



**Cannabis, insulin resistance and steatosis in  
individuals living with HIV and HCV**

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*On behalf of the HEPAVIH study group*



# Why are we interested in cannabis and metabolic disorders in HIV-HCV patients?

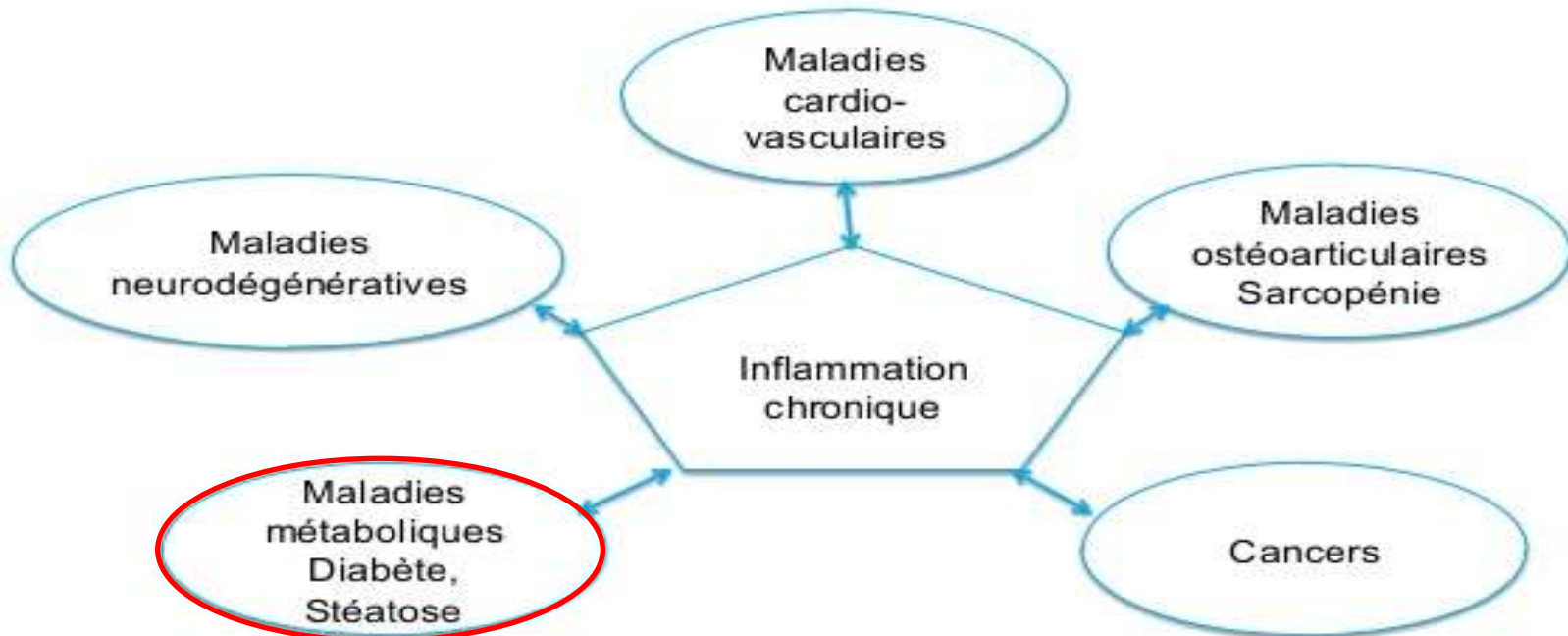
- People living with HIV and HCV at high risk of metabolic disorders => prevalence ranging between 4 % to 44% (Lonardo, Hepatology 2005) (Brown AIDS 2005)
- 40-67% of hepatic steatosis in HIV-HCV co-infected patients
- HIV-HCV co-infected individuals present risk factors for steatosis
  - exposure to antiretroviral agents
  - alcohol problems
  - increased risk of insulin resistance and type II diabetes mellitus
  - HCV infection, especially with genotype 3 virus

## **Why are we interested in cannabis and metabolic disorders in HIV-HCV patients?**

- **HCV clearance is not enough to protect them from metabolic disorders**
- **Cannabis use highly frequent in this group**
- **Cannabis use, insulin resistance and steatosis not yet studied in longitudinal cohorts of HIV-HCV patients**

# Aging, inflammation and HIV

Most complications related to aging are associated with chronic inflammation



**HIV HCV –infected individuals are particularly concerned by an accelerated aging process**



# Cross-sectional studies in the general population

CLINICAL RESEARCH STUDY

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## The Impact of Marijuana Use on Glucose, Insulin, and Insulin Resistance among US Adults

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<sup>c</sup>Cardiovascular Epidemiology Research Unit, Department of Medicine, Beth Israel Deaconess Medical Center, Boston, Mass.

