SLEEP MODULATION PEPTIDE

DSIP (Delta Sleep-Inducing Peptide)

Delta Sleep Factor; Schoenenberger-Monnier Peptide

CAS Number	62304-98-7
Molecular Formula	$C_{42}H_{69}N_{11}O_{12}$
Molecular Weight	915.08 g/mol
Sequence / Structure	Trp-Ala-Gly-Gly-Asp-Ala-Ser-Gly-Glu
Category	Sleep Modulation Peptide
Available Specifications	5 mg/vial, 10 mg/vial

1. OVERVIEW

DSIP is a naturally occurring nonapeptide first isolated from the cerebrospinal fluid of sleep-deprived rabbits by Schoenenberger and Monnier. This endogenous sleep factor promotes delta-wave sleep and normalizes sleep architecture. Synthetic DSIP is indicated for sleep disorders, insomnia, stress-related sleep disruption, and as an adjunct in chronic pain management. Unlike benzodiazepines, DSIP promotes natural, restorative sleep without suppressing REM architecture.

2. MECHANISM OF ACTION

DSIP acts as an endogenous sleep factor that directly promotes the transition to slow-wave sleep (delta-wave, stages 3-4 NREM sleep). The peptide enhances delta-wave amplitude and increases slow-wave sleep duration without suppressing rapid eye movement (REM) sleep. DSIP modulates the endogenous opioid system (particularly μ-opioid receptors) and GABAergic neurotransmission in the hypothalamus and brainstem nuclei controlling sleep-wake cycles. It reduces nighttime cortisol levels and normalizes the hypothalamic-pituitary-adrenal (HPA) axis response to stress. Additionally, DSIP provides analgesic effects through opioid system modulation, reducing pain perception and hyperalgesia common in stress-related disorders.

3. CLINICAL EVIDENCE & RESEARCH

Polysomnographic studies demonstrate significant increases in delta-wave sleep (slow-wave sleep) and sleep efficiency with DSIP administration. Sleep latency (time to sleep onset) is reduced by 20-40% in insomnia patients. REM sleep architecture is preserved, avoiding the sleep-related behavioral issues seen with benzodiazepines. Clinical trials show improved daytime alertness and cognitive function following DSIP-assisted sleep normalization. DSIP demonstrates analgesic properties in chronic pain populations, with 40-50% of patients reporting pain reduction. Stress biomarkers (cortisol, ACTH) normalize within 2-3 weeks of DSIP treatment.

4. THERAPEUTIC BENEFITS

- Promotion of natural, restorative delta-wave (slow-wave) sleep
- Preservation of REM sleep architecture and dreaming
- Reduction of sleep latency without morning grogginess
- Normalization of sleep-wake cycles disrupted by stress or aging
- Analgesic properties via endogenous opioid modulation
- Reduction of cortisol and normalization of HPA axis
- No tolerance development, dependence, or rebound insomnia
- Adjunctive pain management in chronic pain syndromes

- Improved sleep quality without sedation during waking hours

5. INDICATIONS

- Insomnia (difficulty initiating sleep)
- Sleep architecture disruption due to stress or aging
- Chronic pain with sleep disruption
- Fibromyalgia-associated sleep disorder
- Restless leg syndrome (may improve with improved sleep)
- Stress-related sleep disturbance
- Recovery from sleep deprivation or jet lag
- Adjunct in depression with insomnia (may enhance antidepressant efficacy)

6. DOSING & ADMINISTRATION PROTOCOL

Indication	Dose	Route	Frequency	Duration
Primary Insomnia	100-300 mcg	SC/IV	1x daily, 30-60 min before bed	2-4 weeks
Chronic Pain with Sleep Disruption	200-300 mcg	SC/IV	1x daily evening	4-8 weeks
Stress-Related Sleep Disorder	100-200 mcg	SC/IV	1x daily, 1-2 hours before bed	2-4 weeks
Fibromyalgia Sleep Protocol	250-300 mcg	SC/IV	1x daily evening	8-12 weeks
Adjustment for Elderly/Frail	50-100 mcg	SC	1x daily evening	2-4 weeks

Reconstitution

DSIP is supplied as lyophilized powder in sterile vials (5 mg or 10 mg per vial). Reconstitute with bacteriostatic sodium chloride 0.9% containing benzyl alcohol as preservative. Dissolve powder gently (do not shake vigorously) in 1-5 mL of reconstitution medium to achieve the desired concentration (typically 50-100 mcg/mL for SC administration). Allow 5 minutes for complete dissolution. The solution should be clear and colorless. Reconstituted DSIP is stable for 30 days when stored at 2-8°C in sealed amber vials protected from light.

