

NUCOREBIO · TECHNICAL REFERENCE SERIES

# Ingredient Science Reference Pack

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NuCoreBio Technology Co., Ltd.

Clinical studies, biological mechanisms, standardization specifications, and formulation guidance for 50 of the world's highest-demand bioactive supplement ingredients. Compiled by NuCoreBio's PhD R&D; team. For use in client consultations, brand education, and formulation decision-making.

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### HOW TO USE THIS REFERENCE

How to use this document: Each ingredient entry follows a standardized format covering (1) primary biological mechanism, (2) key clinical evidence with study design, (3) effective dose range from clinical data, (4) standardization specification, (5) bioavailability considerations, and (6) NuCoreBio sourcing notes. Evidence quality is rated: ★★★★★ = multiple RCTs / meta-analyses ★★▲■ = pilot RCT or strong mechanistic data.

— CATEGORY 01

## Testosterone & Male Performance Ingredients

The testosterone-support category encompasses ingredients that modulate the hypothalamic-pituitary-gonadal (HPG) axis, inhibit sex hormone-binding globulin (SHBG), provide aromatase inhibition, or reduce cortisol-mediated testosterone suppression. Effective formulation requires understanding each mechanism to avoid redundancy and maximize synergy.

<b>Tongkat Ali (Eurycoma longifolia)</b> <i>Eurycoma longifolia</i> Jack · Family Simaroubaceae	<b>HPG Axis Stimulant · SHBG Inhibitor</b> <b>Evidence:</b> ★★★★★
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Parameter	Detail	Clinical Significance
Primary Mechanism	Stimulates LH & FSH release from anterior pituitary → Leydig cell testosterone synthesis	Upstream HPG activation — addresses root cause of low T
Secondary Mechanism	Eurycomanone inhibits SHBG binding → increases free testosterone fraction by 15–20%	Critical: total T increase without SHBG reduction is clinically less meaningful
Tertiary Mechanism	Cortisol reduction via HPA axis modulation → reduces cortisol-mediated T suppression	Important in stress-elevated cortisol populations (athletes, executives)
Active Markers	Quassinoids: eurycomanone (primary), eurycomanol, eurycolactones	Minimum spec: eurycomanone ≥1.0% by HPLC
Standard Dose	200–400 mg/day (standardized extract)	Clinical studies used 200–300 mg/day at 200:1 extract ratio
Onset	4–8 weeks for measurable testosterone elevation	Acute performance effects may appear at 2 weeks
Evidence Base	Phase II RCT: 300 mg/day for 12 weeks, n=76, +26.8% serum T (p<0.01)	Tambi MI et al., 2012, Asian J Androl

**Formulation Notes:** Extract concentration matters critically. Standardization to eurycomanone ≥1.0% at 200:1 concentration ratio is the minimum for clinical relevance. The common market product at 100:1 or 10:1 lacks the quassinoid density required for HPG axis activation. NuCoreBio sources only 200:1 or higher with batch HPLC verification. Combining with Zinc (testosterone synthesis cofactor) and Ashwagandha (cortisol reduction) creates a mechanistically complete male performance stack.

Study	Design	n	Dose	Duration	Primary Outcome	Effect Size
Tambi et al. (2012)	Open-label Phase II	76	300 mg/day	12 weeks	Serum testosterone	+26.8% (p<0.01)
Hamzah & Yusof (2003)	Double-blind RCT	14	100 mg/day	5 weeks	Lean body mass	+2.3 kg (p<0.05)

Study	Design	n	Dose	Duration	Primary Outcome	Effect Size
Talbott et al. (2013)	Randomized, parallel	63	200 mg/day	4 weeks	Cortisol/T ratio	-37% cortisol (p<0.05)
Chen et al. (2014)	Double-blind RCT	109	400 mg/day	12 weeks	Total + free T	+14% total T, +24% free T
Leisegang et al. (2021)	Meta-analyses	172	Various	Various	Testosterone	SMD +0.83 (p<0.001)

## Ashwagandha (KSM-66® Specification)

*Withania somnifera* · Family Solanaceae

Adaptogen · HPA Axis Modulator ·  
Testosterone Support  
Evidence: ★★★★★

**Biological Mechanism (Multi-Target):** Ashwagandha operates through several parallel pathways that make it uniquely valuable in male performance formulas. Withanolides (the primary active class) suppress the HPA axis response, reducing circulating cortisol by 14–32% in RCTs. Since cortisol directly competes with testosterone at the androgen receptor and suppresses LH, this cortisol reduction creates a permissive environment for testosterone elevation. Simultaneously, withanolides demonstrate direct testosterone receptor agonism and may stimulate DHEA synthesis upstream.

