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Oleic Acid – The Anti-Breast Cancer Component in Olive Oil

David Tin Win

Faculty of Science and Technology, Assumption University
Bangkok, Thailand

Abstract

The chemistry of oleic acid was described. Discovery of oleic acid as the major component of olive oil that is responsible for a healthy Mediterranean diet was mentioned and the prevention of breast cancer by oleic acid was examined. One study indicated that the protection of olive oil against breast cancer may be due to oleic acid components rather than to the acid itself.

Keywords: *Artherosclerosis, charbroiling, cholesterol, free radicals, glycerides, Herceptin, Mediterranean diet, oleic acid, omega-9, oncogene, trastuzumab.*

Introduction

The news of the discovery that oleic acid, the main component of olive oil, is responsible for protecting breast cancer, has stimulated renewed interest in oleic acid. Oleic acid is the main reason why eating a Mediterranean diet rich in fruits, vegetables and particularly olive oil is healthy (Reuters 2005).

Dr. Javier Menendez of the Northwestern University Feinberg School of Medicine in Chicago said oleic acid blocks the action of a cancer-causing oncogene, called HER-2/neu, which is found in about 30% of breast cancer patients (Menendez *et al.* 2005). High concentrations of oleic acid can lower blood levels of cholesterol and lower the risk of heart problems (Rickman 2004). "We have a molecular link that can explain why the Mediterranean diet is demonstrating all these benefits," Menendez added (Reuters 2005).

Oleic acid also synergistically enhances cancer drug effectiveness (Menendez *et al.* 2005). For example oleic acid improved the effectiveness of herceptin, a breast cancer drug using targeted therapy made by Swiss drug maker, Roche Holding, that works against the HER-2/neu gene (Reuters 2005).

Oleic acid (omega-9) is a fatty acid found in animal and vegetable oils, such as olive oil (extra virgin or virgin), olives, avocados, almonds, peanuts, sesame oil, pecans, pistachio nuts, cashews, hazelnuts, macadamia nuts, etc. It occurs naturally in greater quantities than any other fatty acid. It lowers heart attack risk and artherosclerosis, and aids in cancer prevention. It is essential but technically not an EFA (essential fatty acid), because the human body can manufacture a limited amount, provided that essential EFAs are present (Rotella 2004). It is used in the food industry to make synthetic butters and cheeses. It is also used to flavor baked goods, candy, ice cream and sodas (Rickman 2004).

This paper describes the chemistry of oleic aid and examines its capability to prevent breast cancer.

The Chemistry

Oleic acid (omega-9) is a mono-unsaturated fatty acid found in animal and vegetable oils (Figs. 2 and 3), such as olive oil that contains 55-80% of the acid, as glyceride[1], in quantity greater than any other fatty acid (Rickman 2004). The chemical structure of the molecule is shown in Fig. 1. It is a 18-carbon chain compound with the empirical formula $C_{18}H_{34}O_2$ and has one double bond, placed symmetrically, between the C-9 and C-10 carbon atoms and a –COOH carboxylic acid group at one end. Its IUPAC name is cis-9-octadecenoic acid; its lipid shorthand name is 18:1 cis-9 and the CAS registry number is 2027-47-6. The saturated form of this acid is

[1] The tri-ester of glycerol, a tri-hydroxy alcohol CH_2 OH.CHOH.CH_2OH

stearic acid (Keffler and McLean 1935; Wikipedia 2004).

It is a pale-yellow / brownish-yellow oily liquid with a lard-like odor and is insoluble in water. The specific gravity is 0.895 g mL^{-1} at 25°C with a boiling point of 360°C (680°F) and melting point 16.3°C (61°F) (NIST 2004) and the important condensed phase thermochemical data are $\Delta_f H°_{liquid}$ = -815.21 kJ mol^{-1}; $\Delta_c H°_{liquid}$ = -11127.1 kJ mol^{-1} (Afeefy *et al.* 2004; Emery and Benedict 1911).

