

RESEARCH MONOGRAPH . COMPOUND PROFILE

HMB (β -Hydroxy- β -methylbutyrate)

Beta-hydroxy-beta-methylbutyrate; a leucine metabolite that reduces muscle protein breakdown; used in catabolic states and as a supplement.

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AUTHOR	Kodiac biolabs Research
COMPOUND CLASS	Leucine metabolite (anti-catabolic supplement)

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ABSTRACT

HMB (beta-hydroxy-beta-methylbutyric acid; CAS 625-08-1; molecular formula $C_5H_{10}O_3$; molecular weight 118.13; Ca-HMB salt CAS 135236-72-5) is a metabolite of the branched-chain amino acid leucine, produced by approximately 5 percent of leucine catabolism via alpha-ketoisocaproate. Mechanism: HMB reduces muscle protein breakdown via inhibition of the ubiquitin-proteasome pathway and enhanced cell membrane integrity; secondary effects on muscle protein synthesis through mTOR pathway activation. The clinical evidence is strongest in catabolic states (HIV wasting, cancer cachexia, sarcopenia of aging, bedrest, post-surgical recovery) where 3 g/day reduces protein breakdown and preserves lean mass. In healthy resistance-trained athletes, the effect is small. The free acid form (HMB-FA) has improved pharmacokinetics over the calcium salt (Ca-HMB) but most research uses Ca-HMB. Plasma half-life is approximately 2 hours. Used as a reference anti-catabolic supplement.

1. Compound Identification

HMB (β -Hydroxy- β -methylbutyrate) is described as leucine metabolite (anti-catabolic supplement). Beta-hydroxy-beta-methylbutyrate; a leucine metabolite that reduces muscle protein breakdown; used in catabolic states and as a supplement.

1.1 Class summary

Leucine metabolite (anti-catabolic supplement)

1.2 Subtitle

Beta-hydroxy-beta-methylbutyrate; a leucine metabolite that reduces muscle protein breakdown; used in catabolic states and as a supplement.

2. Abstract

HMB (beta-hydroxy-beta-methylbutyric acid; CAS 625-08-1; molecular formula $C_5H_{10}O_3$; molecular weight 118.13; Ca-HMB salt CAS 135236-72-5) is a metabolite of the branched-chain amino acid leucine, produced by approximately 5 percent of leucine catabolism via alpha-ketoisocaproate. Mechanism: HMB reduces muscle protein breakdown via inhibition of the ubiquitin-proteasome pathway and enhanced cell membrane integrity; secondary effects on muscle protein synthesis through mTOR pathway activation. The clinical evidence is strongest in catabolic states (HIV wasting, cancer cachexia, sarcopenia of aging, bedrest, post-surgical recovery) where 3 g/day reduces protein breakdown and preserves lean mass. In healthy resistance-trained athletes, the effect is small. The free acid form (HMB-FA) has improved pharmacokinetics over the calcium salt (Ca-HMB) but most research uses Ca-HMB. Plasma half-life is approximately 2 hours. Used as a reference anti-catabolic supplement.

3. Mechanism of Action

Leucine metabolite; reduces muscle protein breakdown via ubiquitin-proteasome inhibition and enhanced membrane integrity. Secondary mTOR effects.

The mechanistic profile described above represents the consensus position from peer-reviewed literature where available; for compounds with sparse formal characterization, this section reflects vendor-grade reports and structurally-related class pharmacology and should be interpreted with appropriate caution.

4. Pharmacokinetics and Routes of Administration

Pharmacokinetic data are summarized within the abstract for compounds with formal Phase 1 records. Compounds without published human pharmacokinetic studies are noted as such; investigators should treat the absence of data as a research limitation.

5. Reported Research Dose Ranges

Supplement 3 g per oral administration daily, in divided doses.

Doses are scaled from clinical use where the compound is approved as a medicine, from Phase 2/3 trials where development advanced, or from rodent dose-response data scaled by allometric assumptions where the compound has no human clinical record. Investigators should treat dose ranges from research-chemical-grade vendors as starting points for their own pharmacokinetic and tolerability characterization rather than validated dosing recommendations.

6. Sourcing and Quality Verification

Investigators should obtain analytical confirmation of identity (mass spectrometry; for peptides, additionally amino acid analysis or N-terminal sequencing) and purity (HPLC area-percent, ideally greater than 95 percent) on every lot. Vendor certificates of analysis vary in quality; third-party analytical confirmation through independent laboratories (e.g., Janoshik Analytical, Anabolic Lab) is the gold standard for research-grade peptides and small molecules.

For compounds with established pharmaceutical-grade marketing in any jurisdiction, sourcing from the marketed product (where legal and accessible) provides the highest quality assurance.

7. Reconstitution and Handling

Peptides should be reconstituted in bacteriostatic water or sterile water for injection in the volume appropriate to the desired concentration; lyophilized peptides should be allowed to come to room temperature before reconstitution to minimize precipitation. Reconstituted peptides should be stored refrigerated and used within the timeframe specified by the manufacturer (typically 14 to 30 days for bacteriostatic water reconstitutions, shorter for sterile water).

Small molecules: storage conditions vary by compound; consult the certificate of analysis for the specific product. Most are stable at room temperature in dry, dark conditions; oxidation-sensitive compounds (e.g., catecholamine precursors) require cool storage and protection from light.

8. Stack Interaction Considerations

Investigators combining this compound with other research substances should consider receptor-level interactions (additive effects at shared targets), enzyme-level interactions (CYP-mediated drug-drug interactions where applicable), and pharmacodynamic interactions (additive sedation, additive serotonergic activity, additive hemodynamic effects).

The stack interaction section in published monographs of well-characterized compounds is necessarily incomplete for any specific combination; investigators should treat novel combinations with elevated caution and titrate gradually.

9. References

1. Wilson JM, et al. International Society of Sports Nutrition position stand: beta-hydroxy-beta-methylbutyrate (HMB). J Int Soc Sports Nutr 2013.
2. Deutz NE, et al. Effect of beta-hydroxy-beta-methylbutyrate (HMB) on lean body mass during 10 days of bed rest in older adults. Clin Nutr 2013.
3. Nissen S, et al. Effect of leucine metabolite beta-hydroxy-beta-methylbutyrate on muscle metabolism during resistance-exercise training. J Appl Physiol 1996.

This monograph is provided for research use only. Not for medical, diagnostic, or therapeutic purposes. Not for human consumption. Compound class generalizations are noted where compound-specific data are sparse; investigators should weight the evidence accordingly.