

植物多酚對手術誘導骨關節炎及 IL-1 β 誘導軟骨細胞炎症的影響

黃郁家(5123)

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大綱

一、前言

二、天麻素減少 IL-1 β 誘導的細胞凋亡、炎症和骨關節炎軟骨細胞中的基質分解代謝，並減少體內大鼠軟骨退化。

三、黃芩苷透過阻斷人骨關節炎軟骨細胞中的 NF- κ B 抑制 IL-1 β 誘導的炎症細胞因子的表達，並在小鼠骨關節炎模型中顯示出保護作用。

四、丹皮酚通過 PI3K / Akt / NF- κ B 途徑抑制 IL-1 β 誘導的炎症：體內和體外研究。

五、結論

摘要

骨關節炎 (Osteoarthritis, OA) 為一種慢性退化關節疾病，年齡、機械壓力、肥胖人口老化都會使 OA 發病率提升。軟骨細胞可以保持細胞外基質 (Extracellular matrix, ECM) 分解與合成的動態平衡。蛋白質水解酶由軟骨細胞所分泌，可以分解 ECM，發炎之軟骨細胞會產生過多的蛋白質水解酶，使 ECM 之代謝平衡遭到破壞。IL-1 β 已經被證實會透過 NF- κ B 途徑參與促發炎因子的產生，透過抑制 NF- κ B 途徑發現可以降低發炎產物的產生及減少發炎反應。因此本篇希望透過植物多酚來觀察是否可以改善骨關節炎。經手術誘導骨關節炎之大鼠再使用天麻素進行皮下注射後發現可以改善軟骨基質所受到的破壞。經 IL-1 β 誘導發炎之軟骨細胞經天麻素處理後減少了細胞凋亡及 NF- κ B 途徑之發炎因子的釋放。另外，經手術誘導骨關節炎之小鼠再使用黃芩苷進行腹腔注射後證實黃芩苷可以改善軟骨基質厚度及滑膜組織之受損。黃芩苷也可以降低軟骨細胞之發炎產物一氧化氮 (Nitrite) 及前列腺素 (prostaglandin E2, PGE2) 及蛋白質水解酶之產生。給予丹皮酚之軟骨細胞透過抑制 PI3K/AKT/NF- κ B 途徑降低了發炎因子的產生，在動物實驗方面也證實丹皮酚可以改善小鼠的骨關節炎。綜合以上三者，可解釋其皆有潛力成為改善 OA 的天然植物來源。

1 參考文獻

- 2 Altman, R., Brandt, K., Hochberg, M., Moskowitz, R., Bellamy, N., Bloch, D. A., Buckwalter,
3 J., Dougados, M., Ehrlich, G., Lequesne, M., Lohmander, S., Murphy, W. A.,
4 Rosario-Jansen, T., Schwartz, B., & Trippel, S. (1996). Design and conduct of clinical
5 trials in patients with osteoarthritis: Recommendations from a task force of the
6 Osteoarthritis Research Society: Results from a workshop. *Osteoarthritis and*
7 *Cartilage*, 4, 217-243.
- 8 Charni-Ben Tabassi, N., & Garnero, P. (2007). Monitoring cartilage turnover. *Curr Rheumatol*
9 *Rep*, 9, 16-24.
- 10 Chen, C., Zhang, C., Cai, L., Xie, H., Hu, W., Wang, T., Lu, D., & Chen, H. (2017). Baicalin
11 suppresses IL-1 β -induced expression of inflammatory cytokines via blocking NF- κ B
12 in human osteoarthritis chondrocytes and shows protective effect in mice
13 osteoarthritis models. *International Immunopharmacology*, 52, 218-226.
- 14 Chen, D., Shen, J., Zhao, W., Wang, T., Han, L., Hamilton, J. L., & Im, H.-J. (2017).
15 Osteoarthritis: toward a comprehensive understanding of pathological mechanism.
16 *Bone Research*, 5, 16044.
- 17 Chen, J., Gu, Y.-T., Xie, J.-J., Wu, C.-C., Xuan, J., Guo, W.-J., Yan, Y.-Z., Chen, L., Wu, Y.-S.,
18 Zhang, X.-L., Xiao, J., & Wang, X.-Y. (2018). Gastrodin reduces IL-1 β -induced
19 apoptosis, inflammation, and matrix catabolism in osteoarthritis chondrocytes and
20 attenuates rat cartilage degeneration in vivo. *Biomedicine & Pharmacotherapy*, 97,
21 642-651.
- 22 Goldring, M. B. (2012). Chondrogenesis, chondrocyte differentiation, and articular cartilage
23 metabolism in health and osteoarthritis. *Therapeutic advances in musculoskeletal*
24 *disease*, 4, 269-285.
- 25 Johnson, V. L., & Hunter, D. J. (2014). The epidemiology of osteoarthritis. *Best Practice &*

Research Clinical Rheumatology, 28, 5-15.

Lepetsos, P., & Papavassiliou, A. G. (2016). ROS/oxidative stress signaling in osteoarthritis. *Biochimica et Biophysica Acta - Molecular Basis of Disease*, 1862, 576-591.

