

RESEARCH MONOGRAPH . COMPOUND PROFILE

Methallylescaline

A synthetic 4-methallyloxy-3,5-dimethoxyphenethylamine first characterized by Alexander Shulgin, distinguished from mescaline by approximately six-fold greater potency, prolonged duration of action, and a steep dose-response relationship attributable to enhanced lipophilicity and optimized 5-HT_{2A} receptor engagement.

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ABSTRACT

Methallylescaline (MAL; 2-[3,5-dimethoxy-4-(2-methylprop-2-enoxy)phenyl]ethanamine) is a synthetic psychedelic phenethylamine of the scaline structural class, first synthesized and self-administered by Alexander Shulgin in the early 1980s and formally documented in entry number 99 of his 1991 reference work PiHKAL (Phenethylamines I Have Known and Loved). The compound is the 4-methallyloxy homolog of mescaline (3,4,5-trimethoxyphenethylamine), differing from the parent alkaloid by replacement of the 4-methoxy group with a 2-methylprop-2-enyloxy (methallyloxy) substituent. This structural modification increases lipophilicity, enhances blood-brain barrier permeability, and produces a compound with approximately six-fold greater potency than mescaline, an oral dose range of 40 to 65 milligrams (compared to 200 to 400 milligrams for mescaline), and a duration of action of 12 to 16 hours.

The principal molecular target of methallylescaline is the serotonin 5-hydroxytryptamine type 2A (5-HT_{2A}) receptor, at which the compound acts as an agonist to produce the characteristic psychedelic phenomenology of the phenethylamine class: visual distortion, perceptual intensification, synesthesia, and altered cognition. The compound also binds the 5-HT_{2C} receptor and, at higher concentrations, the 5-HT_{1A} receptor (K_i in the low micromolar range). The receptor interaction profile was formally characterized in the Kolaczynska, Luethi, Trachsel, Hoener, and Liechti (2022) systematic study of 4-alkoxy-3,5-dimethoxyphenethylamines (mescaline derivatives) and related amphetamines, which established that scalines as a class bind 5-

HT2A and 5-HT2C receptors with affinities up to 63-fold and 34-fold greater than mescaline, respectively. The study further demonstrated that extending and branching the 4-alkoxy substituent increased binding affinity and activation potency at the 5-HT2A receptor while producing variable effects at the 5-HT2B receptor, a finding with implications for both potency and cardiovascular safety assessment.

Pharmacokinetic data specific to methallylescaline in humans are absent from the peer-reviewed literature. Inferences drawn from mescaline pharmacokinetics (oral absorption with T_{max} of approximately 2 hours, plasma half-life of approximately 3.5 hours, predominant elimination by oxidative deamination and renal excretion of unchanged drug) and from the structural properties of the methallyloxy substituent (increased lipophilicity, probable hepatic O-dealkylation to yield a demethylated phenolic metabolite) suggest that methallylescaline is rapidly absorbed, extensively distributed to central nervous system tissue, and eliminated over a time course consistent with its prolonged 12 to 16 hour subjective duration. The steep dose-response relationship reported by Shulgin, in which small increments in dose produce disproportionately large increases in effect intensity, is characteristic of agonists operating near the inflection point of a sigmoidal concentration-effect curve and may reflect cooperative receptor binding or threshold-dependent downstream signaling amplification.

Preclinical pharmacology data for methallylescaline are limited. The Halberstadt, Chatha, Chapman, and Brandt (2019) study of the mouse head-twitch response (a 5-HT2A receptor-mediated behavioral proxy for psychedelic potency) characterized several mescaline analogs in the scaline series and established the general

principle that extension of the 4-alkoxy chain increases in vivo potency relative to mescaline. No clinical trials, controlled human pharmacology studies, or formal toxicology assessments of methallylescaline have been conducted. The compound has no approved medical indication in any jurisdiction.

This monograph documents the chemistry, synthesis, structural class, and nomenclature of methallylescaline; the receptor pharmacology as characterized in the Kolaczynska et al. (2022) systematic study; inferred pharmacokinetics based on the mescaline pharmacokinetic record and structural analogy; preclinical pharmacology from the scaline head-twitch response literature; the absence of clinical evidence; sourcing and quality verification considerations; reconstitution and handling; stack interaction considerations; adverse events and safety signal; and a comparative assessment of five structurally or mechanistically related phenethylamine psychedelics (mescaline, escaline, allylescaline, proscaline, and 3C-E) against methallylescaline on five competency standards.

1. Compound Identification

1.1 Names, synonyms, and registry identifiers

Common name: Methallylescaline (MAL).

Systematic (IUPAC) name: 2-[3,5-dimethoxy-4-(2-methylprop-2-enoxy)phenyl]ethanamine.

Alternative chemical names: 4-methylallyloxy-3,5-dimethoxyphenethylamine; 4-(2-methylallyloxy)-3,5-dimethoxyphenethylamine; 3,5-dimethoxy-4-(2-methyl-2-propenyloxy)phenethylamine.

Chemical Abstracts Service (CAS) registry number: 207740-41-8 (free base). The hydrochloride salt CAS number is assigned separately; research suppliers typically list the free base CAS.

PiHKAL entry number: 99 (in the Shulgin and Shulgin 1991 compendium). The compound is listed as "MAL" in the PiHKAL index. The name "methallylescaline" was coined by Shulgin as a contraction denoting the methallyl substitution on the mescaline scaffold, though as Shulgin himself noted, the nomenclature is formally imprecise because the compound is not a union of a methallyl group with escaline but rather a mescaline derivative bearing a 2-methylallyloxy group at the 4-position [1].

Other identifiers: The compound appears in the NDEWS (National Drug Early Warning System) alert database as of 2024, reflecting increased online availability and discussion [2]. It is indexed in PubChem, ChemSpider, and commercial chemical databases under the CAS number above.

1.2 Structural class and chemistry

Methallylescaline belongs to the scaline family of phenethylamine psychedelics. Scalines are defined as 4-alkoxy-3,5-dimethoxyphenethylamines; they retain the 3,5-dimethoxy substitution pattern of mescaline but replace the 4-methoxy group with a longer or branched alkoxy chain. The scaline designation encompasses a se-

ries of compounds named by convention after the parent mescaline: escaline (4-ethoxy), proscaline (4-propoxy), isoproscaline (4-isopropoxy), buscaline (4-butoxy), allylescaline (4-allyloxy), and methallylescaline (4-methallyloxy), among others [3].

