**Emerging pharmacotherapy for the treatment of cannabis use disorder**

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**ABSTRACT**

**Introduction**

About one-fifth of cannabis users, the most commonly used illicit substance, have cannabis use disorder (CUD). Psychiatric disorders and suicide are more common in these patients, and the disability-adjusted life years were reported to be 0.69 million. Pharmacotherapy for CUD is an unmet public health need, as current evidence-based therapies have limited efficacy.

**Areas covered**

After explaining the pathophysiology of CUD, the effects of emerging pharmacological interventions in its treatment obtained from randomized controlled trials were reviewed in light of mechanisms of action. Superiority over control of cannabidiol, gabapentin, galantamine, nabilone plus zolpidem, nabiximols, naltrexone, PF-04457845, quetiapine, varenicline, and topiramate were observed through the cannabinoid, glutamatergic, γ-aminobutyric acidergic, serotonergic, noradrenergic, dopaminergic, opioidergic, and cholinergic systems. All medications were reported to be safe and tolerable.

**Expert opinion**

Adding pharmacotherapy to psychotherapy is the optimal treatment for CUD on a case-by-case basis. Drug development to add to psychotherapy is the main path, but time and cost suggest repurposing and repositioning existing drugs. Considering sample size, follow-up, and effect size, further studies using objective tools are necessary. The future of CUD treatment is promising.

KEYWORDS:

* [Adverse drug reaction](https://www.tandfonline.com/keyword/Adverse+drug+reaction)
* [clinical trial](https://www.tandfonline.com/keyword/clinical+trial)
* [combination drug therapy](https://www.tandfonline.com/keyword/combination+drug+therapy)
* [drug approval process](https://www.tandfonline.com/keyword/drug+approval+process)
* [marijuana](https://www.tandfonline.com/keyword/marijuana)
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* [psychiatric disorder](https://www.tandfonline.com/keyword/psychiatric+disorder)
* [state-of-the-art review](https://www.tandfonline.com/keyword/state-of-the-art+review)

**Article highlights**

* The increasing prevalence, comorbidities, and burden of cannabis use disorder necessitate novel therapeutic approaches considering current treatment limitations.
* Drug development as add-ons to psychotherapy is the main path, but time and cost suggest a shortcut called repurposing and repositioning drugs.
* Ten pharmacological interventions based on clinical trials were presented by explaining the pathophysiology of the disorder.
* Tetrahydrocannabinol targets endocannabinoid, glutamatergic, γ-aminobutyric acidergic, serotonergic, noradrenergic, dopaminergic, opioidergic, and cholinergic systems.
* Drugs affecting the cholinergic system may improve cognitive dysfunction, treatment of which was proposed for cannabis addiction.

**Declaration of interest**

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

**Author contributions**

A Shamabadi: Conceptualization, Project administration, Supervision, Data curation, Writing – original draft, Visualization, Writing – review and editing; R.A Bahri: Data curation, Writing – original draft; H Karimi.: Data curation, Writing – original draft, Visualization; E Heidari: Writing – original draft; and S Akhondzadeh: Conceptualization, Project administration, Supervision, Data curation. All authors approved the final version of the manuscript and had accountability for all work aspects.