

Riesgos de los productos nutricionales, deportivos, y drogas de diseño en las personas con VIH ¿Vemos la punta del iceberg?

José Moltó, MD, PhD

Fundació “Lluita contra la sida”

Servicio Enfermedades Infecciosas

Hospital Universitari Germans Trias i Pujol

Badalona



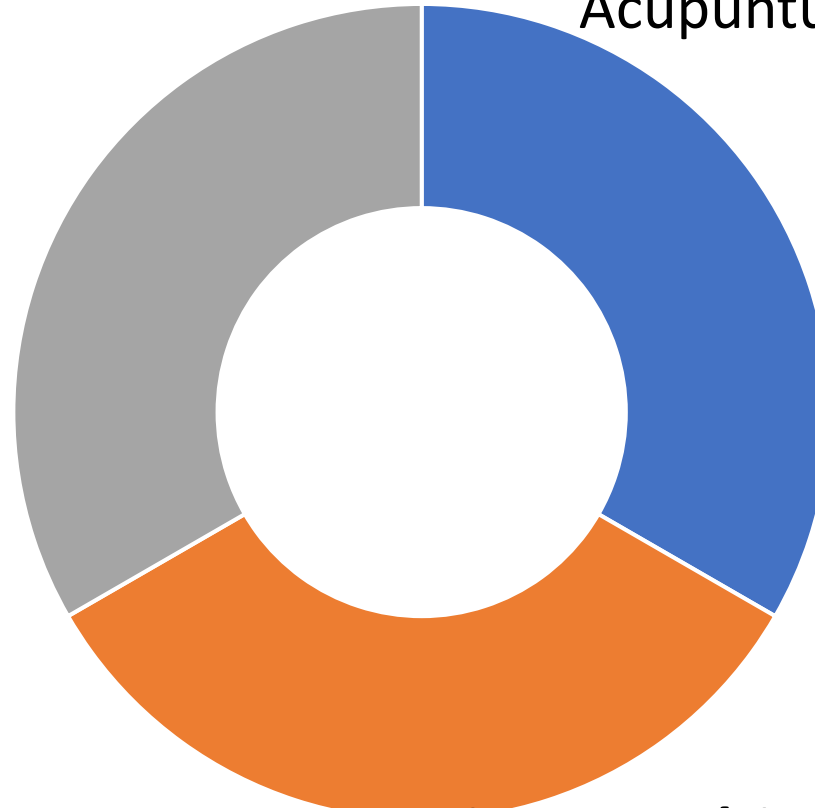
Tratamientos complementarios

Uso por 33-67% de pacientes VIH+

Suplementos alimentarios
Fitoterapia



Terapias físicas
Acupuntura, yoga, masaje...



Terapias energéticas
Meditación, visualización...



Riesgos generales del uso de CAM

- **Uso no controlado**
Ocultación
- **Uso excluyente** del cART / Adherencia
- **Efectos secundarios** aditivos
Efectos secundarios GI, SNC...
- **Interacciones** con el cART



Pan X, et al. Glob Public Health. 2019
Brooks KM, et al. Expert Rev Clin Pharmacol. 2017
Jalloh MA, et al. Int J STD AIDS. 2017

Interacciones INSTI con cationes

		Mg/Al	Ca	Fe	Multivitaminas
RAL	AUC	↓ 49%	↓ 55%		
	Cmax	↓ 44%	↓ 52%		
	Cmin	↓ 63%	↓ 32%		
EVG	AUC	↓ 45%			
	Cmax	↓ 41%			
	Cmin	↓ 47%			
DTG	AUC	↓ 74%	↓ 39%	↓ 54%	↓ 33%
	Cmax	↓ 72%	↓ 37%	↓ 57%	↓ 35%
	Cmin		↓ 39%	↓ 56%	↓ 32%
BIC	AUC	↓ 79%			
	Cmax	↓ 80%			
	Cmin				

Interacciones INSTI con cationes



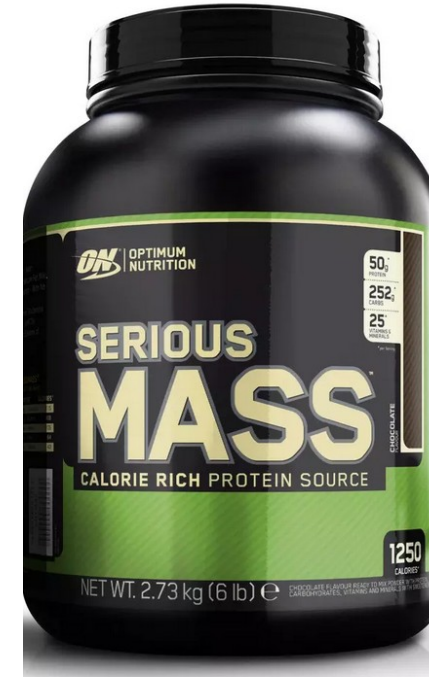
Carbonato
cálcico 267 mg



OH Al 200 mg
OH Mg 200 mg



Magnesio 126 mg



Calcio 167 mg
Magnesio 15.3 mg
Hierro 1.3 mg
Zinc 080 mg, Cu, Mn,
Se, Cr...