Molecular formula: C₁₄H₂₁NO₃ (free base).

Exact mass: 251.1521 g/mol (free base, monoisotopic).

Molecular weight: 251.32 g/mol (free base).

Structural features: The compound comprises a phenethylamine backbone (a phenyl ring bearing a two-carbon ethylamine side chain at position 1) with methoxy groups at positions 3 and 5 and a 2-methylprop-2-enyloxy (methallyloxy) group at position 4. The methallyloxy substituent is a branched, unsaturated three-carbon chain with a terminal methylene (=CH₂) and an internal methyl branch. This substituent is isomeric with the crotyloxy group but differs in branching pattern. The presence of the terminal alkene confers moderate additional lipophilicity relative to the saturated propoxy chain of proscaline and introduces a site for potential metabolic epoxidation.

Lipophilicity: The calculated octanol-water partition coefficient (log P) of methallylescaline is approximately 1.5 to 1.8, intermediate between mescaline (log P approximately 0.78) and the more lipophilic higher-chain scalines. The increased lipophilicity relative to mescaline is a principal determinant of the enhanced blood-brain barrier permeability and the approximately six-fold potency increase [4, 5].

Stereochemistry: Methallylescaline has no stereocenter and is therefore achiral. The compound is supplied and administered as the racemic (or more precisely, non-chiral) free base or as its hydrochloride, fumarate, or other salt forms.

Physical properties: White to off-white crystalline powder (as the hydrochloride salt). Freely soluble in water and polar organic solvents (methanol, ethanol, dimethyl sulfoxide). Sparingly soluble in apolar solvents. Melting point data for the hydrochloride salt are not reported in the peer-reviewed literature; supplier certificates of analysis typically report values in the range of 170 to 190 degrees Celsius.

1.3 Synthesis

The synthesis of methallylescaline follows a two-step route from homosyringonitrile (3,5-dimethoxy-4-hydroxyphenylacetonitrile), a commercially available or readily prepared starting material [1, 3].

Step 1: O-alkylation. The phenolic hydroxyl group of homosyringonitrile is alkylated with methallyl chloride (3-chloro-2-methylpropene) in the presence of a base, typically anhydrous potassium carbonate, in a polar aprotic solvent such as dimethylformamide or acetone. The reaction proceeds at elevated temperature (60 to 80 degrees Celsius) over 6 to 12 hours to yield 3,5-dimethoxy-4-(2-methylallyloxy)phenylacetonitrile. The product is isolated by aqueous workup and purified by column chromatography or recrystallization.

Step 2: Nitrile reduction. The nitrile intermediate is reduced to the primary amine using lithium aluminum hydride in anhydrous diethyl ether or tetrahydrofuran at reflux temperature. After quenching and basification, the free base is extracted into an organic solvent, and the hydrochloride salt is formed by treatment with hydrogen chloride in diethyl ether or isopropanol. The product is purified by recrystallization from ethanol or isopropanol.

Overall yield: Reported yields for the two-step sequence are moderate (50 to 70 percent), consistent with the standard Shulgin phenethylamine synthesis methodology. Alternative reducing agents (sodium borohydride with cobalt chloride, catalytic hydrogenation over palladium) have been described in the general scaline synthesis literature but are less commonly employed for this specific compound [3].

Characterization: The product is confirmed by nuclear magnetic resonance spectroscopy (¹H-NMR showing the characteristic vinyl methylene protons of the methallyl group at approximately 4.9 ppm, the methyl singlet at approximately 1.7 ppm, and the aromatic protons of the 3,5-dimethoxyphenyl ring at approximately 6.3 to 6.5 ppm), mass spectrometry (molecular ion at m/z 251 for the free base, [M+H]⁺ at 252), and melting point determination of the salt.

2. Abstract

Methallylescaline (MAL) is a synthetic psychedelic phenethylamine that belongs to the scaline structural family, a series of 4-alkoxy-3,5-dimethoxyphenethylamines derived from the mescaline scaffold. The compound was first synthesized and self-assayed by Alexander Shulgin in the early 1980s and published as entry number 99 in PiHKAL (1991), where the oral dose range was listed as 40 to 65 milligrams and the duration of action as 12 to 16 hours [1]. The approximately six-fold potency advantage over mescaline (oral dose 200 to 400 milligrams) and the notably steep dose-response curve distinguish methallylescaline within the scaline series and within the broader phenethylamine psychedelic class.

The molecular pharmacology of methallylescaline centers on agonism at the serotonin 5-HT_{2A} receptor, the principal molecular target mediating psychedelic phenomenology in the phenethylamine, tryptamine, and lysergamide classes. The Kolaczynska et al. (2022) systematic study of 4-alkoxy-3,5-dimethoxyphenethylamines established that scalines as a class exhibit enhanced 5-HT_{2A} and 5-HT_{2C} binding affinity relative to mescaline, with the magnitude of enhancement correlating with the length, branching, and unsaturation of the 4-alkoxy substituent [5]. The methallyloxy substituent, combining a three-carbon chain with terminal unsaturation and methyl branching, achieves an optimized balance of size, lipophilicity, and conformational flexibility for 5-HT_{2A} receptor engagement.

No controlled clinical trials, formal pharmacokinetic studies, or regulatory submissions have been conducted for methallylescaline. The compound has no approved medical indication. Preclinical data are limited to the general scaline head-twitch response characterization by Halberstadt et al. (2019), which confirmed the structure-activity relationship between 4-alkoxy chain extension and *in vivo* psychedelic potency in the mouse model [6]. The compound is available from research chemical suppliers as the hydrochloride or fumarate salt at stated purities of 98 percent or greater.

The regulatory status of methallylescaline is variable across jurisdictions. The compound is not explicitly scheduled in the United States Controlled Substances Act but is potentially subject to prosecution under the Federal Analogue Act (21 U.S.C. section 813) when intended for human consumption, on the basis of its struc-

tural and pharmacological similarity to the Schedule I substance mescaline [7]. It is controlled under the New Psychoactive Substances Act (NpSG) in Germany as of November 2016, and is illegal in Sweden.

This monograph reviews the compound identification, synthesis, receptor pharmacology, inferred pharmacokinetics, limited preclinical data, absent clinical evidence, sourcing and quality considerations, handling procedures, stack interactions, adverse events, and comparative positioning of methallylescaline against five related phenethylamine psychedelics.

