Mechanisms of Action of 51 Cannabis Cannabinoids

Marie Seshat Landry

February 19, 2025

Abstract

Cannabis sativa produces a highly complex array of cannabinoids—over 100 have been isolated to date. This paper focuses on 51 of these cannabinoids, organized by chemical class, and provides a summary of their proposed mechanisms of action. Although many of these compounds interact with the endocannabinoid system via the CB_1 and CB_2 receptors, subtle structural variations yield differences in receptor affinity, signaling pathway engagement, and ultimately, physiological effects. Ongoing research will further clarify these mechanisms.

1 Introduction

Cannabis contains many cannabinoids beyond the well-known Δ^9-tetrahydrocannabinol (THC) and cannabidiol (CBD). In fact, researchers have isolated over 100 phytocannabinoids from Cannabis sativa. Here, we review 51 cannabinoids—grouped into several classes—and summarize their current proposed mechanisms of action.

2 Cannabichromenes

2.1 1. Cannabichromene (CBC)

CBC is non-psychoactive. It is thought to modulate inflammation and pain by interacting with transient receptor potential (TRP) channels such as TRPV1 and TRPA1, and it may exert weak effects at cannabinoid receptors.

2.2 2. Cannabichromenic acid (CBCA)

CBCA is the acidic precursor to CBC. It is non-intoxicating until decarboxylated (by heat) to CBC and may itself possess anti-inflammatory properties.

2.3 3. Cannabichromevarin (CBCV)

CBCV is the varin homolog of CBC (with a shorter side chain). Its mechanism is presumed similar to CBC, though with possible differences in potency at TRP channels.

2.4 4. Cannabichromevarinic acid (CBCVA)

CBCVA is the acidic form of CBCV. Like other cannabinoid acids, it is inactive until decarboxylated and is thought to share similar anti-inflammatory actions with its neutral form.

3 Cannabicyclols

3.1 5. Cannabicyclol (CBL)

CBL is a non-psychoactive degradation product of THC. It is believed to have antioxidant and anti-inflammatory properties, although its receptor affinity is low.

3.2 6. Cannabicyclolic acid (CBLA)

CBLA is the acidic precursor of CBL and converts into CBL upon decarboxylation. Its effects are presumed to mirror those of CBL.

3.3 7. Cannabicyclovarin (CBLV)

CBLV, the varin homolog of CBL, likely exhibits similar antioxidant and anti-inflammatory properties with a slightly altered potency.

4 Cannabidiols

4.1 8. Cannabidiol (CBD)

CBD acts as a negative allosteric modulator at CB_1 receptors and interacts with non-cannabinoid targets such as TRPV1, 5-HT_{1A}, and PPARγ. These actions underlie its anxiolytic, anti-inflammatory, and neuroprotective effects.

4.2 9. Cannabidiol monomethylether (CBDM)

A methylated derivative of CBD, CBDM appears to modulate CB_1 receptor activity similarly to CBD, with comparable anti-inflammatory properties.

4.3 10. Cannabidiolic acid (CBDA)

CBDA is the acidic precursor to CBD. It is non-psychoactive until decarboxylation and is reported to have anti-emetic and anti-inflammatory properties.

4.4 11. Cannabidiorcol (CBD-C1)

A minor CBD derivative with a modified side chain, CBD-C1 is presumed to share the indirect receptor modulation of CBD.

4.5 12. Cannabidivarin (CBDV)

CBDV is the varin homolog of CBD. It is non-psychoactive and has shown promise in preliminary studies for anticonvulsant and anti-inflammatory effects.

4.6 13. Cannabidivarinic acid (CBDVA)

CBDVA is the acidic precursor to CBDV and, upon decarboxylation, yields CBDV. Its pharmacology is expected to parallel that of CBDV.

5 Cannabielsoins

5.1 14. Cannabielsoin (CBE)

CBE is a minor cannabinoid that exhibits low-affinity binding to cannabinoid receptors; it may contribute to sedative effects when present alongside other cannabinoids.

