

Cannabidiol as a Potential Treatment for Patients with Chronic Anxiety Disorders

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Anxiety disorders are common and debilitating chronic conditions with a high reported lifetime prevalence of approximately 32%.¹ Despite a multitude of pharmacological treatments currently available for anxiety disorders (e.g., serotonin–norepinephrine reuptake inhibitors, benzodiazepines, etc.), adverse effects, limited response rates, and residual symptoms are associated with these drug classes.²⁻⁵ It is, therefore, evident that a substantial burden remains on individuals with anxiety disorders who cannot tolerate or do not benefit from current pharmacological options. This need for improved therapies highlights the anticipation surrounding cannabis as a potential anxiolytic pharmaceutical treatment.

Many Canadians purposefully target their anxiety by using medical cannabis.^{6,7} In fact, a survey of Canadian cannabis consumers discovered that 63% of individuals sampled substituted prescription medications, such as benzodiazepines and antidepressants, for cannabis.⁷ Despite this, arguments against the usage of medical cannabis for anxiety have been made, stating that a small positive correlation exists between anxiety disorders and cannabis use.⁸ It is important to note, however, that the cannabis usage in these studies included $\Delta 9$ -tetrahydrocannabinol (THC), the psychoactive constituent of cannabis. It should also be noted that certain individuals with anxiety and depressive symptoms achieve relief following low frequency cannabis use, yet symptoms were exacerbated following prolonged use.^{8,9} Although the relationship between anxiety and cannabis is clearly complex and multifactorial, other side effects of cannabis use have been more consistently reported, including transient impairments in psychomotor and cognitive function, which impact working memory, attention, and some executive functions.¹⁰

Existing evidence from preclinical, clinical, and epidemiological studies involving the acute dosing of cannabidiol (CBD)—the phytocannabinoid constituent of *Cannabis sativa* lacking the psychoactive properties of THC—supports many Canadians' claims of CBD's anxiolytic properties against generalized anxiety disorder, panic disorder, social anxiety disorder, obsessive–compulsive disorder, and post-traumatic stress disorder (PTSD).¹¹ Regarding anxiety specifically, a systematic review by Walsh et al. included eight cross-sectional studies that reported anxiolytic effects from CBD.¹¹ It is also notable that one additional cross-sectional study reported a return of anxiety upon the cessation of cannabis use.¹² Further studies involving more long-term dosing of CBD must still be investigated, however, if CBD is to be accepted as a formal treatment for chronic anxiety disorders.

The use of cannabis for non-medical purposes in Canada was formally legalized on October 17th, 2018; this law is likely to promote further and much needed research into the benefits and harms of cannabis.¹³ For instance, insufficient evidence exists for the use of

CBD on patients suffering from PTSD.¹⁴ Studies have only begun to elucidate the neural circuit mechanisms behind the effects of CBD on anxiety and learned fear. In addition, as decades of psychiatry research have shown a large co-occurrence between anxiety-related and substance use disorders, many scientists and physicians have suggested researching the possibility of using CBD to treat both conditions concurrently.¹⁵ Lastly, ongoing research seeks to determine how CBD should be administered, either as an isolated compound or in combination with other closely related molecules and metabolites. Researchers have shown that certain active chemical compounds found in cannabis have increased effects when combined with nonactive chemical groups or metabolites.¹⁶ This synergistic phenomenon is titled the “entourage effect.” Therefore, precise formulations of both active and nonactive chemical metabolites must be combined and tested to optimize the anxiolytic properties of CBD.

Anxiety disorders are one of the most prevalent mental disorders worldwide. The high prevalence and morbidity of anxiety disorders as well as its accompanying economic, healthcare, and physical burdens strongly support the necessity for ongoing and future research.¹⁷ The limited response rates of current anxiolytic pharmacological options combined with the recent legalization of non-medical cannabis magnify the excitement surrounding CBD as a potential anxiolytic. However, with competing evidence that cannabis has both anxiogenic and anxiolytic properties, more research is necessary to elucidate the optimum dosing, frequency, and combination of active and nonactive cannabis metabolites in order to maximize its anxiolytic properties while minimizing its potential adverse effects.

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