3. Discovery and Development History

3.1 Origin

Methallylescaline was first synthesized by Alexander T. Shulgin at his private laboratory in Lafayette, California, as part of a systematic exploration of 4-alkoxy substitutions on the mescaline scaffold [1]. Shulgin's research program, conducted from the late 1960s through the 1990s, produced hundreds of novel phenethylamine and tryptamine analogs, many of which were self-assayed by Shulgin and a small group of experienced volunteers. The methallylescaline synthesis was completed and initial self-administration occurred in 1981, with the discovery of psychedelic activity at the 40 to 65 milligram dose range reported in 1982 [1].

3.2 Publication

The compound was formally documented in Shulgin and Shulgin (1991), PiHKAL: A Chemical Love Story, as entry number 99 under the abbreviation "MAL" [1]. The PiHKAL entry provides the synthesis route from homosyringonitrile, the dose range (40 to 65 milligrams), the duration (12 to 16 hours), and qualitative descriptions of the subjective effects from multiple self-assay sessions at various doses. Shulgin described the compound as producing a "mixed bag" of experiences, with visual effects, body awareness changes, and cognitive alterations that varied considerably across sessions and between individuals. The compound was noted for its steep dose-response characteristics, with the transition from threshold to full psychedelic effect occurring over a narrow dose increment of approximately 10 to 15 milligrams [1].

3.3 Subsequent research

Following the PiHKAL publication, methallylescaline received minimal academic attention for approximately two decades. The compound was included in the Trachsel (2003) comprehensive review of substituted phenethylamines as a classified member of the scaline series [3]. The first systematic pharmacological characterization appeared in the Kolaczynska, Luethi, Trachsel, Hoener, and Liechti (2022) study, which measured receptor binding affinities, activation potencies, and effica-

cies for methallylescaline and related scalines across a panel of serotonin, dopamine, adrenergic, and trace amine receptors [5]. This study represented the first formal in vitro pharmacological profiling of the compound in a peer-reviewed context.

3.4 Emergence in research chemical markets

Beginning approximately 2010 to 2015, methallylescaline became available through online research chemical vendors, initially in Europe and subsequently worldwide. The NDEWS (National Drug Early Warning System) issued an alert in 2024 noting increased online mentions and availability of the compound [2]. The compound has appeared in user experience reports on multiple online databases and forums. No pharmaceutical company has undertaken development of methallylescaline for any therapeutic indication.

3.5 Absence of clinical development

Methallylescaline has not entered any stage of pharmaceutical development. No investigational new drug (IND) application, clinical trial authorization, or equivalent regulatory filing has been submitted for the compound in any jurisdiction. The compound remains exclusively a research chemical and an entry in the historical Shulgin catalog. The broader psychedelic renaissance beginning approximately 2018, which has produced clinical development programs for psilocybin, MDMA, LSD, and mescaline, has not extended to methallylescaline or other scalines as clinical candidates, though interest in the scaline series as a source of novel structure-activity data for 5-HT_{2A} receptor pharmacology continues in academic settings [5, 8].

4. Mechanism of Action

4.1 5-HT_{2A} receptor agonism

The principal molecular target of methallylescaline is the serotonin 5-hydroxytryptamine type 2A (5-HT_{2A}) receptor, a G protein-coupled receptor (GPCR) of the class A rhodopsin family. The 5-HT_{2A} receptor is expressed at high density in layer V pyramidal neurons of the prefrontal cortex, in claustrum, in visual cortex, and in other cortical and subcortical regions. Activation of the 5-HT_{2A} receptor by psychedelic agonists produces the characteristic phenomenology of the psychedelic state: visual hallucinations, perceptual distortion, synesthesia, altered time perception, emotional intensification, and ego dissolution at higher doses [9, 10].

Methallylescaline binds the 5-HT_{2A} receptor at the orthosteric serotonin-binding site. The Kolaczynska et al. (2022) study measured the receptor interaction profiles of a panel of 4-alkoxy-3,5-dimethoxyphenethylamines (scalines) and their corresponding 3,5-dimethoxy-4-alkoxyamphetamine (3C-scaline) analogs using radioligand binding assays and functional activation assays in heterologous expression systems [5]. The scaline series as a class bound the 5-HT_{2A} receptor with affinities ranging from $K_i = 150$ nM to $K_i = 12,000$ nM, with affinity increasing as the 4-alkoxy chain was extended, branched, or unsaturated. Methallylescaline, bearing the branched unsaturated methallyloxy group, falls within the higher-affinity portion of this range. The 5-HT_{2A} binding affinity of the scaline series was up to 63-fold greater than that of mescaline (mescaline K_i at 5-HT_{2A} approximately 7,600 to 12,000 nM depending on assay conditions and radioligand) [5, 11].

Functional activation studies demonstrated that scalines act as agonists at the 5-HT_{2A} receptor, stimulating Gq/11-mediated phospholipase C activation, inositol trisphosphate production, and intracellular calcium release. The activation potency and efficacy at 5-HT_{2A} increased with 4-alkoxy chain extension, paralleling the binding affinity trend [5]. The downstream signaling cascade includes beta-arrestin-2 recruitment, ERK1/2 phosphorylation, and (for some psychedelic agonists) biased signaling toward specific intracellular pathways that may contribute to the distinct qualitative profiles of different psychedelics [10].

4.2 5-HT_{2C} receptor binding

The Kolaczynska et al. (2022) study demonstrated that scalines also bind the 5-HT_{2C} receptor, with affinities up to 34-fold greater than mescaline [5]. The 5-HT_{2C} receptor modulates dopamine and norepinephrine release in mesolimbic and mesocortical circuits and contributes to the anxiogenic, anorectic, and locomotor-suppressive components of the psychedelic response. The scaline series did not show a marked preference for 5-HT_{2A} over 5-HT_{2C} (in contrast to the corresponding 3C-scaline amphetamine analogs, which exhibited a marginal 5-HT_{2A} selectivity), suggesting that methallylescaline engages both serotonin receptor subtypes at pharmacologically relevant concentrations.

4.3 5-HT_{2B} receptor considerations

The 5-HT_{2B} receptor, expressed at high density on cardiac valvular interstitial cells, mediates the valvulopathic effects of chronic serotonergic agonists (the fenfluramine-associated valvular heart disease mechanism). The Kolaczynska et al. (2022) study found that extending the 4-alkoxy substituent enhanced activation potency and efficacy at the 5-HT_{2A} receptor but produced variable and generally lower effects at the 5-HT_{2B} receptor [5]. This dissociation between 5-HT_{2A} agonism (desired psychedelic activity) and 5-HT_{2B} agonism (undesired valvulopathic risk) is pharmacologically favorable, though the data are insufficient to quantify the safety margin for chronic dosing of methallylescaline. The relevance of 5-HT_{2B} activity to acute, single-dose psychedelic administration is limited; the valvulopathic risk is associated with chronic daily exposure over months to years.

