

A Selection of Scientific Research Supporting the Health Benefits of Olive Leaf Extract & Oleuropein

- ANTIBACTERIAL
- ANTIFUNGAL
- ANTI-INFLAMMATORY
- ANTIOXIDANT & FREE RADICAL SCAVENGER
- ANTIVIRAL
- BLOOD PRESSURE (HYPERTENSION)
- CANCER
- CHOLESTEROL, CORONARY & HEART
- COSMETIC
- DIABETES (HYPOGLYCEMIA)
- FEVER
- GENERAL
- HIV/AIDS
- IMMUNE SYSTEM
- RADIO-PROTECTIVE
- RESPIRATORY (INFLUENZA, PNEUMONIA ETC)
- ULCERS

The therapeutic benefits of Olive Leaf Extract have been widely researched and documented in more than 30 medical and scientific publications including:

- American Journal of Chinese Medicine
- Antimicrobial Agents and Chemotherapy
- Applied and Environmental Microbiology
- Arzneim-Forsch
- Belgian Pharmacology Journal
- European Journal of Cancer Farmaceutsk Revy
- Journal of the American Chemists Society
- Journal of Applied Bacteriology
- Journal of Chemical Ecology
- Journal of Ethnopharmacology
- Journal Universel des Sciences Medicales
- Lancet
- Microbiology
- Nature's New Biology
- Nutrition Research
- Phytochemistry
- Planta
- University of Reading, UK
- Positive Health News

Selection of institutes with published reports on the health benefits of olive leaf extract and oleuropein:

- Antwerp University, Belgium
- Cairo University, Egypt
- Durban University, South Africa
- Granada University, Spain

- Harvard Medical School, USA
- King Saud University, Saudi Arabia
- Kobe University, Japan
- Milan University, Italy
- Nebraska University, USA
- New York University School of Medicine, USA
- Rene Descartes University, France
- Wageningen University, Netherlands

Additional publications and institutes can be found inside this document.

ANTIBACTERIAL

TITLE:In vitro antimicrobial activity of olive leaves

AUTHOR:Markin-D; Duek-L; Berdicevsky-I

INSTITUTE:Department of Microbiology, Rappaport Faculty of Medicine, Technion – Institute of Technology, Haifa

SOURCE:Mycoses. 2003; 46(3-4): 132-136

YEAR: 2003

ABSTRACT: We investigated the antimicrobial effect of olive leaves against bacteria and fungi. The microorganisms tested were inoculated in various concentrations of olive leaf water extract. Olive leaf 0.6% (w/v) water extract killed almost all bacteria tested, within 3 h. Dermatophytes were inhibited by 1.25% (w/v) plant extract following a 3-day exposure whereas *Candida albicans* was killed following a 24 h incubation in the presence of 15% (w/v) plant extract. Olive leaf extract fractions, obtained by dialysis, showed antimicrobial activity consisted of particles smaller than 1000 molecular rate cutoffs. Scanning electron microscopic observations of *C. albicans*, exposed to 40% (w/v) olive leaf extract, showed invaginated and amorphous cells. *Escherichia coli* cells, subjected to a similar treatment but exposed to only 0.6% (w/v) olive leaf extract showed complete destruction. These findings suggest an antimicrobial potential for olive leaves.

TITLE: Antimicrobial Properties of Oleuropein and Products of Its Hydrolysis from Green Olives.

AUTHOR: Fleming-HP; Walter-WM Jr; Etchells-JL

YEAR:1973

SOURCE:Applied-Microbiology; 26 (5) 777-782, 14 ref.

ABSTRACT: Antibacterial action of oleuropein and its hydrolysis products against certain species of lactic acid bacteria involved in the brine fermentation of olives was investigated. Oleuropein was not inhibitory, but 2 of its hydrolysis products, the aglycone and elenolic acid, inhibited growth of the 4 species of lactic acid bacteria tested [*Lactobacillus plantarum*, *L. brevis*, *Leuconostoc mesenteroides* and *Pediococcus cerevisiae*]. Another hydrolysis product, beta-3,4dihydroxyphenylethyl alcohol, was not inhibitory. The aglycone of oleuropein and elenolic acid were much more inhibitory when the broth medium contained 5% NaCl; 150 mug of either compound/ml prevented growth of *L. plantarum*. A crude extract of oleuropein, tested by paper disk bioassay, was inhibitory to 3 [*Staphylococcus aureus*, *Bacillus subtilis* and *Pseudomonas solanacearum*] of 17 species of bacteria screened. The acid hydrolysate of the extract was inhibitory to 11 of the bacteria, which included 4 species of lactic acid bacteria and other Gram-positive and Gram-negative species. Neither crude preparation was inhibitory to growth of the 7 species of yeasts tested. A possible explanation is given for the previously reported observation that heating (3 min, 74 degree C) olives prior to brining render them more fermentable by lactic acid bacteria. Results of a brining

experiment indicated that oleuropein is degraded to antibacterial compounds when unheated olives are brined.

TITLE: Studies on the mechanism of the antimicrobial action of oleuropein.

