

# How CBD's Can Effectively Treat Bipolar Disorder Symptoms and Manic Episodes

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As medical marijuana becomes legal in more states across the country, there's been a spike in public interest to see whether cannabis can effectively treat mood disorders such as anxiety, depression, and psychosis that are commonly associated with bipolar disorder. Unfortunately, there are conflicts in scientific consensus for both supporting and opposing views of cannabis use for the treatment of mood disorders. Some **studies** have linked marijuana use with early-onset psychosis, while others **suggest** there are anti-psychotic **benefits** of cannabis in bipolar disorder patients.

It has been **shown** that cannabidiol has anti-psychotic properties, particularly anxiolytic benefits in humans. CBD possesses **hypnotic**, **anti-convulsive**, **neuroprotective**, and **anti-stress** benefits. Based on this evidence, research studies have begun to investigate the anxiolytic and antipsychotic benefits of CBD, which may be useful in effectively treating bipolar disorder.

### **The Neurochemistry of Bipolar Disorder and Cannabinoids**

A dysfunctional endocannabinoid system (EC) has been **implicated** in mood disorders such as bipolar disorder, and modulation of the EC system by exogenous cannabinoids such as cannabidiol, tetrahydrocannabinol and anandamide can potentially treat bipolar disorder symptoms by exerting antipsychotic, anticonvulsant, and anxiolytic effects. Research studies have **demonstrated** the

antipsychotic mechanism of action of cannabidiol. Administration of cannabidiol may indirectly influence endogenous anandamide signaling by inhibiting intracellular metabolism by fatty acid amide hydrolase (FAAH). Elevated levels of anandamide can attenuate mood disturbances and treat bipolar disorder symptoms.

Research studies have **pointed** out the role of the dopamine (DA) system in mood disorders, including bipolar disorder. The key role of the mesoaccumbens DA system has been proven in the reward pathway (neural circuitry) and motivational behaviors. Experimental studies being conducted to **investigate** the efficacy of anti-psychotic drugs are based on the hypothesis of dopamine, glutamate, and other neurotransmitters. These drugs **exhibit** antagonism to dopamine D2 receptors which is commonly **linked** with hyperprolactinemia due to action of anterior-pituitary mammotrophic cells. These drugs are called typical anti-psychotics (Clozapine) which cause Parkinson-like symptoms, while atypical anti-psychotics are also **effective** without causing serious adverse events, which can be **confirmed** by a catalepsy test.

Atypical anti-psychotic drugs **inhibit** hyperlocomotion and the stereotype that results due to dopamine antagonists at lower doses. Effective anti-psychotic action requires the **blocking** of D2 receptors as well as glutamatergic N-methyl-D-aspartate (NMDA) receptors.

A comparative study **assessed** the anti-psychotic efficacy of haloperidol (an anti-psychotic drug) and cannabidiol (CBD) found that CBD inhibited hyperlocomotion without causing catalepsy, even at higher doses; while haloperidol caused prolactin disturbances. The pharmacological action of CBD mimics clozapine. Another neurochemical experimental study **reported** similar results. These results **prove that** CBD acts like an atypical anti-psychotic drug without causing serious and long-term side effects.

**One study** investigated the anti-depressive action of CBD in an experimental animal model (AKA olfactory bulbectomy mouse model) of depression (OBX). The results suggest that cannabidiol exerted rapid and sustained antidepressant action in the depressed animals by significantly augmenting cortical serotonin and glutamate levels in a dose-dependent manner. Receptor studies have shown that the action was exerted via a 5-HT1A receptor-dependent mechanism, which represents novel drug functionality. After prolonged CBD administration notable adaptive changes were documented in pre and post-synaptic 5-HT1A receptor action.

CBD can **inhibit** glutamate toxicity and offers anti-convulsant and mood-stabilizing benefits, which are **similar** to the benefits of conventional therapeutic drugs such as valproate and lithium that are indicated for bipolar disorder. In open-label human clinical trials, CBD has significantly **reduced** psychotic symptoms and normalized motor functions in psychiatric patients. These benefits can be

useful to treat manic episodes in bipolar disorder patients.

Cannabinoids influence mood perceptions and exert anti-depressant action by acting as an agonist in central CB1 receptors. 5-HT is believed to be responsible for mood control and implicated in antidepressant-like actions. Research **evidences** have pointed out the action of CBD in the serotonin (5-HT) system and related neurons. Administration of CB1R agonists such as phytocannabinoids into the ventromedial prefrontal cortex of the brain has resulted in enhanced 5-HT neuronal activity and CB1R-dependent antidepressant-like effects in the experimental animals. This study clearly shows the dose-dependent antidepressant benefit of CBD, which can be particularly useful for the treatment of mood disorders, including bipolar disorder.

