D, Ghazimoradi MM, Shouri S, Tahmasebi S. Longevity and anti-aging effects of curcumin supplementation. Geroscience. 2024 Jun;46 (3):2933-2950. doi: 10.1007/s11357-024-01092-5. Epub 2024 Feb 27. PMID: 38409646; PMCID: PMC11009219.
25. Sadek, M.A., Rabie, M.A., El Sayed, N.S. et al. Neuroprotective Effect of Curcumin Against Experimental Autoimmune Encephalomyelitis-Induced Cognitive and Physical Impairments in Mice: an Insight Into the Role of the AMPK/SIRT1 Pathway. Inflammopharmacol. 2024. 32,1499-1518. https://doi.org/10.1007/S10787-023-01399-3
26. Zhongyuan Zhang, Jiaming Fu, Yihong Di, Honghui Li, Bing Wu, Xueyan Tian, Meiyan Li, Yuging Dai, Zhuoheng Shen, Jinhao Jia, Zeyang Bai, Limeng Xiong, Yuhan Zhang, Xiaoyu Li, Yi Zhao, Hao Hu, Guangjun Wang, Huifang Yang, Rui Zhang, Jian Sun. Imidacloprid Induces Abnormal Glucose Metabolism Through NF-kB-mediated Apoptosis of Pancreatic & Cells Based on Population Exposure levels. Environmental Research. 2025. 10.1016/j.envres.123171,287, (123171)
27. Benameur T, et al. The Effects of Curcumin on Inflammasome: Latest Update. Molecules. 2023. 28(2), 742; https://doi.org/10.3390/molecules280207
28. Nunes YC, et al. Curcumin: A Golden Approach to Healthy Aging. Nutrients. 2024. 16(16), 2721; https://doi.org/10.3390/nu16162721
29. Abu-Hijleh, H. M., Al-Zoubi, R. M., Zarour, A., Al- Ansari, A., & Bawadi, H. The Therapeutic Role of Curcumin in Inflammation and Post-Surgical Outcomes. Food Reviews International. 2023. 40(1), 293-308. https://doi.org/10.1080/87559129.2023.2166525