4.4 5-HT_{1A} receptor binding

Methallylescaline was identified among the scaline phenethylamines that bind the 5-HT_{1A} receptor, albeit with low affinity in the micromolar range (K_i approximately 1.6 to 6.7 micromolar) [5]. The 5-HT_{1A} receptor is a G_i/G_o -coupled GPCR expressed as a somatodendritic autoreceptor on raphe serotonin neurons and as a postsynaptic heteroreceptor in cortex and hippocampus. Activation of postsynaptic 5-HT_{1A} receptors produces anxiolytic and antidepressant-like effects in preclinical models. The low-affinity 5-HT_{1A} binding of methallylescaline is unlikely to contribute substantially to the pharmacological profile at the reported dose range of 40 to 65 milligrams but may become relevant at the upper end of the dose range or in individuals with slow metabolic clearance.

4.5 Trace amine-associated receptor 1 (TAAR1) and other targets

Phenethylamines as a structural class interact with trace amine-associated receptor 1 (TAAR1), a GPCR involved in the modulation of dopaminergic and serotonergic neurotransmission [12]. The Kolaczynska et al. (2022) study included TAAR1 in the receptor panel; scalines showed variable TAAR1 activity. The functional significance of any TAAR1 interaction for the psychedelic or physiological profile of methallylescaline is unclear. No meaningful interactions with dopamine D1 or D2 receptors, adrenergic alpha-1 or alpha-2 receptors, or histamine H1 receptors have been reported for the scaline series at concentrations relevant to the psychedelic dose range.

4.6 Structure-activity relationship and the methallyloxy substituent

The methallyloxy group at the 4-position of the mescaline scaffold represents an optimized balance of three structural features: chain length (three carbons, comparable to the propoxy chain of proscaline), unsaturation (the terminal methylene provides conformational rigidity and a potential hydrogen-bond acceptor via pi-electron density), and branching (the internal methyl group increases van der Waals contact with hydrophobic residues in the 5-HT_{2A} receptor binding pocket). The combination of these features produces a substituent that achieves higher binding affinity and in vivo potency than either the unbranched allyloxy (allylescaline) or the saturated propoxy (proscaline) analogs, consistent with the structure-activity principle that optimal 5-HT_{2A} receptor engagement in the scaline series requires both appropriate chain length and conformational constraint [5, 6].

5. Pharmacokinetics and Routes of Administration

5.1 Preliminary considerations

No formal pharmacokinetic study of methallylescaline has been conducted in humans or in preclinical species. The pharmacokinetic profile presented in this section is inferred from the mescaline pharmacokinetic record, from structural analogy within the scaline series, and from first-principles analysis of the physicochemical properties of the methallyloxy substituent. These inferences are provisional and should be treated with appropriate caution.

5.2 Absorption

The oral route is the only route of administration documented for methallylescaline in the Shulgin PiHKAL entry and in subsequent user reports. Onset of subjective effects is reported within approximately 1 hour of oral ingestion, with peak effects reached within approximately 2 to 3 hours [1, 13]. This time course is consistent with rapid gastrointestinal absorption and is similar to the oral absorption profile of mescaline (Tmax approximately 2.0 hours in controlled studies) [14, 15].

The increased lipophilicity of methallylescaline relative to mescaline (calculated log P approximately 1.5 to 1.8 versus 0.78 for mescaline) may facilitate transcellular absorption and blood-brain barrier permeability, potentially contributing to the enhanced central nervous system potency. Oral bioavailability has not been measured; by analogy with mescaline (estimated oral bioavailability of at least 53 percent based on unchanged urinary recovery), methallylescaline is likely to have moderate to high oral bioavailability [14].

5.3 Distribution

The increased lipophilicity and moderate molecular weight (251.32 g/mol) of methallylescaline predict substantial tissue distribution and efficient blood-brain barrier penetration. The volume of distribution has not been measured. The com-

pound contains a primary amine that is protonated at physiological pH (predicted pKa approximately 9.5 to 10.0), which influences protein binding and tissue partitioning. Plasma protein binding has not been characterized.

5.4 Metabolism

The metabolism of methallylescaline has not been directly studied. By analogy with mescaline and with general principles of phenethylamine metabolism, the following pathways are predicted:

Oxidative deamination. The primary amine of methallylescaline is expected to undergo oxidative deamination by monoamine oxidase (MAO) and possibly diamine oxidase (DAO) or aldehyde oxidase, producing the corresponding phenylacetic acid metabolite (3,5-dimethoxy-4-(2-methylallyloxy)phenylacetic acid). This is the principal metabolic pathway of mescaline, which is predominantly converted to 3,4,5-trimethoxyphenylacetic acid [14, 16].

O-dealkylation. The methallyloxy group at the 4-position is an ether that may undergo hepatic O-dealkylation by cytochrome P450 enzymes, yielding the corresponding 4-hydroxy metabolite (a catechol-type intermediate). This pathway would regenerate a phenol and release methacrolein (2-methylpropenal) as the aldehyde byproduct. The cytochrome P450 isoforms most likely to catalyze this O-dealkylation are CYP2D6 and CYP3A4, based on their established role in the metabolism of related phenethylamines and methoxyamphetamines [17].

Epoxidation. The terminal alkene of the methallyloxy group is a potential substrate for cytochrome P450-mediated epoxidation, producing a reactive epoxide intermediate. Whether this pathway contributes meaningfully to the elimination of methallylescaline and whether the epoxide intermediate has toxicological significance are unknown.

N-acetylation. Mescaline undergoes N-acetylation to produce N-acetylmescaline, a minor metabolite. The analogous N-acetylmethallylescaline would be expected as a minor metabolic product.

5.5 Elimination

Mescaline is eliminated predominantly by renal excretion, with approximately 53 percent of an oral dose recovered unchanged in urine and the remainder excreted as the phenylacetic acid and N-acetyl metabolites [14]. The elimination half-life of mescaline in plasma is approximately 3.5 hours based on recent controlled studies using validated analytical methods [14, 15]. The 12 to 16 hour duration of methallylescaline suggests either a longer elimination half-life (plausible given the increased lipophilicity and tissue distribution), slower receptor dissociation kinetics (prolonging pharmacodynamic effect beyond the plasma residence time), or both. A plasma half-life in the range of 4 to 8 hours would be a reasonable provisional estimate, though this figure is speculative and awaits direct measurement.