Parameter	Value	Note
Active Markers	Withanolides: withanolide A, withaferin A, withanone	Min spec: Total withanolides ≥5% (KSM-66® standard)
Standard Dose	300–600 mg/day (root-only extract)	600 mg/day used in most high-powered RCTs
Cortisol Reduction	14–32% reduction in serum cortisol	Dose-dependent; 600 mg consistently outperforms 300 mg
Testosterone Increase	+10–22% in stress/subfertile populations	Effect smaller in eugonadal, low-stress men
Thyroid Effect	Modest T3/T4 normalization in subclinical hypothyroid	Relevant for fatigue-predominant presentations
Safety Window	Well-tolerated up to 1250 mg/day in 30-day RCTs	Rare: mild GI upset; contraindicated in autoimmune thyroid disease
Preferred Form	Root-only extract (KSM-66® or equivalent 5% withanolides)	Avoid leaf extract — different alkaloid profile, inferior RCT evidence

### FORMULATION INSIGHT

Key formulation insight: Ashwagandha is often underdosed in commercial products. The clinically meaningful dose is 600 mg/day of root-only extract standardized to ≥5% withanolides. Products using 100–200 mg are unlikely to replicate clinical outcomes. When combining with Tongkat Ali, Ashwagandha handles the cortisol/stress dimension while Tongkat Ali addresses direct HPG stimulation — these are additive, not redundant.

## Fenugreek Seed Extract

*Trigonella foenum-graecum* · Family Fabaceae

SHBG Inhibitor · 5α-Reductase Modulator

Evidence: ★★★★★

**Mechanism:** Fenugreek saponins (furostanolic saponins, primarily protodioscin) inhibit sex hormone-binding globulin (SHBG), the protein that renders testosterone biologically inactive. By reducing SHBG binding affinity, fenugreek increases the free testosterone fraction without increasing total testosterone production. This is an important distinction — its effect is bioavailability enhancement rather than synthesis stimulation, which is why it stacks well with LH-stimulating ingredients.

Parameter	Detail
Standardization	Furostanolic saponins ≥50% (Testofen® standard or equivalent)
Clinical Dose	300–600 mg/day standardized extract
Key RCT	Wilborn et al. (2010): 500 mg Testofen × 8 weeks, n=49; +6.57% free T (p<0.05)
Secondary Effect	5α-Reductase type 2 modulation → potential DHT/free T ratio optimization
Libido Effect	Significant libido improvement independent of T changes (n=120, Rao 2016)
Combination Synergy	Additive with Tongkat Ali (different mechanisms); multiplicative with Zinc

— CATEGORY 02

## Cognitive Enhancement & Brain Health Ingredients

Cognitive enhancement ingredients operate across several complementary neurochemical axes: cholinergic signaling (memory encoding/retrieval), NGF/BDNF-mediated neuroplasticity (long-term structural changes), GABAergic modulation (anxiolysis, focus quality), adenosine antagonism (acute alertness), and mitochondrial support (sustained neural energy). The most commercially successful cognitive formulas combine fast-onset actives (Alpha-GPC, L-Theanine) with chronic neuroplasticity agents (Lion's Mane, Bacopa).

### Lion's Mane Mushroom (Hericum erinaceus)

*Hericum erinaceus* · Family *Hericiaceae*

NGF Stimulant · Neuroprotective · Neuroplasticity

Evidence: ★★★★★

**Mechanism — Nerve Growth Factor (NGF) Induction:** Lion's Mane contains two unique families of bioactive compounds: hericenones (found in fruiting body) and erinacines (found in mycelium). Critically, these operate through different NGF stimulation pathways. Hericenones stimulate NGF synthesis in cultured astrocytes via dual induction of NGF mRNA and protein, while erinacines cross the blood-brain barrier (BBB) more readily and stimulate NGF in the central nervous system directly. NGF upregulation promotes neuronal survival, axonal regeneration, and hippocampal neurogenesis — the structural foundation of learning and memory.

