β-Hydroxybutyrate

β-Hydroxybutyrate (β-HB) is a chemical compound that belongs to the group of ketone bodies.

It serves as one of the primary alternative energy sources to glycogen during periods of low carbohydrate availability, such as prolonged fasting or a ketogenic diet. β-HB is produced in the liver through the oxidation of fatty acids and, along with other ketone bodies like acetoacetate and acetone, is transported to various organs, particularly the brain and muscles, where it can be converted into energy.

This compound is significant because:

- **Energy source**: It provides an efficient fuel for the brain and body during carbohydrate scarcity.

- **Brain function**: β-HB can cross the blood-brain barrier, offering an alternative energy source for neurons.

- **Metabolic benefits**: It may support improved metabolic health by promoting fat metabolism and influencing pathways related to cellular energy.

The ketogenic diet (KD) has demonstrated efficacy in ameliorating inflammation in rats with osteoarthritis (OA). However, the long-term safety of the KD and the underlying mechanism by which it delays OA remain unclear. Cai et al. found that while long-term KD could ameliorate OA, it induced severe hepatic steatosis in mice. Consequently, they developed two versions of ketogenic-based diets: KD supplemented with vitamin D and intermittent KD. Both KD supplemented with vitamin D and intermittent KD effectively alleviated OA by significantly reducing the levels of inflammatory cytokines, cartilage loss, sensory nerve sprouting, and knee hyperalgesia without inducing hepatic steatosis. Furthermore, β-hydroxybutyrate (β-HB), a convenient energy carrier produced by adipocytes, could ameliorate OA without causing liver lesions. Mechanistically, β-HB enhanced chondrocyte autophagy and reduced apoptosis through the activation of the Erb-B2 receptor tyrosine kinase 3 (ERBB3) signaling pathway; a pathway which was down-regulated in the articular chondrocytes from both OA patients and mice. Collectively, the findings highlighted the potential therapeutic value of β-HB and KD supplemented with vitamin D and intermittent KD approaches for managing OA [1].

1)
Cai Z, Zhang Z, Leng J, Xie M, Zhang K, Zhang J, Zhang H, Hu H, Deng Y, Bai X, Song Q, Lai P. β-hydroxybutyrate ameliorates osteoarthritis through activation of the ERBB3 signaling pathway in mice. J Bone Miner Res. 2024 Nov 5:zjae176. doi: 10.1093/jbmr/zjae176. Epub ahead of print. PMID: 39498503.