5.6 Routes of administration

The oral route is the standard and only well-documented route of administration. Methallylescaline has been administered as the hydrochloride or fumarate salt dissolved in water or encapsulated in gelatin capsules. Intranasal, sublingual, and parenteral routes have not been formally characterized; user reports of intranasal administration suggest rapid onset with increased irritation and no clear potency advantage. The compound is expected to be bioavailable by multiple routes given its favorable physicochemical properties.

6. Preclinical Pharmacology

6.1 Head-twitch response studies

The mouse head-twitch response (HTR) is a validated behavioral proxy for 5-HT_{2A} receptor-mediated psychedelic activity. The HTR is elicited by serotonergic hallucinogens and is abolished by selective 5-HT_{2A} receptor antagonists (M100907/volinanserin), confirming its receptor specificity [6, 18].

The Halberstadt, Chatha, Chapman, and Brandt (2019) study examined the head-twitch response profiles of mescaline and several scaline analogs (escaline, proscaline) and their corresponding 3C-amphetamine homologs in C57BL/6J mice [6]. The study established that extension of the 4-alkoxy chain from methoxy (mescaline) to ethoxy (escaline, ED₅₀ = 11.2 micromol/kg) to propoxy (proscaline, ED₅₀ = 8.09 micromol/kg) produces progressive increases in in vivo potency. Escaline was approximately two-fold and proscaline approximately three-fold more potent than mescaline in the HTR assay [6].

Methallylescaline was not directly tested in the Halberstadt et al. (2019) study. However, the structure-activity relationship established by the series (increasing potency with chain extension and with unsaturation/branching) predicts that methallylescaline, bearing a branched unsaturated three-carbon substituent, would exhibit HTR potency comparable to or exceeding that of proscaline. The approximately six-fold potency advantage over mescaline reported by Shulgin from human self-assay is consistent with this prediction.

6.2 In vitro receptor profiling

The Kolaczynska et al. (2022) systematic study profiled the scaline series against a panel of receptors including 5-HT_{2A}, 5-HT_{2B}, 5-HT_{2C}, 5-HT_{1A}, dopamine D₂, adrenergic alpha-1 and alpha-2, and TAAR1, using radioligand binding assays ([³H]-ketanserin displacement for 5-HT_{2A}; [³H]-mesulergine displacement for 5-HT_{2C}) and functional activation assays (calcium mobilization, IP₁ accumulation) in HEK293 cells stably expressing the target receptors [5].

The study demonstrated that the scaline series uniformly exceeds mescaline in 5-HT_{2A} and 5-HT_{2C} binding affinity, with the magnitude of enhancement dependent on the 4-alkoxy substituent. Activation potency and efficacy at 5-HT_{2A} also increased with chain extension. The study further demonstrated that the scaline series produced variable and generally lower activation at the 5-HT_{2B} receptor, providing a favorable (though not definitive) preliminary signal for the dissociation of psychedelic activity from valvulopathic risk.

6.3 Absence of toxicology data

No formal toxicology studies (acute toxicity, subchronic toxicity, genotoxicity, reproductive toxicity, carcinogenicity) have been conducted for methallylescaline. The lethal dose in any species is unknown. Therapeutic index estimates are therefore not available. Investigators using the compound in animal models should conduct pilot dose-range-finding studies and monitor for acute cardiovascular, neurological, and behavioral toxicity signals.

7. Clinical Evidence Base

7.1 Absence of clinical trials

No controlled clinical trial, Phase 1 pharmacokinetic study, or observational clinical study of methallylescaline has been conducted or registered in any clinical trial database (ClinicalTrials.gov, EudraCT, ANZCTR) as of the current monograph revision date.

7.2 Self-assay data from Shulgin

The only systematic human exposure data for methallylescaline are the self-assay reports published in PiHKAL entry 99 [1]. Shulgin and his research group administered the compound at doses ranging from approximately 20 milligrams (threshold) to 65 milligrams (full psychedelic experience) by the oral route. The qualitative reports describe:

At 40 milligrams: mild visual enhancement, awareness of body sensations, slight time distortion, duration approximately 12 hours.

At 50 to 55 milligrams: pronounced visual effects including geometric patterns and color intensification, significant cognitive alteration, emotional amplification, duration approximately 14 hours.

At 60 to 65 milligrams: intense open-eye and closed-eye visual phenomena (described as neon colors and kaleidoscopic imagery), strong body awareness, profound cognitive and perceptual changes, duration approximately 16 hours [1, 13].

The steep dose-response relationship was consistently noted: a 10 milligram increment (from 40 to 50 milligrams, a 25 percent increase in dose) produced a disproportionately large increase in effect intensity. This characteristic distinguishes methallylescaline from mescaline, which exhibits a more gradual dose-response curve over its 200 to 400 milligram range.

7.3 User experience reports

Uncontrolled user experience reports collected on online databases (Erowid, PsychonautWiki, Bluelight) describe effects broadly consistent with the Shulgin self-assay data: onset within 1 hour, peak at 2 to 4 hours, total duration of 8 to 16 hours depending on dose, with visual, cognitive, and somatic effects typical of the phenethylamine psychedelic class [13]. Multiple reports note a significant "body load" (somatic discomfort including nausea, muscle tension, and gastrointestinal disturbance) that is more pronounced than with mescaline at equivalent psychedelic intensity. These reports lack dose verification, analytical confirmation of compound identity, and controlled conditions and cannot be considered clinical evidence.

7.4 Potential research applications

Although no clinical development is underway, the pharmacological profile of methallylescaline suggests potential research utility in several domains: (a) as a tool compound for studying the structure-activity relationships of 5-HT_{2A} receptor agonism in the scaline series; (b) as a comparator compound in studies of phenethylamine psychedelic pharmacology, offering a potency intermediate between mescaline and the more potent 2C and DOx series; (c) as a probe for investigating the contribution of 4-alkoxy substituent geometry to psychedelic receptor selectivity and downstream signaling bias. These applications are purely investigational and do not imply clinical utility.

8. Sourcing and Quality Verification

8.1 Research chemical suppliers

Methallylescaline is available from multiple online research chemical suppliers as the hydrochloride salt or the fumarate salt at stated purities of 98 percent or greater. The compound is not available from major pharmaceutical-grade chemical suppliers (Sigma-Aldrich, Tocris, Cayman Chemical) through their standard research chemical catalogs. Availability is primarily through specialized research chemical vendors operating in jurisdictions where the compound is not explicitly scheduled.

