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**ANTIOXIDANT CAPACITY
INCREASES AFTER OLIVE OIL
SUPPLEMENTATION IN PATIENTS
WITH METABOLIC SYNDROME**

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- The prevalence of the metabolic syndrome (MetS) is increasing rapidly throughout the world, in parallel with the increasing prevalence of diabetes and obesity; thus, it is now considered as a major public health problem

King H, Aubert RE, Herman WH. Diabetes Care 1998;21:1414-31.

- According to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) definition, prevalence of the MetS in Europe, Asia, Australia, and North and South America ranges between 9.6% and 55.7%;

Day C. Diab Vasc Dis Res 2007;4:32-8.

- MetS is considered to be a clustering of metabolic alterations conferring a high risk of developing type 2 diabetes (T2D), cardiovascular disease (CVD) and all-causes of mortality.

Eckel RH, et al. Lancet 2010;375:181-3

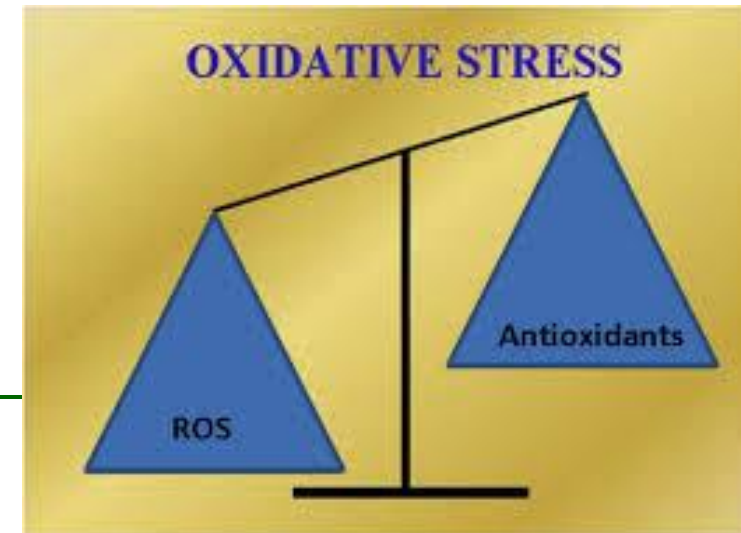
- Several compounds of MetS are related to inflammatory abnormalities, suggesting that the mechanism underlying this syndrome could be a chronic low-grade inflammatory and oxidative state.

NCEP ATP III: Clinical Identification of the Metabolic Syndrome (≥ 3 of 5 criteria)

