# Cannabis potential effects to prevent or attenuate SARS-COV2 contagion

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## Abstract

Medical cannabis has gained an exponential interest in recent years. Therapeutic targets have been broadened from specific applications over pain control, chemotherapy side effects, treatment-resistant epilepsies and multiple sclerosis, among others. Several in vitro and animal studies, along with few human controlled studies, suggest cannabinoids have a potential therapeutic role over medical conditions comporting inflammatory mechanisms. Given the tremendous world-wide impact of the COVID-19 pandemic, research efforts are converging towards the use of cannabinoids to attenuate severe or fatal forms of the disease. The present survey aims to explore possible correlations between cannabis use, either recreational or medical, over the presence of SARS-COV-2 contagion, along with the symptom's severity. 4026 surveys were collected via electronic form. Results suggest a relation between any type of cannabis use and a lower risk of SARS-COV-2 contagion (p=0,004; OR=0,689, IC95% 0,534-0,889). Despite several methodological limitations, the present survey steps up the urge to expand our understanding on cannabinoids potential use on human controlled studies, that can better arm us in the fight against the current COVID-19 pandemic and other infectious diseases.

## Introduction

Cannabinoids have been regarded as a possible therapeutic clue for the SARS-COV-2 pandemic. Even though, till date there is limited evidence towards a specific therapeutic role for cannabinoids on viral infections [1]. Cannabinoids anti-inflammatory mechanisms have been only explored during the recent years, mainly tested in vitro, in vivo, animals and computational settings[2,3]. Comparatively, human controlled studies are still scarce[4].

THC and CBD anti-inflammatory effects are highly suspected given their therapeutic potential use in diverse conditions having a physiopathological core around inflammation and immune cells[1,5–7]. Based on available literature, it is reasonable to think that cannabinoids may play multiple therapeutic roles in front of SARS-COV2 contagion, as well as on other viral infections. These perspectives embrace a potential preventive role through replication inhibition mechanisms, and a direct therapeutic role linked to a possible modulation of angiotensin-converting enzyme 2 (ACE2) [8–10] and cytokines cascades [11], both related to the most severe and fatal SARS-COV-2 issues [3].

The present survey aims to explore possible correlations between cannabis use, either recreational or medical, over the presence of SARS-COV-2 contagion, along with the symptom's severity.

## Methods

*Study design and population*

We carried out a cross-sectional study through a self-administered online survey among a non-probabilistic sample in Colombia. The survey remained online from 1st to 30th of November, 2020.

*Sample size calculation and sampling strategy*

We calculated sample size with an expected frequency of 50%, an acceptable error of 5%, and a design effect of 1 for a population survey, with a resulting sample size of 384 participants.

Sampling was obtained with a virtual snowball method, by posting the survey in social media groups and contacts (WhatsApp©, Telegram®, Facebook®) asking to answer and share the link with multiple contacts.

We did not use any imputation method after trying to collect the information. After giving their agreement, participants were allowed to answer the survey: *1. Age, 2. "Have you been diagnosed with COVID-19?", 3. "If you have had COVID-19, what was the intensity of your symptoms?", 4. "Has any of the people you live with, or with whom you have very close contact, been infected with COVID-19?", 5. "Please indicate the number of people close to you who have been infected", 5."Do you drink or consume any type of cannabis?", 6. "If you answered 'yes', please indicate which type (recreational, sativa oil, indica oil, hemp mother tincture, topic or uncontrolled preparations)", 7. "How frequently do you use these products? (daily, occasionally)".*

After completing the scheduled data collection, a visual inspection was conducted to verify the database completion. A semi-automated procedure was applied to homogenize outputs. Statistical analyses were conducted on IBM SPSS Statistics for Mac, Version 26.0. Data distribution was checked to verify sphericity, skewness and kurtosis. Parametric analysis (univariate and bivariate analysis) through Chi-square test and risk estimation were conducted.

