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OSTEOARTHRITIS

PROCYANIDIN B3 PREVENTS OA *IN VIVO*

Procyanidin B3 (B3), a proanthocyanidin extracted from grape seeds, has been shown to prevent the progression of osteoarthritis (OA) and heterotopic cartilage formation in an OA mouse model. "B3 administration markedly prevented OA progression in articular cartilage *in vivo*," notes author Yoshinori Asou (Toyko Medical and Dental University), "the effect of B3 on heterotopic cartilage formation was unexpected."

"Oxidative stress is among one of the key inflammatory mediators involved in the progression of OA," says Asou. In the quest to find molecules for prevention of disease progression, Asou and co-workers reasoned that grape seed proanthocyanidins such as B3 could have potential therapeutic benefit in OA because of powerful antioxidant activity.

To investigate the therapeutic properties of B3, Asou and colleagues first tested the molecule *in vitro*. Using this approach, the researchers found that B3 blocked several negative effects of oxidative stress on chondrocytes: H_2O_2-induced chondrocyte apoptosis; production of inducible nitric oxide synthase (iNOS); and suppression of extracellular matrix synthesis.

Next, Asou *et al.* examined the effects of B3 *in vivo* in a surgical mouse model of OA. Daily oral B3 administration (1 mg/10 g body weight) prevented cartilage destruction in the surgically treated mice; histological OA grading in B3-treated animals was around half that of controls. Moreover, heterotopic cartilage and pseudocapsule formation near the surgical site (as a result of chronic inflammation) was also prevented by B3 administration. Finally, Asou and colleagues found that iNOS expression was enhanced in control mice, but reduced in B3-treated mice, indicating that B3 prevented cartilage degeneration, at least in part, through suppression of iNOS.

The authors are now planning further work to study the effects of other procyanidin dimers and trimers found in grape seed extracts on cartilage and bone metabolism. Moreover, Asou hopes to elucidate the molecular target of B3 in chrondrocyte metabolism: "although B3-mediated iNOS inhibition may be one means by which B3 prevents OA, the molecular target of B3 is still unknown".

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Original article Aini, H. *et al.* Procyanidin B3 prevents articular cartilage degeneration and heterotopic cartilage formation in a mouse surgical osteoarthritis model. *PLoS ONE* **7**, e37728 (2012)