THE SCIENCE BEHIND EXTRA VIRGIN OLIVE OIL:

HOW POLYPHENOLS INFLUENCE LDL OXIDATION, ENDOTHELIAL FUNCTION, AND CARDIOVASCULAR HEALTH

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

EXTRA VIRGIN OLIVE OIL (EVOO)

- Continues hydroxytyrosol (HT)
- Olive Oil has 3 phenolic compounds that scavenge ROS
  - Peroxynitrite ($ONOO^-$)
  - Hydrogen peroxide (H_2O_2)
  - Hydroxyl (OH^-)
- Reactive Oxygen Species (ROS) damages all tissues especially fatty cellular membranes, in a process called lipid peroxidation

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

POLYPHENOLS IN EVOO

HT dissociates Nrf2 from Keap1 in cytoplasm of cells and releases Nrf2 which then binds to antioxidant response element (ARE) or DNA.
This then presents in anti-inflammatory pathway activation.

This decreases NF-κB, IL-6, and STAT-3 hence shuts down inflammation

HT blocks NF-κB attachment to endothelial cells and mitochondria and reduces ROS

HT increases LDL receptor lifespan

HT reduces ox LDL formation

HT activates PPAR-δ in macrophages which induces reverse cholesterol transport and less NLRP3 inflammasome production

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

EVOO

- **Oleuropein** causes the pungent, bitter taste and it is converted to HT
- **Oleocanthal** has a peppery burn and it inhibits COX and COX-2 and hence anti-inflammatory

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

EVOO

- Poly Unsaturated Fatty Acids (PUFAs) have saturated hydrogen bonds and hence get oxidized. They are prone to attack by ROS.

- PUFAs are incorporated into cellular membranes and LDL particles. Hence you get lipid peroxidation and oxidized LDL. Lipid peroxidation causes Nitric Oxide (NO) depletion

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

EVOO

Dose:
20 g + 1.5-2 tablespoons
minimal phenol content is 250mg/kg

High phenol content oil (500-800) use 1 tablespoon
Raw - not cooked
Mix as finishing oil

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

EVOO

Linoleic Acid (Omega 6)

Found in seed oils

Oxidizes 10 - 40x faster than OLEic Acid (MUFA)

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

MONOUNSATURATED FATTY ACIDS (MUFA)

EVOO has OLEic Acid

- It resists oxidation
- OLEiC Acid is also found in high oleic safflower oil, canola oil, and avocado oil but do NOT give the same health benefit as EVOO because of the absence of polyphenols!

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

DOI: 10.1056/NEJMoa1800389

EVOO

Eurolive Clinical Trial

Showed dose dependant reduction in oxidized LDL (oxLDL) with polyphenol content in EVOO

So...polyphenols prevent lipd peroxidation

Endothelial dysfunction is associated with reduced nitric oxide (NO) bioavailability and is attenuated postprandially by extra virgin olive oil (EVOO), but not by refined olive oil.

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

EVOO

Polyphenol content

Low = 50mg/kg

High = 7250mg/kg

26% of retail olive oil is low content

50% is ~ 400 mg/kg

25% is 7625 mg/kg

Refrigerator Test: 4 tablespoons 48 hours

Semi-solid = Good

Clear = low quality

Sniff Test: Body temp in cap

smells like grass or green tomatoes = Good

crayon smell = Bad

Cough Test : Bitterness in the throat

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

DOI: 10.1056/NEJMoa1800389

PREDIMED STUDY

7447 Patients

with

T2DM or 3 risk factors for CAD

No CAD at baseline

DIET

Mediterranean + Extra Virgin Olive Oil (EVOO)

- 1 Liter of EVOO per week
- EVOO + 300-400mg/kg polyphenol content

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

DOI: 10.1056/NEJMoa1800389

PREDIMED STUDY RESULTS

30% decrease in cardiovascular events

NNT = 61 over 5 years

CRP reduced by 0.54

IL-6 reduced by 1.3

ICAM reduced by 50

TNF-α no change

CD40 lingand reduction

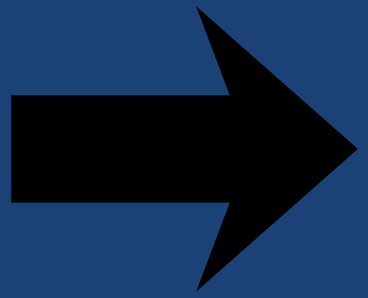
Overall,
IL-6 + CRP reduction predicted outcomes

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

DOI: 10.1016/S0140-6736(22)00122-2

OLIVE OIL IN CAD POINTS

CORDIOPREV TRIAL



- 1002 patients with CAD
- 1 liter of EVOO vs Low Fat Diet
- 7-year follow-up
- 26-28% Relative Risk Reduction
- NNT 20-25!
- Reduction in IL-6 + hsCRP

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

DOI: 10.1016/j.jacc.2021.10.041

NON MEDITERRANEAN DIET POPULATION STUDY

60582 Women Nurses Health

31801 patients in Health Professional follow-up study

Non-CAD patients

½ tablespoon of olive oil a day

- 14% reduced risk
- 18% reduced CAD risk

Breakdown: Most benefit was with EVOO vs ordinary olive oil

This confirmed benefit NOT just from OLEiC acid but due to polyphenol content

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

DOI: 10.1079/phn2005935

SUN COHORT STUDY

- 2200 subjects over 14 years
- 2 tablespoons of EVOO
- 44% reduced relative risk
- Mostly due to CRP + IL-6 reaction
- 16% reduced risk for every additional 25 grams of EVOO per day