5.2 15. Cannabielsoin acid A (CBEA-A)

As the acidic form of CBE, CBEA-A converts to CBE on decarboxylation and is under investigation for potential anti-inflammatory actions.

5.3 16. Cannabielsoin acid B (CBEA-B)

Similar to CBEA-A, CBEA-B is an acidic variant that, after decarboxylation, produces CBE and may help modulate inflammatory responses.

6 Cannabigerols

6.1 17. Cannabigerol (CBG)

CBG is a precursor to THC, CBD, and CBC. It acts as a partial agonist at both CB_1 and CB_2 receptors and may also inhibit endocannabinoid reuptake, offering neuroprotective, anti-inflammatory, and antibacterial benefits.

6.2 18. Cannabigerol monomethylether (CBGM)

A methylated derivative of CBG, CBGM is presumed to have similar receptor interactions and therapeutic potential as CBG.

6.3 19. Cannabigerolic acid (CBGA)

CBGA is the precursor molecule for many cannabinoids. While it has minimal direct receptor activity, it may exhibit anti-inflammatory properties.

6.4 20. Cannabigerolic acid monomethylether (CBGAM)

CBGAM is the methylated acidic form of CBGA; decarboxylation yields active CBG.

6.5 21. Cannabigerovarin (CBGV)

CBGV is the varin homolog of CBG with a shortened side chain, which may slightly alter its receptor binding and potency.

6.6 22. Cannabigerovarinic acid (CBGVA)

CBGVA is the acidic precursor to CBGV and converts to CBGV upon decarboxylation.

7 Cannabinols and Cannabinodiols

7.1 23. Cannabinol (CBN)

CBN is a mildly psychoactive cannabinoid produced by the degradation of THC. It exhibits weak agonism at CB_1 and CB_2 receptors and is commonly associated with sedation.

7.2 24. Cannabinol methyl ether (CBNM)

CBNM is a methylated form of CBN that may modify its receptor affinity slightly relative to CBN.

7.3 25. Cannabinol-C2 (CBN-C2)

An isomer of CBN with a shortened alkyl chain, CBN-C2's receptor interactions are still being elucidated.

7.4 26. Cannabinol-C4 (CBN-C4)

Another homolog of CBN with an extended alkyl chain, CBN-C4 may affect its sedative potency.

7.5 27. Cannabinolic acid (CBNA)

CBNA is the acidic precursor to CBN; decarboxylation converts it to CBN, thereby imparting similar sedative effects.

7.6 28. Cannabiorcool (CBN-C1)

Also known as cannabiorcool, CBN-C1 is a variant of CBN with subtle structural differences that may affect its low-level receptor activity.

7.7 29. Cannabinodiol (CBND)

CBND is a lesser-studied cannabinoid that appears to act as a partial agonist at cannabinoid receptors, contributing modest sedative or anti-inflammatory actions.

7.8 30. Cannabinodivarin (CBN-DV)

CBN-DV is the varin homolog of CBND, expected to show similar activity with slight potency differences due to its shorter side chain.

8 Cannabitriols

8.1 31. Cannabitriol (CBT)

CBT is a minor cannabinoid with limited psychoactivity; it may help modulate the overall receptor signaling when combined with other cannabinoids.

8.2 32. Cannabitriolvarin (CBTV)

CBTV, the varin homolog of CBT, is presumed to have similar modulatory properties with potentially different potency.

8.3 33. 10-Ethoxy-9-hydroxy-δ6a-tetrahydrocannabinol

This derivative, with an ethoxy and a hydroxy substitution, is thought to modulate CB1 receptor activity; its exact effects require further study.

8.4 34. 8,9-Dihydroxy-δ6a-tetrahydrocannabinol

This dihydroxy derivative likely interacts with cannabinoid receptors and may influence inflammatory signaling.

8.5 35. Trihydroxy-δ9-tetrahydrocannabinol (triOH-THC)

TriOH-THC is proposed to have a unique CB1 receptor signaling profile that can affect both psychoactive and anti-inflammatory pathways.