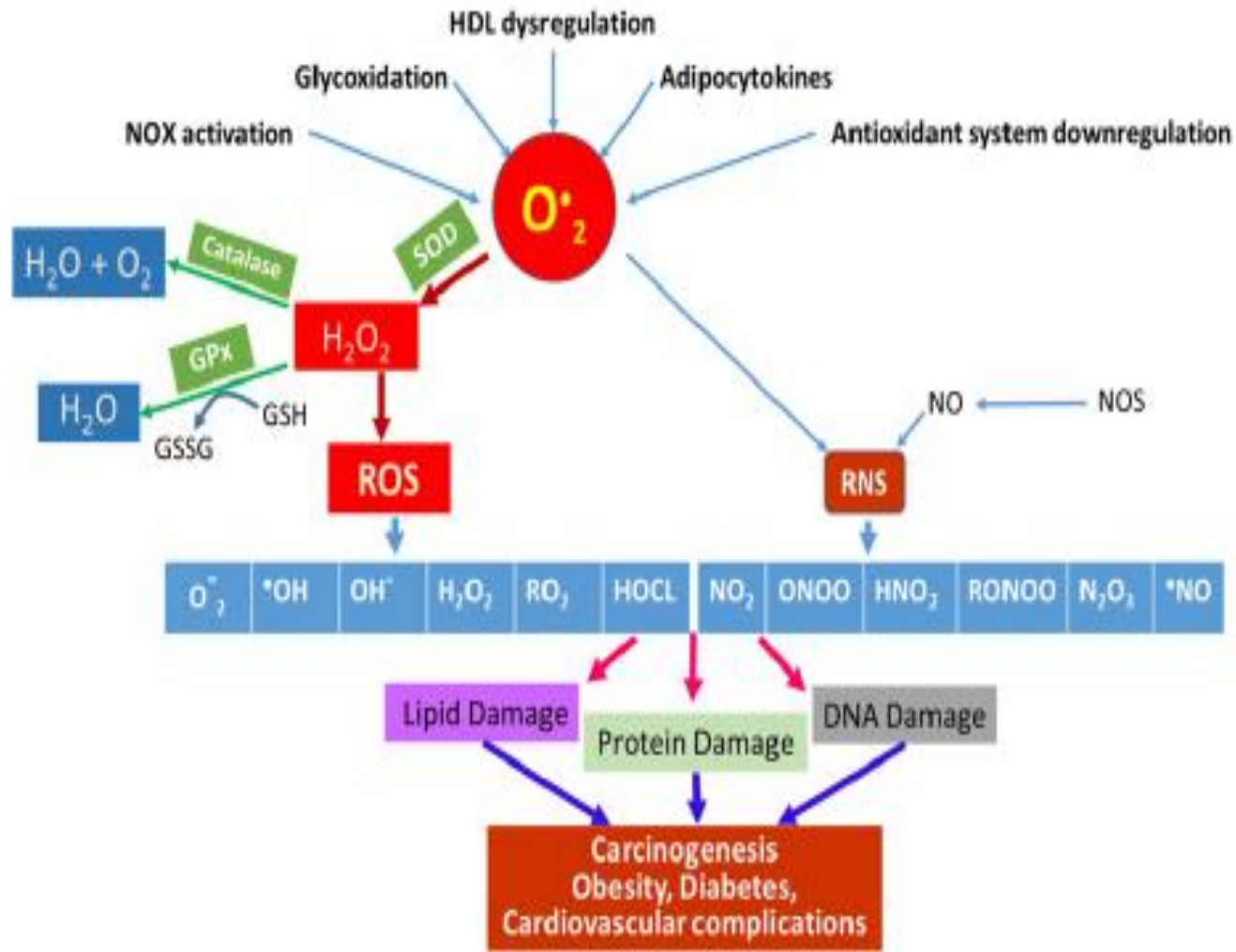
D-R-O-P	Risk Factor	Defining Level
D = <i>Dyslipidemia</i>	Triglycerides	≥ 150 mg/dL
	HDL cholesterol	Men: < 40 mg/dL Women: < 50 mg/dL
R = <i>Insulin resistance</i>	Fasting glucose	≥ 100 mg/dL
O = <i>Obesity</i>	Abdominal Obesity (Waist Circumference)	Men: > 102 cm (> 40 "") Women: > 88 cm (> 35 "")
P = <i>Blood pressure</i>	Blood pressure	$\geq 130/85$ mm Hg

- Oxidative stress is characterized by an increased production of cellular **oxidants** (i.e., superoxide anion and hydrogen peroxide) and a decreased concentration of circulating **antioxidants**

Fang, Yang, & Wu, 2002



Introduction



- Epidemiologic studies have now confirmed that olive oil is related to a decreased risk of chronic diseases such as cardiovascular disease (CVD) and its risk factors and of certain cancers

Ruiz-Canela M, Martinez-Gonzalez MA. *Maturitas* 2011;68:245–50.
Bendinelli B, et al. *Am J Clin Nutr* 2011;93:275–83.
Pelucchi C, et al. *Curr Pharm Des* 2011;17:805–12.

- Reports suggest that consuming extra virgin olive oil as the main dietary fat can be important because of its action in preventing oxidative stress

Covas, 2007; Covas et al., 2006; Marrugat et al., 2004;
Perona et al., 2006; Vissers et al., 2004

- Olive oil is rich in monounsaturated fatty acids (MUFAs) and antioxidant compounds, mainly phenolic compounds, and is capable of reducing one or more risk factors of MetS.

Minich DM, Bland JS. Nutr Rev 2008;66:429–44.



