MEDICINAL PLANT COMMUNICATIONS
© / ISSN 2452 4433 / www.mpc.ms-editions.cl
https://doi.org/10.37360/mpc.22.5.2.07

Short Communication

Influence of decarboxylation on *Cannabis sativa*'s antioxidant activity and flavonoid profile: A preliminary study

[El efecto de la decarboxilación de *Cannabis sativa* sobre su actividad antioxidante y el perfil de flavonoides: un estudio preliminar]

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Abstract: *Cannabis sativa* L. is used to treat drug-resistant epilepsy. Cannabinoids and phenolic compounds were identified in its composition. It is known that decarboxylation transforms acid cannabinoids into their neutral, usually more active, forms. Our aim was to determine the effect of the decarboxylation on *C. sativa*´s resin (CSR) antioxidant effect and its relationship with cannabinoids and polyphenolic compounds. The DPPH scavenger activity, the inhibition of lipid peroxidation and the metal chelating activities were determined for the raw CSR and decarboxylated C. sativa´s resin (CSRD). The phytochemical composition was studied by HPLC. The decarboxylation process modified the HPLC flavonoids profile and increased the resin's antioxidant activities. The EC_{50} of CSRD for DPPH activity was 2.5 times lower than CSR EC_{50} (p<0.001); for the inhibition of lipid peroxidation, CSRD presented an EC_{50} 2.7 times lower than CSR (p<0.001). CSR did not exert metal chelating activity. In view of these results, it could be promising to decarboxylate CSR to improve its antiepileptic and antioxidant effects.

Keywords: Cannabis; Antioxidant; Flavonoids; Cannabinoids; HPLC.

Resumen: *Cannabis sativa* L. es utilizada para el tratamiento de la epilepsia resistente a fármacos. En su composición se identificaron cannabinoides y compuestos fenólicos. Se sabe que la decarboxilación transforma a los ácidos cannabinoides en su forma neutral, que usualmente es más activa. Nuestro objetivo fue determinar el efecto de la decarboxilación de la resina de *C. sativa* (CSR) sobre la actividad antioxidante y su relación con cannabinoides y compuestos polifenólicos. Se determinaron la actividad eliminadora del radical DPPH, la inhibición de la peroxidación lipídica y la actividad quelante de metales para CSR cruda y decarboxilada (CSRD). La composición fitoquímica se estudió mediante HPLC. El proceso de decarboxilación modificó el perfil de flavonoides y aumentó la actividad antioxidante de la resina. La EC_{50} de CSRD para la actividad DPPH fue 2.5 veces menor que la de CSR (p<0.001); en la inhibición de la peroxidación lipídica CSRD presentó una EC_{50} 2.7 veces menor que CSR (p<0.001). CSR no mostró actividad quelante de metales. Teniendo en cuenta estos resultados, podría ser interesante decarboxilar CSR para mejorar sus efectos antiepilépticos y antioxidantes.

Palabras clave: Cannabis; Antioxidante; Flavonoides; Cannabinoides; HPLC.

This article must be cited as: Saint Martin M, Marrassini C, Peralta I, Cogoi L, Alonso MR, Anesini C. 2022. Influence of decarboxylation on *Cannabis sativa* antioxidant activity and flavonoid profile: A preliminary study. **Med Plant Commun** 5 (2): 38 – 47.

INTRODUCCIÓN

Cannabis sativa L. (marihuana) is a dioicous plant of the Cannabaceae family widely distributed worldwide that has been used as a psychoactive drug, a folk medicine ingredient and a source of textile fiber since ancient times (Andre *et al.*, 2016). Nowadays, *C. sativa* is used to treat chronic pain, fibromyalgia, depression, arthritis, neuropathy (Ware *et al.*, 2005; Aggarwal *et al.*, 2009; Fiz *et al.*, 2011, Lal *et al.*, 2011) and inflammatory bowel disease (Hamerle *et al.*, 2014). Moreover, medicinal Cannabis and its derivatives are used in the treatment of drug-resistant epilepsy (Russo, 2017; Porter & Jacobson, 2013). *C. sativa* is characterized by a complex chemical composition, including phenolic compounds, terpenes, carbohydrates, fatty acids and their esters, amides, amines, phytosterols and the specific compounds of this plant, namely the cannabinoids, such as CBD and THC which are terpenophenolic compounds (Andre *et al.*, 2016).

It is known that *C. sativa*'s resin exerts antioxidant activity (Muscará *et al.*, 2021), which could be useful to mitigate oxidative stress during epilepsy. Moreover, the antioxidant activity of polyphenols and cannabinoids, such as CBD is also well known (Mendes Hacke *et al.*, 2019).

