BIOMOD LABS · RESEARCH PEPTIDE CO.

RESEARCH COMPOUND MONOGRAPH · SERIES 1 · NO. 006

KPV

Lys-Pro-Val — the C-terminal tripeptide of α-melanocyte-stimulating hormone (α-MSH 11-13), identified by Hiltz and Lipton in 1989 as the minimal anti-inflammatory pharmacophore of the parent 13-residue α-MSH hormone, retaining inflammation-modulating activity without the pigmentation effects of the full-length molecule.

CAS REGISTRY	CATALOG REFERENCE	CLASS	DATE OF ISSUE
67727-97-3	BM-LYO-006	Synthetic tripeptide · 3 a.a.	May 2026

KPV is a tripeptide of sequence Lys-Pro-Val corresponding to the C-terminal residues 11–13 of α-melanocyte-stimulating hormone (α-MSH), a 13-residue peptide hormone derived from the proopiomelanocortin (POMC) precursor protein. The anti-inflammatory pharmacology of α-MSH was systematically dissected through the 1980s by James Lipton, Anna Catania, and colleagues, who identified the C-terminal KPV tripeptide in 1989 (Hiltz and Lipton, FASEB J) as retaining significant anti-inflammatory activity despite lacking the core melanocortin-receptor-binding sequence (His-Phe-Arg-Trp at α-MSH positions 6–9). Subsequent work has characterised KPV's anti-inflammatory mechanism as partly melanocortin-receptor-mediated (engagement of MC1R at higher concentrations) and partly receptor-independent, including direct effects on IL-1β signalling and possible transport via the PepT1 intestinal peptide transporter — a complex mechanistic picture that remains incompletely reconciled in the published literature. ***This monograph summarises published cellular pharmacology and preclinical findings for laboratory research reference only.***

01 Compound Profile

COMMON DESIGNATION	KPV · α-MSH (11-13) tripeptide · Lysyl-prolyl-valine
PRIMARY SEQUENCE	Lys-Pro-Val (K-P-V)
CAS REGISTRY	67727-97-3
MOLECULAR FORMULA	$C_{16}H_{30}N_4O_4$
AVERAGE MOLECULAR MASS	342.43 g · mol^{-1}
PARENT PEPTIDE	α-Melanocyte-stimulating hormone (α-MSH), 13 residues: Ac-Ser-Tyr-Ser-Met-Glu-His-Phe-Arg-Trp-Gly-Lys-Pro-Val-NH_2; KPV corresponds to positions 11–13
PROPOSED MOLECULAR TARGETS	Melanocortin-1 receptor (MC1R) — partial engagement at higher concentrations; receptor-independent IL-1β-pathway interaction; PepT1 transporter (gastrointestinal preparations)[1,3]
PHYSICAL FORM	White lyophilised solid
SOLUBILITY (LAB RECONSTITUTION)	Highly water-soluble; the small size and lack of hydrophobic residues confer excellent aqueous solubility
STORAGE (RESEARCH HANDLING)	Lyophilised solid: −18 °C, desiccated; reconstituted solution refrigerated 2–8 °C short-term; aliquoted long-term at −18 °C
ANALYTICAL SPECIFICATION	≥ 99 % purity by HPLC (BIOMOD Labs internal release specification)

02 Origin and Chemistry

α-Melanocyte-stimulating hormone (α-MSH) is a 13-residue peptide hormone derived from the proopiomelanocortin (POMC) precursor protein by tissue-specific proteolytic processing. POMC is a "molecular Swiss Army knife" that is processed differently in different cell populations to yield ACTH, β-endorphin, and the three melanocyte-stimulating hormones (α-MSH, β-MSH, γ-MSH). α-MSH was originally characterised for its melanocyte-stimulating activity (driving pigmentation through MC1R engagement on melanocytes), but Lipton, Catania, and colleagues established through the 1980s that the molecule also exhibited substantial anti-inflammatory and antipyretic activity — properties not predicted by its pigmentation-focused original characterisation.[2]

