

1 **Abstract**

2 **Nitro-fatty acids as novel Virgin olive oil quality markers**

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5 Virgin Olive oil (VOO) consumption exerts beneficial health effects and helps reduce the
6 risk of infectious, cardiovascular, liver, and neurodegenerative diseases, among others.
7 Nitro-fatty acids (NO₂-FA) are endogenously formed in VOO as well as in gastric condi-
8 tions, exhibiting pleiotropic anti-inflammatory responses. In this review, we analyzed the
9 conditions which favor the formation of VOO-derived NO₂-FA. Firstly, will discuss the
10 formation of NO₂-FA in contrasting varieties of VOO showing a strong correlation be-
11 tween the formation of NO₂-FA and the type of cultivar. The variation of NO₂-FA levels
12 with the stage of maturation will be discussed, observing maximum levels of NO₂-FA in
13 intermediate stages. It should be considered that VOO has other key bioactive compo-
14 nents such as polyphenols. We will discuss how polyphenols play a role in modulating
15 NO₂-FA formation and how all these components would be acting synergistically to exert
16 antioxidant/anti-inflammatory protection. Finally, will discuss how VOO supplementa-
17 tion is capable of improving cellular respiration in hepatic mitochondria from Non-alco-
18 holic fatty liver disease (NAFLD) animal model, mainly due to the presence of NO₂-FA.
19 There appears to be a strong positive correlation between NO₂-FA formation from VOO
20 intake and mitochondrial protection. Updated data collection strongly supports the pro-
21 posal of NO₂-FA as novel VOO quality markers. The information reviewed here can be
22 useful to make recommendations about which cultivars to use and at what stages of mat-
23 uration the oil should be extracted to maximize the concentration of these compounds that
24 are so beneficial to human health.
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26 **Biography.** Dr. Rubbo has investigated the biological production of nitric oxide (•NO)
27 and reactive oxygen species and their central role in the pathogenesis of acute and chronic
28 diseases. His independent research on the biological chemistry and pharmacology of •NO
29 has critically contributed to unraveling new and pathophysiologically relevant
30 information about the reactions of •NO and oxidized lipids and demonstrated the products
31 of this reaction to be essential mediators of tissue oxidant protection. Investigations were
32 particularly focused on the antioxidant roles that •NO plays at the biochemical and
33 cellular levels. Understanding the reactions of •NO-derived reactive species with
34 unsaturated fatty acids forming nitro-fatty acids (NFA, nitroalkenes) has been a central
35 focus of Rubbo's research and is of significance because it unifies eicosanoid and •NO
36 cell signaling pathways so critical for the regulation of tissue and inflammatory function.
37 Dr. Rubbo's research has progressed, with •NO and oxidative stress-related investigation
38 now active and fertile grounds for understanding general mechanisms of key events such
39 as inflammatory injury. In recent years, Dr. Rubbo carried out pioneering research on the
40 chemical-structural characterization of NFA, describing key anti-inflammatory signaling
41 actions. These studies have allowed propose a modulating role of NFA on arachidonic
42 acid signaling cascades through activation of antioxidant pathways. His lab is performing
43 oxy-lipidomics and metabolomics with the aim of discovering new molecules to diagnose
44 and treat neurodegenerative diseases, particularly oxylipins as new monitoring markers,
45 providing a platform for developing novel pharmacologic interventional strategies
46 directed toward modulating inflammatory tissue injury. Finally, within the framework of
47 the collaboration with olive oil industry, Dr. Rubbo has demonstrated the presence of
48 NFA in extra virgin olive oils, as new quality indicators. He has published over ninety

49 original research and high-cited review articles, as well as several Master's and Doctorate
50 Theses and collaboration with international reference laboratories. **Orcid: 0000-0002-**
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