The cannabinoids are synthesized in the plant in their acidic forms, such as Δ9-tetrahydrocannabinolic acid (THCA) and cannabidiolic acid (CBDA), which can decarboxylate to render their neutral forms upon heating (Moreno-Sanz, 2016). Because the acidic forms poorly cross the brain blood barrier (BBB) and CBD has a stronger anticonvulsant activity than its acidic counterpart, the resin is submitted to a further decarboxylation. During this process Cannabis compounds could be affected as well as its pharmacological activity (Moreno-Sanz *et al.*, 2020). Moreover, Citti *et al.* (2018), revealed that if the decarboxylation process takes place at high temperatures (over 100°C), a significant loss (up to 60%) of the total concentration of CBDA and CBD is observed, denoting that it is an aggressive process on the extract and could lead to the degradation of bioactive molecules. Nothing is known about how decarboxylation could influence the antioxidant activity of the resin in relation to polyphenolic compounds, when it is submitted to this process.

The objective of this work was to determine the effect of decarboxylation upon the antioxidant effect of *C. sativa´*s resin and its relationship to polyphenols and cannabinoids content. To do this, DPPH scavenger activity, inhibition of lipid peroxidation and metal chelating activities were determined on raw *C. sativa* resin (CSR) and decarboxylated *C. sativa* resin (CSRD). Also, the phytochemical composition regarding polyphenolic content, specially flavonoids, and cannabinoids such as CBD was studied by HPLC.

MATERIALS AND METHODS

Plant material, resin preparation and decarboxylation process

Inflorescences from *Cannabis sativa* var. NN-AV011, a Non-Psychoactive Cannabis cultivar from Dr Ignacio Peralta's owned crops, upon REPROCANN program (Registry number: 77984, decree 883/20, law 27350 Ministerio de Ciencia y Técnica de la República Argentina-MINCYT) were used in this work.

The plant was identified by morphological, anatomical and histochemical criteria by Dr. Hernán Gerónimo Bach from the Museum of Pharmacobotany, School of Pharmacy and Biochemistry, University of Buenos Aires. One voucher specimen was deposited at the Museum of Pharmacobotany. The resin was obtained from the dried female flowers, through extraction in absolute ethanol for 10 min at 0°C. The extract was filtered and the solvent was evaporated on a rotary evaporator at 40°C. The resin obtained was stored at -20°C until use. The final yield was 9.17% (w/w) of plant material.

Decarboxylation of CSR to obtain CSRD was performed in a magnetic stirrer heating plate, using an oil bath at 130 ± 5°C for 30 min. The magnetic stirrer was used to promote even heat distribution throughout the experiment.

Determination of total polyphenols and total flavonoids

The total polyphenols content was determined by spectrophotometry according to the Folin-Ciocalteu's method using gallic acid as standard. Briefly, the CSR and CSRD extracts were dissolved in absolute ethanol. 5 mL of the Folin-Ciocalteu's reagent diluted at 10% (v/v) were added to 1.0 ml of the extracts. After 3 to 8 min, 4 mL of a 7.5% (w/v) sodium carbonate solution were added. Solutions were then allowed to stand at room temperature for 60 min and then the absorbance at 765 nm was measured using an UV-vis spectrophotometer. The concentration of polyphenols in

samples was derived from a standard curve of gallic acid ranging from 10 to 50 μg/mL (Pearson's correlation coefficient: r2 = 0.9996). Results were expressed as % w/w (ISO 14502-1, 2005) (Hosseinzadeh *et al.*, 2013).

Total flavonoids were also determined on the extracts according to Chang *et al.*, (2002). Quercetin was used as a standard (0-300 μg/mL). Briefly, 0.5 mL of the diluted extracts or standard were mixed with 1.5 ml of ethanol, 0.1 ml of 10% (w/v) aluminum chloride, 0.1 mL of 1 M potassium acetate and 2.8 mL of ethanol. After incubation at room temperature for 30 min the absorbance at 415 nm was measured using an UV-vis spectrophotometer. Results were expressed as %w/w.

