BIOMOD LABS · RESEARCH PEPTIDE CO.

RESEARCH COMPOUND MONOGRAPH · SERIES 1 · NO. 019

DSIP

Delta Sleep-Inducing Peptide — a nonapeptide (WAGGDASGE) first isolated by Schoenenberger and Monnier in 1977 from the cerebral venous blood of rabbits during induced delta-wave EEG sleep states.

CAS REGISTRY	CATALOG REFERENCE	CLASS	DATE OF ISSUE
62568-57-4	BM-LYO-019	Synthetic nonapeptide · 9 a.a.	May 2026

Delta Sleep-Inducing Peptide (DSIP) is a naturally occurring nonapeptide of sequence Trp-Ala-Gly-Gly-Asp-Ala-Ser-Gly-Glu (WAGGDASGE), originally isolated by the Schoenenberger–Monnier group in Switzerland in the 1970s from extracorporeal dialysates of cerebral venous blood in rabbits subjected to hypnogenic electrical stimulation of the intralaminar thalamic area. DSIP-like immunoreactive material has subsequently been documented in rabbit, rat, and other mammalian brain and peripheral tissues, and in human plasma, cerebrospinal fluid, urine, and breast milk. Preclinical investigation in rodent and rabbit preparations has reported delta-EEG-enhancing activity, stress-protective observations, antiseizure activity, and immunomodulating effects. The molecule's biological target remains incompletely characterised. ***This monograph summarises published preclinical findings for laboratory research reference only.***

01 Compound Profile

COMMON DESIGNATION	DSIP · Delta Sleep-Inducing Peptide
PRIMARY SEQUENCE	Trp-Ala-Gly-Gly-Asp-Ala-Ser-Gly-Glu
ONE-LETTER SEQUENCE	WAGGDASGE
CAS REGISTRY	62568-57-4
MOLECULAR FORMULA	$C_{35}H_{48}N_{10}O_{15}$
AVERAGE MOLECULAR MASS	848.81 g · mol^{-1}
STEREOCHEMISTRY NOTE	Only the α-aspartyl (Asp5 in α-linkage) isomer carries reported activity; the β-Asp isomer is reported inactive in the original characterisation work[2]
PHYSICAL FORM	White lyophilised solid
SOLUBILITY (LAB RECONSTITUTION)	Soluble in sterile water and bacteriostatic water; the molecule is amphiphilic and crosses the blood–brain barrier in cited rabbit/rodent work[3]
STORAGE (RESEARCH HANDLING)	Lyophilised solid: −18 °C, desiccated, light-protected (Trp residue); reconstituted solution refrigerated short-term, light-protected; freeze–thaw minimised
ANALYTICAL SPECIFICATION	≥ 99 % purity by HPLC (BIOMOD Labs internal release specification)

02 Origin and Chemistry

DSIP was identified through a series of experiments conducted by Marcel Monnier and Guido Schoenenberger and colleagues at the University of Basel, Switzerland, beginning in the late 1960s. In their preparation, rabbits were subjected to intralaminar thalamic electrical stimulation that reliably produced slow-wave EEG patterns; cerebral venous blood collected during these episodes contained, after extracorporeal dialysis, a material that — when subsequently infused intraventricularly into recipient rabbits — reproduced the donor's EEG pattern with high specificity.[1] Amino acid analysis, sequence determination, and chemical synthesis of the nonapeptide followed in 1977. Synthetic and natural preparations were tested under double-blind conditions against several metabolic fragments and modified analogues; the parent α-aspartyl nonapeptide retained the EEG-modifying activity, with a mean increase of approximately 35 % in delta activity in neocortex and limbic cortex compared with vehicle controls.[2]

Chemically, DSIP is unusual among neuroactive peptides for the absence of basic residues — its net charge at neutral pH is acidic, dominated by the two aspartate and glutamate side chains. The tryptophan residue confers UV absorbance at 280 nm and a known photo-oxidation susceptibility, with implications for handling. The Asp5-Gly6 peptide bond is susceptible to

spontaneous hydrolysis under acidic conditions, and lyophilised storage with strict desiccation is the standard preservation strategy in published methodology.[4]