*Ethical considerations*

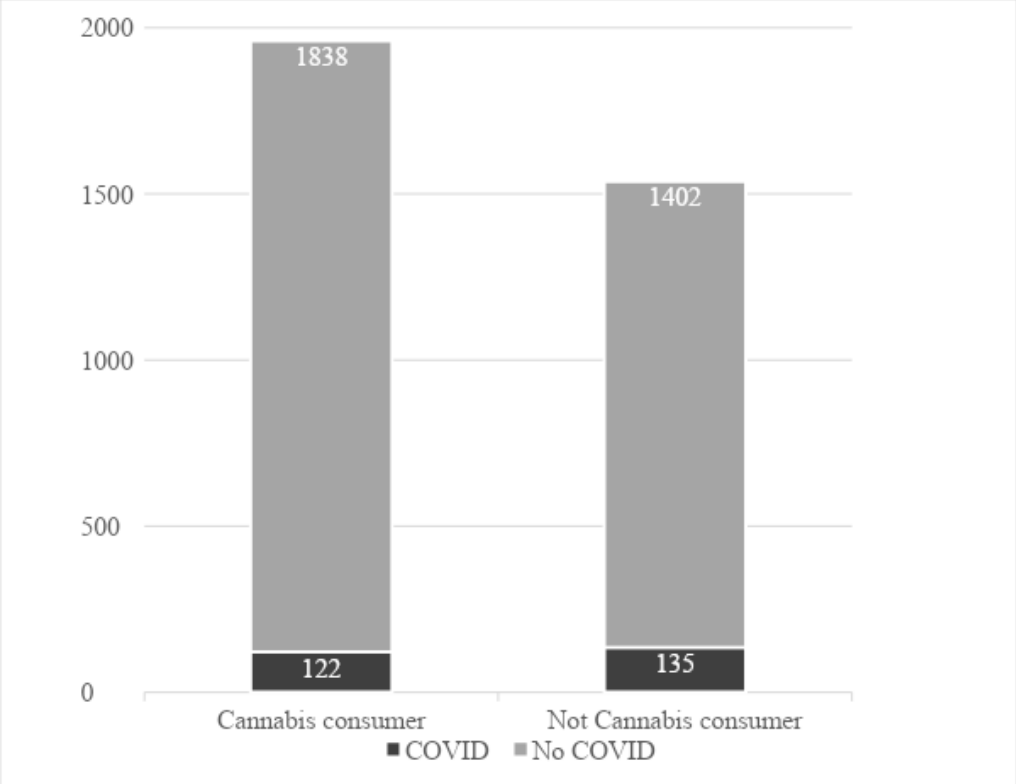
Ethical principles, confidentiality and the Declaration of Helsinki were respected. Once participants entered the survey link, they were explicitly told that participation is voluntary and data gathered will be processed anonymously and solely for investigative purposes. Participants were not asked to give their name or any contact information.

## Results

4026 surveys were collected through an online questionnaire. 76 people declared to be under legal majority age. Data obtained from them were excluded before any further analysis. 453 participants (11.5% of the population) expressed doubts about the SARS-COV2 infection

due to the presence of related symptoms but without having a confirmatory test. These subjects were not included in the statistical analysis process, coding their answers as Missing data. The final sample retained to apply statistical analysis consisted of 3950 participants, with 3497 participants declaring to be sure about COVID-19 diagnosis. The mean age was 34.9 years (SD 11.6; min 18, max 86). Confirmed SARS-COV-2 contagion was reported by 7.3% (257) participants. Gathering those participants reporting some type of symptom, regardless any confirmatory tests, the number rises to 24.7% (n= 975). 30% informed having had strong symptoms and 70% mild symptoms. Figure 1 shows the distribution of frequencies of the sample according to cannabis consumption and COVID-19 confirmed infection.