≈ 199 mg

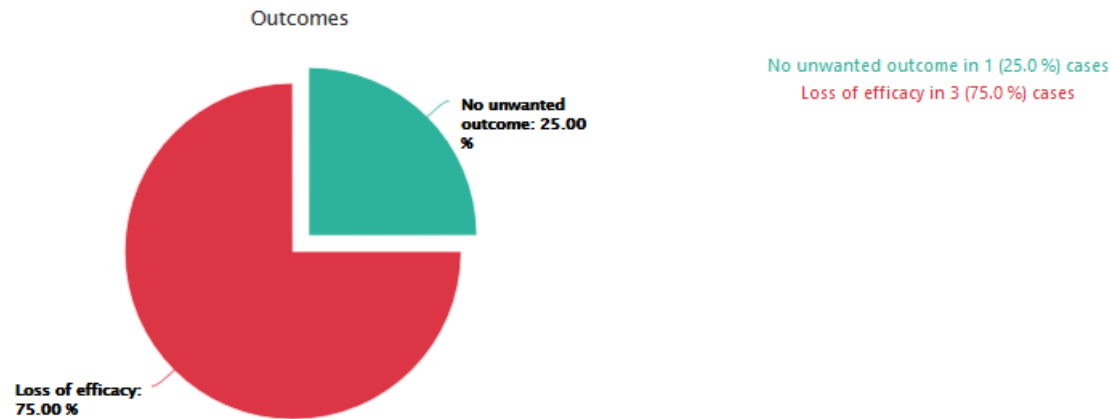


Magnesio 247 mg

Clinical cases including ARVs and Mineral Supplements

There are 4 clinical cases including any of the components of and Mineral Supplements in our database.

Out of these, the clinical outcome was as follows:



Reported case interaction between Dolutegravir and Mineral Supplements

Drugs suspected to be involved in the DDI

Drug A Dolutegravir (Victim)		
Daily Dose 50 (mg)	Dose adjustment performed No	Administration Route Oral
Start date Dec. 2, 2015	End date Ongoing	

Drug B Mineral Supplements (Perpetrator)		
Daily Dose Unknown	Dose adjustment performed No	Administration Route Oral
Start date Unknown	End date Ongoing	

Complete list of drugs taken by the patient

Antiretroviral treatment Dolutegravir/Abacavir/Lamivudine
--

Complete list of all comedications taken by the patient, included that involved in the DDI Cimicifuga, echinacea, licorice, giner, perilla, vitD3
--

Reported clinical cases involving ARVs and Mineral Supplements

Legend: P=Perpetrator V=Victim

	date	ARV involved	Comedication	Dose adjustment	Outcome
details	13 May 2019	Dolutegravir (V)	Mineral Supplements (P)	-	No unwanted outcome
details	29 May 2019	Raltegravir (V)	Mineral Supplements (P)	-	Loss of efficacy
details	28 Jun 2019	Raltegravir (V)	Mineral Supplements (P)	Yes	Loss of efficacy
details	11 Jul 2019	Raltegravir (V)	Mineral Supplements (P)	-	Loss of efficacy