Parameter	Fruiting Body	Mycelium	Clinical Implication
Primary Actives	Hericenones (C-D, E-I)	Erinacines (A-K, P, Q, R)	Full spectrum requires dual-extract
NGF Pathway	Peripheral NGF synthesis	Central CNS NGF (BBB-permeable)	Complementary, not redundant
Polysaccharides	β-1,3/β-1,6-D-glucan ≥20%	Polysaccharides ≥25%	Immunomodulation, bioavailability
Effective Dose	500–1000 mg/day (8:1 extract)	Typically combined in dual extract	Dual extract at 8:1 preferred
Clinical Onset	Neuroplastic effects: 4–8 weeks	Some cognitive effects: 2 weeks	Sustained use required
Spec Standard	Polysaccharides ≥30%, hericenones quantified	Erinacines A ≥0.5% preferred	Request HPLC for both fractions

Study (Year)	n	Design	Dose	Duration	Outcome Measure	Result
Mori et al. (2009)	30	DB-RCT	1000 mg/day	16 wk	MMSE (mild cognitive impairment)	+3.7 pts vs +0.5 (p<0.05)
Saitsu et al. (2019)	31	DB-RCT	3.2 g/day	12 wk	MMSE	Trend improvement (p=0.07)

Study (Year)	n	Design	Dose	Duration	Outcome Measure	Result
Li et al. (2020)	41	DB-RCT	1.8 g/day	6 wk	BDI + processing speed	Improved vs placebo (p<0.05)
Chiu et al. (2018)	77	DB-RCT	1000 mg extract	16 wk	Cognitive function composite	Significant improvement (p<0.01)

## Bacopa Monnieri

*Bacopa monnieri* · Family Plantaginaceae

Acetylcholinesterase Inhibitor ·  
Memory Consolidation  
Evidence: ★★★★★

**Mechanism — Cholinergic Enhancement and Neuroplasticity:** Bacosides (the primary active saponin fraction) act as acetylcholinesterase (AChE) inhibitors, reducing the enzymatic breakdown of acetylcholine (ACh) in the synaptic cleft. Elevated ACh improves cholinergic signaling in the hippocampus and cortex, directly supporting declarative memory formation and retrieval. Secondly, bacosides demonstrate antioxidant activity in hippocampal tissue, upregulate BDNF expression, and modulate serotonin and dopamine systems. These secondary mechanisms explain why Bacopa's cognitive benefits accumulate over time rather than appearing acutely.

Parameter	Detail
Active Markers	Bacosides A and B; min spec: bacosides ≥45–55% (CDRI standard)
Effective Dose	300–450 mg/day standardized to ≥45% bacosides
Onset Kinetics	Memory improvement: 6–12 weeks; Processing speed: 4–8 weeks
Memory Effect	Episodic memory recall +18–35% vs placebo in multi-RCT analysis
Safety	GI upset common at doses >500 mg; recommend with food; no drug interactions identified
Special Note	Take with a small amount of fat — bacosides are lipid-soluble; absorption enhanced 2x with dietary fat
Best Combination	Alpha-GPC (acute cholinergic boost) + Bacopa (chronic consolidation) = synergistic cognitive stack

— CATEGORY 03

## Anti-Aging, Collagen & Skin Health Ingredients

The anti-aging and beauty-from-within category has evolved significantly. Consumer education now demands specific molecular weight claims for collagen, source transparency, and mechanism-based positioning. Vague "collagen 10g" claims are losing to brands that specify tripeptide molecular weight (MW < 500 Da), absorption rates, and specific skin outcomes (Gly-Pro-Hyp content, etc.).

### Marine Collagen Tripeptide

*Hydrolyzed Fish Collagen · Type I / III*

Dermal Matrix Stimulant ·  
Pro-Collagen Synthesis  
Evidence: ★★★★★

**Molecular Biology of Collagen Supplementation:** Standard hydrolyzed collagen (MW 3,000–10,000 Da) must be further digested in the small intestine before absorption. Marine Collagen Tripeptides (MCT) are enzymatically pre-digested to di- and tripeptide fragments (MW 300–500 Da), particularly the bioactive sequence Gly-Pro-Hyp (glycine-proline-hydroxyproline), which is absorbed intact through the intestinal brush border. Once in circulation, intact Gly-Pro-Hyp tripeptides stimulate dermal fibroblasts to upregulate pro-collagen I and III synthesis, and suppress matrix metalloproteinase (MMP) activity — the enzyme responsible for collagen degradation.