AUTHOR:Juven-B; Henis-Y; Jacoby-B

INSTITUTE: Div. of Food Tech., Volcani Inst. of Agric. Res., Rehovot, Israel

YEAR: 1972

SOURCE: Journal-of-Applied-Bacteriology; 35 (4) 559-567, 25 ref.

ABSTRACT: This work was undertaken to investigate the mechanism of the antimicrobial action of the phenolic glycoside, oleuropein, the bitter principle of green olives. It was shown to be surface active, and this, in conjunction with its damaging effect on the permeability of cell membranes, seemed to be the basis of its antimicrobial activity. Oleuropein affected a significant leakage of glutamate, K and inorganic phosphate from *Lactobacillus plantarum*. Oleuropein had no effect on the rate of glycolysis when added to resting cells of *L. plantarum*, but it caused a decrease in the ATP content of the cells.

TITLE: Inhibition of Salmonella enteritidis by oleuropein in broth and in a model food system.

AUTHOR:Tassou,-C-C; Nychas,-GJ

INSTITUTE:National Agricultural Research Foundation, Institute of Technology of Agricultural Products, Lycovrysi, Athens, Greece.

SOURCE: Lett-Appl-Microbiol. 1995 Feb; 20(2): 120-4

YEAR: 1995

ABSTRACT: The inhibitory effect of commercial 'pure' oleuropein was tested against *Salmonella enteritidis* in a coliform broth and in reconstituted milk (model food system). It was found that the inhibition of this organism in the broth was influenced by the initial inoculum size, the pH of the medium and the concentration of additive. The inhibition was more pronounced in samples with low pH and low inoculum size. No such inhibition was evident in the model food system.

TITLE:Modeling the effectiveness of a natural antimicrobial on Salmonella enteritidis as a function of concentration, temperature and pH,using conductance measurements.

AUTHOR:Koutsoumanis,-K; Tassou,-C-C; Taoukis,-P-S; Nychas,-G-J

INSTITUTE: Agricultural University of Athens, Department of Food Science and Technology, Hellas, Greece.

SOURCE: J-Appl-Microbiol. 1998 Jun; 84(6): 981-7

YEAR: 1998

ABSTRACT: The growth of *Salmonella enteritidis* in a brain heart infusion medium was monitored using the traditional viable count method and by conductance measurements using a Rabbit impedance instrument. Growth curves (log₁₀ cfu ml⁻¹ vs time) at three different concentrations of oleuropein (0, 0.2 and 0.8%), pH values in the range of 5-8 and incubation temperatures from 22 to 42 degrees C were modeled using the Gompertz equation. A good correlation between the maximum growth rate from the viable count method and the maximum slope of the conductance curve from the impedance instrument was established. Based on this correlation, the maximum specific growth rate of *Salm. enteritidis* was modeled as a function of the oleuropein concentration, initial pH values and the incubation temperature with a quadratic equation, using a new, large dataset of growth measurements by conductance. The developed model was validated by statistical comparison of predicted growth rates with growth rates determined by the viable count method, within the limits of the antimicrobial, pH and temperature domain.

TITLE:Characterization of an oleuropein degrading strain of *Lactobacillus plantarum*. Combined effects of compounds present in olive fermenting brines (phenols, glucose and NaCl) on bacterial activity.

AUTHOR:Marsilio,-V; Lanza,-B.

SOURCE: J-sci-food-agric. Sussex : John Wiley & Sons Limited. Apr 1998. v. 76 (4) p. 520-524

YEAR:1998

ABSTRACT:This study aims to examine the effects of glucose and NaCl on the ability of an oleuropein degrading strain of *Lactobacillus plantarum*, strain B21, to grow in the presence of oleuropein, its degradation product, hydroxytyrosol, and p-coumaric acid. Oleuropein (10 g litre⁻¹) and 2 g litre⁻¹ hydroxytyrosol combined with NaCl did not inhibit bacterial growth, whereas 1 g litre⁻¹ p-coumaric acid showed low inhibitory activity. This study also presents that bacterial beta-glucosidase and esterase are involved in the breakdown of oleuropein. Oleuropein (10 g litre⁻¹) incorporated in the cultivation medium without glucose was completely degraded to derivative products within 20 days, whereas in the presence of glucose, at concentrations up to 50 g litre⁻¹ beta-glucosidase activity was partially inhibited, and 30-70% of oleuropein residual content remained in the cultivation medium. Esterase activity involved in the second step of biodegradation process, was not influenced by glucose. Incorporation of glucose in the growth medium adversely affected the ability of *L. plantarum* to break-down oleuropein. The findings of this study are significant since it could lead to the development of a new biotechnology for removing the bitter principle, oleuropein, from olives replacing the traditional alkali treatment used for debittering olives.

TITLE:Inhibition of *Staphylococcus aureus* by olive phenolics in broth and in a model food system.

AUTHOR: Tassou,-C.C.; Nychas,-G.J.E.

SOURCE: J-food-prot. Des Moines, Iowa : International Association of Milk, Food and Environmental Sanitarians. Feb 1994. v. 57 (2) p. 120-124.