Clinical case description

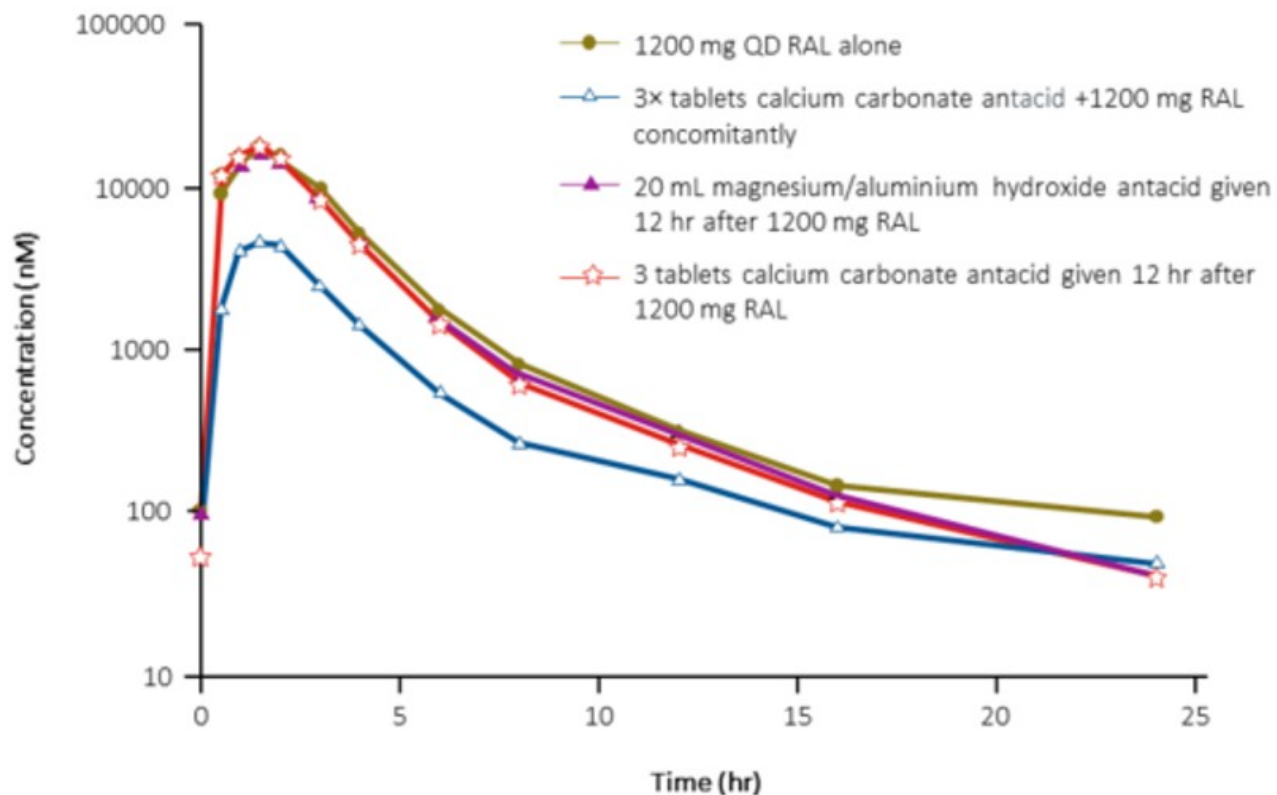
Gender Female	Age 51	eGFR (mL/min) >60	Liver function impairment No
------------------	-----------	----------------------	---------------------------------

Description

Patient taking Triumeq plus different alternative medicines including zinc supplements. Potential interaction between zinc and Triumeq. It was recommended to take the supplements and the rest of complementary treatments separately 12h from Triumeq.

Effect of metal-cation antacids on the pharmacokinetics of 1200 mg raltegravir

Krishna R et al. J Pharm Pharmacol 2016;68:1359-65.



	GMR		
	Calcium carbonate concomitantly	Calcium carbonate 12h after RAL	Mg/Al antacid 12h after RAL
C_{max}	0.26	0.98	0.86
AUC_{0-24}	0.28	0.90	0.86
C_{24}	0.52	0.43	0.42



Seednative

Plantas y plantas



Hypericum

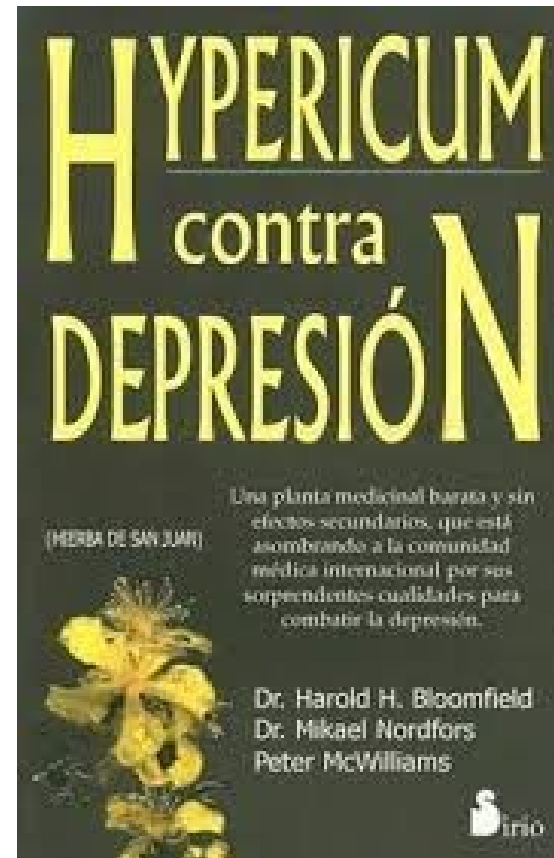


St John's Wort Supplements Endanger the Success of Organ Transplantation

Arch Surg. 2002;137:316-319

Interaction Between Cyclosporine and *Hypericum perforatum* (St. John's Wort) After Organ Transplantation

Am J Kidney Dis. 2001 Nov;38(5):1105-7





[\[Red yeast rice as the presumed cause of acute kidney and liver failure\].](#)

Peterslund P, Christensen HD, Urbahnke J, Cappeln AV.

Ugeskr Laeger. 2019 Sep 30;181(40). pii: V02190107. Danish.