9 Delta-8-Tetrahydrocannabinols

9.1 36. Delta-8-tetrahydrocannabinol (8-THC)

An isomer of 9-THC with the double bond on the eighth carbon, 8-THC binds to CB1 and CB2 receptors with slightly lower affinity, yielding milder psychoactive effects.

9.2 37. Delta-8-tetrahydrocannabinolic acid (8-THCA)

The acidic, non-psychoactive precursor of 8-THC; decarboxylation converts it to 8-THC and it may also have inherent anti-inflammatory properties.

10 Delta-9-Tetrahydrocannabinols

10.1 38. Delta-9-tetrahydrocannabinol (9-THC)

The primary psychoactive constituent of cannabis, 9-THC acts as a partial agonist at CB1 receptors (in the central nervous system) and CB2 receptors (peripherally), affecting pain, mood, and memory.

10.2 39. Delta-9-tetrahydrocannabinol-C4 (THC-C4)

A homolog of 9-THC with a modified alkyl side chain that may alter its binding affinity and potency.

10.3 40. Delta-9-tetrahydrocannabinolic acid A (THCA-A)

The non-psychoactive acidic precursor to 9-THC, THCA-A converts to 9-THC upon heating and may possess its own anti-inflammatory effects.

10.4 41. Delta-9-tetrahydrocannabinolic acid B (THCA-B)

Another variant of THCA that, upon decarboxylation, produces 9-THC; subtle differences in its structure may affect its pharmacokinetics.

10.5 42. Delta-9-tetrahydrocannabinolic acid-C4 (THCA-C4)

An acidic variant with a modified side chain; decarboxylation yields 9-THC with possibly altered potency.

10.6 43. Delta-9-tetrahydrocannabiorcol (THC-C1)

A degradation product or alternative isomer of 9-THC with reduced psychoactivity due to its modified receptor binding profile.

10.7 44. Delta-9-tetrahydrocannabivarin (THCV)

THCV is the varin homolog of 9-THC. It exhibits dose-dependent effects: at low doses, it may act as a CB1 antagonist (possibly suppressing appetite), and at higher doses as a partial agonist.

10.8 45. Delta-9-tetrahydrocannabivarinic acid (THCVA)

The acidic precursor to THCV, THCVA is non-psychoactive until decarboxylated, and is believed to share THCV's appetite-suppressing and anti-inflammatory properties.

11 Miscellaneous Cannabinoids

11.1 46. 10-Oxo-δ6a-tetrahydrocannabinol (OTHC)

OTHC features an oxo group substitution and is believed to exhibit moderate CB1 receptor activity.

11.2 47. Cannabichromanon (CBCF)

A derivative of CBC, CBCF is less studied but may possess anti-inflammatory effects through modulation of TRP channels.

11.3 48. Cannabifuran (CBF)

CBF is a trace cannabinoid thought to arise from thermal degradation, with low direct activity at cannabinoid receptors and possible antioxidant properties.

11.4 49. Dehydrocannabifuran (DCBF)

DCBF is an oxidized form of CBF that exhibits minimal receptor activity but might contribute to the overall entourage effect.

11.5 50. Delta-9-cis-tetrahydrocannabinol (cis-THC)

cis-THC is an isomer of 9-THC with a different three-dimensional configuration, resulting in lower psychoactivity and altered receptor kinetics.

11.6 51. Tryhydroxy-δ9-tetrahydrocannabinol (triOH-THC)

TriOH-THC (when considered as distinct from the triOH-THC listed among cannabitriols) is believed to modulate cannabinoid receptor activity with a unique signaling profile that may balance psychoactive and anti-inflammatory effects.

12 Conclusion

The 51 cannabinoids presented here demonstrate the vast chemical diversity of Cannabis sativa. Although many share common pathways—most notably interactions with the CB_1 and CB_2 receptors—the subtle structural differences lead to a range of pharmacological effects. This diversity underpins the so-called entourage effect, where multiple cannabinoids and terpenes work synergistically. Ongoing research continues to elucidate the precise mechanisms of action of these compounds, offering promise for the development of targeted therapies with improved efficacy and safety.

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