Identification and quantification of CBD and CBDA by HPLC-UV

The CBD and CBDA content were determined in CSR and CSRD by HPLC. A Varian Pro Star instrument equipped with a Rheodyne injection valve (20 μL), a photodiode array detector set a 240 nm and a reversed-phase Agilent Zorbax Eclipse XDB-C18 (250 mm x 4.6 mm and 5 μ pd) column were used. Samples were dissolved in acetonitrile and eluted at 35°C with a gradient of A: H_2O with 0.085% phosphoric acid and B: acetonitrile with 0.085% phosphoric acid at a flow rate of 1.6 mL/min according to the method of Mandrioli *et al.* (2019). The gradient elution was 70% of B for 3 min, 85% of B at 7 min, 95% of B from 7.01 up to 8.00 min, and 70% of B up to 10 min. The identification and quantification of CBD and CBDA was carried out by comparing the retention time and areas obtained with those of commercial standards (CBD Avicanna; CBDA Restek®). A reference standard of THCA was also used to evaluate its presence on the extracts (THCA Restek®). The water employed to prepare the working solution was of ultrapure quality (Milli-Q). Acetonitrile (J.T. Baker) and phosphoric acid (Carlo Erba Reagents) were HPLC grade.

Study of flavonoids profile by HPLC

Regarding the analysis of flavonoids and related compounds, a method from Pellati et al. with slight modifications was used (Pellati *et al.*, 2018). Briefly, a Varian Pro Star instrument equipped with a Rheodyne injection valve (20 μL), a photodiode array detector set a 342 nm and a reversed-phase Agilent Zorbax Eclipse XDB-C18 (150 mm x 4.6 mm and 5 μ pd) column were used. Samples were eluted at 30°C with a gradient of 0.1% HCOOH in both (A) H_2O and (B) ACN as follows: 40% B for 5 min, 40% to 80% B from 5 to 20 min, 80% to 90% B from 20 to 35 min, condition that was held for 10 min. The flow rate was 1.0 mL/min. The water employed to prepare the working solution was of ultrapure quality (Milli-Q). Acetonitrile (J.T. Baker) and formic acid (Sintorgan) were HPLC grade.

Antioxidant activities

DPPH free radical scavenger activity

The antioxidant activity measured through the scavenging capacity of the free radical diphenyl-2-picrylhydrazyl (DPPH) was performed according to the methodology described by Blois (1958). Briefly, CSR or CSRD were diluted in absolute ethanol in order to obtain solutions with final concentrations in the reaction tube ranging from 1 to 1000 μg/mL. Sample blanks were prepared using ethanol. Vitamin C was used as the antioxidant reference standard. One hundred μL of each sample solution were placed in a vial. Four hundred μL of 100 mM Tris-hydrochloric buffer and 500 μL of a 500 μM DPPH solution in absolute ethanol were added. Samples were incubated in the dark for 20 min and the absorbance at 517 nm was measured. A DPPH control was prepared in100 mM Tris-hydrochloric buffer.

The antioxidant activity was determined by comparing the absorbance obtained with the reference solutions or the sample solutions to that obtained with the DPPH control. Results were expressed as percentage with respect to the control according to the following equation:

Radical Scavenger Act. DPPH: [(Control Abs.- Sample Abs.) / Control Abs.] X 100

Inhibition of lipid peroxidation: TBARS determination of egg yolk

The antioxidant activity was determined in an egg yolk phospholipid peroxidation model described by Dissanayake et al. (2009), with modifications. Briefly, 25 μl of diluted extracts, with final concentrations in the reaction tube ranging from 0.1 to 1000 of either CSR or CSRD, were mixed with 100 μL of distilled water and 125 μL of a 10% (v/v) egg yolk solution prepared in 1.15% (w/v) potassium chloride. A volume of 375 μL of a 20% solution of acetic acid and 375 μL of 1% (w/v) thiobarbituric acid (TBA) in 1.1% (w/v) sodium laureth sulfate (SD) solution were added. This mixture was kept in a water bath at 95°C for 90 min. A volume of 1.250 mL of butanol was added to each tube and vortexed for

10 sec. After centrifuging at 3000 rpm for 10 min, the absorbance of the butanol layer was measured at 532 nm in a UV-vis spectrophotometer. Butylhydroxytoluene (BHT) was used as the antioxidant reference standard. The percentage inhibition of peroxidation was calculated with the following equation:

$$\% \text{ Inhibition: } [(A0 - As) / A0] \times 100$$

where A0 was the absorbance of the oxidation control and As was the sample absorbance.

Metal Chelating activity

Metal chelating activity was measured by adding 250 μL of 0.25 mM $FeSO_4$ and 250 μL of 3 mM ferrozine subsequently into 500 μl of CSR or CSRD extracts (0.01-2500 μg/mL). After incubating at room temperature for 10 min, absorbance was measured at 562 nm. EDTA (1000 μg/mL) was used as the positive control. The ability of the extracts to chelate the ferrous ion was calculated using the following formula:

$$\text{Metal chelating activity} = (\text{Acontrol} - \text{Asample})/\text{Acontrol} \times 100$$

Where Acontrol is the absorbance of control reaction (without plant extract), and Asample is the absorbance in the presence of a plant extract.

