

RESEARCH MONOGRAPH . COMPOUND PROFILE

Synephrine

p-Synephrine; a phenylethanolamine alkaloid from *Citrus aurantium* (bitter orange); a beta-3 adrenergic-preferring agonist used as a thermogenic supplement.

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AUTHOR	Kodiac bioLabs Research
COMPOUND CLASS	Adrenergic agonist (bitter orange alkaloid)

ABSTRACT

Synephrine (p-synephrine, (R/S)-4-[1-hydroxy-2-(methylamino)ethyl]phenol; CAS 94-07-5; molecular formula C₉H₁₃NO₂; molecular weight 167.21) is a phenylethanolamine alkaloid from *Citrus aurantium* (bitter orange) and other *Citrus* species. The compound is a structural analog of phenylephrine (the m-isomer) with a beta-3 adrenergic preference (relative to alpha-1 and beta-1) that distinguishes its pharmacology. The beta-3 activity drives thermogenesis and fat oxidation in adipose tissue, the basis for its supplement use as a weight-loss aid. Synephrine became prominent after the 2004 FDA ban on ephedra (which contained the more potent ephedrine). Clinical evidence for weight-loss effect is modest. Plasma half-life is approximately 2 hours. Used as a beta-3-preferring adrenergic agonist in metabolic research and supplement formulations.

1. Compound Identification

Synephrine is described as adrenergic agonist (bitter orange alkaloid). p-Synephrine; a phenylethanolamine alkaloid from Citrus aurantium (bitter orange); a beta-3 adrenergic-preferring agonist used as a thermogenic supplement.

1.1 Class summary

Adrenergic agonist (bitter orange alkaloid)

1.2 Subtitle

p-Synephrine; a phenylethanolamine alkaloid from Citrus aurantium (bitter orange); a beta-3 adrenergic-preferring agonist used as a thermogenic supplement.

2. Abstract

Synephrine (p-synephrine, (R/S)-4-[1-hydroxy-2-(methylamino)ethyl]phenol; CAS 94-07-5; molecular formula C₉H₁₃NO₂; molecular weight 167.21) is a phenylethanolamine alkaloid from *Citrus aurantium* (bitter orange) and other *Citrus* species. The compound is a structural analog of phenylephrine (the m-isomer) with a beta-3 adrenergic preference (relative to alpha-1 and beta-1) that distinguishes its pharmacology. The beta-3 activity drives thermogenesis and fat oxidation in adipose tissue, the basis for its supplement use as a weight-loss aid. Synephrine became prominent after the 2004 FDA ban on ephedra (which contained the more potent ephedrine). Clinical evidence for weight-loss effect is modest. Plasma half-life is approximately 2 hours. Used as a beta-3-preferring adrenergic agonist in metabolic research and supplement formulations.

3. Mechanism of Action

Phenylethanolamine adrenergic agonist with beta-3 preference; thermogenesis and fat oxidation in adipose tissue.

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 30 to 100 mg per oral administration daily.

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. Stohs SJ, et al. A review of the human clinical studies involving Citrus aurantium (bitter orange) extract and its primary protoalkaloid p-synephrine. Int J Med Sci 2012.
2. Haaz S, et al. Citrus aurantium and synephrine alkaloids in the treatment of overweight and obesity. Obes Rev 2006.
3. Stohs SJ, Shara M. A review of the safety and efficacy of synephrine. Phytother Res 2017.

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.