

## Editorial

# Punicalagin from pomegranate: a polyphenolic modulator of inflammation and cartilage homeostasis in knee and joint pain

Aavrati Rastogi<sup>1\*</sup>, Roop B. Kalia<sup>1</sup>, Pradeep K. Meena<sup>1</sup>, Mukesh Bairwa<sup>2</sup>

<sup>1</sup>Department of Orthopedics, AIIMS Rishikesh, Uttarakhand, India

<sup>2</sup>Department of Internal Medicine, AIIMS Rishikesh, Uttarakhand, India

**Received:** 01 June 2026

**Accepted:** 18 July 2026

### \*Correspondence:

Dr. Aavrati Rastogi,

E-mail: [aavrati26@gmail.com](mailto:aavrati26@gmail.com)

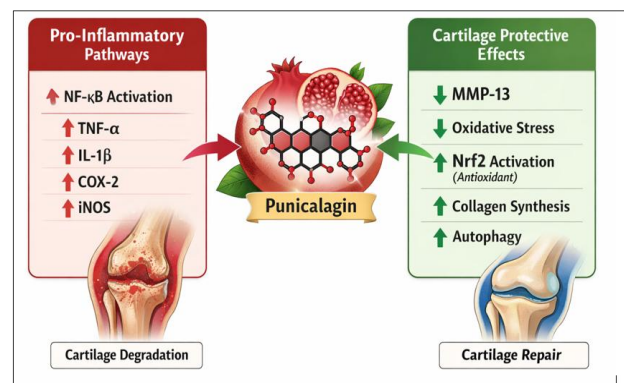
**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Knee osteoarthritis is increasingly recognized as a multifactorial disorder rather than simple “wear and tear.” Pain and cartilage degradation are caused by oxidative stress, metabolic imbalance, and chronic low-grade inflammation. NF  $\kappa$ B is a significant therapeutic target because it is a key regulator of inflammation which promotes the production of cytokines and matrix breakdown.<sup>1,2</sup>

Pomegranates contain punicalagin, a significant ellagitannin that has shown promise as a nutraceutical with the ability to alter illness. After consumption, it is broken down into urolithins and ellagic acid, both of which have systemic bioactivity. Punicalagin maintains collagen integrity by suppressing NF  $\kappa$ B activation, lowering COX 2 and iNOS production, and downregulating matrix metalloproteinases such MMP 13.<sup>2,3</sup> Additionally, it stimulates Nrf2, strengthening antioxidant defenses and preventing apoptosis in chondrocytes.<sup>4</sup> Recent research uncovers more functions in epigenetic regulation, such as chromatin remodeling mediated by Brd4 and modulation of the Foxo1/Prg4/HIF3 $\alpha$  axis, which may have a wider impact on cartilage homeostasis.<sup>8,9</sup>

Pomegranate peel extract supplementation has been shown in clinical trials to reduce inflammatory biomarkers (hs CRP, IL 6, and MMP 1) and improve knee OA patients' pain, stiffness, and function.<sup>5-7</sup> Individual responses vary, though, as punicalagin metabolism is impacted by gut flora diversity. The amount response studies, bioavailability enhancers, and standardized formulations are needed to optimize clinical translation.<sup>9</sup>

Punicalagin is an excellent example of how dietary polyphenols might influence osteoarthritis's catabolic and anabolic pathways. It could be a useful supplement to precision nutrition and multimodal rehabilitation techniques with additional validation from large randomized controlled studies.



**Figure 1: Punicalagin molecular pathways in osteoarthritis.**

Punicalagin lowers matrix metalloproteinases (MMP 13), activates Nrf2 antioxidant pathways, decreases NF $\kappa$ B signaling (TNF  $\alpha$ , IL 1 $\beta$ , COX-2, iNOS), and increases chondrocyte survival through autophagy and epigenetic regulation (Foxo1/Prg4/HIF3 $\alpha$ ).

Together, these benefits promote cartilage regeneration while reducing oxidative stress, inflammation, and cartilage disintegration.<sup>2,4,8,9</sup>

## REFERENCES

1. Shukla M, Gupta K, Rasheed Z, Khan KA, Haqqi TM. Consumption of hydrolyzable tannin-rich pomegranate extract suppresses inflammation and improves clinical symptoms in patients with knee osteoarthritis. *Nutrition*. 2008;24(7-8):733-43.
2. Rasheed Z, Akhtar N, Khan A, Haqqi TM. Anti-inflammatory effects of pomegranate extract on human osteoarthritis chondrocytes. *Arthritis Res Ther*. 2009;11(2):R47.
3. Ismail T, Sestili P, Akhtar S. Pomegranate peel and fruit extracts: A review of potential anti-inflammatory and antioxidant properties. *J Ethnopharmacol*. 2012;143(2):397-405.
4. Xu J, Cao K, Liu X, Zhao L, Feng Z, Liu J. Punicalagin regulates NF- $\kappa$ B, MAPK, and PI3K/Akt pathways in chronic inflammation. *Antioxidants (Basel)*. 2021;11(1):29.
5. Rafrat M, Khadem Haghighian M, Molani Gol R, Hemmati S, Asghari-Jafarabadi M. Effects of pomegranate peel extract on inflammation and MMP-1 in women with knee osteoarthritis: a randomized controlled trial. *Nutr Metab Insights*. 2024;17:11786388241243266.
6. Rafrat M, Hemmati S, Jafarabadi MA, Moghaddam A, Haghighian MK. Pomegranate peel hydroalcoholic extract reduces pain and improves symptoms in knee osteoarthritis: randomized controlled trial. *Iran Red Crescent Med J*. 2017;19(1):e38577.
7. Haghighian MK, Rafrat M, Hemmati S, Haghravan S, Asghari-Jafarabadi M. Pomegranate peel extract supplementation improves lipid profile and antioxidant status in obese women with knee osteoarthritis. *Adv Integr Med*. 2021;8(2):107-13.
8. Li H, Li Q, Wan T, Wang Y, Zhang S. Punicalagin attenuates inflammatory osteolysis via Brd4-mediated chromatin remodeling. *Sci Rep*. 2026;16:12948.
9. Bone. Punicalagin attenuates osteoarthritis progression via Foxo1/Prgh4/HIF3 $\alpha$  axis. *Bone*. 2021;152:116070.

**Cite this article as:** Rastogi A, Kalia RB, Meena PK, Bairwa M. Punicalagin from pomegranate: a polyphenolic modulator of inflammation and cartilage homeostasis in knee and joint pain. *Int J Community Med Public Health* 2026;13:4776-7.