- The mechanisms by which extra virgin olive oil can exert its protective antioxidant effect can be explained by the activity of polyphenols or by the combined protective effect of both **polyphenols and MUFA content**.
- Extra virgin olive oil has been shown to counteract both metal- and radical-dependent LDL oxidation, also acting as chain-breaking antioxidant for lipid peroxidation

- Several bioavailability studies have confirmed that extra virgin olive oil antioxidants, such as polyphenols, are dose-dependently absorbed

Marrugat et al., 2004; Vissers, Zock, & Katan, 2004; Zbakh & El Abbassi, 2012

- And cooperate to increase plasma antioxidant capacity
 - Covas, 2007; Covas et al., 2006; Franconi et al., 2006;
 - Perona, Cabello- Moruno, & Ruiz-Gutierrez, 2006

- The aim of this study was verified if extra-virgin olive oil is capable to improve the antioxidant capacity in MetS patients.
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Patients and Methods

- Fifth and five (41 female and 14 male) patients with MetS (aged 51.45 years) from the ambulatory of the University Hospital of Londrina, Paraná, Brazil participated in this intervention study.
- Control group (CG) n:42 maintained their usual diet
- Olive oil group (OO) n: 13 received 10mL/d of extra-virgin olive oil.
- Assessments were performed at baseline and after 90 days.

- After fasting for 12 hours, the subjects underwent the following laboratory blood analysis: triacylglycerol (TG), total cholesterol, HDL-C, LDL-C, fasting glucose, uric acid which were evaluated by a biochemical auto-analyzer (Dimension Dade AR, Dade Behring, Deerfield, IL, USA), using Dade Behring kits. The total radical-trapping antioxidant parameter (TRAP) was determined by chemiluminescence.

- Data are expressed as median and interquartiles (25%-75%). Wilcoxon test was performed to verify changes from baseline (intra-group changes). Kruskal-Wallis with post hoc Dunn`s test was performed to verify differences across treatment groups (inter-group changes). Correlations were evaluated by Spearman`s rank correlation.
- The results were considered significant when $p < 0.05$. A statistical analysis program (Graph Pad Instat; Graph Pad Software, Inc, California, CA, USA) was used for evaluations.

Results

Table 1: Clinical, anthropometric and biochemical parameters in patients with metabolic syndrome at the beginning and after 90 days of the study

Parameters	CG (n: 42)		OO (n: 13)	
	baseline	90-d	Baseline	90-d
Age	51.7±8.2		51.9±7.4	
Sex (female/male)	33/9		8/5	
BMI (kg/m ²)	37.70 (27.14-50.95)	35.60 (26.70-50.20)	32.50 (26.74-48.10)	32.68 (26.00-48.00)
WC (cm)	113.0 (88.0-153.0)	113.0 (88.0-140.0)	104.0 (88.0-129.0)	102.0 (80.0-126.0)
WHR	0.96 (0.79-1.12)	0.94 (0.75-1.08)	0.97 (0.86-1.09)	0.94 (0.82-1.07)
SBP (mmHg)	125.0 (76.0-170.0)	129.0 (78.0-180.0)	130.0 (100.0-181.0)	125.0 (120.0-149.0)
DBP (mmHg)	79.0 (38.0-109.0)	75.0 (53.0-119.0)	84.0 (70.0-120.0)	70.0 (85.0-115.0)
Triacylglycerol (mg/dL)	192.0 (48.0-404.0)	150.0 (60.0-573.0)	191.0 (80.0-326.0)	157.0 (81.0-415.0)
TC (mg/dL)	207.0 (128.0-313.0)	212.0 (121.0-357.0)	216.0 (167.0-262.0)	204.0 (139.0-296.0)
HDL-C (mg/dL)	46.0 (29.0-67.0)	47.0 (28.0-69.0)	45.0 (29.0-69.0)	43.0 (22.0-56.0)
LDL-C (mg/dL)	116.50 (50.0-229.0)	121.0 (58.0-175.0)	126.0 (77.0-166.0)	125.50 (58.0-215.0)
Fasting glucose (mg/dL)	102.0 (81.0-280.0)	102.0 (75.0-310.0)	93.0 (79.0-150.0)	86.0 (75.0-132.0)
Uric acid (mg/dL)	4.98 (2.70-10.18)	5.17 (1.01-8.96)	4.75 (2.61-6.35)	4.79 (3.42-7.53)
TRAP(equivalent of μM Trolox)/Uric acid ratio	161.89 (95.28-245.07)	128.13 (87.64-537.91)	132.88 (90.15-199.35)	158.48 (121.67-234.70)*