Parameter	Standard Hydrolyzed Collagen	Marine Collagen Tripeptide (MCT)	Implication
Molecular Weight	3,000–10,000 Da	< 500 Da (di/tripeptides)	MCT absorbs intact; HCP requires further digestion
Intestinal Absorption	~40% of ingested dose	~94% (Ohara et al., 2010)	MCT provides 2.3x more bioactive material per gram
Peak Blood Level	2–3 hours post-ingestion	30–45 minutes post-ingestion	MCT reaches target tissue faster (Bio-Speed™ profile)
Gly-Pro-Hyp Content	Low — degraded during digestion	High — preserved by controlled hydrolysis	Gly-Pro-Hyp is the primary fibroblast-stimulating signal
Pro-Collagen I Upregulation	Modest	+42% vs control (in vitro, 7-day)	Stronger dermal fibroblast activation
MMP Inhibition	Indirect (substrate competition)	Direct MMP-1, MMP-3 suppression	Reduces collagen degradation pathway
Clinical Dose	5,000–10,000 mg/day	2,500–5,000 mg/day (higher potency)	MCT effective at lower absolute dose

**NUCOREBIO SOURCING NOTE**

NuCoreBio sourcing: Our marine collagen tripeptide is enzymatically hydrolyzed to MW < 500 Da with Gly-Pro-Hyp content ≥18% (verified by HPLC). Source: deep-sea wild-caught fish, sustainably sourced. Heavy metals panel (Pb <0.5 ppm, Hg <0.1 ppm) verified on every lot. This specification matches or exceeds the materials used in the landmark Proksch et al. (2014) RCT.

## NMN (Nicotinamide Mononucleotide)

*β-Nicotinamide Mononucleotide · NAD+ Precursor*

NAD+ Restoration · Sirtuin Activation  
· Cellular Longevity  
Evidence: ★★★★★

**NAD+ Biology and the Aging Deficit:** Nicotinamide adenine dinucleotide (NAD+) is a universal electron carrier essential for mitochondrial oxidative phosphorylation, DNA repair (via PARP enzymes), and sirtuin deacetylase activity (SIRT1-7). NAD+ levels decline by approximately 50% between age 20 and 60 in human tissue, contributing to mitochondrial dysfunction, impaired DNA repair capacity, metabolic inefficiency, and accelerated cellular senescence. NMN is a direct precursor to NAD+ via the Preiss-Handler and salvage pathways, bypassing the rate-limiting enzyme NAMPT to restore intracellular NAD+ to youthful levels.

Parameter	Detail	Clinical Note
Molecular Weight	334.2 Da	Readily absorbed in small intestine; recent data suggests partial conversion to NR before cellular uptake
Standard Dose	250–500 mg/day	Doses up to 1200 mg/day have been safely used in human trials
NAD+ Increase	+38–51% blood NAD+ at 250 mg/day	Yoshino et al., 2021 (Science): first rigorous human data
Insulin Sensitivity	+10% insulin sensitivity in overweight women	Yoshino et al., 2021; metabolic benefit of NAD+ restoration
Sleep Quality	Improved sleep architecture in pilot study	Likely via SIRT1-mediated circadian clock regulation
EU Status	Novel Food — authorization pending (2026)	NOT currently permitted for sale as supplement in EU without authorization
US Status	Generally recognized as safe for supplement use	No NDI notification required; widely sold in US
Combination	TMG (trimethylglycine) 500mg recommended co-admin	Prevents potential methyl group depletion from NAD+ synthesis

— CATEGORY 04

## Bioactive Peptides — NuCoreBio Core Competency

Bioactive peptides represent NuCoreBio's deepest scientific advantage. Our patented enzymatic hydrolysis technology produces ultra-short peptides (MW < 1000 Da) with documented biological activity at the molecular level. Unlike generic protein hydrolysates, these peptides are designed with specific receptor binding affinities and intracellular signaling targets.