### **The Neuroprotective, Anti-psychotic, and Anxiolytic Benefits of CBD**

Recent **studies** have found that CBD can **provide** neuro-protection in acute and chronic neurodegenerative disorders. **Published studies** have **shown** that oxidative stress and free radical generation may play an **important role** in the pathogenesis of bipolar disorder. **In vitro studies** and **in vivo** studies have confirmed that CBD possess neuroprotective properties.

CBD can **exert** anti-oxidative (scavenging free radicals) and neuroprotective benefits in humans. In this study, CBD was found to be an inhibitor of oxidative damage (free radicals) and increased BDNF (brain-derived neurotrophic factor) levels in the brain regions. BDNF is vital for synaptic plasticity and hence for neuro-protection. Similar results were **reported** by another study. By mitigating the oxidative stress in the brain, cannabidiol can treat and prevent the symptoms of bipolar disorder.

Not only research studies, but even anecdotal, subjective reports and **case studies** have shown anti-psychotic benefits of cannabis. Most of the bipolar disorder patients studied use cannabis either to treat the symptoms or to reduce the side effects of conventional therapeutic drugs, such as lithium. Although this evidence looks promising, stringent laws and anti-drug campaigns have made it impossible to conduct large-scale, controlled studies to fully explore the anti-psychotic benefits of marijuana to treat bipolar disorder.

One **prospective study** that collected mood data of bipolar disorder patients over two years has reported marijuana use was associated with complete abstinence of substance abuse in bipolar disorder patients. Although cannabis did not reduce total number of days of abnormal mood, marijuana increased the number of hypomanic days and decreased the number of depressed days in bipolar disorder patients.

Bipolar disorder patients often report subjective mood improvement after marijuana use. A small research study that enrolled 43 bipolar disorder patients **reported** remarkable reduction in total mood disturbance in marijuana smokers, while a slight worsening of symptoms was observed in pure marijuana users. Most of the patients who reported mood improvements were diagnosed with worse mood ratings before marijuana use. This empirical evidence can support the anecdotal claims that cannabis can treat mood-related symptoms.

One open-label **clinical trial study** that enrolled a 19-year old schizophrenic woman who suffered serious adverse events after standard anti-psychotic therapeutic drugs use has compared the use of CBD oil followed by interruption of treatment and placebo administration. Finally, the patient was treated with increasing doses of haloperidol. The treatment benefits were assessed by the Brief Psychiatric Rating Scale (BPRS). Significant improvement in mood symptoms was observed during the CBD oil treatment period, and found to be worsening during treatment the interruption period and placebo treatment. These reported improvements were not further improved by haloperidol treatment. This evidence clearly shows that bipolar disorder symptoms are poorly controlled by conventional therapies, while marijuana is a reliable option to treat mood disorders, including bipolar disorder. By employing the Ugvalg for Kliniske Undersgelses (UKU) scale, the study observed no serious side effects after marijuana use.

In a double-blind, placebo-controlled study, CBD was **equally effective** in treating anxiety, compared with diazepam and ipsapirone, in humans. The study results were concordant with another clinical trial study as **evidenced** by cerebral activity pattern.

This evidence is further strengthened by other independent academic studies that **indicated** cannabidiol as an effective and safer anti-psychotic treatment option for bipolar disorder. **One study** has reported that CBD has a similar pharmacological profile as like mood stabilizing drugs, albeit without serious side effects.

Bipolar disorder is **characterized** by impaired learning abilities and verbal fluency. One study **reported** that cannabis treatment can significantly improve learning abilities and verbal fluency in bipolar disorder patients. However, comparatively slighter improvements were observed in patients who were treated with conventional therapies such as antidepressants and lithium. Cannabis therapy generally causes fewer but temporary side effects, whereas conventional therapy can cause prolonged and serious adverse events.

In addition to human clinical trial evidence, let's have a look at the pre-clinical studies that demonstrate the benefits of cannabis on symptoms of bipolar disorder. CBD's anti-psychotic effect has been **demonstrated** in several experimental studies based on encouraging results in

conditioned emotional response, the Vogel conflict test, and the elevated plus-maze studies.

Considering this evidence, we can clearly see the anti-psychotic benefits of marijuana for treatment of bipolar disorders. Based on all of this irrefutable scientific proof, large-scale, prospective, controlled clinical studies should be conducted by renowned academic institutions to provide sound evidence to support the use of CDB to treat bipolar disorder, and therefore benefit mankind.

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Prakash is a biomedical researcher and medical writer by profession with extensive experience in pharmacology, molecular oncology, stem cells science and clinical trials. He authored medical textbooks and several research publications in peer-reviewed medical journals. Prakash is an ardent advocate of medical marijuana, wants to educate the science of medical marijuana to general public.