The concentration of the extract able to inhibit 50% of the initial DPPH, phospholipid peroxidation or metal chelation (EC_{50}) was calculated from concentration-response curves using a mathematical method based upon the principles of a right-angled triangle:

$$EC_{50} = D\text{-}[(A\text{-}50\% \text{ max response}).\ X]/\ Y$$

where A is the immediately higher response of 50% maximum response; B is the immediately lower response of 50% maximum response; D= log concentration corresponding to A response; C= log concentration corresponding to B response; X= D-C; Y= A-B (Alexander *et al.*, 1999).

Statistical analysis

The statistical analysis was done with three or more independent experiments performed in triplicate. In all cases, the mean and the standard error of the mean (SEM) were determined. The significance between the means was analyzed by Student´s t test. In all cases, the differences were considered significant when $p<0.05$.

RESULTS AND DISCUSSION

First, the phytochemical composition of CSR and CSRD regarding polyphenols, flavonoids and cannabinoids was analyzed. As it can be seen in Table No. 1, both extracts present the same content of polyphenols and flavonoids.

On the other hand, the content of CBD determined by HPLC was 8.9 times higher in CSRD than CSR (Figure No. 1B, Figure No. 1C and Figure No. 1D; Table No. 1). Moreover, CBDA was detected in CSR but not in CSRD, indicating that the decarboxylation process was successful (Figure No. 1A, Figure No. 1C and Figure No. 1B; Table No. 1). To confirm this, the sum of CBDA + CBD in both the raw and the decarboxylated extract was determined. Being CBDA+CBD 65.659 ± 1.613 g% (w/w) in CSR and 62.360 ± 1.572 g% (w/w) in CSRD ($p>0.05$ Student´s T test) no significant difference was observed between the extracts, indicating the whole transformation of CBDA into CBD during the decarboxylation process.

The presence of polyphenolic compounds in *C. sativa* is well known. Three major classes of phenolic compounds, namely flavonoids, stilbenoids, and lignans, have been described in Cannabis (Isidore *et al.*, 2021). More than 20 flavonoids have been identified in *C. sativa*, most of which are flavone (apigenin and luteolin) and flavonol (kaempferol and quercetin) aglycones and glycosides (Flores- Sanchez & Verportee, 2008; Radwan *et al.*, 2008, Isidore *et al.*, 2021). Moreover, three prenylated/geranylated flavones, cannflavin A, B, and C, were isolated from *C. sativa* and are unique to this species. In addition, several studies have quantified individual phenolic compounds, such as caffeic acid, gallic acid, rosmarinic acid, p-OH-benzoic acid, ferulic acid, 3,4-dihydroxybenzoic acid, p-coumaric acid, syringic acid, quercetin,

luteolin, canniprene, cannflavin A, cannflavin B, catechin, naringenin, isorhamnetin, resveratrol, rutintrihydrate, apigenin, and apigenin7-glucoside in C. Sativa extracts (Allegrone *et al.*, 2017).