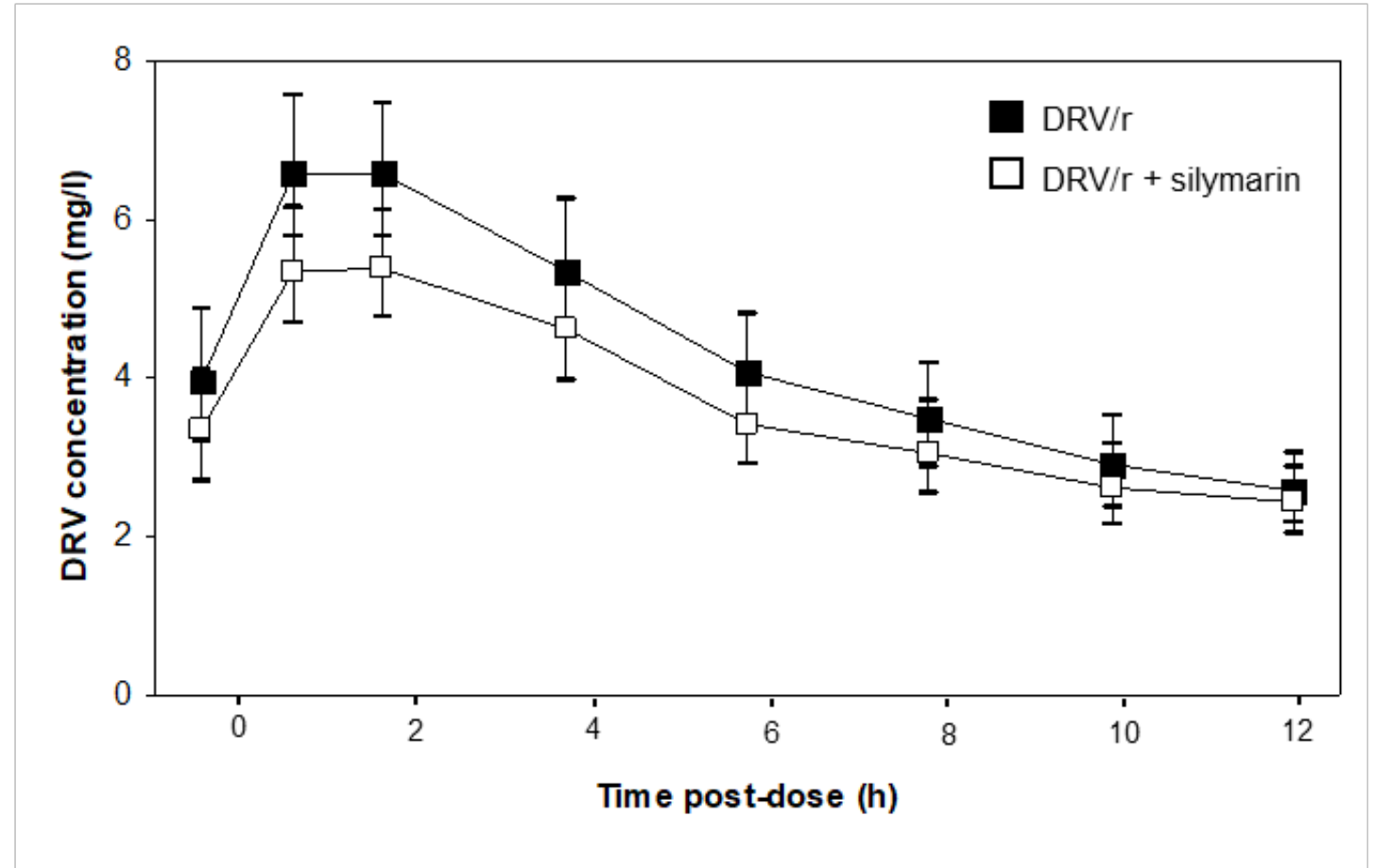


[Acute liver injury induced by red yeast rice supplement.](#)

Loubser L, Weider KI, Drake SM.

BMJ Case Rep. 2019 Mar 25;12(3). pii: e227961. doi: 10.1136/bcr-2018-227961.

Protectores hepáticos. Silimarina



Y otras....



Esteroides anabolizantes



- Derivados sintéticos de la testosterona

Esteroides orales

- Anadrol (oximetolona)
- Oxandrín (oxandrolona)
- Dianabol (metandrostenolona)
- Winstrol (estanozolol)

