

Enveric Biosciences Inc - Chemical Library Catalogue Brochure: *Novel Psilocin Prodrug (NPP) Series*

Enveric’s NPP Series:

This series contains seven novel psilocin prodrugs designed to be specifically metabolized to release therapeutic levels of systemic psilocin at varying rates. Included in this series are four compounds that can be metabolized upon direct intravenous injection. These may bypass first-pass metabolism, making them amenable to non-oral forms of administration (eg. intranasal, sublingual, buccal).

Background:

Psilocybin is a natural prodrug produced by hallucinogenic mushroom (“Magic Mushrooms”). Upon ingestion, psilocybin is dephosphorylated within the acidic gastrointestinal tract, generating the readily absorbed, psychoactive agent psilocin. To modify the metabolic profile of psilocybin,

Enveric has generated an extensive library of novel psilocin prodrugs with enhanced GI stability, increased absorption properties, and variable cleavable substitutions producing altered pharmacokinetic properties.

Key Features of the NPP Series:

- All NPP compounds are metabolized completely into psilocin at varying rates when administered orally in mice
- NPP-01 to -04 are metabolized by human serum *in vitro* to release psilocin; results suggest that these prodrugs can bypass first pass metabolism when administered directly (eg. intravenous, intranasal)
- Effective intranasal administration is confirmed for NPP-01 and NPP-02, producing comparable psilocin levels relative to oral dosing in plasma and brain in mice

Summary Pharmacology of Novel Psilocin Prodrugs:

Prodrug Metabolism Studies

Compound	In vitro Metabolism Assays		Mouse PK Study
	<i>in vitro</i> Human Liver Metabolism (Half-Life)	<i>in vitro</i> Human Serum Metabolism (Half-life)	<i>in vivo</i> Plasma Psilocin Exposure (oral)
Psilocybin			+++
NPP-01	✓✓✓	✓✓✓	++
NPP-02	✓	✓✓✓	+
NPP-03	✓✓✓	✓✓✓	++
NPP-04	✓✓✓	✓✓✓	++
NPP-05	✓✓✓		++
NPP-06	✓		+
NPP-07	✓		+

Confirmed Intranasal Dosing