Kruskal-Wallis with post hoc Dunn`s test

* $p < 0.05$

Table 2: Spearman's correlation between metabolic parameters and antioxidant capacity in olive oil group after 90 days

Parameters	TRAP/uric acid ratio
Glucose (mg/dL)	-0,19
TC (mg/dL)	-0,004
HDL-C (mg/dL)	0,39 (0,001)
LDL-C (mg/dL)	-0,07
TG (mg/dL)	-0,32 (0,009)

r (p)

- In relation to baseline values, there was a significant increase ($p < 0.05$) in total antioxidant capacity, evaluated by TRAP, in OO group.
 - TRAP also was positively correlated with HDL-C and negatively correlated with triacylglycerol after 90 days.
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- Olive oil was associated with a decreased risk of overall mortality and an important reduction in CVD mortality in a large Mediterranean cohort conducted by Buckland G. et al (2012) in the Spanish population (EPIC-Spain).

Buckland G. et al. Am J Clin Nutr 2012;96:142–9.

- In this Spanish cohort there were a significant 26% decrease in overall mortality and a 44% decrease in CVD mortality associated with olive oil intake in the highest quartile

- Oxidative stress may play an important role in the etiology of various risk factors of MetS-related manifestations, including atherosclerosis, hypertension, type 2 diabetes, adiposity, and insulin resistance

Roberts CK, Sindhu KK. Life Sci 2009;84:705–12.

- In the present study, OO showed a statistically significant increase in TRAP/uric acid ratio.
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- Me and my colleagues conducted a study which aimed to verify if extra virgin olive oil and fish oil have a synergistic effect on lipid and oxidative stress parameters in patients with metabolic syndrome (MetS).
- Olive oil group also showed a statistically significant increase in **TRAP/uric acid ratio.**

- In the same study, we demonstrated that patients who received both, extra virgin olive oil and fish oil, presented a significant decrease in LDL-C ($P < 0.05$), TC/HDL-C ($P < 0.05$) and LDL-C/HDL-C ($P < 0.05$) indexes after 90 d when compared with baseline values

- The use of TRAP has been proposed to explore plasma antioxidant capacity. TRAP evaluates the antioxidant capacity due to known and unknown antioxidants present in the sample as well as their cooperation.

Skalicky J.,. Et al. Clin Chem Lab Med 2008;46:499–505.

- Additionally, TRAP analysis in conditions associated with **hyperuricemia**, as in patients with MetS, may be jeopardized because uric acid concentration is responsible for **60%** of plasma TAC and some reports have verified an unexpected increase in TAC in patients with MetS
- Thus, a correction of TAC based on uric acid concentration is needed

- A study conducted with 45 healthy adults, showed that extra virgin olive oil (EVOO) increased significantly the plasma antioxidant capacity after 30 d of intake ($p < 0.001$, $n = 32$).

Oliveras-López, MJ, et al. Journal of functional foods 10(2014), 475-484

- In a large, multicentre, randomized controlled trial involving people with high cardiovascular risk, a Mediterranean diet supplemented with extra-virgin olive oil was associated with a smaller increase in the prevalence of metabolic syndrome compared with advice on following a low-fat diet.

PREDIMED Study Investigators. CMAJ, November 18, 2014, 186(17)

- In a recent study, plasmatic antioxidant capabilities and xanthine oxidase activity were determined in 75 metabolic syndrome (MetS) patients after 5 years intervention with Mediterranean Diet (MeDiet) supplemented with extra-virgin olive oil (MeDiet+EVOO) or with nuts or with low-fat diet (the PREDIMED study).
- **A MeDiet enriched with either virgin olive oil or nuts enhances the plasma antioxidant capabilities and decreases xanthine oxidase activity in patients with the metabolic syndrome**

- The present study has several limitations to consider.
 - First, the small number of participants;
 - Second, although the patients were instructed not to change their usual diets or other lifestyle factors throughout the intervention period, those variables were not directly measured.

- This study provides evidence that extra-virgin olive oil can improve the antioxidant capacity in MetS patients.
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Thank you!