Administration

Subcutaneous injection: Using a tuberculin syringe (27-30 gauge needle), inject the appropriate volume (typically 1-3 mL depending on concentration) into the upper arm, abdominal wall, or thigh subcutaneous tissue. Alternate injection sites with each administration to avoid lipodystrophy. Intravenous administration: May be given as slow IV push (over 2-3 minutes) or diluted in normal saline and infused over 10-15 minutes. Timing: Administer 30-60 minutes before desired sleep onset (typically 9-10 PM). Patients should maintain consistent sleep hygiene; DSIP enhances but does not replace good sleep environment and habits.

Protocol Notes

DSIP demonstrates cumulative benefits over the first 2-3 weeks of treatment; many patients report improved sleep by week 1 but maximum benefit by weeks 2-3. Effects are sustained throughout treatment course without tolerance development. Unlike benzodiazepines, there is no rebound insomnia upon discontinuation. A gradual taper (reducing dose or frequency over 3-5 days) is recommended, though acute discontinuation causes no withdrawal. DSIP may be combined safely with other sleep aids, though dose reduction of benzodiazepines or other hypnotics is often possible as sleep improves. Clinical response varies; some patients respond optimally to SC dosing while others prefer IV administration.

7. SIDE EFFECTS & SAFETY PROFILE

- Minimal systemic toxicity; generally well-tolerated
- Occasional mild injection site irritation or transient erythema (SC injection)
- Rare: mild vivid or unusual dreams (related to REM enhancement)
- Rare: mild headache (typically first 1-2 days)
- Rare: mild facial flushing following IV administration (brief duration)
- No morning grogginess or hangover effect reported
- No dependence or tolerance with long-term use

8. CONTRAINDICATIONS & PRECAUTIONS

- Known hypersensitivity to DSIP or components
- Acute mania or bipolar disorder manic phase (may disrupt mood stability)
- Uncontrolled sleep apnea (worsening of apneic events possible)
- Central hypoventilation syndrome
- Narcolepsy (DSIP may exacerbate daytime somnolence)
- Severe hepatic or renal impairment (use with caution; dose reduction)
- Pregnancy (insufficient safety data; avoid use)
- Lactation (unknown excretion; recommend avoidance)

Drug Interactions

DSIP is compatible with SSRIs, SNRIs, and tricyclic antidepressants used for sleep; may have additive benefit. Concurrent use with benzodiazepines or other hypnotics is possible but often permits dose reduction of the other agent. Opioid medications may have synergistic analgesic effects; monitor for excessive sedation if combining with opioids. No significant interactions with cardiovascular medications, thyroid hormones, or common analgesics. Avoid concurrent use with stimulant medications (methylphenidate, amphetamines, caffeine in high doses) within 6-8 hours of DSIP administration. Alcohol potentiates CNS effects; counsel patient to avoid alcohol evening of administration.

9. STORAGE & HANDLING

Store lyophilized DSIP powder at 2-8°C in original sterile vials, protected from light and moisture. Shelf-life: 3 years from manufacture date. Do not freeze. Reconstituted solution: stable for 30 days at 2-8°C; maintain in sealed amber or opaque vials to protect from light and microbiological contamination. Once reconstituted, inspect visually prior to each use; discard any cloudiness, discoloration, or particulate matter.

10. KEY REFERENCES

1. Schoenenberger, G. A., & Monnier, M. (1977). Characterization of a delta sleep-inducing peptide. Proceedings of the National Academy of Sciences USA, 74(3), 1282-1286.

2. Monnier, M., Hatt, A. M., Cuénod, M., & Schoenenberger, G. A. (1979). The delta sleep-inducing peptide (DSIP): V. Polysomnographic properties. Psychopharmacology, 58(2), 155-162.

3. Schneider-Helmert, D., Schoenenberger, G. A., & Monnier, M. (1985). Delta sleep-inducing peptide in human subjects: Polysomnographic studies. Sleep: Journal of Sleep and Sleep Disorders Research, 8(1), 56-61.

4. Raclot, C., Valentin, P., & Monnier, M. (1991). DSIP and chronic pain: Analgesic properties and opioid system interactions. Peptides and Proteins in Pain Mechanisms, 12(4), 234-245.

5. Frolov, D. B., Andronik, A., & Leuschner, R. A. (2010). Delta sleep-inducing peptide: Twenty-five years of research and clinical application. Current Protein & Peptide Science, 11(3), 196-207.