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

DOI: 10.1038/s41430-024-01442-8

MOLI-SANI COHORT

22892 Patients - 12-year study

37% reduction in CV adverse outcomes

25% reduced risk in CV mortality

20% lower all-causes of mortality

1 ½ tablespoons of EVOO needed compared to ordinary olive oil to produce benefit

BP + HR lower

CRP + D-Dimer lower

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

DOI: 10.1038/s41430-024-01442-8

MOLI-SANI COHORT

- EVOO’s phenolic compounds are active antioxidants
- Inhibit NF-κB translation into the nucleus of endothelial cells and macrophages
- Reduce Il-6, TNF, MCP-1, COX-2and suppress the NLRP3 complex

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

COMPARATIVE NUMBER NEEDED TO TREAT (NNT)

Transcendental meditation in CAD
NNT = 10 over 5 years
ARR + 10%

Transcendental meditation in primary prevention
NNT~ 30-50

Predimed 10 Prevention
Mediterranean Diet
NNT = 30

DASH Diet
Implied NNT= 40-60

Tobacco abstinence
NNT = 20 in 1 year

Statins in primary prevention
NNT = 50-80 over 5 years

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

KEY HIGHLIGHTS

- A study showed a 30% decrease in cardiovascular events
- Another study showed a reduction in IL-6 + hsCRP
- ½ tablespoon of EVOO a day showed a 14% reduced risk and 18% reduced CAD risk
- 37% reduction in CV adverse outcomes, 25% reduced risk in CV mortality, 20% lower all-causes of mortality
- EVOO's phenolic compounds are active antioxidants
- Polyphenols prevent lipd peroxidation
- Quality olive oil has a high polyphenol count
- Good EVOO has a pungent, bitter taste and peppery burn

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

References

- **PREDIMED Study**

Estruch, R., Ros, E., Salas-Salvadó, J., Covas, M. I., Corella, D., Arós, F., Gómez-Gracia, E., Ruiz-Gutiérrez, V., Fiol, M., Lapetra, J., Lamuela-Raventos, R. M., Serra-Majem, L., Pintó, X., Basora, J., Muñoz, M. A., Sorlí, J. V., Martínez, J. A., Fitó, M., Gea, A., Hernán, M. A., … PREDIMED Study Investigators (2018). Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. The New England journal of medicine, 378(25), e34. https://doi.org/10.1056/NEJMoa1800389

- **CORDIOPREV Trial**

Delgado-Lista, J., Alcala-Diaz, J. F., Torres-Peña, J. D., Quintana-Navarro, G. M., Fuentes, F., Garcia-Rios, A., Ortiz-Morales, A. M., Gonzalez-Requero, A. I., Perez-Caballero, A. I., Yubero-Serrano, E. M., Rangel-Zuñiga, O. A., Camargo, A., Rodriguez-Cantalejo, F., Lopez-Segura, F., Badimon, L., Ordovas, J. M., Perez-Jimenez, F., Perez-Martinez, P., Lopez-Miranda, J., & CORDIOPREV Investigators (2022). Long-term secondary prevention of cardiovascular disease with a Mediterranean diet and a low-fat diet (CORDIOPREV): a randomised controlled trial. Lancet (London, England), 399(10338), 1876–1885. https://doi.org/10.1016/S0140-6736(22)00122-2

- **Nurses' Health Study**

Guasch-Ferré, M., Li, Y., Willett, W. C., Sun, Q., Sampson, L., Salas-Salvadó, J., Martínez-González, M. A., Stampfer, M. J., & Hu, F. B. (2022). Consumption of Olive Oil and Risk of Total and Cause-Specific Mortality Among U.S. Adults. Journal of the American College of Cardiology, 79(2), 101–112. https://doi.org/10.1016/j.jacc.2021.10.041

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP

References

- **The SUN cohort study**
  Martínez-González M. A. (2006). The SUN cohort study (Seguimiento University of Navarra). Public health nutrition, 9(1A), 127–131. https://doi.org/10.1079/phn2005935

- **Moli-Sani Study cohort**
  Ruggiero, E., Di Castelnuovo, A., Costanzo, S., Esposito, S., De Curtis, A., Persichillo, M., Cerletti, C., Donati, M. B., de Gaetano, G., Iacoviello, L., Bonaccio, M., & Moli-sani Study Investigators (2024). Olive oil consumption is associated with lower cancer, cardiovascular and all-cause mortality among Italian adults: prospective results from the Moli-sani Study and analysis of potential biological mechanisms. European journal of clinical nutrition, 78(8), 684–693. https://doi.org/10.1038/s41430-024-01442-8

- **The EUROLIVE study**
  Cicero, A. F., Nascetti, S., López-Sabater, M. C., Elosua, R., Salonen, J. T., Nyyssönen, K., Poulsen, H. E., Zunft, H. J., Kiesewetter, H., de la Torre, K., Covas, M. I., Kaikkonen, J., Mursu, J., Koenbick, C., Bäumler, H., Gaddi, A. V., & EUROLIVE Study Group (2008). Changes in LDL fatty acid composition as a response to olive oil treatment are inversely related to lipid oxidative damage: The EUROLIVE study. Journal of the American College of Nutrition, 27(2), 314–320. https://doi.org/10.1080/07315724.2008.10719705

Dr. Pradip Jamnadas, MD
MBBS, FACC, FSCAI, FCCP, FACP