Potential use of phytocannabinoids in Atherosclerosis

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Introduction

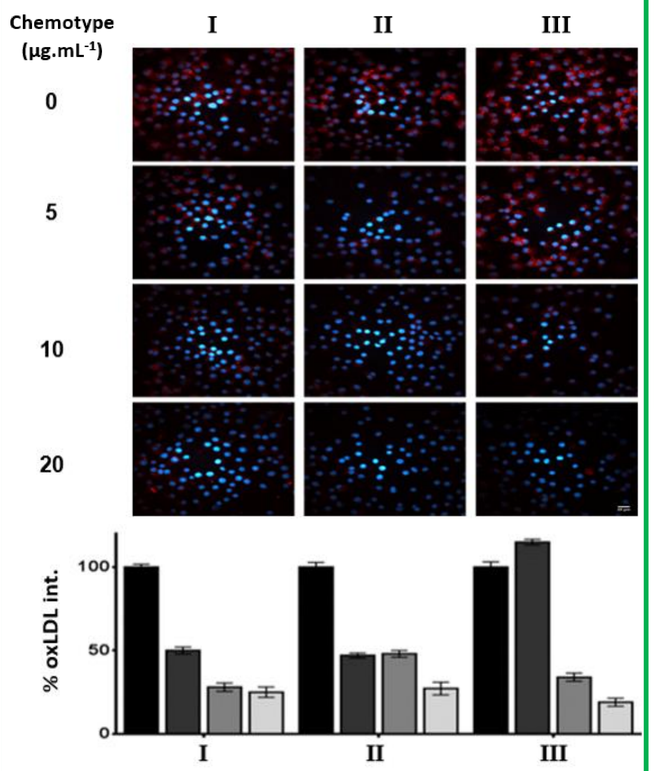
Atherosclerosis is a chronic inflammatory condition where arteries narrow due to formation of foam cells (macrophages full of oxidized LDL). Atherosclerosis is the primary cause of heart disease and stroke, being the leading cause of mortality in the world. Phytocannabinoids act as antioxidants and modulate the immune response. Hence, there is rational basis to consider them to treat or prevent atherosclerotic plaque formation.

Cannabis sativa extracts chemotype profile

Solvent extracts from three Cannabis sativa chemotypes were obtained, dried and analyzed by UPLC. Cannabinoids content was determined using analytical grade standards.

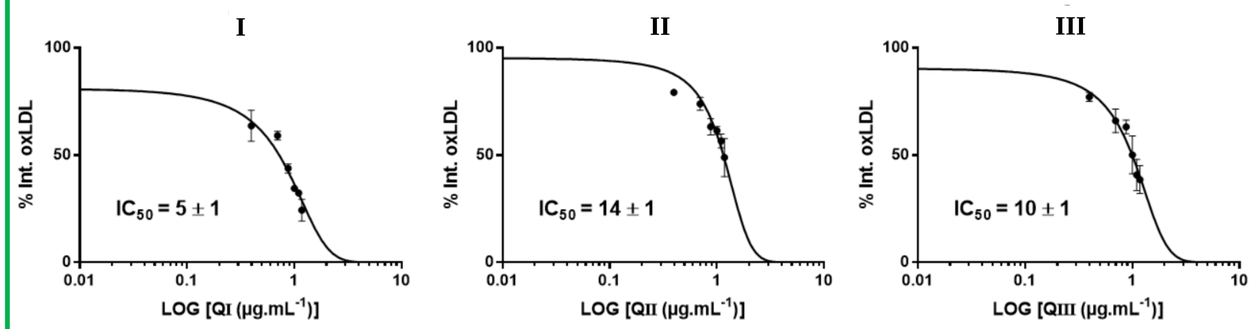
Cannabinoid	RT (min)	I	II	III
		%	%	%
CBDV	2,35	0,4	-	0,3
CBDA	2,84	2,5	30,3	9,2
CBGA	3,20	0,3	3,2	0,4
CBG	3,80	0,5	0,3	0,8
CBD	3,83	0,7	2,0	19,8
CBN	4,96	0,3	0,1	0,1
Δ9-THC	5,45	7,3	3,0	0,9
Δ8-THC	5,68	3,1	0,3	> 0,1
Δ9-THCA	5,81	43,0	13,4	> 0,1
CBC	6,60	0,1	0,2	3,0
Total (%)		58	53	35
THCA+THC CBDA+CBD		16	0.51	0.03
Chemotype		I or Drug	II or Intermediate	III or Fiber

Foam cell formation



J774 cells were incubated with vehicle (0.2% DMSO) or 5-20 µg.mL^{-1} of extracts (**I**, **II** or **III**) and oxLDL labeled with the florescent probe DiI (oxLDL-DiI) for 4 hs at 37° C. Foam cells were visualized by confocal fluorescence microscopy and bars correspond to average intensity/Area ± SEM expressed as percentage of vehicle condition. One hundred cells from eight different fields were evaluated in two independent experiments.

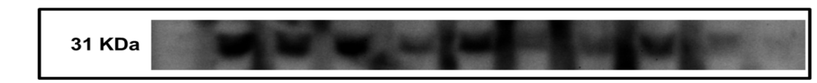
Inhibition of oxLDL internalization



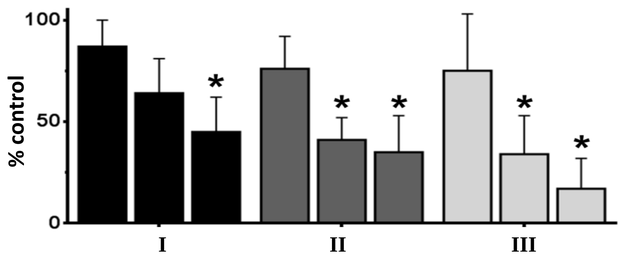
J774 cells were incubated with vehicle (0.2% DMSO) or 1-15 µg.mL^{-1} of the extracts (**I**, **II** or **III**) and oxLDL-DiI (10 µg/mL) for 24 hs at 37°C. The oxLDL-DiI internalized was determined by fluorimetry and is expressed as percentage of vehicle condition ± SD. Three independent experiments were performed.

Anti-inflammatory effect

Chem. (µg.mL-1)	-	-	I			II			III		
			2	10	20	2	10	20	2	10	20
INFγ +LPS	-	+	+	+	+	+	+	+	+	+	+



Densitometric analysis



Western Blot analysis of proIL-1β production. J744 cells were incubated with extracts (**I**, **II** or **III**) and INFγ+LPS for 4 hs at 37°C. Bars represent percentage of control condition ± SD of four independent experiments.

Conclusions

- The three extracts analyzed exerted a decrease in the internalization of oxLDL; as determined by microscopy and fluorimetry.
- The three extracts inhibited the production of proIL-1β after INFγ+LPS assault.

Perspectives

We are currently working towards determining the molecular mechanisms behind the effects observed.