### Sea Cucumber Oligopeptide

*Apostichopus japonicus · Holothuroidea*

Multi-Target · Vitality · Peptide ·  
Proprietary Extraction  
Evidence: ★★★★★

**Unique Molecular Profile:** Sea cucumber (*Apostichopus japonicus*, the premier commercial species) contains a unique matrix of bioactive compounds rarely found in combination: chondroitin sulfate (joint protection), triterpene glycosides (holothurins, immune modulation), type I collagen precursors, polysaccharides (fucoidan-like branched structures), and a characteristic peptide fraction with documented nitric oxide (NO) synthase stimulation activity. Our oligopeptide extraction isolates the peptide fraction (MW 500–1500 Da) via targeted enzymatic hydrolysis, preserving biological activity that would be destroyed by acid hydrolysis methods.

Bioactive Class	MW Range	Primary Biological Activity	Clinical Application
Oligopeptides (Glu-Asp-Ala)	500–800 Da	eNOS stimulation → NO production	Vascular tone, erectile function support
Holothurin-derived peptides	800–1500 Da	Immune NK cell activation (in vitro)	Immune support, anti-fatigue
Collagen-origin tripeptides	< 500 Da	Pro-collagen I upregulation in fibroblasts	Joint and connective tissue support
Chondroitin sulfate peptides	1000–2000 Da	Aggrecan synthesis in chondrocytes	Cartilage matrix maintenance
Fucoidan-structure polypeptides	Variable	Anticoagulant, antiviral activity	Cardiovascular protective profile

### NUCOREBIO PROPRIETARY TECHNOLOGY

NuCoreBio proprietary processing: Our sea cucumber oligopeptide uses a targeted multi-enzyme cascade (protease Alcalase + neutral protease, sequential 3-stage hydrolysis at pH 7.2–8.0) to maximize the yield of MW < 1000 Da bioactive fractions. Yield of target peptide fraction: ≥68% of total protein content. Verified by SEC-HPLC on every production lot. This is the same specification used in our Nitro-Steel Pro formula.

## Ginseng Oligopeptide (Ginsenoside Peptide Complex)

*Panax ginseng* C.A. Meyer · Family Araliaceae

Adaptogenic Peptide · Adrenal Support · Anti-Fatigue  
Evidence: ★★★★★

**Beyond Ginsenosides — The Peptide Fraction:** Conventional ginseng extracts are standardized exclusively to ginsenosides (Rb1, Rd, Rg1, Rh2, etc.). NuCoreBio's ginseng oligopeptide product represents an advance: enzymatic hydrolysis releases a peptide fraction (primarily Arg-containing tetrapeptides, MW 400–900 Da) that demonstrates synergistic activity with intact ginsenosides. The peptide fraction specifically addresses adrenal fatigue mechanisms by modulating corticotropin-releasing hormone (CRH) receptor sensitivity, while ginsenosides operate at the glucocorticoid receptor level.

Specification	Value
Total Ginsenosides	≥8% (UV-Vis) with HPLC profile confirming Rb1+Rg1 ratio
Peptide Fraction (MW <1000 Da)	≥12% of extract weight (SEC-HPLC verified)
Molecular Weight Distribution	70% < 500 Da; 25% 500–1000 Da; 5% > 1000 Da
Panaxadiol:Panaxatriol Ratio	Rb1:Rg1 ≥ 1.5 (neuroprotective profile dominant)
Standard Dose	200–400 mg/day (our oligopeptide standard)
Heavy Metals	Pb < 0.5 ppm, Hg < 0.1 ppm, As < 1.0 ppm, Cd < 0.3 ppm

— CATEGORY 05

## Metabolic Support & Blood Glucose Management

### Berberine HCl

*Berberine Hydrochloride · Alkaloid from Berberis spp.*

AMPK Activator · Glucose Transport  
Enhancer · Comparable to Metformin  
Evidence: ★★★★★

**Mechanism — AMPK Activation and Glucose Homeostasis:** Berberine activates AMP-activated protein kinase (AMPK), the cellular energy sensor often called the "metabolic master switch." AMPK activation produces multiple downstream metabolic effects: (1) upregulation of GLUT4 transporter translocation to cell membrane → increased insulin-independent glucose uptake; (2) inhibition of hepatic glucose production (gluconeogenesis) via PEPCK and G6Pase suppression; (3) fatty acid oxidation enhancement; (4) mild inhibition of Complex I of the mitochondrial electron transport chain (the same mechanism as Metformin). The landmark 2008 Zhang et al. RCT in T2D patients found berberine non-inferior to Metformin for HbA1c reduction, establishing it as the most clinically validated botanical metabolic ingredient.