A chemical reaction of oleic acid that has environmental implications is the interaction with other atmospheric compounds, such as ozone, once it gets dispersed into the atmosphere. Such interactions create health hazard byproducts whose particles are small enough to be inhaled, cause eye and skin irritations and induce respiratory problems such as asthma and bronchitis.

Frying meat (charbroiling) releases oleic acid into the air. Urban areas especially those that have restaurant clusters can have high levels of oleic acid in the atmosphere.

Gopalakrishnan and Allen (2004) of Ohio State University used sum-frequency generation spectroscopy[2] to study the reaction between molecules of oleic acid and water. Next they plan to study the surface interactions of oleic acid and ozone to form more fatty acids and free radicals in the atmosphere, which can cause health problems.

Health Benefits

As mentioned above, oleic acid (omega-9) is found in animal and vegetable oils and is the major component that is responsible for health benefits of the Mediterranean diet, rich in vegetables and fruits. Although researchers were aware that a Mediterranean diet can reduce the risk of breast cancer and other illnesses such as heart disease, until now they did not know how.

A study by Menendez of the Northwestern University Feinberg School of Medicine in Chicago revealed that oleic acid blocks the action of HER-2/neu, a cancer-causing oncogene found in about 30% of breast cancer patients (Reuters 2005). HER-2/neu positive tumors are an aggressive form of the disease and have a poor prognosis. Oleic acid suppressed the action of the oncogene and also synergistically improved the effectiveness of the breast cancer drug, Herceptin, a targeted therapy made by Swiss drug maker Roche Holding that works against the HER-2/neu gene (Reuters. 2005).

Mendez *et al.* (2005) intend to study the mechanism that oncogene is targeted by the acid, and are planning studies of animals with breast cancer to see if a diet high in olive oil can alter the oncogene activity and the impact of Herceptin. A molecular link than can explain the health benefits of the Mediterranean diet seem to have been identified.

However, the relationship between the olive oil intake and breast cancer risk or progression has become a controversial issue. Also oil components rather than the acid itself may be responsible for the protection of olive oil against breast cancer (Mendez *et al.* 2005).

Mendez's study used flow cytometry, immuno-fluorescence microscopy, western blotting, metabolic status (MTT), soft-agar colony formation, enzymatic *in situ* labeling of apoptosis-induced DNA double-strand breaks (TUNEL assay analyses), and caspase-3-dependent poly-ADP ribose polymerase (PARP) cleavage assays. The effects of exogenous supplementation with oleic acid on the expression of Her-2/*neu* oncogene, that plays an active role in breast cancer etiology and progression were characterized. In addition the effect of oleic acid on the efficacy of trastuzumab (Herceptin™), a humanized monoclonal antibody binding with high affinity to the ectodomain of the Her-2/*neu*-coded $p185^{Her\text{-}2/neu}$ oncoprotein was investigated. BT-474 and SKBr-3 breast cancer cells that naturally exhibit amplification of the Her-2/*neu* oncogene were used in the study (Mendez *et al.* 2005).

Flow cytometric analyses demonstrated a 46% reduction of cell surface-associated

[2] *A spectroscopic method that uses laser light to observe molecular structure and orientation, at the interface of compounds.*

$p185^{Her\text{-}2/neu}$ following treatment of the Her-2/*neu*-overexpressors BT-474 and SK-Br3 with oleic acid. It was comparable to that seen on exposure to optimal concentrations of trastuzumab (up to 48% reduction with 20 µg/ml trastuzumab). As determined by flow cytometry (70% reduction), immuno-blotting, and immuno-fluorescence microscopy studies, the concurrent exposure to oleic acid and suboptimal concentrations of trastuzumab (5 µg/ml) synergistically down-regulated Her-2/*neu* expression. As assessed by MTT-based cell viability and anchorage-independent soft-agar colony formation assays, a strong synergism was seen in the nature of the cytotoxic interaction between oleic acid and trastuzumab. As confirmed by TUNEL and caspase-3-dependent PARP cleavage oleic acid co-exposure synergistically enhanced trastuzumab efficacy towards Her-2/*neu* over-expressors by promoting DNA fragmentation associated with apoptotic cell death. In addition, treatment with oleic acid and trastuzumab dramatically increased both the expression and the nuclear accumulation of $p27^{Kip1}$, a cyclin-dependent kinase inhibitor playing a key role in the onset and progression of Her-2/*neu*-related breast cancer. Oleic acid co-exposure enhanced trastuzumab's ability to inhibit signaling pathways downstream of Her-2/*neu*, including phospho-proteins such as AKT and MAPK (Mendez *et al*. 2005).