03 Proposed Mechanisms in Preclinical Models

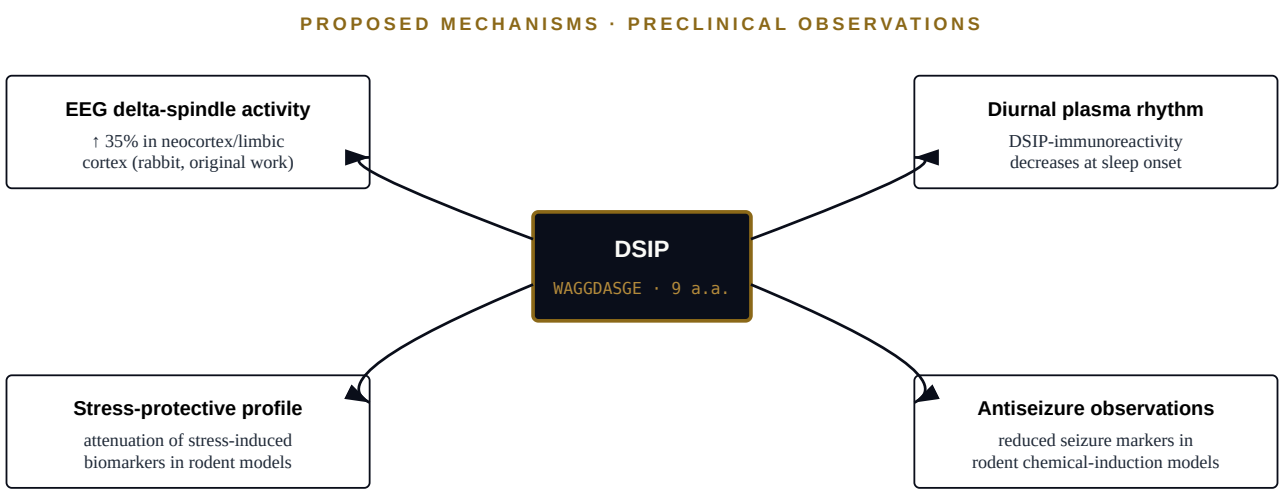

FIGURE 1 Schematic of proposed pathways and observed effects reported in preclinical animal investigations of DSIP. Compiled from refs 1, 2, 4, 5.

3.1 DELTA EEG-ENHANCING ACTIVITY IN THE ORIGINATING PREPARATION

The defining characterisation of DSIP — and the source of its name — is the work of Schoenenberger and colleagues in rabbits. Synthetic DSIP and several related peptides (truncated fragments, single- and double-amino-acid analogues, and the β-aspartyl isomer) were infused intraventricularly into rabbits under double-blind conditions. Fast-Fourier-transformed EEG from frontal neocortex and limbic archicortex demonstrated a highly specific delta- and spindle-EEG-enhancing effect of the synthetic α-aspartyl nonapeptide that was not shared by any of the tested fragments or analogues. The mean increase in delta activity reached approximately 35 % relative to cerebrospinal-fluid-vehicle controls.[2]

3.2 DISTRIBUTION IN TISSUES AND DIURNAL PATTERN

DSIP-like immunoreactive material has been documented in the brain and peripheral organs of the rat, in the plasma of several mammalian species, and in human cerebrospinal fluid and urine.[4] A separate line of work reported a diurnal rhythm of plasma DSIP-like immunoreactivity in mammals, with a decrease at the transition from wakefulness to sleep — consistent with a role of the peptide in mechanisms involved in sleep initiation, although the molecular target driving this association has not been identified.[6]

3.3 STRESS-PROTECTIVE AND ANTISEIZURE OBSERVATIONS

Beyond the original EEG work, multiple preclinical studies in rodents have examined DSIP in models of stress and chemically induced seizure activity. The compound has been reported to attenuate stress-related biomarker rises in rodent paradigms and to reduce seizure-associated markers in defined chemical-induction models. The mechanism underlying these observations remains hypothesis-generating; no high-affinity receptor for DSIP has been definitively characterised in the published literature.[5] PRECLINICAL · RODENT

3.4 IMMUNOMODULATORY OBSERVATIONS

Studies in cell-culture and rodent immune preparations have reported modulation of cytokine output and lymphocyte responses to DSIP exposure, expanding the originally sleep-focused characterisation to a broader neuroimmune profile. These observations remain at the in-vitro and rodent-preclinical level.[7]

04 Preclinical Findings Summary

SYSTEM	ANIMAL MODEL / PREPARATION	REPORTED OBSERVATION	REF.
Cortical EEG	Rabbit intraventricular infusion	↑ ~35% delta & spindle activity in neocortex and limbic cortex	2
Tissue distribution	Rat brain & peripheral organs; mammalian plasma	DSIP-like immunoreactivity in brain & periphery	4
Diurnal rhythm	Mammalian plasma sampling	Decrease in DSIP-IR at wakefulness-to-sleep transition	6
Stress markers	Rodent stress paradigms	Attenuation of stress-induced biomarker rises	5
Antiseizure	Rodent chemical-induction models	Reduced seizure-associated markers	5
Immunomodulation	Cell-culture & rodent immune cell preparations	Modulation of cytokine output, lymphocyte response	7

05 Research Synthesis & Limitations

METHODOLOGICAL NOTES

The DSIP corpus has a distinctive history: a vigorous research period in the 1970s–1980s tapered substantially in subsequent decades, in part because the molecule's biological target was never definitively characterised and replication of some of the earlier behavioural findings was inconsistent across groups. The strongest body of evidence remains the originating EEG work in rabbits and the documentation of endogenous DSIP-like material in mammalian tissues. Researchers should treat mechanistic claims at the receptor or signal-transduction level with caution, given the incomplete molecular characterisation, while regarding the cortical-EEG observations as relatively well-established within the originating preparation.

06 Laboratory Handling, Reconstitution, and Storage

DSIP is supplied as a lyophilised powder under research-use specifications. Published methodology reconstitutes the peptide in sterile water for injection or physiological saline; the molecule is moderately water-soluble and amphiphilic. **Three handling features warrant attention.** First, the tryptophan residue is photo-oxidation susceptible — lyophilised storage and any reconstituted solutions should be light-protected. Second, the Asp5–Gly6 peptide bond is susceptible to spontaneous hydrolysis at acidic pH, so neutral aqueous vehicles are preferred. Third, solution stability is limited relative to many peptides of similar size; aliquoted long-term storage at −18 °C with

minimal freeze–thaw is the conventional approach. Working concentrations are determined by the investigator's experimental design.

07 References

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