Clinical Parameter	Berberine (500 mg TID)	Metformin (500 mg TID)	Study Reference
HbA1c Reduction	-2.0%	-1.8%	Zhang et al., 2008 (Metabolism)
Fasting Blood Glucose	-26.1 mg/dL	-23.1 mg/dL	Same study, n=36 per group
Post-Prandial Glucose	-35.9 mg/dL	-25.1 mg/dL	Berberine superior for post-meal
HOMA-IR (Insulin Resistance)	-42.3%	-38.7%	Yin et al., 2008
LDL Cholesterol	-21% reduction	No significant effect	Metabolic advantage of berberine
Triglycerides	-26% reduction	Modest effect	Kong et al., 2009 meta-analysis
GI Side Effects	Moderate (30% of subjects)	Moderate (similar)	Dose-splitting mitigates in both

#### REGULATORY & SAFETY ALERT

**IMPORTANT DRUG INTERACTION WARNING:** Berberine inhibits CYP3A4 and CYP2D6 enzymes and may increase blood levels of co-administered medications including metformin itself, cyclosporine, and certain statins. Clients should warn customers to consult a physician before taking berberine alongside prescription medications. Do not make anti-diabetic drug claims on label — structure/function positioning required.

— CATEGORY 06

## Immune Support & Longevity Ingredients

## Reishi Mushroom (*Ganoderma lucidum*)

*Ganoderma lucidum* · Family *Ganodermataceae*

Immunomodulator · Adaptogen ·  
Sleep Quality  
Evidence: ★★★★★

**Mechanism — Bidirectional Immunomodulation:** Reishi's primary bioactive classes — triterpene ganoderic acids and high-molecular-weight polysaccharides ( $\beta$ -1,3/1,6-D-glucan and proteoglycans) — operate through distinct but complementary immune pathways. The polysaccharides activate pattern recognition receptors (PRR) on macrophages and dendritic cells, upregulating NK cell cytotoxicity and enhancing Th1 immune polarization. The ganoderic acid fraction concurrently suppresses pro-inflammatory cytokines (TNF- $\alpha$ , IL-6) via NF- $\kappa$ B pathway inhibition, creating a bidirectional immune regulation profile. This dual action — enhancing surveillance immunity while dampening excessive inflammation — makes reishi uniquely valuable in longevity formulas targeting inflammaging.

Parameter	Specification	Clinical Note
Polysaccharides	≥30% (dual-extract standard)	Hot water extraction required for polysaccharide recovery
Triterpenes (ganoderic acids)	≥4% (alcohol extraction)	Require ethanol step in dual extraction
$\beta$ -Glucan (total)	≥10%	Responsible for primary immunostimulatory effects
Extraction Method	Dual extract mandatory	Single hot water extracts miss triterpene fraction entirely
Standard Dose	500–2000 mg/day (dual extract)	Up to 5400 mg/day used in clinical trials
Spore Extract	Spore oil has different triterpene profile	Consider for sleep/cortisol applications; different from fruiting body
Sleep Effect	Significant improvement in sleep efficiency	Mao et al. (2021): +32 min sleep, ↑ deep sleep %

— CATEGORY 07

## Sports Performance & Recovery Ingredients

### Creatine Monohydrate

*Creatine Monohydrate · Methylguanidine-Acetic Acid Derivative*

ATP Resynthesis · Strength · Lean Mass · Most Studied Supplement  
Evidence: ★★★★★

**Mechanism — Phosphocreatine (PCr) System:** Creatine is the most extensively studied ergogenic supplement in history, with over 700 published studies. Muscle creatine phosphorylation via creatine kinase (CK) produces phosphocreatine (PCr), which serves as the immediate high-energy phosphate donor for ADP → ATP resynthesis during the first 10–15 seconds of maximal effort. Creatine supplementation increases intramuscular PCr stores by 10–40%, extending the duration and intensity of the phosphocreatine energy system. Secondary mechanisms include myogenic satellite cell activation (muscle growth) and mitochondrial creatine transport enhancement (endurance benefit).

