

RESEARCH MONOGRAPH . COMPOUND PROFILE

2- Arachidonoylglycerol (2-AG)

A monoacylglycerol endocannabinoid; the principal full agonist at CB1 and CB2 receptors and the higher-abundance endocannabinoid in brain.

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COMPOUND CLASS	Endocannabinoid (monoacylglycerol)

ABSTRACT

2-Arachidonoylglycerol (2-AG; CAS 53847-30-6; molecular formula $C_{23}H_{38}O_4$; molecular weight 378.55) is a monoacylglycerol endocannabinoid identified by Mechoulam and Sugiura groups in 1995. The compound is a full agonist at both CB1 and CB2 receptors, with higher concentrations in brain than anandamide. Synthesis is calcium-dependent via diacylglycerol lipase (DAGL); degradation is via monoacylglycerol lipase (MAGL) producing arachidonic acid and glycerol. The on-demand synthesis-degradation kinetics produce phasic retrograde signaling, particularly at synapses where 2-AG mediates short-term and long-term presynaptic depression. Plasma half-life is short (minutes) owing to MAGL-mediated degradation. Used as the canonical full-agonist endocannabinoid in neuroscience research; pharmacological elevation is achieved via MAGL inhibitors (JZL184, KML29). The 2-AG signaling pathway is central to retrograde synaptic communication and is the primary mechanism for endocannabinoid-mediated neuroplasticity.

1. Compound Identification

2-Arachidonoylglycerol (2-AG) is described as endocannabinoid (monoacylglycerol). A monoacylglycerol endocannabinoid; the principal full agonist at CB1 and CB2 receptors and the higher-abundance endocannabinoid in brain.

1.1 Class summary

Endocannabinoid (monoacylglycerol)

1.2 Subtitle

A monoacylglycerol endocannabinoid; the principal full agonist at CB1 and CB2 receptors and the higher-abundance endocannabinoid in brain.

2. Abstract

2-Arachidonoylglycerol (2-AG; CAS 53847-30-6; molecular formula $C_{23}H_{38}O_4$; molecular weight 378.55) is a monoacylglycerol endocannabinoid identified by Mechoulam and Sugiura groups in 1995. The compound is a full agonist at both CB1 and CB2 receptors, with higher concentrations in brain than anandamide. Synthesis is calcium-dependent via diacylglycerol lipase (DAGL); degradation is via monoacylglycerol lipase (MAGL) producing arachidonic acid and glycerol. The on-demand synthesis-degradation kinetics produce phasic retrograde signaling, particularly at synapses where 2-AG mediates short-term and long-term presynaptic depression. Plasma half-life is short (minutes) owing to MAGL-mediated degradation. Used as the canonical full-agonist endocannabinoid in neuroscience research; pharmacological elevation is achieved via MAGL inhibitors (JZL184, KML29). The 2-AG signaling pathway is central to retrograde synaptic communication and is the primary mechanism for endocannabinoid-mediated neuroplasticity.

3. Mechanism of Action

Endogenous full agonist at CB1 and CB2 receptors. Calcium-dependent synthesis via DAGL; degradation via MAGL. Mediates retrograde synaptic signaling.

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. 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. Reported Research Dose Ranges

Research substrate; not used clinically owing to short half-life.

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. 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. 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. References

1. Mechoulam R, et al. Identification of an endogenous 2-monoglyceride, present in canine gut, that binds to cannabinoid receptors. *Biochem Pharmacol* 1995.
2. Sugiura T, et al. 2-Arachidonoylglycerol: a possible endogenous cannabinoid receptor ligand in brain. *Biochem Biophys Res Commun* 1995.
3. Kano M, et al. Endocannabinoid-mediated control of synaptic transmission. *Physiol Rev* 2009.

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