Esteroides inyectables

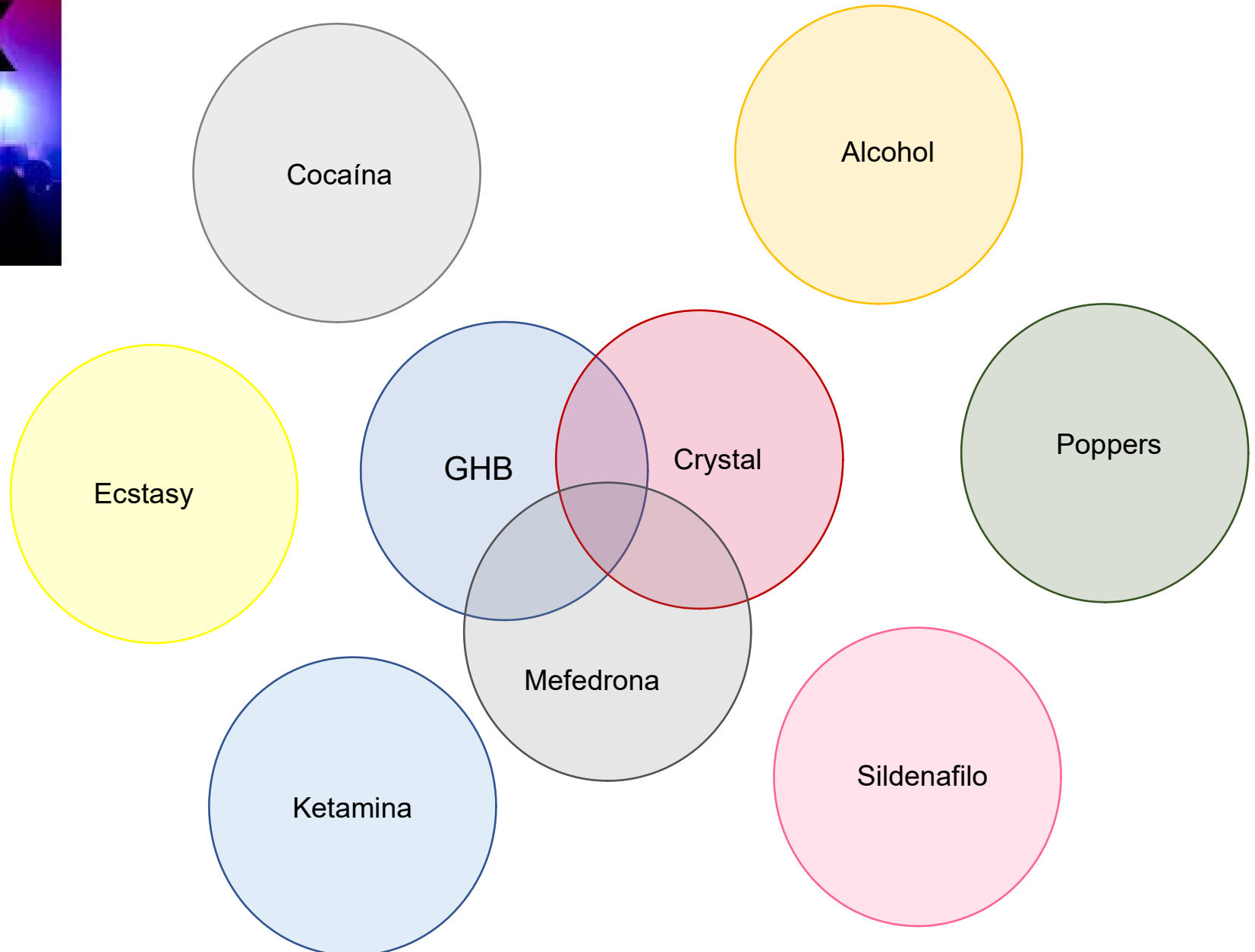
- Deca-Durabolín (decanoato de nandrolona)
- Durabolín (fenilpropionato de nandrolona)
- Depo-testosterona (cipionate de testosterona)
- Equipoise (undecilenato de boldenona)
- Tetrahydrogestrinona (THG)

- Usados por 17-22% de MSM-HIV+
Ciclos, piramidalización, “stacking”....



Riesgos asociados al uso de anabolizantes

- **Efectos secundarios**
 - Cutáneos: acné severo
 - SNC: insomnio, agresividad, paranoia, manía
 - Hepatotoxicidad, hepatocarcinoma (?)
 - Miocardiopatía dilatada
 - Hipercoagulabilidad: TVP
 - Endocrino: ginecomastia, atrofia testicular, infertilidad, hipertrofia-ca próstata
- Mayor consumo de drogas (MDMA, anfetaminas) y sexo anal sin preservativo
- Metabolismo por 5 α/β reductasas (**bajo riesgo DDIs con inhibidores P450**)