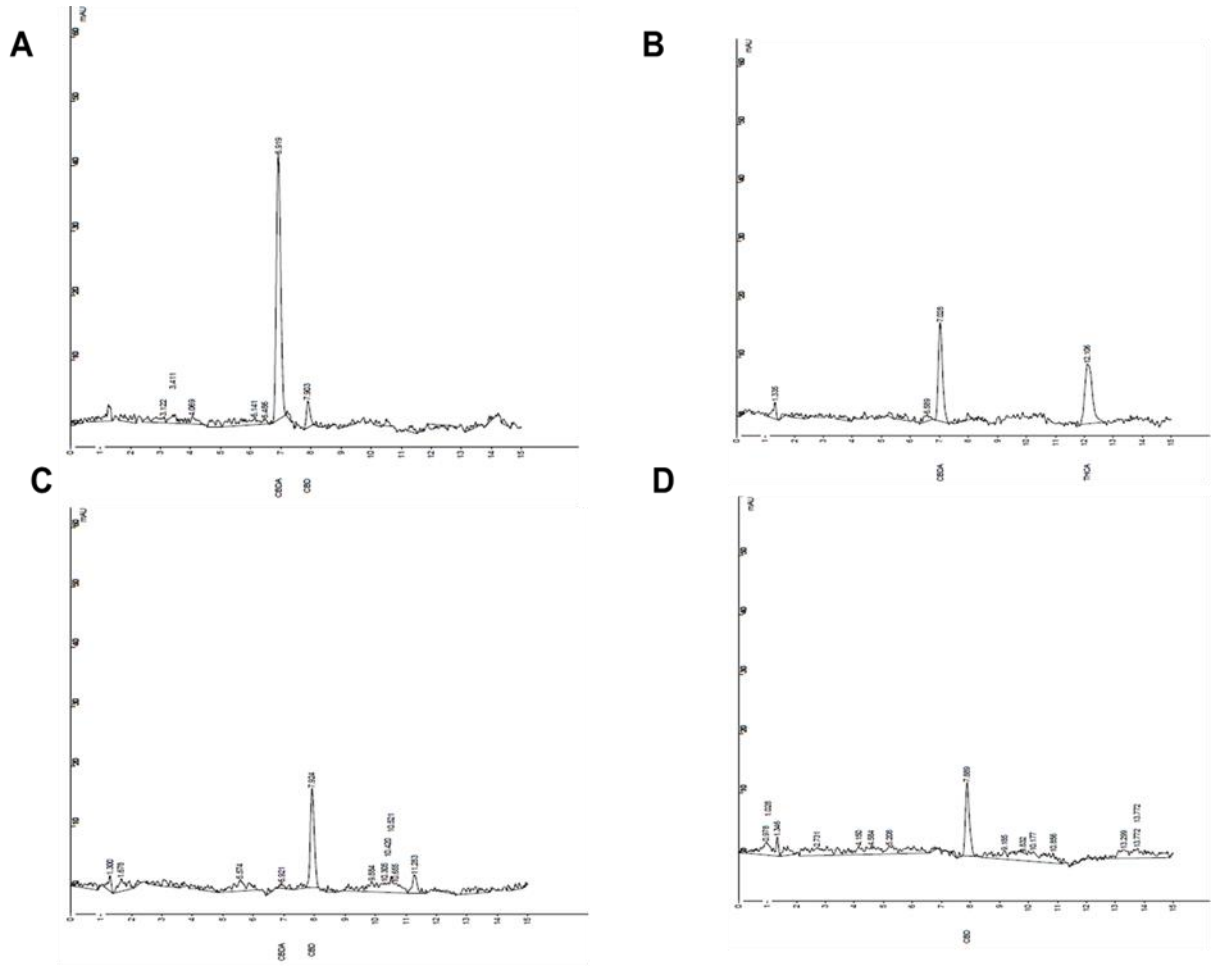


Figure No. 1
Chromatograms of CSR and CSRD obtained by HPLC
A. Chromatogram of CSR, B. Chromatogram of CBDA and THCA, C. chromatogram of CSRD D. Chromatogram of CBD. The chromatograms are representatives of three performed. CSR: raw Cannabis resin; CSRD: decarboxylated Cannabis resin.

Table No. 1
Content of polyphenols, flavonoids and cannabinoids in CSR and CSRD

	Content g% (w/w)	
	CSR	**CSRD**
Polyphenols	**18.664 ± 1.159**	**18.463 ± 1.474**
Flavonoids	**0.3674 ± 0.0081**	**0.3509 ± 0.0048**
CBD	**7.02 ± 0.08**	**62.36 ± 1.57*****
CBDA	**58.64**	**ND**

Results represent the mean ± SEM of two or three determinations. ** $p<0.001$ between CSR and CSRD in accordance to Student´s T test. ND: no detected

The flavonoids profile in CSR and CSRD was studied by HPLC with a specific method for their detection in *C. sativa* (Figure No. 2A and Figure No. 2B) (Pellati *et al.*, 2018). Despite searching for the presence of quercetin, kaempferol, apigenin and luteolin in the extracts using reference standards, none of these compounds could be detected (data not shown). However, some of the peaks in the chromatogram could correspond to cannflavins.