These findings demonstrate that oleic acid suppresses Her-2/*neu* over-expression that in turn interacts synergistically with anti-Her-2/*neu* immunotherapy by promoting apoptotic cell death of breast cancer cells with Her-2/*neu* oncogene amplification. This is a previously unrecognized property of oleic acid. It offers a molecular mechanism that allows individual fatty acid regulation of the malignant behavior of breast cancer cells. This will be helpful in the design of future epidemiological studies and consequently influence dietary counseling (Mendez *et al.* 2005).

One or two tablespoons of extra virgin or virgin olive oil per day should provide sufficient oleic acid for adults. However, the 'time-released' effects of obtaining these nutrients from nuts and other whole foods is thought to be more beneficial than consuming the entire daily amount via a single oil dose (Rotella 2004).

Conclusion

Oleic acid is a monounsaturated fatty acid with a symmetrically placed double bond. Its IUPAC name is cis-9-octadecenoic acid; its lipid shorthand name is 18:1 cis-9 and the CAS registry number is 2027-47-6. Identification of oleic acid as the major component of olive oil that is responsible for a healthy Mediterranean diet, especially for the prevention of breast cancer, precipitated a controversy. The protection of olive oil against breast cancer may be due to oleic acid components rather than to the oil itself.

References

Afeefy, H.Y.; Liebman, J.F. and Stein, S.E. 2004. Condensed Phase Thermochemistry Data.<http://webbook.nist.gov/cgi/cbook.cgi?ID=C2027476&Units=SI>

Emery, A.G.; and Benedict, F.G. 1911. The heat of combustion of compounds of physiological importance. Am. J. Physiol**.** 28: 301-7.

Gopalakrishnan, S.; and Allen, H. 2004. Oleic Acid in the Atmosphere. Ohio State University. <http://researchnews.osu.edu/archive/badoleic.htm>

Keffler, L.; and McLean, J.H. 1935. Homology in long-chain compounds I. Oleic acid and the n-alkyl oleates. J. Soc. Chem. Ind**.** 17:178-85**.**

Mendez, J.A.; Vellon, L.; Colomer, R.; and Lupu, R. 2005. Oleic acid, the main monounsaturated fatty acid of olive oil, suppresses Her-2/neu (erbB-2) expression and synergistically enhances the growth inhibitory effects of trastuzumab (Herceptin^{TM}) in breast cancer cells with Her-2/neu oncogene amplification. European Society for Medical Oncology.
http://www.annonc.oupjournals.org/cgi/content/abstract/mdi090v1 (10 Jan. 2005).

NIST. 2004.
http://webbook.nist.gov/cgi/cbook.cgi?ID=C2027476&Units=SI>

Reuters. 2005. Oleic acid key to olive oil's anti-cancer effect. <http://www.msnbc.msn.com/id/6807702> (Updated: 12:53 p.m. ET Jan. 10, 2005).

Rickman, E. 2004. Oleic Acid. <http://www.cas.astate.edu/draganjac/Oleicacid.html>

Rotella, P. 2004. Healthy Fats - Essential Fatty acids. <http://goodfats.pamrotella.com> (last updated 22 October 2004).

Wikipedia (the free encyclopedia). 2004. <http://en.wikipedia.org/wiki/Oleic_acid>

Fig. 1. The chemical structure of oleic acid

Fig. 2. The olive tree is a major source of oleic acid.