**Figure 1. SARS-COV-2 contagion frequencies according to cannabis consumption in a Colombian sample, 2020.**

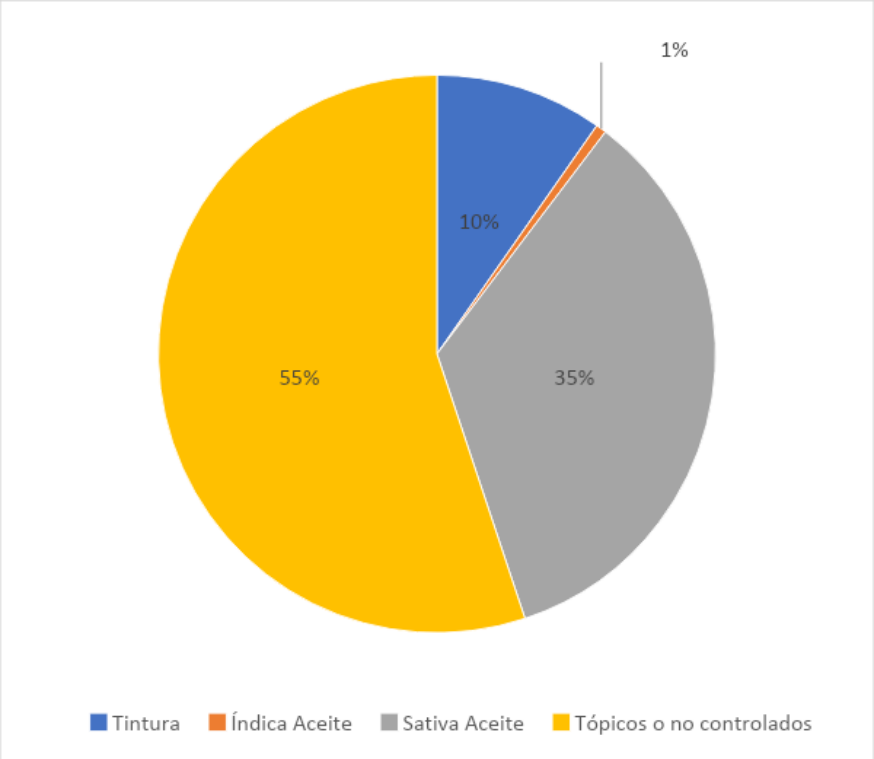


In regard to the question *"Do you have any member of your family or people with whom you live under the same roof, that has been positive to SARS-COV2 contagion?"*, 47% participants answer *"yes"*, and 40% expressed living with more than 1 person with a confirmed infection.

57.24% participants informed of any type of cannabis use (n=2261). Recreational use was reported by 1797 people, medical use by 797 and both recreational and medical by 333 people.

Referring to the type of medicinal cannabis employed, participants mainly declared the use of topical or uncontrolled preparations (55%), followed by Cannabis sativa oil (34%), hemp mother tincture (10%) and Cannabis indica oil (1%) (See figure 1).

**Figure 1. Cannabis type distributions**



Bivariate analysis was conducted, examining all variables in study (Cannabis consumption, confirmed infection, presence of symptoms, severity of symptoms, Close-related people with COVID-19 confirmed infection, number of close-related people with COVID-19 confirmed infection, type of cannabis if consumed, recreational or medical use of cannabis, simultaneous use, quantity and frequency of cannabis if used). Relation between any type of cannabis use and a lower risk of SARS-COV-2 contagion was found (p=0,004; OR=0,689, IC95% 0,534-0,889). No adjustments were made in the OR since only one of the Chi-square tests yielded significant results.

**Discussion**

The present study found that there is a relation between any type of cannabis use and a lower risk of SARS-COV-2 contagion (p=0,004; OR=0,689, IC95% 0,534-0,889). No other relations nor associations were found in the population survey.

Despite of estimated sample size declared in Methodology (N=384), total data obtained from online survey was used to complete the statistical analysis (N=3950). Given the conditions declared about the non-probabilistic sampling, the association found in the statistical analysis only can be suggested, not assured, due to selection bias. Another limitation is the impossibility to obtain dosing quantification and biomarkers of endocannabinoid response in individuals consuming cannabis exposed to SARS-COV-2 confirmed cases or patients with COVID-19 confirmed infection, in order to compare effects among different populations, dosing quantification, doses-response relation, biological and sociodemographic characteristics, etc.