YEAR:1994

ABSTRACT:The commercial 'pure' oleuropein and phenolics extracted from olives inhibited the growth and enterotoxin production by *Staphylococcus aureus* S-6 in broth as well as in reconstituted milk (model food system). It was found that the inhibition of this organism in N-Z amine A broth was influenced by the initial inoculum size, the pH of the media, and the concentration of additive. In particular, growth and enterotoxin B production by *S. aureus* were inhibited in broth with a high concentration of oleuropein (0.6%). The inhibition was more pronounced in samples with low pH and low inoculum size. In the case of milk, enterotoxin B production was also influenced by the initial concentration of extract. [Extracts from olives have been shown to inhibit or delay the rate of growth of a range of bacteria and micro fungi such as *Pseudomonas fluorescens*, *Lactobacillus plantarum*, *Bacillus megaterium*, *Staphylococcus aureus*, *Enterobacteriaceae*, *Aspergillus* spp., *Saccharomyces*, *Pichia*, *Torulopsis*, *Candida*.]

TITLE:The effect of the olive phenolic compound, oleuropein, on growth and enterotoxin B production by *Staphylococcus aureus*.

AUTHOR:Tranter,-H.S.;Tassou,-S.C.;Nychas,-G.J

SOURCE: J-Appl-Bacteriol. Oxford : Blackwell Scientific Publications. Mar 1993. v. 74 (3) p. 253-259.

YEAR:1993

ABSTRACT:The presence of low concentrations (0.1% w/v) of oleuropein, a phenolic compound extracted from olives, delayed the growth of *Staphylococcus aureus* in NZ amine A and brain heart infusion media modified by the addition of growth factors and glucose (NZA+ and BHI+), as indicated by changes in conductance, whilst higher concentrations (0.4-0.6% w/v) inhibited growth completely. Intermediate concentrations of oleuropein (0.2%) prevented growth in BHI+ but allowed growth to occur in NZA+ despite an extended lag phase (30 h). Concentrations of oleuropein > 0.2% inhibited growth and production of

enterotoxin B in both types of media. Lower levels (0.1 %) did not affect the final viable count and production of toxin in BHI+ but decreased the number of viable organisms and reduced the toxin production in NZA+ by eightfold. An increase in the concentration of oleuropein resulted in a decrease in the amount of glucose assimilated and consequently the amount of lactate produced. In addition, oleuropein prevented the secretion of a number of exoproteins. Addition of oleuropein during the exponential phase appeared to have no effect on the growth of *Staph. aureus* in NZA+.

TITLE:Bactericidal action of oleuropein extracted from green olives against *Lactobacillus plantarum*.

AUTHOR:Ruiz-Barba,-J-L; Garrido-Fernandez,-A; Jimenez-Diaz,-R

INSTITUTE:Correspondence (Reprint) address, R. Jimenez-Diaz, Unidad Estructural de Biotecnologia de Alimentos, Inst. de la Grasa y sus Derivados (CSIC), Avda. Padre Garcia Tejero 4, Apdo. 1078, 41012 Seville, Spain

SOURCE: Letters-in-Applied-Microbiology. 1991; 12(2): 65-68 ; 15 ref.

YEAR:1991

ABSTRACT:The phenolic compound oleuropein extracted from green olives was shown to be bactericidal against 9 strains of *Lactobacillus plantarum* isolated from green olive fermentation brines. Heat-treated oleuropein also demonstrated a strong bactericidal effect but not alkali-treated oleuropein, which allowed survival of most of the strains tested. The bactericidal effect was accompanied by changes in the typical bacillary structure and Gram-positive strain of *L. plantarum*.

TITLE:In vitro antimycoplasmal activity of oleuropein.

AUTHOR:Furneri,-P-M; Marino,-A; Saija,-A; Uccella,-N; Bisignano,-G

INSTITUTE: Department of Microbiological Sciences and Gynecological Sciences, University of Catania, via Androne 81, 95124, Catania, Italy.furneri@mbox.unit.it

SOURCE: Int-J-Antimicrob-Agents. 2002 Oct; 20(4): 293-6

YEAR: 2002

ABSTRACT: The activity of oleuropein, a phenolic glycoside contained in olive oil, was investigated in vitro against *Mycoplasma hominis*, *Mycoplasma fermentans*, *Mycoplasma pneumoniae* and *Mycoplasma pirum*. Oleuropein inhibited mycoplasmas at concentrations from 20 to 320 mg/l. The MICs of oleuropein to *M. pneumoniae*, *M. pirum*, *M. hominis* and *M. fermentans* were 160, 320, 20 and 20 mg/l, respectively.

TITLE: On the in-vitro antimicrobial activity of oleuropein and hydroxytyrosol.

AUTHOR:Bisignano,-G; Tomaino,-A; Lo-Cascio,-R; Crisafi,-G; Uccella,-N; Saija,-A

INSTITUTE: Department Farmaco-Biologico, University of Messina, Italy.