Cocaina

Alcohol

Ecstasy

GHB

Crystal

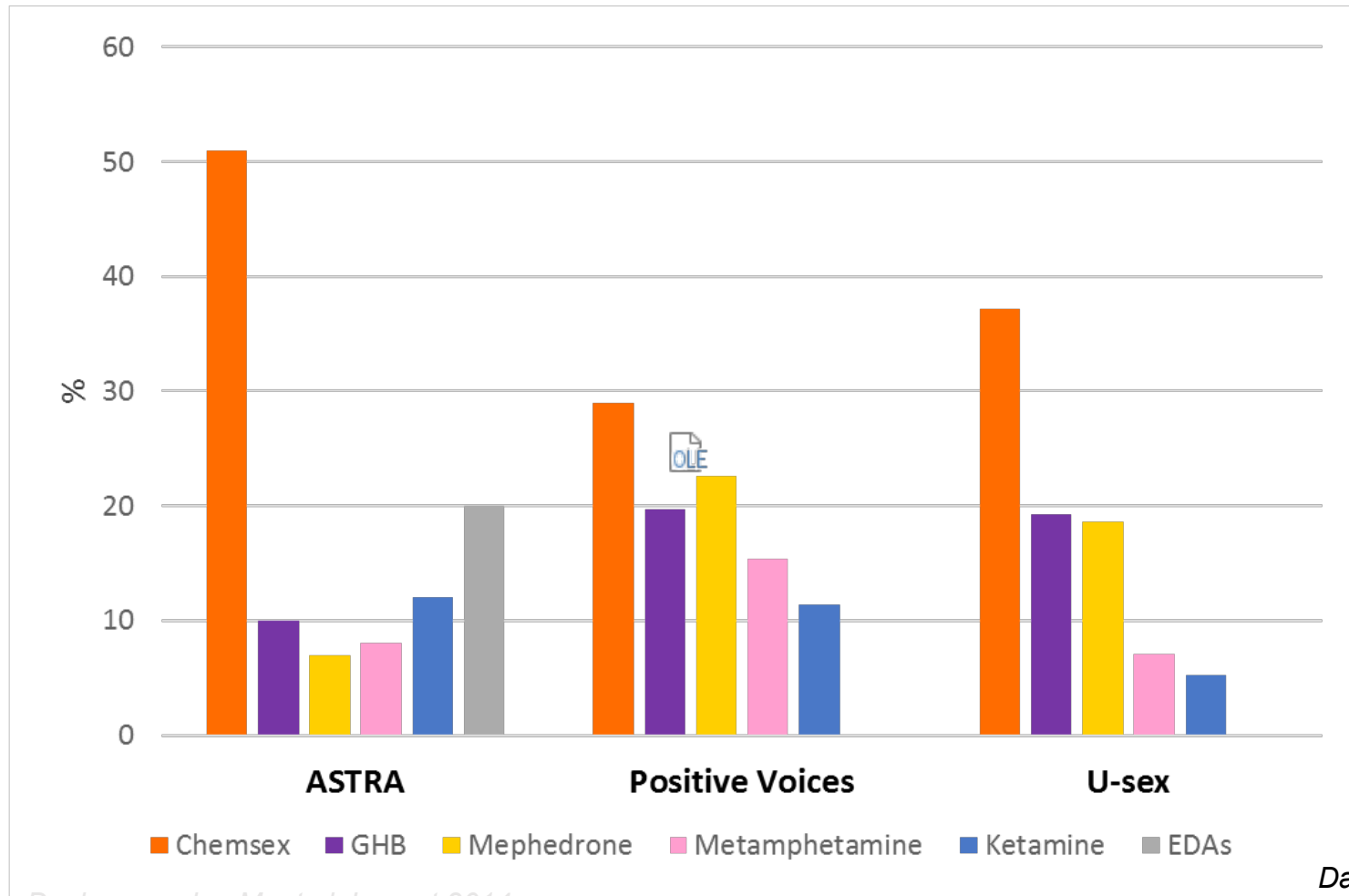
Poppers

Ketamina

Mefedrona

Sildenafil

Chemsex. Uso en HSH VIH+



Daskaopaoulou M, et al. Lancet 2014
Pufall EL, et al. CROI 2016
Ryan P, et al. GESIDA 2016

Daskaopaoulou M, et al. Lancet 2014
Pufall EL, et al. CROI 2016
Ryan P, et al. GESIDA 2016


Chemsex. Riesgos potenciales



**Transmisión
ITS**



**Trastornos
psiquiátricos**



**Adherencia TARV
Interacciones &
sobredosis**

HOW CHEMSEX ADDICTION IS KILLING THE UK GAY COMMUNITY

METRO

NEWS... BUT NOT AS YOU KNOW IT

London is being hit by a GHB death epidemic – and postmortem drug screenings aren't even picking it up.