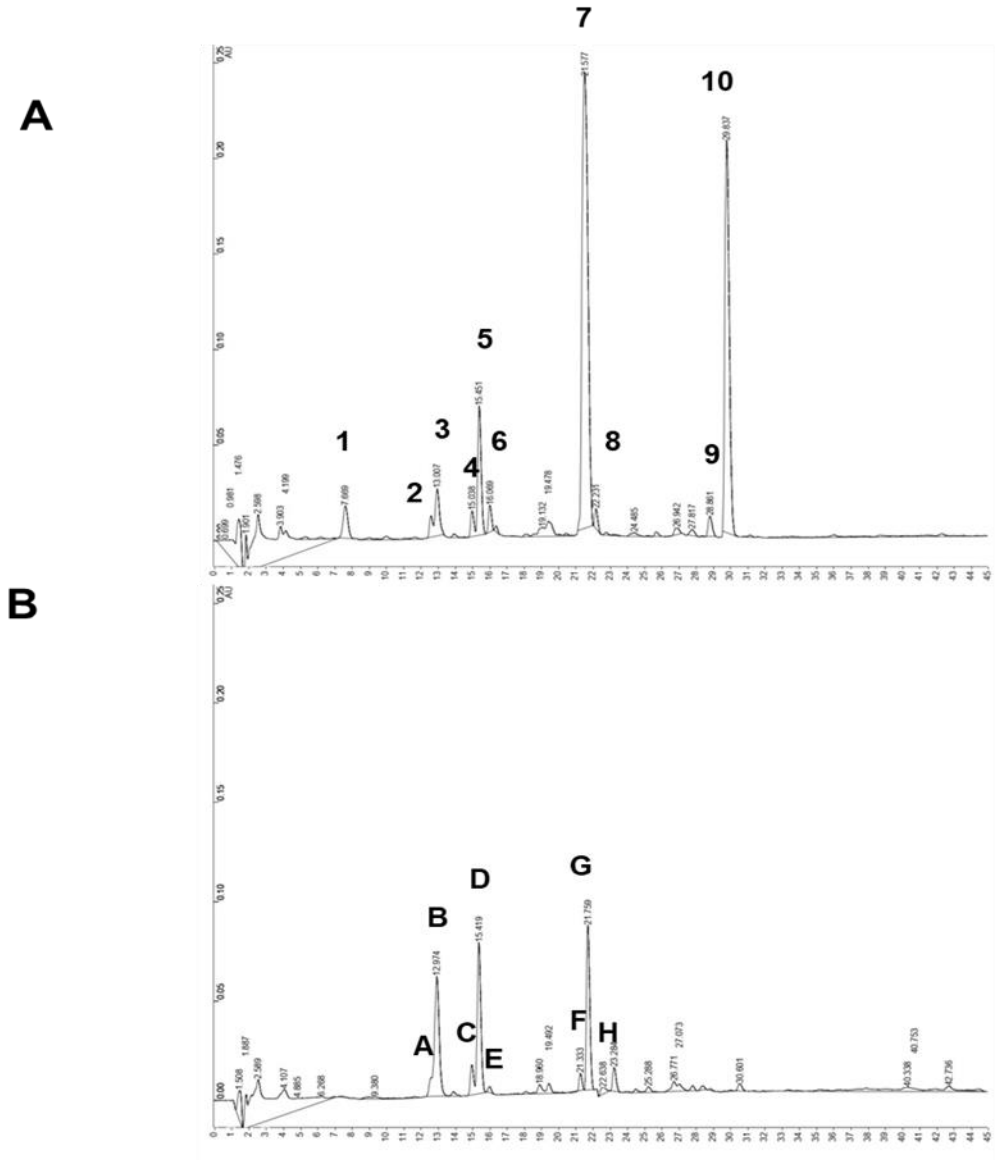


Figure No. 2
Flavonoids profile obtained by HPLC
A. HPLC chromatogram of CSR. B. HPLC chromatogram of CSRD performed at 342 nm. The chromatogram is representative of three performed. Inserted on graphs: Retention time (RT) of different peaks. Numbers 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 indicated different peaks in CSR and letters A, B, C, D, E, F, G and H indicated different peaks in CSRD. CSR: raw Cannabis resin; CSRD: decarboxylated Cannabis resin.

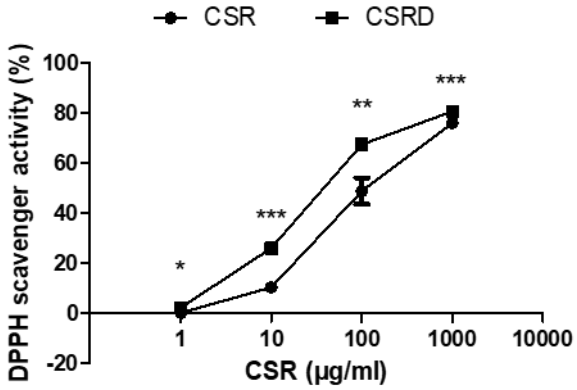
The obtained peaks were analyzed through their UV spectra, retention time (RT) and peak height. It is known that the height of each peak is proportional to the amount of the particular component present in the sample mixture. It can be seen that the HPLC profile changed when *C. sativa*'s resin was decarboxylated, even beyond those peaks corresponding to cannabinoid compounds (Figure No. 2A and Figure No. 2B). It could be hypothesized that certain compounds, some of which had the characteristic absorption bands I (300-380 nm) and II (240-280 nm) from flavonoids, disappeared, others increased their absorption, others appeared and some stayed without modifications when submitted