Although there is still a long way ahead to fully grasp phytocannabinoids pharmacological properties, available data strongly suggests two broad therapeutic uses in regard to the SARS-COV2 infection: a preventive potential role, possibly linked to Caflanone strong binding affinity to two proteases related to SARS-COV2 replication inside human cells, allegedly acting as infection regulation[12]. The other role is related to the anti-inflammatory CBD properties with suggested evidence to restrict lung and systemic damage and cytokines

cascades, through modulation of ACE2, interleukin (IL)-2, IL-6, IL-1a and B, interferon gamma, tumor necrosis factor-a, only to name some [13].

Further research is always needed, even though available reports on medical cannabis keep on throwing lights on their enormous therapeutic potentials, with a particular hope as a powerful tool to cope with our global health challenge in front of the COVID-19 pandemic.

References


1. Hill KP. Cannabinoids and the Coronavirus. Cannabis Cannabinoid Res. 2020 Jun 1;5(2):118–20. https://www.liebertpub.com/doi/10.1089/can.2020.0035
2. Raj V, Park JG, Cho K-H, Choi P, Kim T, Ham J, et al. Assessment of antiviral potencies of cannabinoids against SARS-CoV-2 using computational and in vitro approaches. Int J Biol Macromol. 2020 Dec 5; http://www.ncbi.nlm.nih.gov/pubmed/33290767
3. Khodadadi H, Salles ÉL, Jarrahi A, Chibane F, Costigliola V, Yu JC, et al. Cannabidiol Modulates Cytokine Storm in Acute Respiratory Distress Syndrome Induced by Simulated Viral Infection Using Synthetic RNA. Cannabis Cannabinoid Res. 2020 Sep 1;5(3):197–201.
4. Friedman D, French JA, Maccarrone M. Safety, efficacy, and mechanisms of action of cannabinoids in neurological disorders [Internet]. Vol. 18, The Lancet Neurology. Lancet Publishing Group; 2019. p. 504–12. https://pubmed.ncbi.nlm.nih.gov/30910443/
5. Mechoulam R. Looking Back at Cannabis Research. Curr Pharm Des. 2005 Mar 25;6(13):1313–22. https://pubmed.ncbi.nlm.nih.gov/10903394/
6. Lowe H, Steele B, Bryant J, Toyang N, Ngwa WF. Non-Cannabinoid Metabolites of Cannabis sativa with Therapeutic Potential. 2020; www.preprints.org
7. Mecha M, Feliú A, Iñigo PM, Mestre L, Carrillo-Salinas FJ, Guaza C. Cannabidiol provides long-lasting protection against the deleterious effects of inflammation in a viral model of multiple sclerosis: A role for A2A receptors. Neurobiol Dis. 2013 Nov;59:141–50.
8. Zhang H, Penninger JM, Li Y, Zhong N, Slutsky AS. Angiotensin-converting enzyme

2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. Intensive Care Med. 2020 Apr 1;46(4):586–90.

9. Costiniuk CT, Jenabian MA. Acute inflammation and pathogenesis of SARS-CoV-2 infection: Cannabidiol as a potential anti-inflammatory treatment? Vol. 53, Cytokine and Growth Factor Reviews. Elsevier Ltd; 2020. p. 63–5.
10. Wang Q, Zhang Y, Wu L, Niu S, Song C, Zhang Z, et al. Structural and Functional Basis of SARS-CoV-2 Entry by Using Human ACE2. Cell. 2020 May 14;181(4):894-904.e9.
11. Sims JT, Krishnan V, Chang CY, Engle SM, Casalini G, Rodgers GH, et al. Characterization of the cytokine storm reflects hyperinflammatory endothelial dysfunction in COVID-19. J Allergy Clin Immunol. 2020;
12. Ngwa W, Kumar R, Thompson D, Lyerly W, Moore R, Reid TE, et al. Potential of Flavonoid-Inspired Phytomedicines against COVID-19. Molecules. 2020 Jun 11;25(11). https://pubmed.ncbi.nlm.nih.gov/32545268/
13. Stebbing J, Phelan A, Griffin I, Tucker C, Oechsle O, Smith D, et al. COVID-19: combining antiviral and anti-inflammatory treatments [Internet]. Vol. 20, The Lancet Infectious Diseases. Lancet Publishing Group; 2020. p. 400–2. https://pubmed.ncbi.nlm.nih.gov/32113509/