- Cross-sectional in the general population (N=4657)
- Compared to non-users, cannabis users had insulin and insulin resistance values 16% and 17% lower, respectively
- Among users, no dose-response relationship was found

# Cross-sectional studies in the general population



## Decreased prevalence of diabetes in marijuana users: cross-sectional data from the National Health and Nutrition Examination Survey (NHANES) III

Tripathi B Rajavashisth,<sup>1,2</sup> Magda Shaheen,<sup>3</sup> Keith C Norris,<sup>3</sup> Deyu Pan,<sup>3</sup> Satyesh K Sinha,<sup>1</sup> Juan Ortega,<sup>1</sup> Theodore C Friedman<sup>1</sup>

- **Cross-sectional study in the general population N=10896**
- **Cannabis users had a 64% risk reduction of have diabetes than non users**
- **The results suggest that the effect is attributable to anti-inflammatory properties of cannabis as an association with cannabis and markers of inflammation was found**

# The ANRS HEPAVIH cohort

- Started in 2005-2006, it included 1364 patients enrolled in 24 hospital specialised services for HIV and HCV (first wave)
- Double data collection: clinical, using medical records and socio-behavioral based on yearly self-administered questionnaires
- HOMA-IR was used as indicator of insuline resistance risk ( $>2.77$ )
- Steatosis measured by ultrasound examination
- Five –year follow-up

## Objective

- => To study the relationship between cannabis use, IR and steatosis
- in HIV-HCV co-infected patients

# Methods

**Two analyses :**

## **HOMA-IR**

**1. Longitudinal to study the effect of cannabis use on HOMA IR over time (Carrieri CID 2014)**

## **Steatosis**

**2. Cross sectional: to study the effect of cannabis use on steatosis**

**(Nordmann J Vir Hep 2017)**

**Cannabis use was based on self-reports**



# Résultats



# Results: HOMA-IR

## Analysis on HOMA-IR

- **703 patients (1287 visits),**
- **323 (46%) had HOMA-IR  $> 2.77$  for at least 1 follow-up visit**
- **319 (45%) reported cannabis use in the 6 months before the first available visit.**
- **Cannabis use was associated with lower body mass index, history of injecting drug use and drinking 3 or more cups of coffee**

# Results: Cannabis use reduces by 60% the risk of insulin resistance

		OR	95% CI	p
BMI	Underweight	0.5	0.3 – 1.0	0.04
	Normal	1		
	Overweight	3.2	1.8 – 5.5	
Exposure to D4T	No	1	1.1 – 2.9	0.01
	Yes	1.8		
Sex	Males	1	0.3 – 0.7	<10 <sup>-2</sup>
	Females	0.4		
Viral load	Detectable	0.6	0.4-1.0	0.04
	Undetectable	1		
Coffee	<3 cups/day	1	0.4-1.0	0.05
	≥ 3 cups/day	0.6		
Cannabis use	No	1	0.2 – 0.6	<10 <sup>-3</sup>
	Yes	0.4		

# Results: Steatosis

Among study sample patients (n=838),

- **40.1% had steatosis**
- **14% reported daily cannabis use**
- **11.7% regular use**
- **74.7% no use or occasional use (“never or sometimes”)**

# Results: Daily cannabis use reduces by 40% the risk of **steatosis**

		OR	95% CI	p
BMI	Underweight	1		
	Normal	1.44	0.89 - 2.30	0.13
	Overweight	1.93	1.11 - 3.38	0.02
Exposure to Lamivudine zidovudine	No	1		
	Yes	1.51	1.12 – 2.01	0.01
Hazardous alcohol use	No	1		
	Yes	1.73	1.06 – 2.83	0.03
Cannabis use	Never/sometimes	1		
	Regular	0.98	0.62 – 1.53	0.91
	<b>Daily</b>	<b>0.64</b>	<b>0.42 – 0.99</b>	<b>0.04</b>