SOURCE:J-Pharm-Pharmacol. 1999 Aug; 51(8): 971-4

YEAR: 1999

ABSTRACT: Secoiridoides (oleuropein and derivatives), one of the major classes of polyphenol contained in olives and olive oil, have recently been shown to inhibit or delay the rate of growth of a range of bacteria and microfungi but there are no data in the literature concerning the possible employment of these secoiridoides as antimicrobial agents against pathogenic bacteria in man. In this study five ATCC standard bacterial strains (*Haemophilus influenzae* ATCC 9006, *Moraxella catarrhalis* ATCC 8176, *Salmonella typhi* ATCC 6539, *Vibrio parahaemolyticus* ATCC 17802 and *Staphylococcus aureus* ATCC 25923) and 44 fresh clinical isolates (*Haemophilus influenzae*, eight strains, *Moraxella catarrhalis*, six strains, *Salmonella* species, 15 strains, *Vibrio cholerae*, one strain, *Vibrio alginolyticus*, two strains, *Vibrio parahaemolyticus*, one strain, *Staphylococcus aureus*, five penicillin-susceptible strains and six penicillin-resistant strains), causal agents of intestinal or respiratory tract infections in man, were tested for in-vitro susceptibility to two olive (*Olea europaea*) secoiridoides, oleuropein (the bitter principle of olives) and hydroxytyrosol (derived

from oleuropein by enzymatic hydrolysis and responsible for the high stability of olive oil). The minimum inhibitory concentrations (MICs) calculated in our study are evidence of the broad antimicrobial activity of hydroxytyrosol against these bacterial strains (MIC values between 0.24 and 7.85 microg mL⁻¹) for ATCC strains and between 0.97 and 31.25 microg mL⁻¹) for clinically isolated strains). Furthermore oleuropein also inhibited (although to a much lesser extent) the growth of several bacterial strains (MIC values between 62.5 and 500 microg mL⁻¹) for ATCC strains and between 31.25 and 250 microg mL⁻¹) for clinical isolates); oleuropein was ineffective against *Haemophilus influenzae* and *Moraxella catarrhalis*. These data indicate that in addition to the potential employment of its active principles as food additives or in integrated pest-management programs, *Olea europaea* can be considered a potential source of promising antimicrobial agents for treatment of intestinal or respiratory tract infections in man.

TITLE: Comparative antibacterial and antifungal effects of some phenolic compounds.

AUTHOR:Aziz,-N-H; Farag,-S-E; Mousa,-L-A; Abo-Zaid,-M-A

INSTITUTE: National Centre for Radiation Research and Technology, Nasr City, Cairo, Egypt.

SOURCE:Microbios. 1998; 93(374):43-54

YEAR: 1998

ABSTRACT:The antimicrobial potential of eight phenolic compounds isolated from olive cake was tested against the growth of *Escherichia coli*, *Klebsiella pneumoniae*, *Bacillus cereus*, *Aspergillus flavus* and *Aspergillus parasiticus*. The phenolic compounds included p-hydroxy benzoic, vanillic, caffeic, protocatechuic, syringic, and p-coumaric acids, oleuropein and quercetin. Caffeic and protocatechuic acids (0.3 mg/ml) inhibited the growth of *E. coli* and *K. pneumoniae*. The same compounds apart from syringic acid (0.5 mg/ml) completely inhibited the growth of *B. cereus*. Oleuropein, and p-hydroxy benzoic, vanillic and p-coumaric acids (0.4 mg/ml) completely inhibited the growth of *E. coli*, *K. pneumoniae* and *B. cereus*. Vanillic and caffeic acids (0.2 mg/ml) completely inhibited the growth and aflatoxin production by both *A. flavus* and *A. parasiticus*, whereas the complete inhibition of the moulds was attained with 0.3 mg/ml p-hydroxy benzoic, protocatechuic, syringic, and p-coumaric acids and quercetin.

TITLE: Effect of Phenolic Compounds and Oleuropein on the Germination of Bacillus-cereus T Spores.

AUTHOR:TASSOU-C-C {a}; NYCHAS-G-J-E; BOARD-R-G

INSTITUTE: {a} INST FOOD TECHNOL, MINISTRY AGRIC, S VENIZELOU 1, LYCOVRISI 14123, ATHENS, GREECE

SOURCE:Biotechnology-and-Applied-Biochemistry. 1991; 13 (2): 231-237.

YEAR:1991

ABSTRACT: The phenolic compounds extracted from olives with ethyl acetate inhibited germination and outgrowth of *Bacillus cereus* T spores. Purified oleuropein, a well-characterized component of olive extract, inhibited these processes also. The addition of oleuropein and olive extracts 3 or 5 min after germination began, immediately decreased the rate of change of phase bright to phase dark spores and delayed significantly outgrowth.

ANTIFUNGAL

TITLE:In vitro antimicrobial activity of olive leaves

AUTHOR: Markin-D; Duek-L; Berdicevsky-I

INSTITUTE: Department of Microbiology, Rappaport Faculty of Medicine, Technion – Institute of Technology, Haifa

SOURCE: Mycoses-. 2003; 46(3-4):132-136,

YEAR: 2003

ABSTRACT: We investigated the antimicrobial effect of olive leaves against bacteria and fungi. The microorganisms tested were inoculated in various concentrations of olive leaf water extract. Olive leaf 0.6% (w/v) water extract killed almost all bacteria tested, within 3 h. Dermatophytes were inhibited by 1.25% (w/v) plant extract following a 3-day exposure whereas *Candida albicans* was killed following a 24 h incubation in the presence of 15% (w/v) plant extract. Olive leaf extract fractions, obtained by dialysis, showed antimicrobial activity consisted of particles smaller than 1000 molecular weight cutoffs. Scanning electron microscopic observations of *C. albicans*, exposed to 40% (w/v) olive leaf extract, showed invaginated and amorphous cells. *Escherichia coli* cells, subjected to a similar treatment but exposed to only 0.6% (w/v) olive leaf extract showed complete destruction. These findings suggest an antimicrobial potential for olive leaves.