8.2 Analytical verification

Investigators should confirm compound identity and purity on every lot through:

- High-performance liquid chromatography (HPLC) area-percent purity, target greater than 98 percent.
- Mass spectrometry confirmation of molecular weight (free base $[M+H]^+ = 252.16$; hydrochloride salt molecular weight 287.78).
- Nuclear magnetic resonance spectroscopy (1H -NMR) confirmation of structural identity, with specific attention to the diagnostic vinyl methylene protons (approximately 4.9 ppm) and methyl singlet (approximately 1.7 ppm) of the methallyloxy group.
- Differential scanning calorimetry or melting point determination for salt form confirmation.
- Residual solvent analysis by gas chromatography for common synthesis solvents (dimethylformamide, tetrahydrofuran, diethyl ether, ethanol).

8.3 Counterfeit and mislabeling risk

The research chemical market for novel psychedelic phenethylamines carries a non-trivial risk of mislabeling, substitution, or contamination. Methallylescaline could be confused with or substituted by structurally related scalines (allylesca-

line, escaline, proscaline) that differ in potency and duration. Analytical confirmation of identity is essential for any investigation in which dose-response precision, receptor pharmacology interpretation, or safety assessment is important.

8.4 Pricing and availability

Pricing at the time of monograph preparation is in the range of \$30 to \$100 per 250 milligrams of the hydrochloride salt at stated 98 percent or greater purity. Supply quantities are typically in the 100 milligram to 5 gram range. Availability is variable and dependent on supplier inventory and regulatory environment.

9. Reconstitution and Handling

9.1 Solubility and stock preparation

Methallylescaline hydrochloride is freely soluble in water at room temperature. For research applications, stock solutions are typically prepared at 10 to 50 mg/mL in:

- Distilled or deionized water for oral dosing studies in animal models.
- Normal saline (0.9 percent sodium chloride) for parenteral administration in animal models.
- Dimethyl sulfoxide (DMSO) at high concentration (100 mM) for in vitro cell-based assays, with subsequent dilution into aqueous assay buffer. Final DMSO concentration in cell assays should not exceed 0.1 to 0.5 percent to avoid vehicle effects.

9.2 Storage

The solid compound (hydrochloride or fumarate salt) should be stored at 2 to 8 degrees Celsius in a sealed container, protected from moisture. The compound is expected to be stable at refrigerated conditions for at least 12 months based on general stability data for crystalline phenethylamine salts. Aqueous stock solutions should be prepared fresh or stored at minus 20 degrees Celsius in single-use aliquots to avoid repeated freeze-thaw cycles. Light protection is not specifically required but is reasonable practice.

9.3 Handling precautions

Methallylescaline is a psychoactive compound. Standard laboratory handling precautions for psychoactive research chemicals apply: use of personal protective equipment (gloves, laboratory coat, eye protection), avoidance of inhalation or dermal exposure, and containment measures appropriate to the quantities handled. The compound is active at low milligram doses; weighing should be performed with an analytical balance in a well-ventilated space or fume hood.

10. Stack Interactions and Combinations

10.1 Monoamine oxidase inhibitors

Monoamine oxidase inhibitors (MAOIs), including both pharmaceutical agents (phenelzine, tranylcypromine, moclobemide) and botanical sources (*Banisteriopsis caapi*, *Peganum harmala*), would be expected to potentiate and prolong the effects of methallylescaline by inhibiting the oxidative deamination pathway that is likely a principal route of metabolic clearance. The combination of a psychedelic phenethylamine with an MAOI carries a risk of hypertensive crisis from unopposed sympathomimetic activity and of serotonin syndrome from combined serotonergic stimulation. This combination has not been studied and cannot be recommended for research without careful dose titration and physiological monitoring [19].

10.2 Selective serotonin reuptake inhibitors

Chronic selective serotonin reuptake inhibitor (SSRI) therapy produces adaptive downregulation of postsynaptic 5-HT_{2A} receptor density, which would be expected to attenuate the psychedelic effects of methallylescaline. Acute SSRI co-administration elevates synaptic serotonin and may produce unpredictable interactions with a 5-HT_{2A} agonist. The clinical significance of SSRI interactions with methallylescaline is unknown and is inferred from the broader psychedelic-SSRI interaction literature [20].

10.3 Other serotonergic agents

Concurrent administration with other serotonin receptor agonists (tryptamine psychedelics, lysergamides, MDMA/entactogens) produces additive serotonergic stimulation and increases the risk of serotonin syndrome. The combination of methallylescaline with other psychedelics has not been studied and is not recommended for research without established safety margins.

10.4 CYP2D6 inhibitors and inducers

If hepatic O-dealkylation by CYP2D6 contributes to methallylescaline clearance (as predicted by structural analogy), strong CYP2D6 inhibitors (paroxetine, fluoxetine, bupropion, quinidine) may elevate plasma concentrations and prolong the duration of action. CYP2D6 inducers (dexamethasone, rifampin) may accelerate clearance. These interactions are speculative and have not been characterized.

10.5 Lithium

The combination of lithium with serotonergic psychedelics (principally LSD and psilocybin) has been associated in case reports with severe adverse reactions including seizures. The mechanism is incompletely understood but may involve lithium-mediated sensitization of 5-HT_{2A} receptor signaling through inhibition of glycogen synthase kinase 3 beta (GSK-3 β) and inositol monophosphatase. Whether this interaction extends to methallylescaline is unknown; caution is warranted [21].

10.6 Cardiovascular agents

The 5-HT_{2B} receptor agonism demonstrated for the scaline class (albeit at lower potency and efficacy than 5-HT_{2A} agonism) raises a theoretical concern for interaction with agents that affect cardiac valvular tissue remodeling. The practical relevance to acute, single-dose administration is minimal.

11. Adverse Events and Safety Signal

11.1 Reported adverse effects

The following adverse effects are reported from the Shulgin self-assay data and from uncontrolled user experience reports. No controlled safety data exist.

Gastrointestinal: Nausea (common, particularly during onset; likely reflects peripheral 5-HT_{2A} and 5-HT₃ receptor activation in enteric neurons and area postrema). Abdominal discomfort. Occasional vomiting at higher doses. The gastrointestinal effects are consistent with the broader phenethylamine psychedelic class and are similar in character to mescaline-associated nausea, though user reports suggest that the body load of methallylescaline may be more pronounced than that of mescaline at equivalent psychedelic intensity [1, 13].

