

RESEARCH MONOGRAPH . COMPOUND PROFILE

Valproic Acid (Topical Hair)

The histone deacetylase inhibitor valproic acid in topical formulation, studied as a Wnt-pathway-activating agent for androgenetic alopecia in academic dermatology research.

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ABSTRACT

Valproic acid (2-propylpentanoic acid; CAS 99-66-1; molecular formula $C_8H_{16}O_2$; molecular weight 144.21) is a branched short-chain fatty acid in widespread clinical use as the antiepileptic and mood-stabilizer Depakote (sodium valproate; KDC-MN; sodium-valproate). The systemic monograph for sodium valproate is published separately. The topical use of valproic acid for hair regrowth is the subject of this monograph and represents a research-application of the same chemical entity. The pharmacological argument for topical valproic acid in hair is derived from the histone deacetylase inhibitor activity of the compound and the dependence of canonical Wnt/beta-catenin signaling on histone acetylation at Wnt target gene promoters; HDAC inhibition increases Wnt target gene expression and promotes anagen-phase hair follicle activity. Korean academic groups (notably Yonsei University, with the same investigator group developing the PTD-DBM peptide; KDC-MN-1347) have published case-series and small randomized trial data on topical 8.3 percent valproic acid solution for androgenetic alopecia, reporting hair count and density improvements over 24 weeks at frequencies suggestive of meaningful efficacy. The combination with topical PTD-DBM has been studied as a synergistic Wnt-activating regimen with reported additive efficacy in *ex vivo* and *in vivo* models. Topical valproic acid is not FDA-approved for any indication; it is compounded by specialty pharmacies for off-label hair use. The systemic safety considerations of valproic acid (hepatotoxicity, teratogenicity, neural tube defects) are substantially mitigated in topical use owing to the extensive first-pass metabolism if absorbed and the limited cumulative dose, but

pregnancy contraindication should be observed. Reconstitution into a topical solution typically uses ethanol, propylene glycol, and water; the 8.3 percent (50 mg/mL) solution is the most-studied concentration.

1. 1. Compound Identification

Valproic Acid (Topical Hair) is described as hdac inhibitor and topical hair regrowth research compound. The histone deacetylase inhibitor valproic acid in topical formulation, studied as a Wnt-pathway-activating agent for androgenetic alopecia in academic dermatology research.

1.1. 1.1 Class summary

HDAC inhibitor and topical hair regrowth research compound

1.2. 1.2 Subtitle

The histone deacetylase inhibitor valproic acid in topical formulation, studied as a Wnt-pathway-activating agent for androgenetic alopecia in academic dermatology research.

2. Abstract

Valproic acid (2-propylpentanoic acid; CAS 99-66-1; molecular formula C₈H₁₆O₂; molecular weight 144.21) is a branched short-chain fatty acid in widespread clinical use as the antiepileptic and mood-stabilizer Depakote (sodium valproate; KDC-MN; sodium-valproate). The systemic monograph for sodium valproate is published separately. The topical use of valproic acid for hair regrowth is the subject of this monograph and represents a research-application of the same chemical entity. The pharmacological argument for topical valproic acid in hair is derived from the histone deacetylase inhibitor activity of the compound and the dependence of canonical Wnt/beta-catenin signaling on histone acetylation at Wnt target gene promoters; HDAC inhibition increases Wnt target gene expression and promotes anagen-phase hair follicle activity. Korean academic groups (notably Yonsei University, with the same investigator group developing the PTD-DBM peptide; KDC-MN-1347) have published case-series and small randomized trial data on topical 8.3 percent valproic acid solution for androgenetic alopecia, reporting hair count and density improvements over 24 weeks at frequencies suggestive of meaningful efficacy. The combination with topical PTD-DBM has been studied as a synergistic Wnt-activating regimen with reported additive efficacy in ex vivo and in vivo models. Topical valproic acid is not FDA-approved for any indication; it is compounded by specialty pharmacies for off-label hair use. The systemic safety considerations of valproic acid (hepatotoxicity, teratogenicity, neural tube defects) are substantially mitigated in topical use owing to the extensive first-pass metabolism if absorbed and the limited cumulative dose, but pregnancy contraindication should be observed. Reconstitution into a topical solution typically uses ethanol, propylene glycol, and water; the 8.3 percent (50 mg/mL) solution is the most-studied concentration.

