

- (4) The primary mode of action of HMB appears to be through its dual mechanism to enhance muscle protein synthesis and suppress muscle protein breakdown. HMB's activation of mTORC1 is independent of the leucine-sensing pathway (Sestrin2-GATOR2 complex).
- (5) HMB may help reduce muscle damage and promote muscle recovery, which can promote muscle growth and repair. HMB may also have anti-inflammatory effects, which could contribute to reducing muscle damage and soreness.
- (6) HMB consumption in close proximity to an exercise bout may be beneficial to increase muscle protein synthesis and attenuate the inflammatory response. HMB can provide a beneficial physiological effect when consumed both acutely and chronically in humans.
- (7) Daily HMB supplementation at 38 mg/kg body weight in combination with exercise training may potentially improve body composition through increasing lean mass and/or decreasing fat mass with benefits in participants across age, biological sex, and baseline training status. The most pronounced of these improvements in body composition with HMB have been observed in studies with robust resistance training programs and dietary control.
- (8) HMB may improve strength and power in untrained individuals, but its performance benefits in trained athletes are mixed and increase with an increase in study duration (>6 weeks). Furthermore, HMB's beneficial effects on athletic performance are thought to be driven by improved recovery.
- (9) HMB supplementation appears to potentially have a positive impact on aerobic performance, especially in trained athletes. The proposed mechanisms of the effects are unknown.
- (10) HMB supplementation may be important in a non-exercising sedentary and aging population to improve muscle strength, functionality, and muscle quality. The effects of HMB supplementation with exercise are varied, but the combination may have a beneficial effect on the treatment of age-associated sarcopenia under select conditions.
- (11) HMB may be effective in countering muscle disuse atrophy during periods of inactivity due to illness or injury. The modulation of mitochondrial dynamics and lipid metabolism by HMB may be a potential mechanism for preventing disuse atrophy and aiding rehabilitation beyond HMB's effects on rates of muscle protein synthesis and degradation.
- (12) The efficacy of HMB in combination with certain nutrients may be enhanced under select conditions.

Disclosure statement

JAR is currently employed by MTI Biotech Inc., Ames IA and continues his research with HMB studies. JAR was a principal investigator for clinical and animal studies with HMB while previously employed at Metabolic Technologies, Inc., which until recently had marketed HMB-Ca and HMB-FA. JAR is listed as an inventor on a number of active HMB-related patents. JAR has received federal grants to conduct research on HMB-Ca.