to this process. For example: Peak 1 in CSR (RT: 7.669) disappeared in CSRD; peak 2 in CSR (RT: 12.651) resulted to be equal to peak A in CSRD (RT: 12.638) as their UV spectra could be overlapped; peak 3 in CSR (RT: 13.007) resulted to be equal to peak B in CSRD (and RT:12.974) as their spectra could be overlapped, but the latest has a bigger peak height and area; peak 4 in CSR (RT:15.038) could not be detected in CSRD as its UV spectra did not overlapped with peak C in CSRD nor with any other (RT: 15.013); UV spectra of peak 5 in CSR (RT: 15.451) could be overlapped with that of peak D in CSRD (RT:15.419) but again it presented a slightly bigger peak height and area when the resin was decarboxylated; peak 6 in CSR (RT: 16.069) seemed to be similar to peak E in CSRD (RT: 16.034) but in this case a decrease in peak height and area was observed and we cannot confirm it is the same compound; peak 7 in CSR (RT: 21.577) had some similar absorption peaks as peak G in CSRD (RT: 21.759) but their whole UV spectra does not overlap and peak G does not appear to be pure. It is important to consider that CBDA reference standard has an RT of 21.849 min in this method and could contribute to peak 7 absorbance (although its UV spectra does not overlap with CBDA UV spectra). The peak 8 from CSR had a RT: 22.231 with UV spectra similar to that of an acid cannabinoid as well as peaks 9 (RT: 28.861) and 10 (RT: 29.837) that did not appear in the decarboxylated resin.

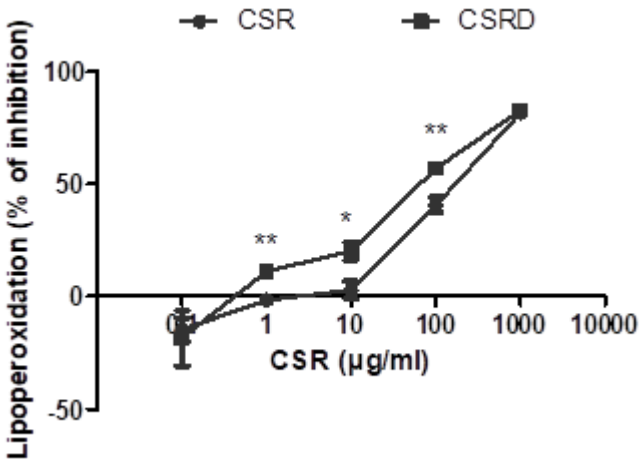
The peak H in CSRD (RT:23.284) has a similar UV spectrum than CBD reference standard (RT: 23.144) but peak H does not seem to be entirely pure because CBD doesn't have any absorption at 342 nm. Peak F with a UV spectra similar to that of a flavonoid compound only appeared in CSRD (RT:21.333).

These last results suggest that the decarboxylation process appears to affect the chemical structure of compounds other than cannabinoids, such as flavonoids. More studies are necessary for a better understanding of this process.

Studying the antioxidant activity of the resins, CSR and CSRD exerted antioxidant activity in a concentration dependent manner for both DPPH scavenger activity and inhibition of lipid peroxidation, reaching a maximum at 1000 µg/mL (Figure No. 3A and Figure No. 3B). For the inhibition of lipid peroxidation the effect of CSR and CSRD was observed over 1 µg/mL, meanwhile lower concentrations exerted pro-oxidative action. CSRD exerted a higher antioxidant activity than CSR for both activities. For example, the EC_{50} of CSRD for DPPH scavenger activity was 2.5 times lower than the EC_{50} of CSR ($p<0.001$) (Table No. 2) denoting its higher potency. The same occurs for the inhibition of lipid peroxidation for which CSRD presents an EC_{50} 2.7 times lower than the EC_{50} of CSR ($p<0.001$) (Table No. 2). On the other hand, CSR did not exert metal chelating activity (Figure No. 3C).



A



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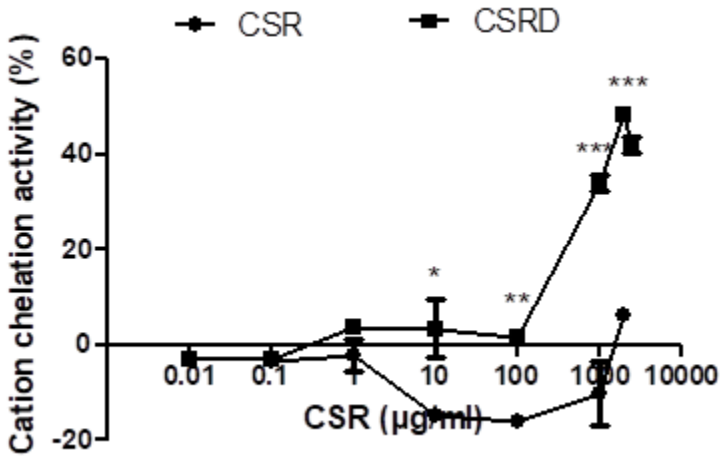