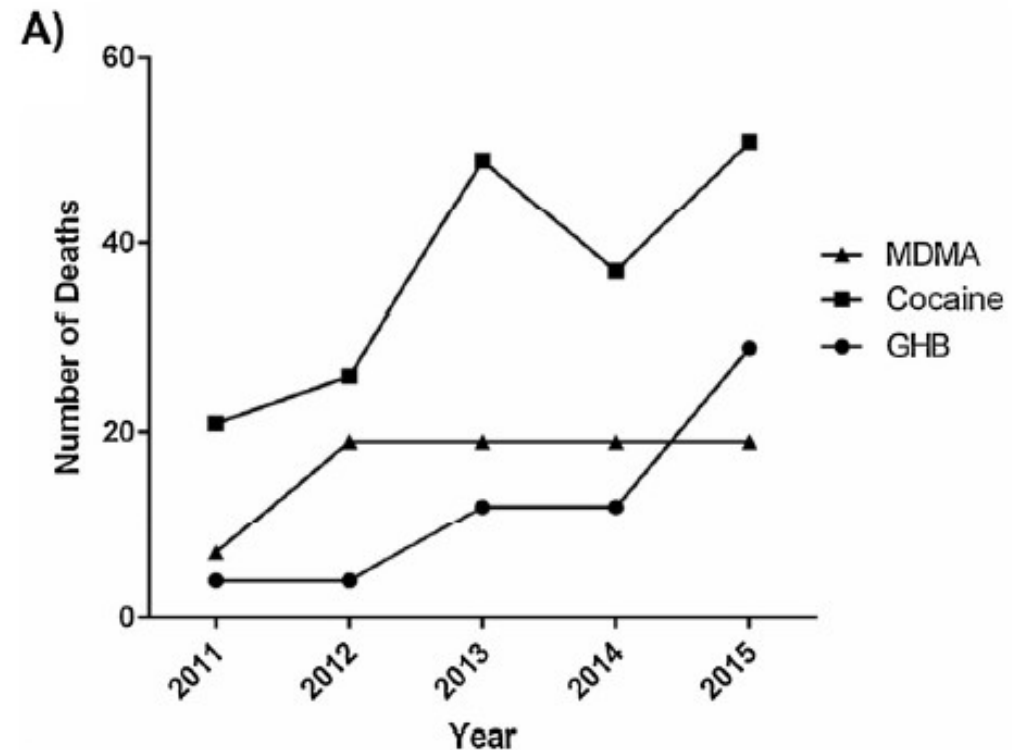
According to a disturbing new study, the number of people dying after taking GHB in the capital rose by 119% in just a year. In fact, someone was dying from GHB or GBL every 12 days in London in 2015.



Saturday 14 Jan 2017 !

An observed rise in γ -hydroxybutyrate-associated deaths in London: Evidence to suggest a possible link with concomitant rise in chemsex

Joanna Hockenull^{a,*}, Kevin G. Murphy^b, Sue Paterson^a



Chemsex & TARV. Riesgo de sobredosis

- Drogas con intervalo terapéutico estrecho
 - GHB
- Algunos antirretrovirales inhiben transportadores y enzimas implicados en la PK de las drogas recreativas
 - Potenciadores (RTV o COBI)
 - Riesgo de interacciones PK

Bases teóricas sobre interacciones TARV y drogas chemsex

Droga	Mefedrona	Metanfeta- mina	GHB	Éxtasis	Cocaína	Sildenafil y otros ADE	Ketamina
Metabolic pathway	CYP2D6	CYP2D6	Deshidro- genasas CYP2D6 (?)	CYP2D6	Esterasas 10% CYP3A4	CYP3A4	CYP3A4

Alto riesgo interacciones!!

CYP450 enzyme IC ₅₀ (μM)	1A2	2B6	2C8	2C9	2C19	2D6	3A
COBI	>25	2.8	30	>25	>25	9.2	0.2
RTV	>25	2.9	5.5	4.4	>25	2.8	0.2

≈155 ng/mL

≈144 ng/mL

	C _{max} (ng/mL)	C _{tau} (ng/mL)	AUC (ng.h/mL)
COBI	1700	35	12300
RTV	840	80	6600

Bases teóricas sobre interacciones TARV y drogas chemsex

Droga	Mefedrona	Metanfeta- mina	GHB	Éxtasis	Cocaína	Sildenafil y otros ADE	Ketamina
Metabolic pathway	CYP2D6	CYP2D6	Deshidro- genasas CYP2D6 (?)	CYP2D6	Esterasas 10% CYP3A4	CYP3A4	CYP3A4



Riesgo interacciones ?

CYP450 enzyme IC ₅₀ (μM)	1A2	2B6	2C8	2C9	2C19	2D6	3A
COBI	>25	2.8	30	>25	>25	9.2	0.2
RTV	>25	2.9	5.5	4.4	>25	2.8	0.2

≈7139 ng/mL

≈2016 ng/mL

	C _{max} (ng/mL)	C _{tau} (ng/mL)	AUC (ng.h/mL)
COBI	1700	35	12300
RTV	840	80	6600

German et al.
12th IWCPHT 2011

Riesgo de interacciones con dosis bajas de RTV/COBI?