The systematic Lipton-Catania programme to identify the minimal anti-inflammatory pharmacophore of α-MSH tested truncation fragments and identified the C-terminal Lys-Pro-Val tripeptide as retaining significant anti-inflammatory potency despite lacking the central His-Phe-Arg-Trp core sequence that mediates melanocortin receptor binding in the parent

molecule. The 1989 Hiltz and Lipton paper in *FASEB J* documented antipyretic activity, and subsequent work extended the anti-inflammatory characterisation across multiple model systems.[1]

03 Proposed Mechanisms in Preclinical Models

The mechanism of KPV's anti-inflammatory activity is incompletely characterised but appears to involve multiple parallel pathways. **Partial MC1R engagement** — KPV binds melanocortin-1 receptor with lower affinity than full-length α-MSH, and at higher concentrations engages downstream Gαs / cAMP signalling. **Receptor-independent IL-1β pathway interaction** — Getting and colleagues (2003) demonstrated that KPV retains anti-inflammatory activity in recessive-yellow e/e mice, which carry a non-functional MC1R, suggesting that significant KPV activity is independent of melanocortin-receptor engagement and may operate through direct interference with IL-1β signalling. **PepT1-mediated transport** — in gastrointestinal preparations, KPV is taken up by the intestinal di-/tripeptide transporter PepT1, providing a mechanism for direct uptake by intestinal epithelial cells without classical receptor engagement. **Cytokine modulation** — KPV exposure attenuates TNF-α, IL-6, and IL-1β production in cell-culture and animal-model inflammation preparations.[3] PRECLINICAL · MOUSE

04 Preclinical Findings

SYSTEM	ANIMAL MODEL / PREPARATION	REPORTED OBSERVATION	REF.
Antipyretic activity	Rabbit fever model	Hiltz & Lipton 1989: KPV retains antipyretic activity of parent α-MSH	1
Anti-inflammatory in IL-1β model	Mouse peritonitis (IL-1β induced)	Anti-inflammatory effect preserved in MC1R-defective mice — receptor-independent activity	3
Murine colitis	DSS-induced colitis mouse model	Reduced colon inflammation; Kannengiesser et al. 2008 demonstrated efficacy in murine IBD	4
Dermatitis	Allergic contact dermatitis mouse models	Reduced ear swelling; attenuated inflammatory cell infiltrate	5
PepT1 transport	Intestinal epithelial cell preparations	KPV transported by PepT1; allows direct epithelial uptake	6
Cytokine production	Macrophage / monocyte cell culture	↓ TNF-α, IL-6, IL-1β in LPS-stimulated cells	5

05 Research Synthesis & Limitations

METHODOLOGICAL NOTES

KPV is one of the better-characterised small-peptide anti-inflammatory tools, with consistent observations across rodent models from independent laboratories. The principal mechanistic complexity for researchers is that the parent α-MSH literature attributes activity primarily to melanocortin receptor engagement, while the KPV-specific literature documents substantial receptor-independent activity — including efficacy in MC1R-null mouse models. The PepT1 transport finding adds a route by which the molecule enters cells without classical receptor engagement. These observations have not been fully reconciled in the published literature, and researchers should design experiments capable of distinguishing receptor-mediated from receptor-independent contributions to KPV's activity in their specific model system.

06 Laboratory Handling, Reconstitution, and Storage

Lyophilised KPV is supplied under research-use specifications. The peptide is highly water-soluble and reconstitutes readily in sterile water for injection, phosphate-buffered saline, or bacteriostatic water. Lyophilised storage at −18 °C, desiccated; reconstituted solutions at refrigerated 2–8 °C for short-term work; aliquoted long-term storage at −18 °C with minimised freeze–thaw. The small molecular size and absence of oxidation- or photo-sensitive residues make KPV one of the more handling-tolerant peptides in the catalog. Working concentrations are determined by the investigator's experimental design.

07 References

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