C

Figure No. 3
Antioxidant activities exerted by CSR and CSRD
A. DPPH scavenger activity, B. Inhibition of lipoperoxidation and C. Cation chelation activity. CSR: raw Cannabis resin; CSRD: decarboxylated Cannabis resin. Results represent the mean ± SEM of three experiments made by triplicate. *p<0.05, **p<0.01, ***p<0.001 significant differences between CSR y CSRD values in accordance to Student´s t test

Table No. 2
EC_{50} of CSR and CSRD for different antioxidant activities

	EC50 (µg/ml)	
	CSR	**CSRD**
DPPH scavenger activity	**58.88 ± 0.244**	**23.98 ± 0.20 *****
Inhibition of lipid peroxidaction	**102.32 ± 5.00**	**37.75 ± 1.25*****
Chelation activity	**----------**	**503.50 ± 8.99**

Results represent the mean ± SEM of two or three determinations. EC_{50} were calculated from graphics of Figure No. 1. ***p<0.001 between CSR and CSRD in accordance to Student´s T test

The fact that the resins exerted DPPH scavenger activity and, at the same time, inhibited lipid peroxidation, suggests that they could be acting through neutralizing free radicals, behaving like a primary antioxidant. Also, CSRD could act as secondary antioxidant eliminating Fe^{2+}, demonstrated by its metal chelating activity, consequently inhibiting Fenton's reaction. This last effect represents a valuable antioxidant property, hindering metal-catalyzed oxidative reactions. In this context, it is known that Fe^{2+} cations are powerful pro-oxidants that generate reactive oxygen species (ROS) in vivo, which are involved in the lipid peroxidation process; therefore, Fe^{2+} chelators could offer protection against oxidative damage, while Fe^{3+} cations are predominant in foods and produce radicals from peroxides as well, but at a lower rate than Fe^{2+} (Gulcin *et al.*, 2012).

In conclusion, it was observed herein that the decarboxylation process improved the antioxidant activity of Cannabis resin. This effect was also observed by other authors. For example, Petrovici *et al.* (2021), demonstrated that a hemp oil submitted to decarboxylation exerted higher Fe^{2+} chelating activity, free radicals scavenger activity and inhibition of lipid peroxidation under oxidative conditions. At the same time the decarboxylation process improved the antiproliferative action of the hemp oil in cancer cells and promoted fibroblasts proliferation. Other authors demonstrated the distinctive pharmacological activity of Cannabis extracts with different decarboxylation degrees at

cannabinoid receptors (Lewis-Bakker *et al*., 2019). These effects were related to the fact that, decarboxylation not only acts by transforming acid cannabinoids into their neutral forms, but also potentially affecting other organic acids and thermally-labile substances that may be present in the extract.

The higher antioxidant effects observed after decarboxylation could be related to both the increase in CBD content, given that its antioxidant activity is reported (Tura *et al*., 2019), and to a chemical oxidation of other polyphenolic compounds, such as flavonoids. For instance, it was reported that under decarboxylation conditions some flavonoids such as quercetin suffer oxidation giving different compounds like 3,4-dihydroxy-benzoic (protocatechuic) and 2,4,6-trihydroxybenzoic (phloroglucinic) acids, as well as the decarboxylation product of the latter, 1,3,5-trihydroxybenzene (phloroglucinol). In accordance with the literature data, this process involves the cleavage of the γ-pyrone fragment (ring C) of the quercetin molecule by oxygen, with primary formation of 4,6-dihydroxy-2-(3,4-dihydroxybenzoyloxy)benzoic acid (depside) (Zenkevich *et al*., 2007). These compounds are shown to exert antioxidant activity both "*in vivo*" and "*in vitro*" (Quéguineur *et al*., 2012; Zhang *et al*., 2021). Reinforcing this hypothesis, using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay, Ramos et al. (2006) reported that while some quercetin oxidation products retained the scavenging properties of quercetin, others were slightly more potent.

CONCLUSIONS

Considering these results, it could be promising to decarboxylate Cannabis resin to improve its antiepileptic as well as its antioxidant activities. This preliminary study opened further investigation pathways to study how and which flavonoids or other phenolic compounds could be affected during the decarboxylation process with the aim of obtaining standardized preparations.

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