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ANTI-INFLAMMATORY

TITLE: Olea europaea L.: stimulant, anti-ulcer and anti-inflammatory effects

AUTHOR: Fehri-B; Aiache-JM; Mrad-S; Korbi-S; Lamaison-JL

INSTITUTE: Dept. of Pharmacol. and Toxicol., Soc. of Pharm. Industries of Tunisia Fondouk Choucha, Rades 2040, Tunisia

SOURCE: Boll-Chim-Farm (Bollettino-Chimico-Farmaceutico); 1996; 135(Jan); 42-49,

YEAR: 1996

ABSTRACT: The dried aqueous extract of the leaf of *Olea europaea* containing 3.25% oleuropein was studied for pharmacological effects using the hole board, open field, rota rod, and automatic reflex conditioner tests. At low doses, the preparation stimulated the CNS, but at high doses it caused CNS depression. The extract induced dose dependent and significant anti-inflammatory effects on carrageenin induced edema in rats. It also provided pronounced protection against aspirin induced gastric ulcers.

TITLE: Oleuropein, the bitter principle of olives, enhances nitric oxide production by mouse macrophages.

AUTHOR: Visioli,-F; Bellosa,-S; Galli,-C

INSTITUTE: Institute of Pharmacological Sciences, Milan, [Italy. Francesco.Visioli@unimi.it](mailto:Francesco.Visioli@unimi.it)

SOURCE:Life-Sci. 1998; 62(6): 541-6

YEAR:1998

ABSTRACT: The Mediterranean diet, rich in fresh fruits and vegetables, has been associated with a lower incidence of cardiovascular disease and cancer, partly because of its high proportion of bioactive compounds such as vitamins, flavonoids and polyphenols. The major lipid component of such diet is the drupe-derived olive oil, which can be distinguished from other seed oils for the peculiar composition of its non-triglyceride fraction. In fact, several minor components, including polyphenols, grant the oil its particular taste and aroma. Oleuropein, the most abundant among these components, has been shown to be a potent antioxidant endowed with anti-inflammatory properties. We investigated the effects of oleuropein on NO release in cell culture and its activity toward nitric oxide synthase (iNOS) expression. The results show that oleuropein dose-dependently enhance nitrite production in LPS-challenged mouse macrophages. This effect was blocked by the iNOS inhibitor L-NAME, indicating increased iNOS activity. Also, Western blot analysis of cell homogenates show that oleuropein increases iNOS expression in such cells. Taken together, our data suggest that, during endotoxin challenge, oleuropein potentiates the macrophage-mediated response, resulting in higher NO production, currently believed to be beneficial for cellular and organismal protection.

TITLE: Effect of minor components of virgin olive oil on topical antiinflammatory assays

AUTHOR:de-la-Puerta-Rocio {a}; Martinez-Dominguez-Eugenia; Ruiz-Gutierrez-Valentina

INSTITUTE: {a} Department of Pharmacology, Faculty of Pharmacy, University of Seville, 41012, Seville: puerta@fajar.us.es, Spain

SOURCE: Zeitschrift-fuer-Naturforschung-Section-C-Journal-of-Biosciences. [print] September-October, 2000; 55 (9-10): 814-819.

YEAR: 2000

ABSTRACT:Interest in the health-promoting effects of virgin olive oil, an important part of the "Mediterranean diet", prompted us to determine the anti-inflammatory effects of erythrodiol, beta-sitosterol and squalene, identified as major components of the so-called "unsaponifiable fraction" of virgin olive oil, as well as of the phenolic compounds from the "polar fraction": oleuropein, tyrosol, hydroxytyrosol and caffeic acid. Their activities were compared to those of both, total unsaponifiable and polar fractions. This study was designed to analyse the antiinflammatory effect of these specific compounds from virgin olive oil on edema in mice induced by either arachidonic acid (AA) or 12-O-tetradecanoylphorbol acetate (TPA). The inhibition of the myeloperoxidase (MPO), marker enzyme of the accumulation of neutrophils in the inflamed tissue, was also investigated by the TPA model. The topical application of the olive oil compounds (0.5 mg/ear) produced a variable degree of anti-inflammatory effect with both assays. In the auricular edema induced by TPA, beta-sitosterol and erythrodiol from the unsaponifiable fraction of the oil showed a potent anti-edematous effect with a 61.4% and 82.1% of inhibition respectively, values not very different to that of the reference indomethacin (85.6%) at 0.5 mg/ear. The four phenolics exerted a similar range of inhibition (33-45%). All compounds strongly inhibited the enzyme myeloperoxidase, indicating a reduction of the neutrophil influx in the inflamed tissues. The strongest inhibitor of AA edema was the total unsaponifiable fraction which inhibition was 34%, similar to that obtained by the reference drug dexamethasone at 0.05 mg/ear. Among the phenolics, oleuropein also produced an inhibition of about 30% with the same dose, but all the other components were found less active in this assay. The anti-inflammatory effects exerted by both unsaponifiable and polar compounds might contribute to the potential biological properties reported for virgin olive oil against different pathological processes.