3. Mechanism of Action

HDAC inhibition increases histone acetylation at Wnt target gene promoters. Disinhibition of canonical Wnt/beta-catenin signaling drives anagen-phase hair follicle activation. Independent of the GABA-elevation mechanism that drives the systemic anticonvulsant activity.

The mechanistic profile described above represents the consensus position from peer-reviewed literature where available; for compounds with sparse formal characterization, this section reflects vendor-grade reports and structurally-related class pharmacology and should be interpreted with appropriate caution.

4. 4. Pharmacokinetics and Routes of Administration

Pharmacokinetic data are summarized within the abstract for compounds with formal Phase 1 records. Compounds without published human pharmacokinetic studies are noted as such; investigators should treat the absence of data as a research limitation.

5. 5. Reported Research Dose Ranges

Topical 8.3 percent solution applied to the scalp once or twice daily for 24-week courses. Combination protocols add PTD-DBM topical at 100 micrograms per application.

Doses are scaled from clinical use where the compound is approved as a medicine, from Phase 2/3 trials where development advanced, or from rodent dose-response data scaled by allometric assumptions where the compound has no human clinical record. Investigators should treat dose ranges from research-chemical-grade vendors as starting points for their own pharmacokinetic and tolerability characterization rather than validated dosing recommendations.

6. Sourcing and Quality Verification

Investigators should obtain analytical confirmation of identity (mass spectrometry; for peptides, additionally amino acid analysis or N-terminal sequencing) and purity (HPLC area-percent, ideally greater than 95 percent) on every lot. Vendor certificates of analysis vary in quality; third-party analytical confirmation through independent laboratories (e.g., Janoshik Analytical, Anabolic Lab) is the gold standard for research-grade peptides and small molecules.

For compounds with established pharmaceutical-grade marketing in any jurisdiction, sourcing from the marketed product (where legal and accessible) provides the highest quality assurance.

7. 7. Reconstitution and Handling

Peptides should be reconstituted in bacteriostatic water or sterile water for injection in the volume appropriate to the desired concentration; lyophilized peptides should be allowed to come to room temperature before reconstitution to minimize precipitation. Reconstituted peptides should be stored refrigerated and used within the timeframe specified by the manufacturer (typically 14 to 30 days for bacteriostatic water reconstitutions, shorter for sterile water).

Small molecules: storage conditions vary by compound; consult the certificate of analysis for the specific product. Most are stable at room temperature in dry, dark conditions; oxidation-sensitive compounds (e.g., catecholamine precursors) require cool storage and protection from light.

8. 8. Stack Interaction Considerations

Investigators combining this compound with other research substances should consider receptor-level interactions (additive effects at shared targets), enzyme-level interactions (CYP-mediated drug-drug interactions where applicable), and pharmacodynamic interactions (additive sedation, additive serotonergic activity, additive hemodynamic effects).

The stack interaction section in published monographs of well-characterized compounds is necessarily incomplete for any specific combination; investigators should treat novel combinations with elevated caution and titrate gradually.

9. 9. References

1. Jo SJ, et al. Valproic acid promotes human hair growth in in vitro culture model. J Dermatol Sci 2014.
2. Lee SH, et al. Valproic acid induces hair regeneration in murine model and activates alkaline phosphatase activity in human dermal papilla cells. PLoS One 2012.
3. Ryu YC, et al. Combination treatment with PTD-DBM and valproic acid restores androgen-responsive hair regrowth. Br J Dermatol 2021.

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