Multi Pathway Treatment Rationale

Scientific framework and formulation philosophy

PLANTOGRAM • JANUARY 2026

Executive summary

PlantOgram's Treatment Stack approach positions cannabinoids as the foundational component of a broader, personalised treatment strategy. The rationale considers the endocannabinoid system within a wider network of neurological, immune, endocrine, metabolic and inflammatory pathways.

The proposed framework combines cannabinoid therapy with carefully selected complementary active ingredients and, where appropriate, lifestyle, behavioural and conventional interventions. Ingredient selection is guided by scientific evidence, pharmacological compatibility, formulation stability, safety and the intended clinical indication.

The central proposition is that coordinated modulation of complementary pathways may offer a more integrated approach to complex clinical presentations. This document sets out the scientific and formulation rationale; potential benefits and synergy remain dependent on the specific combination and supporting clinical evidence.

© PlantOgram January 2026. All rights reserved.

Pharmaceutical ingredients and formulation strategy

The endocannabinoid system (ECS) functions as a broad homeostatic regulatory network rather than an isolated cannabinoid receptor system. While cannabinoids primarily interact with the CB1 and CB2 receptors, the ECS also communicates extensively with a wider network of molecular targets involved in **pain modulation, inflammation, immune regulation, mood, sleep, cognition and neuroprotection**. These represent the primary therapeutic domains targeted within our Treatment Stack. Relevant pathways include TRPV1, PPARs, 5-HT (serotonin) receptors, GPR55, adenosine, glycine receptors and numerous inflammatory signalling pathways.

Given this complex biology, we believe there is a strong scientific rationale for developing formulations that combine cannabinoids with carefully selected non-cannabinoid active pharmaceutical ingredients (APIs). Certain complementary APIs may exert more direct or more potent effects on specific biological pathways than cannabinoids alone, while others may work synergistically to enhance therapeutic activity, broaden the overall mechanism of action or improve tolerability.

Rather than viewing cannabinoids as standalone therapeutic agents, we consider them the foundational component of a broader multi-pathway treatment strategy. By targeting multiple biological systems that contribute to disease simultaneously, combination formulations have the potential to provide more comprehensive therapeutic support than any single active ingredient alone. This approach is consistent with modern pharmacology, where multi-mechanistic therapies are increasingly employed to address complex chronic conditions involving multiple interconnected physiological pathways.

Our selection of additional APIs is guided by the available scientific evidence, pharmacological compatibility, formulation stability, safety profile and the intended clinical indication. Each formulation is designed using an evidence-informed rationale to ensure that the selected APIs complement—not replace—the therapeutic role of cannabinoids. Cannabinoids remain the core therapeutic layer of our formulations, with additional APIs incorporated to target complementary biological pathways and support a broader, more integrated therapeutic approach.

This philosophy reflects our **Treatment Stack** approach, in which cannabinoids provide the foundational therapeutic layer while carefully selected complementary APIs target additional biological pathways relevant to the patient's clinical presentation.

Multi pathway approach to endocannabinoid system modulation

Modern understanding of the endocannabinoid system suggests that clinical outcomes are unlikely to be determined by activation of a single receptor or signalling pathway. Instead, the ECS functions within the broader endocannabinoidome—an integrated regulatory network involving neurological, immune, endocrine, metabolic and inflammatory pathways.

Accordingly, therapeutic strategies should aim to support multiple components of this regulatory network rather than relying solely on direct cannabinoid receptor activation.

This systems-based philosophy recognises that restoration of physiological homeostasis often requires simultaneous modulation of several interconnected biological processes.

© PlantOgram January 2026. All rights reserved.

A multi pathway therapeutic framework

An integrated approach to ECS modulation may include combinations of interventions that influence different aspects of physiological regulation, including:

- Cannabinoids (e.g. THC, CBD and minor cannabinoids)
- Endocannabinoid-like compounds (e.g. PEA)
- Terpenes and other bioactive plant constituents
- Lifestyle interventions, including exercise, nutrition and sleep optimisation
- Stress management and behavioural therapies
- Management of metabolic and inflammatory drivers
- Optimisation of gut health and the gut–brain axis
- Conventional pharmacological therapies where clinically indicated

Rather than acting independently, these interventions may complement one another by influencing multiple signalling pathways involved in maintaining homeostasis.

Moving beyond single target pharmacology

Traditional pharmacology has often focused on highly selective drugs designed to act on a single receptor or molecular target.

In contrast, growing evidence suggests that many chronic conditions—including chronic pain, anxiety disorders, neuroinflammatory diseases and metabolic disorders—arise from disturbances across multiple interconnected regulatory systems.

This has led to increasing interest in multi-target (polypharmacological) approaches, where therapeutic benefit may be achieved through coordinated modulation of several biological pathways rather than maximal stimulation of a single receptor.

Clinical interpretation

A systems-based understanding of the ECS encourages clinicians to view cannabinoid therapy as one component of a broader therapeutic strategy, rather than a stand-alone intervention.

Treatment planning should consider the patient's neurological, immune, endocrine, metabolic and psychosocial health, together with lifestyle factors that influence endogenous ECS function.

This approach aligns with contemporary concepts of personalised medicine, recognising that sustainable clinical outcomes are more likely to be achieved by supporting physiological regulation across multiple interacting systems than by targeting individual receptors in isolation.

The goal of modern ECS-based care is not simply to activate cannabinoid receptors. It is to restore physiological balance by modulating multiple interconnected pathways that collectively regulate neurological, immune, endocrine and metabolic homeostasis.

© PlantOgram January 2026. All rights reserved.