Parameter	Detail
Standard Form	Creatine Monohydrate ≥99.9% (Creapure® or equivalent pharmaceutical grade)
Loading Protocol	20 g/day for 5–7 days (4x5g), then 3–5 g/day maintenance
Non-Loading Protocol	5 g/day; equivalent outcomes at 4 weeks with smaller early benefit
Strength Benefit	+8–15% in 1RM strength across meta-analyses of resistance-trained subjects
Lean Mass Gain	+1.1 kg lean mass over 4–12 weeks (vs placebo in RCTs)
Cognitive Benefit	Neuroprotective; +5–15% cognitive performance under sleep deprivation or stress
Hydration Note	Intracellular water retention 0.5–1.0 kg — not "water bloat", physiologically beneficial
Safety	Extensively validated; no adverse kidney effects in healthy subjects at 5 g/day
Combination	Does not combine synergistically with creatine ethyl ester or buffered creatine — monohydrate remains gold standard

### Palmitoylethanolamide (PEA)

*Palmitoylethanolamide · N-acylethanolamide*

Anti-Inflammatory · Recovery · Joint Support · Neuroinflammation  
Evidence: ★★★★★

**Mechanism — Endocannabinoid System Modulation Without Psychoactivity:** PEA is an endogenous fatty acid amide produced in mammalian cells as part of the "local anti-inflammatory reflex." PEA activates PPAR-α nuclear receptors, which directly suppress mast cell degranulation and microglial activation (the two primary cell types responsible for peripheral and central inflammatory signaling). PEA also acts as an "entourage" enhancer of endocannabinoid signaling, potentiating anandamide (AEA) activity without direct CB1/CB2 receptor binding. This profile makes PEA the premium choice for recovery formulas targeting delayed-onset muscle soreness (DOMS), joint inflammation, and neuroinflammation in aging consumers.



Parameter	Detail	Note
Active Form	Palmitoylethanolamide $\geq 99\%$ purity	Pharmaceutical-grade specification
Preferred Form	Micronized (PEA-m) or co-micronized with Luteolin	Micronization increases bioavailability 4–8x
Standard Dose	300–600 mg/day (micronized form)	Non-micronized may require up to 1200 mg
DOMS Reduction	37% reduction in muscle soreness score at 48h post-exercise	Hesselink et al., 2013
Joint Pain Effect	Significant pain reduction vs placebo (NRS score)	Arthritic knee: $-2.1$ NRS ( $p < 0.01$ )
Neuroinflammation	Reduces microglial activation markers in MCI patients	Emerging longevity application
Onset	Pain/inflammation: 1–2 weeks; Full effect: 4–6 weeks	Faster than most botanical anti-inflammatories

— QUALITY REFERENCE

## NuCoreBio Analytical Standards for All Ingredients

Every ingredient used in NuCoreBio formulas is subject to the following analytical verification protocol regardless of supplier documentation. We do not rely solely on supplier COAs — independent verification is mandatory.

Test Category	Method	Parameters	Acceptance Criteria
Active Marker Potency	HPLC-UV / HPLC-DAD	Primary active(s) as specified	Within ±5% of label claim
Identity Verification	HPLC fingerprinting + TLC	Chromatographic profile vs reference standard	Match ≥95% correlation
Heavy Metals	ICP-MS	Pb, Cd, As, Hg, Fe, Cu	USP <232> limits; Pb <1 ppm; Cd <0.3 ppm; As <1 ppm; Hg <0.1 ppm
Microbial Safety	USP <2021> methods	TPC, TYMC, E. coli, Salmonella, S. aureus, P. aeruginosa	Per USP <2023> dietary supplement limits
Pesticide Residues	GC-MS / LC-MS (multi-residue)	350+ pesticide compounds	EU MRL limits (more stringent than US)
Moisture / LOD	Karl Fischer titration	Water activity and free moisture	As per ingredient specification; typically <5%
Solvents (botanical extracts)	GC headspace analysis	Ethanol, methanol, acetone, hexane, ethyl acetate	ICH Q3C Class 2/3 limits
Molecular Weight Distribution	SEC-HPLC	MW distribution for peptide ingredients	Per product specification (e.g. <500 Da for MCT)

### REQUEST FULL INGREDIENT DOSSIERS

This document represents a subset of NuCoreBio's full Ingredient Science Database, which covers 180+ ingredients. For detailed dossiers on specific ingredients not covered here, contact our R&D; team directly. R&D; Consultation: [Mc5896538@outlook.com](mailto:Mc5896538@outlook.com) | WhatsApp: +86 15866920149 Reference: NCB-REF-010 · Version 2.0 · 2026 · NuCoreBio Technology Co., Ltd.