Cardiovascular: Modest increases in heart rate and blood pressure are expected based on the sympathomimetic properties of the phenethylamine scaffold, though no formal cardiovascular monitoring data exist for methallylescaline. Mescaline at clinical doses produces modest tachycardia (increase of approximately 10 to 20 beats per minute) and systolic blood pressure elevation (increase of approximately 10 to 20 mmHg) [15].

Neurological and psychological: Anxiety, confusion, disorientation, and panic reactions are reported at higher doses and in unfavorable settings, consistent with the general adverse event profile of psychedelic substances. The steep dose-response curve of methallylescaline increases the risk of inadvertent overdose, which may precipitate intense and prolonged psychological distress.

Thermoregulatory: Chills, sweating, and temperature instability are reported, consistent with central serotonergic effects on hypothalamic thermoregulation.

Musculoskeletal: Muscle tension and jaw clenching (bruxism) are reported, consistent with serotonergic and possibly adrenergic activation of skeletal muscle tone.

11.2 Steep dose-response and overdose risk

The unusually steep dose-response relationship is the most significant safety concern specific to methallylescaline within the scaline class. A dose increment of 10 to 15 milligrams (approximately 20 to 30 percent of a moderate dose) can transition the effect from mild perceptual enhancement to intense psychedelic experience lasting 16 hours or longer. This characteristic increases the risk of unintended overdose, particularly for naive users or when compound purity is uncertain. No lethal dose data exist for methallylescaline in any species [1].

11.3 Long duration

The 12 to 16 hour duration of action is among the longest in the phenethylamine psychedelic class (comparable to DOx amphetamines at 12 to 24 hours, considerably longer than mescaline at 8 to 12 hours). Prolonged psychedelic experiences are associated with increased fatigue, dehydration, sleep disruption, and psychological distress, particularly in uncontrolled settings.

11.4 Serotonin syndrome risk

As a 5-HT_{2A} receptor agonist with additional serotonergic activity at 5-HT_{2C} and 5-HT_{1A} receptors, methallylescaline carries a theoretical risk of serotonin syndrome when combined with other serotonergic agents. No cases of serotonin syndrome associated with methallylescaline have been reported in the literature.

11.5 Cardiac safety

The 5-HT_{2B} receptor agonism demonstrated for the scaline class raises a theoretical concern for valvulopathic effects with chronic administration. This risk is relevant only to repeated, sustained dosing regimens and is unlikely to be clinically significant for single-dose or infrequent administration.

11.6 Absence of formal safety data

The absence of formal toxicology, pharmacokinetic, and clinical safety data for methallylescaline is a fundamental limitation. All safety assessments are inferred from structural analogy, from the limited self-assay data, and from uncontrolled

user reports. The compound should be treated as a research chemical with an unknown safety profile.

12. Comparative Assessment

This section presents a structured comparative assessment of five phenethylamine psychedelics against methallylescaline, evaluated against five competency standards: novelty of mechanism, effect size (psychedelic potency), promising potential (research trajectory and data availability), side-effect profile, and overall validation. The five comparators were selected for their structural or mechanistic relationship to methallylescaline: mescaline (the parent compound), escaline (the ethoxy scaline), allylescaline (the unbranched allyloxy scaline), proscaline (the propoxy scaline), and 3C-E (4-ethoxy-3,5-dimethoxyamphetamine, the alpha-methyl homolog of escaline that bridges the scaline and 3C-scaline series).

12.1 Mescaline (3,4,5-trimethoxyphenethylamine)

Mechanism: 5-HT_{2A} receptor agonist. Mescaline is the parent compound of the scaline series and the naturally occurring psychedelic alkaloid of the peyote cactus (*Lophophora williamsii*) and San Pedro cactus (*Echinopsis pachanoi*). It binds the 5-HT_{2A} receptor with relatively low affinity (K_i approximately 7,600 to 12,000 nM) and requires oral doses of 200 to 400 milligrams for full psychedelic effect [11, 14, 15].

Novelty: Low. Mescaline is one of the oldest known psychedelic compounds, with ethnobotanical use spanning millennia and scientific characterization beginning with Heffter (1897) and Spath (1919). Its pharmacology is thoroughly characterized.

Effect size: Moderate. Mescaline produces reliable psychedelic effects across the 200 to 400 milligram dose range, with subjective intensity comparable to psilocybin (20 to 30 milligrams) and LSD (100 to 200 micrograms) in cross-comparison studies. The high dose requirement limits experimental convenience [15].

Promising potential: High. Mescaline is currently in active clinical research, with controlled pharmacokinetic and pharmacodynamic studies published by the Liechti laboratory (2022 to 2025) and with increasing regulatory interest in its therapeutic potential [14, 15].

Side-effect profile: Nausea is the principal dose-limiting adverse effect, occurring in a majority of subjects at psychedelic doses and contributing to the traditional association between peyote ingestion and vomiting. Cardiovascular effects are modest. The safety profile at single doses is well characterized [15].

Overall validation: High. Mescaline is the best-characterized phenethylamine psychedelic, with extensive ethnobotanical, chemical, pharmacological, and emerging clinical data.

Comparison to methallylescaline: Methallylescaline is approximately six-fold more potent, has a longer duration (12 to 16 versus 8 to 12 hours), and has a steeper dose-response curve. Mescaline has vastly more validation data, an established clinical research program, and centuries of human use history. Methallylescaline offers experimental convenience through lower dose requirement but lacks the safety and pharmacokinetic characterization of mescaline.

12.2 Escaline (4-ethoxy-3,5-dimethoxyphenethylamine)

Mechanism: 5-HT_{2A} receptor agonist. Escaline is the shortest-chain scaline, replacing the 4-methoxy of mescaline with a 4-ethoxy group. Oral dose range is 40 to 60 milligrams with a duration of 8 to 12 hours [1, 3].

Novelty: Low. Escaline was characterized by Shulgin in PiHKAL and is a straightforward chain-extension analog.

Effect size: Moderate. Approximately five- to eight-fold more potent than mescaline. HTR ED₅₀ = 11.2 micromol/kg in the Halberstadt et al. (2019) study [6].

Promising potential: Low. No clinical development. Limited academic interest beyond the Kolaczynska et al. (2022) receptor profiling study [5].

Side-effect profile: Body load (nausea, muscle tension) reported as comparable to or greater than mescaline at equipotent psychedelic doses. No formal safety data [1].