## Discussion and perspectives

- First study exploring the relationship between cannabis use, insulin resistance and steatosis in HIV-HCV patients
- Results consistent with those in the general population including a very recent study [Adejumo et al. Plos one 2017](#)
- Relationship between cannabis et IR is robust => it holds when changing a cutoff (3.8) and when using HOMA-IR as a continuous variable
- But smoking is dangerous for HIV patients => propose alternative to smoking = > proposing les harmful modes of consumption

=> Which is the therapeutic agent ?

# Which is the therapeutic agent?



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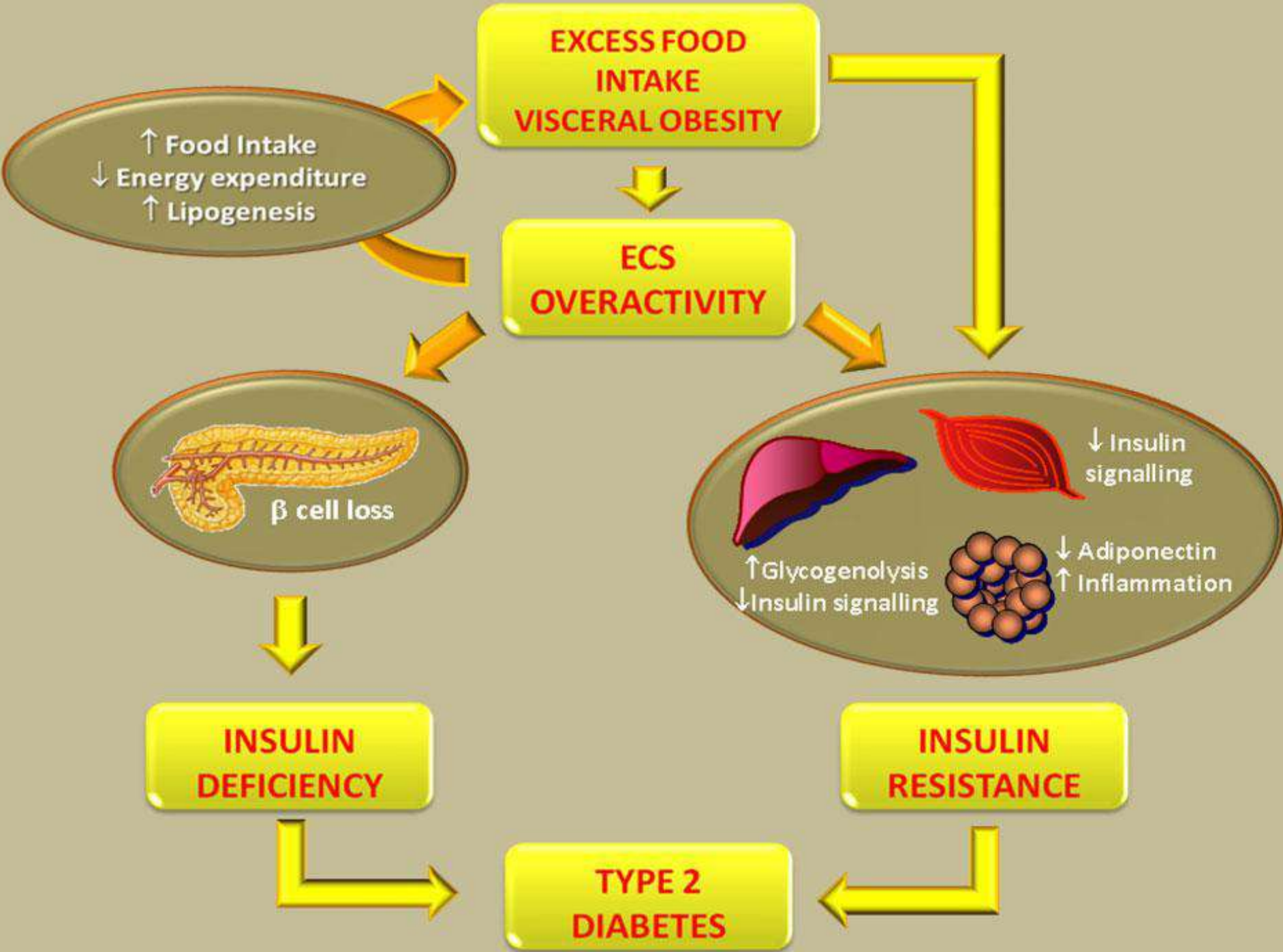
Themed Section: Endocannabinoids

