

Enveric Biosciences Inc - Chemical Library Catalogue Brochure: *Novel Neuroplastic Antidepressant (NAD-01)*

Enveric's Novel Antidepressant - NAD-01:

NAD-01 is a novel antidepressant molecule designed to induce neuroplasticity, promoting long-term therapeutic benefit in patients suffering from severe depressive mood disorders. Literature indicates activation of 5-HT_{2A}, commonly linked to hallucination in humans, also induces neuroplasticity. NAD-01 demonstrates low 5-HT_{2A} binding yet induces neuroplastic effects *in vitro*.

Background:

Traditional anti-depressants increase availability of key neurotransmitters in the brain by interacting with receptors that modify the extracellular levels of these molecules. These drugs produce adverse side-effects and fail to achieve long-term benefit.

Recently, clinical trials have reported promising results for the use of psilocybin to treat patients with severe depression and anxiety, showing apparent long-term benefit. Psilocin, the active metabolite of psilocybin, can induce neuroplasticity leading to increased synapse density and positive neuronal function. Unfortunately, the potency and duration of the

psychedelic experience limits the clinical application of psilocybin. Efforts are ongoing to design novel drugs with reduced hallucinogenic potential while retaining neuroplasticogenic activity.

Key Features of NAD-01:

- Demonstrates neuroplasticogenic activity comparable to known 5-HT_{2A} agonist DMT
- Demonstrates weak 5-HT_{2A} binding and activation *in vitro*
- Demonstrates lower Head Twitch Response (HTR) relative to psilocin and DMT in mice; literature considers HTR a predictive indicator for hallucination in humans
- Demonstrates recovery of sucrose preference (SP) in stressed mice; literature suggests the SP test is an accepted model for evaluation of antidepressant functionality
- Novel therapeutic profile:
 - Weak 5-HT_{2A} binding affinity
 - Demonstrated SERT binding *in vitro*
 - Suggests a novel molecular mechanism that induces neuroplasticity independent of 5-HT_{2A} agonism

Summary of Pharmacology Data:

Functional Parameter	Neuroactive Molecule			
	5-MeO-DMT	Psilocin	DMT	NAD-01
5-HT _{1A} Binding (K _i)	0.01-0.1 μM*	0.05-0.5 μM*	0.87 μM	1.2 μM
SERT Binding (K _i)	3.6 μM*	3.8 μM*	2.58 μM	0.37 μM
5-HT _{2A} Binding (K _i)	0.18 μM	0.03 μM	1.51 μM	9.22 μM
5-HT _{2A} Activation (EC ₅₀)	21 μM	58 μM	414 μM	>1000 μM
5-HT _{2A} Inhibition (IC ₅₀)	1.01 μM	0.12 μM	0.49 μM	1.17 μM
Neuroplasticity	Yes	Yes	Yes	Yes

* As reported in literature sources