ANTIOXIDANT & FREE RADICAL SCAVENGER

TITLE: Antioxidant activity of phenolics extracted from *Olea europaea* L. leaves

AUTHOR: Benavente-Garcia-O; Castillo-J; Lorente-J; Ortuno-A; Del-Rio-JA

INSTITUTE: Research/Development Department, Furfural Espanol S.A., Camino Viejo de Pliego s/n, 80320 Alcantarilla, Murcia

SOURCE: FOOD-CHEM. Food-Chemistry. 2000-168(4):457-462

YEAR: 2000

ABSTRACT: The purpose of this study was to identify the main phenolic compounds present in an olive leaf extract (OL) in order to delineate the differential antioxidant activities of these compounds through the extent of their abilities to scavenge the ABTS([.]+) radical cation and to clarify the structural elements conferring antioxidant capacity in aqueous systems. The results show that the relative abilities of the flavonoids from olive leaf to scavenge the ABTS([.]+) radical cation are influenced by the presence of functional groups in their structure, mainly the B-ring catechol, the 3-hydroxyl group and the 2,3-double bond conjugated with the 4-oxo function. For the other phenolic compounds present in OL, their relative abilities to scavenge the ABTS([.]+) radical cation are mainly influenced by the number and position of free hydroxyl groups in their structure. Also, both groups of compounds show synergic behaviour when mixed, as occurs in the OL. Copyright (C) 2000 Elsevier Science Ltd.

TITLE: In vitro evaluation of the antioxidant activity and biomembrane interaction of the plant phenols oleuropein and hydroxytyrosol

AUTHOR: Saija-A; Trombetta-D; Tomaino-A; Lo-Cascio-R; Castelli-F; et-al

INSTITUTE: Dept. Farmaco-Biol., Sch. of Pharm., Univ. of Messina, 98168 Messina, Italy **SOURCE:** Int-J-Pharm (International-Journal-of-Pharmaceutics); 1998; 166(May 18); 123-133

YEAR: 1998

ABSTRACT: The scavenging activity against the stable 1,1-diphenyl-2-picrylhydrazyl free radical, the antioxidant activity in a model system consisting of dipalmitoyllecithin (dipalmitoylphosphatidylcholine)/linoleic acid unilamellar vesicles and a water soluble azo compound as a free radical generator, and the biomembrane interaction with dimyristoyllecithin (dimyristoylphosphatidylcholine) vesicles of the plant phenols oleuropein and 3,4-dihydroxyphenethyl alcohol (hydroxytyrosol) were studied in vitro. The results showed that both oleuropein and hydro.

TITLE: *Olea europaea* L. leaf extract and derivatives: antioxidant properties.

AUTHOR: Briante,-R; Patumi,-M; Terenziani,-S; Bismuto,-E; Febbraio,-F; Nucci,-R Correspondence (Reprint) address, R. Nucci, Istituto di Biochimica delle Proteine ed

INSTITUTE: Enzimologia del CNR, Via Marconi 10, 80125 Naples, Italy. Tel./Fax +39-0817257300. E-mail nucci@dafne.ibpe.na.cnr.it

SOURCE: Journal-of-Agricultural-and-Food-Chemistry. 2002; 50(17): 4934-4940 ; 44 ref,

YEAR: 2002

ABSTRACT: A simple and fast method to collect eluates containing high amounts of hydroxytyrosol from *Olea europaea* (olive cv. Moraiolo) leaf extract is described. Biotransformation of *O. europaea* leaf extract was carried out using a thermophilic beta-glycosidase immobilized on chitosan, and some of the phenols in the leaf tissue and in the eluates were identified. Antioxidative activity of the eluates was compared with that of the leaf extract from which they originated. The eluates possessed a higher concentration of simple phenols (characterized by stronger antioxidative activity) than those in extra virgin olive oils and in many commercial olive leaf extract tablets.

TITLE: Anti hypertensive, antiatherosclerotic and antioxidant activity of triterpenoids isolated from *Olea europaea*, subspecies *africana* leaves.

AUTHOR:Somova,-LI; Shode,-FO; Ramnanan,-P; Nadar,-A

SOURCE: J-Ethnopharmacol. 2003 Feb; 84(2-3): 299-305,

YEAR: 2003

ABSTRACT: For the first time a bioassay-directed study of triterpenoids isolated from the leaves of *Olea europaea* from Greece, from wild African olive and from a cultivar of *O. europaea* grown in Cape Town was reported. The experiment was undertaken since our preliminary analyses showed that the African wild olive leaf is rich in triterpenoids and contain only traces of the glycoside oleuropein, which is typical for the European olive leaves. The isolate of the African wild olive leaves (AO) used in the experiments was found to contain 0.27% 1:1 mixture of oleanolic acid and ursolic acid, named oleuafricein. The isolate of Greek olive leaves (GO) was found to contain 0.71% oleanolic acid, and the Cape Town cultivar (CT) contained 2.47% oleanolic acid. No ursolic acid was found in either GO or CT. The antihypertensive, diuretic, antiatherosclerotic, antioxidant and hypoglycemic effects of authentic oleanolic and ursolic acid and the three isolates (GO, AO and CT) were studied on Dahl salt-sensitive (DSS), insulinresistant rat genetic model of hypertension. All three isolates, in a dose 60 mg/kg b.w. for 6 weeks treatment, prevented the development of severe hypertension and atherosclerosis and improved the insulin resistance of the experimental animals. GO, OA and CT isolates could provide an effective and cheap treatment of this particular, most common type of salt-sensitive hypertension in the African population. Xytyroso.