Lin, C., Lin, H.-Y., Chen, J.-H., Tseng, W.-P., Ko, P.-Y., Liu, Y.-S., Yeh, W.-L., & Lu, D.-Y. (2015). Effects of paeonol on anti-neuroinflammatory responses in microglial cells. *International journal of molecular sciences*, 16, 8844-8860.

Liu, B., Li, F., Shi, J., Yang, D., Deng, Y., & Gong, Q. (2016). Gastrodin ameliorates subacute phase cerebral ischemia-reperfusion injury by inhibiting inflammation and apoptosis in rats. *Molecular medicine reports*, 14, 4144-4152.

Liu, Y., Gao, J., Peng, M., Meng, H., Ma, H., Cai, P., Xu, Y., Zhao, Q., & Si, G. (2018). A Review on Central Nervous System Effects of Gastrodin. *Frontiers in pharmacology*, 9, 24-24.

Loeser, R. F., Goldring, S. R., Scanzello, C. R., & Goldring, M. B. (2012). Osteoarthritis: A disease of the joint as an organ. 64, 1697-1707.

Nakata, K., Ono, K., Miyazaki, J., Olsen, B. R., Muragaki, Y., Adachi, E., Yamamura, K., & Kimura, T. (1993). Osteoarthritis associated with mild chondrodysplasia in transgenic mice expressing alpha 1(IX) collagen chains with a central deletion. *Proceedings of the National Academy of Sciences of the United States of America* 90, 2870-2874.

Rahmati, M., Mobasheri, A., & Mozafari, M. (2016). Inflammatory mediators in osteoarthritis: A critical review of the state-of-the-art, current prospects, and future challenges. *Bone*, 85, 81-90.

Sandell, L. J., Aigner, T. J. A. R., & Therapy. (2001). Articular cartilage and changes in Arthritis: Cell biology of osteoarthritis. *Arthritis Research & Therapy*, 2001, 3:107.

Santangelo, K. S., Nuovo, G. J., & Bertone, A. L. (2012). In vivo reduction or blockade of interleukin-1 β in primary osteoarthritis influences expression of mediators implicated in pathogenesis. *Osteoarthritis and Cartilage*, 20, 1610-1618.

- Stampella, A., Monteagudo, S., & Lories, R. (2018). Wnt signaling as target for the treatment of osteoarthritis. *Best Practice & Research Clinical Rheumatology*.
- Vincenti, M. P., & Brinckerhoff, C. E. (2002). Transcriptional regulation of collagenase (MMP-1, MMP-13) genes in arthritis: integration of complex signaling pathways for the recruitment of gene-specific transcription factors. *Arthritis Res*, 4, 157-164.
- Wang, H. Z., Wang, H. H., Huang, S. S., Zhao, H., Cao, Y. G., Wang, G. Z., Wang, D., Wang, Z. G., & Liu, Y. H. (2014). Inhibitory effect of baicalin on collagen-induced arthritis in rats through the nuclear factor-kappaB pathway. *The Journal of pharmacology and experimental therapeutics*, 350, 435-443.
- Wang, J.-W., Liu, Y.-M., Zhao, X.-F., & Zhang, H. (2017). Gastrodin protects retinal ganglion cells through inhibiting microglial-mediated neuroinflammation in an acute ocular hypertension model. *International journal of ophthalmology*, 10, 1483-1489.
- Wu, Y., Chen, L., Wang, Y., Li, W., Lin, Y., Yu, D., Zhang, L., Li, F., & Pan, Z. (2015). Overexpression of Sirtuin 6 suppresses cellular senescence and NF- κ B mediated inflammatory responses in osteoarthritis development. *Scientific Reports*, 5, 17602.
- Yang, W., Li, H., Cong, X., Wang, X., Jiang, Z., Zhang, Q., Qi, X., Gao, S., Cao, R., & Tian, W. (2016). Baicalin attenuates lipopolysaccharide induced inflammation and apoptosis of cow mammary epithelial cells by regulating NF-kappaB and HSP72. *Int Immunopharmacol*, 40, 139-145.
- Young, I.-C., Chuang, S.-T., Gefen, A., Kuo, W.-T., Yang, C.-T., Hsu, C.-H., & Lin, F.-H. (2017). A novel compressive stress-based osteoarthritis-like chondrocyte system. 242, 1062-1071.
- Yuan, X., Chen, J., & Dai, M. (2016). Paeonol promotes microRNA-126 expression to inhibit monocyte adhesion to ox-LDL-injured vascular endothelial cells and block the activation of the PI3K/Akt/NF-kappaB pathway. *International Journal of Molecular Medicine*, 38, 1871-1878.

- 1 Zhang, Z., Zhou, J., Song, D., Sun, Y., Liao, C., & Jiang, X. (2017). Gastrodin protects
- 2 against LPS-induced acute lung injury by activating Nrf2 signaling pathway.
- 3 Oncotarget, 8, 32147-32156.