## REVIEW

# Role of the endocannabinoid system in diabetes and diabetic complications

G Gaudin<sup>1</sup>, F Baratta<sup>1</sup>, G Kuroki<sup>2</sup> and P Pacher<sup>2</sup>

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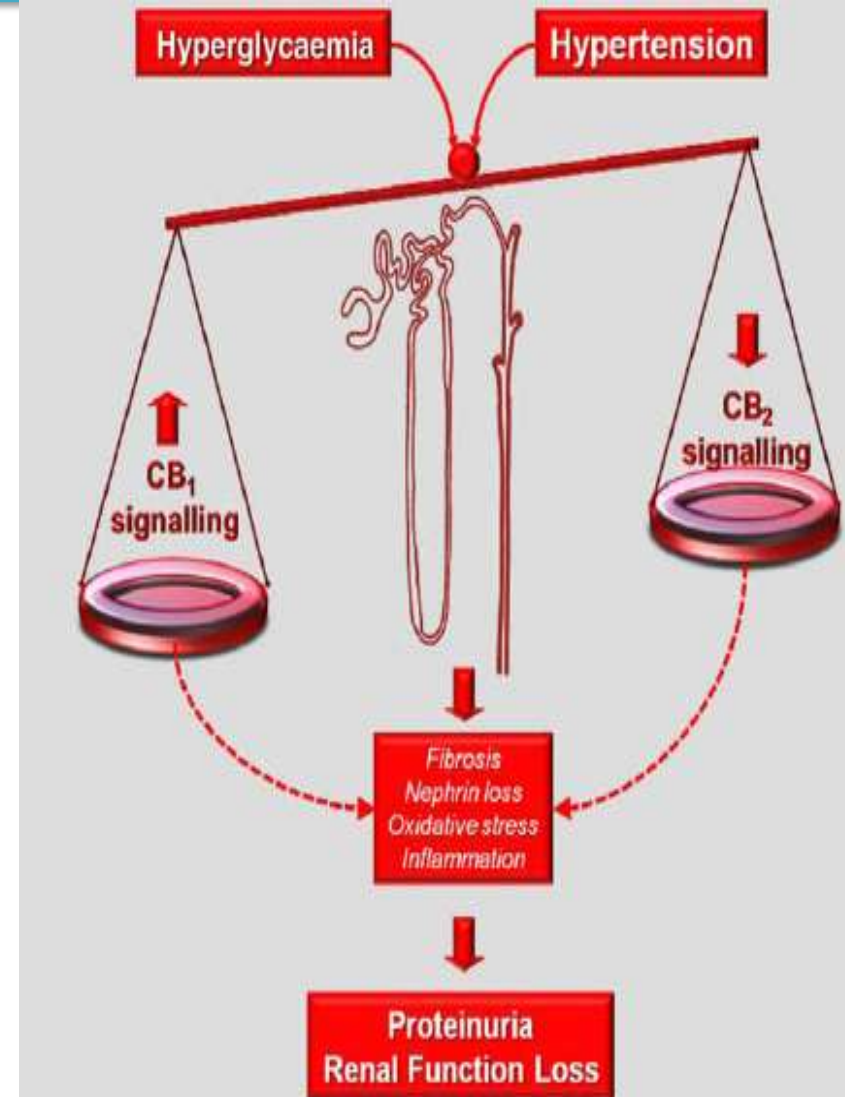
# Which is the therapeutic agent?



G Gruden et al.

## Cannabidiol for diabetes and diabetic complications

- Cannabidiol has anti-oxidant, anti-inflammatory, and tissue protective effects
- It has a potential for use not only for refractory epilepsy or glioblastoma but also for human diabetes and its complications



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