TITLE: Bioactive derivatives from oleuropein by a biotransformation on *Olea europaea* leaf extracts.

AUTHOR:Briante,-R; La-Cara,-F; Febbraio,-F; Patumi,-M; Nucci,-R

INSTITUTE: Istituto di Biochimica delle Proteine ed Enzimologia del Consiglio Nazionale delle Ricerche, Via Marconi 10, 80125 Napoli, Italy.

SOURCE: J-Biotechnol. 2002 Feb 14; 93(2): 109-19

YEAR:2002

ABSTRACT: A very simple method is proposed to produce, using non-homogeneous hyperthermophilic beta-glycosidase immobilised on chitosan, 3,4-dihydroxy-phenylethanol (hydroxytyrosol), a commercially unavailable compound with well known biological properties which justify a potential commercial application. Leaf extracts from *Olea europaea* with high oleuropein content are selected as substrate for biotransformation. Under the biotransformation conditions, high amounts of hydroxytyrosol are collected within a short space of time after being preliminarily purified by a non-treated chitosan column. This is possible due to the capacity of amino groups on the chitosan to bind aldehydic groups of molecules present at the end of the reaction. We have produced a natural and non-toxic product from vegetal source, as opposed to the molecule obtainable through chemical synthesis, as a candidate to test in vivo its biological properties. The proposed process may prove useful for a further application for recycling *Olea europaea* leaves. The radical-scavenging properties of the bioreactor eluates and their capacity to inhibit fatty acid peroxidation rates are characterized in order to make them candidates as substitutes for synthetic antioxidants commonly used to increase the shelf-life of food products as well as for their possible protective effect in human cells.

TITLE: Isolation and characterization of the antioxidant component 3,4dihydroxyphenylethyl 4-formyl-3-formylmethyl-4-hexenoate from olive (*Olea europaea*) leaves.

AUTHOR:Paiva-Martins,-F; Gordon,-M-H

INSTITUTE: Centro de Investigacao em Quimica, Departamento de Quimica, Faculdade de Ciencias, Universidade do Porto, Rua do Campo Alegre, number 687, 4169-007 Porto, Portugal

SOURCE: J-Agric-Food-Chem. 2001 Sep; 49(9): 4214-9,

YEAR: 2001

ABSTRACT:Storage of olive (*Olea europaea*) leaves for 22 h at 37 degrees C in closed plastic bags caused the content of a nonglycosidic secoiridoid, 3,4-dihydroxyphenylethyl 4-formyl-3formylmethyl-4-hexenoate (3,4-DHPEA-EDA) to rise from 15% to 50% of the phenolic extract with corresponding falls in the content of oleuropein and two oleuropeindials, which were identified as precursors of 3,4-DHPEA-EDA. Pure product was isolated from one set of stored olive leaves in a 0.16% yield. Storage of olive leaves under various conditions showed that the moisture present in closed plastic bags was important for the formation of 3,4-DHPEA-EDA. The time taken to reach the maximum concentration of the product varied widely for different. I showed good free scavenging activity and antioxidant effects. samples of olive leaves, with a shorter time for the sample with lower initial oleuropein content. The oleuropeindial precursors of the product were readily hydrolyzed to carboxylic acid derivatives, which have been identified by NMR. The antiradical activity of 3,4-DHPEA-EDA, evaluated by scavenging of 2,2-diphenyl-1-picrylhydrazyl radicals, was comparable to that of alpha-tocopherol.

TITLE: Protective effect of oleuropein, an olive oil biophenol, on low density lipoprotein oxidizability in rabbits.

AUTHOR: Coni,-E; Di-Benedetto,-R; Di-Pasquale,-M; Masella,-R; Modesti,-D; Mattei,-R; Carlini,-E-A

INSTITUTE: Food Department, Istituto Superiore di Sanita, Rome, [Italy. e.coni@iss.it](mailto:e.coni@iss.it)