Overall validation: Low. Limited to PiHKAL self-assay data, one in vitro receptor profiling study, and one in vivo HTR study.

Comparison to methallylescaline: Similar dose range and onset characteristics. Methallylescaline has a longer duration (12 to 16 versus 8 to 12 hours) and a steeper dose-response curve. Neither compound has meaningful clinical validation.

12.3 Allylescaline (4-allyloxy-3,5-dimethoxyphenethylamine)

Mechanism: 5-HT_{2A} receptor agonist. Allylescaline is the unbranched allyloxy analog, differing from methallylescaline by the absence of the 2-methyl branch on the allyl group. Oral dose range is 20 to 35 milligrams with a duration of 8 to 12 hours [1, 3].

Novelty: Low. Characterized in PiHKAL as the allyloxy scaline.

Effect size: High within the scaline series. Allylescaline is among the most potent scalines, with a lower dose range than methallylescaline (20 to 35 versus 40 to 65 milligrams as reported in PiHKAL), suggesting higher in vivo potency. The allyloxy substituent, with its unbranched unsaturated chain, achieves high 5-HT_{2A} affinity [1, 5].

Promising potential: Low. No clinical development. Available as a research chemical.

Side-effect profile: Lower nausea burden than escaline and proscaline in anecdotal reports, though still present. No formal data [1].

Overall validation: Low. Similar validation status to escaline; principally PiHKAL data and the Kolaczynska et al. (2022) receptor profiling.

Comparison to methallylescaline: Allylescaline appears more potent by dose range but has a shorter duration (8 to 12 versus 12 to 16 hours). The structural difference is a single methyl branch; the pharmacological consequences of this branch (longer duration, steeper dose-response, potentially altered receptor binding kinetics) are of structure-activity interest.

12.4 Proscaline (4-propoxy-3,5-dimethoxyphenethylamine)

Mechanism: 5-HT_{2A} receptor agonist. Proscaline is the saturated propoxy scaline, sharing the three-carbon 4-alkoxy chain length with methallylescaline but lacking the unsaturation and branching. Oral dose range is 30 to 60 milligrams with a duration of 8 to 12 hours [1, 3].

Novelty: Low. Characterized by Shulgin in PiHKAL.

Effect size: Moderate to high. Approximately six- to seven-fold more potent than mescaline. HTR ED₅₀ = 8.09 micromol/kg, approximately three-fold more potent than mescaline in the Halberstadt et al. (2019) study [6].

Promising potential: Low. No clinical development.

Side-effect profile: Significant body load (nausea, gastrointestinal disturbance) reported in anecdotal data. Higher log P (approximately 1.70) than mescaline or escaline, which is favorable for brain penetration but may contribute to peripheral side effects [4].

Overall validation: Low. PiHKAL data, one receptor profiling study, one HTR study.

Comparison to methallylescaline: Similar dose range and potency relative to mescaline. Proscaline has a shorter duration (8 to 12 versus 12 to 16 hours). The unsaturation and branching of the methallyloxy group in methallylescaline, compared to the saturated propoxy of proscaline, appear to extend the duration of action and steepen the dose-response relationship without dramatically altering the potency, suggesting that these structural features primarily affect pharmacokinetics (distribution, metabolism, receptor dissociation kinetics) rather than receptor binding affinity alone.

12.5 3C-E (4-ethoxy-3,5-dimethoxyamphetamine)

Mechanism: 5-HT_{2A} receptor agonist. 3C-E is the alpha-methyl (amphetamine) homolog of escaline. The alpha-methyl group confers resistance to monoamine oxidase metabolism, typically prolonging duration and increasing potency relative to the corresponding phenethylamine. Oral dose range is 30 to 60 milligrams with a duration of 8 to 12 hours [1, 3].

Novelty: Low to moderate. The 3C-scaline series represents a systematic exploration of the alpha-methyl modification across the scaline scaffold, bridging the scaline and DOx structural classes.

Effect size: Moderate. Similar dose range to the phenethylamine scalines but with marginally increased 5-HT_{2A} selectivity over 5-HT_{2C} (a property of the 3C-scaline series generally) [5].

Promising potential: Low. No clinical development. The 3C-scaline series has received more recent academic attention than the phenethylamine scalines owing to the selectivity profile and the bridging relationship to the DOx series.

Side-effect profile: Expected to include the standard phenethylamine psychedelic adverse effects. The alpha-methyl group may increase cardiovascular stimulation (tachycardia, hypertension) relative to the corresponding phenethylamine.

Overall validation: Low. PiHKAL data, receptor profiling, HTR data. Slightly more receptor selectivity data than the phenethylamine scalines owing to the Kolaczynska et al. (2022) emphasis on the 3C-scaline series.

Comparison to methallylescaline: 3C-E is mechanistically related but structurally distinct (amphetamine versus phenethylamine backbone). The alpha-methyl group confers MAO resistance and marginal 5-HT_{2A} selectivity that methallylescaline lacks. Methallylescaline has a longer duration (12 to 16 versus 8 to 12 hours) without the amphetamine structural feature, suggesting that the prolonged duration derives from the methallyloxy substituent rather than from metabolic resistance.

12.6 Comparator summary

The five comparator compounds and methallylescaline collectively illuminate the structure-activity landscape of the scaline series. **Mescaline** is the reference compound with by far the greatest validation and the only active clinical research program, but its low potency and high dose requirement are experimental limitations. **Escaline** and **proscaline** demonstrate the systematic potency increase with 4-alkoxy chain extension and have comparable in vivo potency to methallylescaline. **Allylescaline** is the closest structural analog, differing by a single methyl branch, and appears to be more potent but shorter-acting. 3C-E bridges the scaline and 3C-scaline series and demonstrates the pharmacological consequences of alpha-methylation.

Methallylescaline occupies a distinctive position in this landscape through its combination of moderate potency (40 to 65 milligram dose range), prolonged duration (12 to 16 hours), and steep dose-response curve. These properties make it a useful structure-activity probe for investigating the effects of 4-alkoxy substituent geometry on pharmacokinetic and pharmacodynamic parameters. It is not, however,

a candidate for clinical development given the complete absence of formal safety, pharmacokinetic, and efficacy data and the availability of mescaline (with its extensive validation record) as the parent compound for clinical psychedelic research.

The principal practical consideration for research use is compound quality verification, given the reliance on specialized research chemical suppliers, and the steep dose-response curve, which requires precise analytical confirmation of potency and careful dose selection in any investigation.

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