Potential Interaction
Darunavir/cobicistat
GHB (Gamma-hydroxybutyrate)

Potential Interaction
Darunavir/cobicistat
Mephedrone

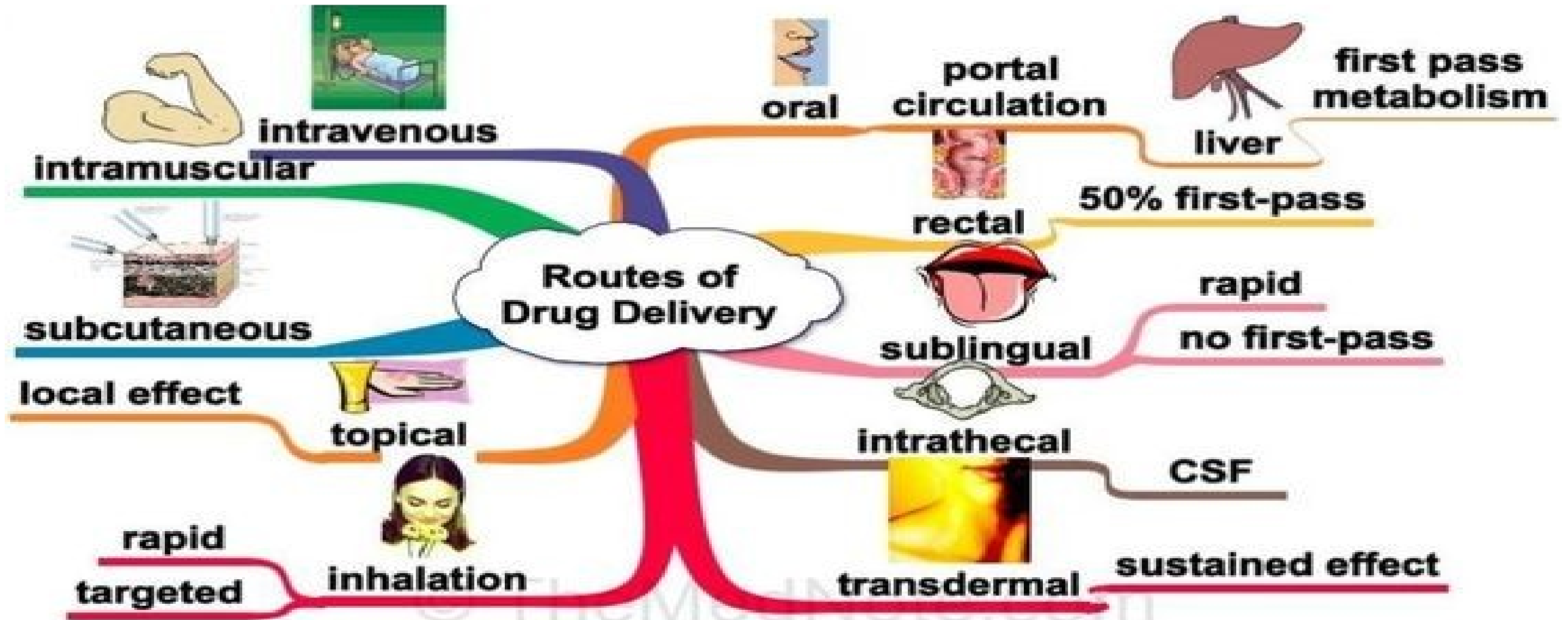
Potential Interaction
Darunavir/cobicistat
Methamphetamine

Quality of evidence: Very Low

Summary:

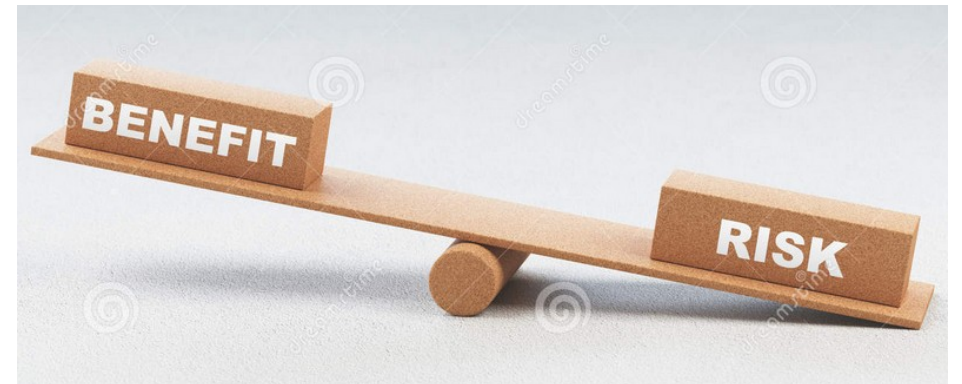
Coadministration has not been studied.

Vía de administración



Conclusiones

- Existe otra polifarmacia diferente a la de los pacientes mayores con comorbilidades...
- Una proporción destacable de nuestros pacientes consumen suplementos y otros CAM o drogas recreativas.
- Este hecho y los potenciales riesgos deben ser abordados proactivamente.
 - Necesidad de la indicación
 - Posibles efectos secundarios
 - Potenciales interacciones



Gracias!