YEAR:2000

ABSTRACT:On the basis of the results obtained with pilot studies conducted in vitro on human low density lipoprotein (LDL) and on cell cultures (Caco-2), which had indicated the ability of certain molecules present in olive oil to inhibit pro-oxidative processes, an in vivo study was made of laboratory rabbits fed special diets. Three different diets were prepared: a standard diet for rabbits (diet A), a standard diet for rabbits modified by the addition of 10% (w/w) extra virgin olive oil (diet B), a modified standard diet for rabbits (diet C) differing from diet B only in the addition of 7 mg kg⁻¹ of oleuropein. A series of biochemical parameters was therefore identified, both in the rabbit plasma and the related isolated LDL, before and after Cu-induced oxidation. The following, in particular, were selected: (i) biophenols, vitamins E and C, uric acid, and total, free, and ester cholesterol in the plasma; (ii) proteins, triglycerides, phospholipids, and total, free, and ester cholesterol in the native LDL (for the latter, the dimensions were also measured); (iii) lipid hydroperoxides, aldehydes, conjugated dienes, and relative electrophoretic mobility (REM) in the oxidized LDL (ox-LDL). In an attempt to summarize the results obtained, it can be said that this investigation has not only verified the antioxidant efficacy of extra virgin olive oil biophenols and, in particular, of oleuropein, but has also revealed a series of thus far unknown effects of the latter on the plasmatic lipid situation. In fact, the addition of oleuropein in diet C increased the ability of LDL to resist oxidation (less conjugated diene formation) and, at the same time, reduced the plasmatic levels of total, free, and ester cholesterol (-15, -12, and -17%, respectively), giving rise to a redistribution of the lipidic components of LDL (greater phospholipid and cholesterol amounts) with an indirect effect on their dimensions (bigger by about 12%).

TITLE:Oleuropein evaluated in vitro and in vivo as an antioxidant

AUTHOR:Speroni-E; Guerra-MC; Minghetti-A; Crespi-Perellino-N; Pasini-P; Piazza-F; Roda-A

INSTITUTE:Department of Pharmacology, Bologna University, Via Imerio, 48, 40126 Bologna

SOURCE:Phytotherapy-Research. 1998; 12(SUPPL. 1): S98-S100,

YEAR: 1998

ABSTRACT: Oleuropein is a phenolic compound extracted from the leaves of *Olea europaea*. The antioxidant activity of this natural product has been evaluated in vitro and in vivo by means of a chemiluminescent assay, based on a luminol-horseradish peroxidase p-iodophenol O₂ mediated light emission system. In vitro, oleuropein had a remarkable antioxidant activity. Serum samples obtained from treated animals exhibited an antioxidant activity comparable to controls. Bile samples obtained from the

same treated animals showed a significant inhibition (90%) of the light emission in the chemiluminescent assay, when compared with the control sample.

TITLE: Effect of phenolic compounds of virgin olive oil on LDL oxidation resistance.

AUTHOR: Moreno-JA; Lopez-Miranda-J; Gomez-P; Fatiha-Benkhalti; El-Boustani-E; PerezJimenez-F

INSTITUTE: Unidad de Lipidos y Arteriosclerosis, Hospital Universitario Reina Sofia, Avda. Menendez Pidal, s/n. 14004 Cordoba, Spain.

SOURCE: Medicina-Clinica-Barcelona. 2003, 120: 4, 128-131; 41 ref.

YEAR:2003

ABSTRACT: Background and objective: Several epidemiological and experimental studies have associated the intake of antioxidants, which are abundant in the Mediterranean diet, with a low incidence of cardiovascular disease. One possible mechanism of this action is the oxidative protection in low density lipoproteins (LDL). The aim of our study was to compare the antioxidative activity of diverse phenolic compounds present in virgin olive oil on these lipoproteins. Subjects and method: LDL was isolated from blood plasma of healthy volunteers by sequential ultracentrifugation. This was followed by oxidation with CuCl₂ in the presence of different concentrations of phenolic compounds and virgin olive oil extract. Production of conjugated dienes was determined by the continuous monitoring of increased absorbency at 234 nm as an indicator of LDL oxidation. Results: Virgin olive oil extract prolonged the latency phase and significantly lowered the progression rate ($p < 0.05$) at low concentrations (2 Ng/ml). This antioxidative effect was also observed with low concentrations (2 NM) of caffeic acid and oleuropein ($p < 0.05$). However, it was necessary to increase the concentration of flavone up to 50 times to observe a similar effect ($p < 0.05$). Conclusion: Both virgin olive oil extract enriched in phenolic compounds and phenolic compounds present in olive oil (caffeic acid and oleuropein) are potent antioxidants at very low concentrations. Thus, the beneficial effects of a Mediterranean diet may be partly due to the protective action of these compounds.

TITLE: Antioxidant and other biological activities of phenols from olives and olive oil.

AUTHOR: Visioli-F; Poli-A; Galli-C

INSTITUTE: Department of Pharmacological Sciences, University of Milan, Via Balzaretti 9, 20133 Milan, Italy.

SOURCE: Medicinal-Research-Reviews. 2002, 22: 1, 65-75; 68 ref.

YEAR: 2002

ABSTRACT: Olive oil is the principal source of fat in the Mediterranean diet, which has been associated with a lower incidence of coronary heart disease and certain cancers. Phenolic compounds, e.g., hydroxytyrosol and oleuropein, in extra-virgin olive oil are responsible for its peculiar pungent taste and for its high stability. Recent findings demonstrate that olive oil phenolics are powerful antioxidants, both in vitro and in vivo, and possess other potent biological activities that could partially account for the observed healthful effects of the Mediterranean diet.

TITLE: Antioxidative activities of Olea europaea leaves and related phenolic compounds.

AUTHOR: Le-Tutour,-B.; Guedon,D.

SOURCE: Phytochemistry. Oxford : Pergamon Press. Apr 1992. v. 31 (4) p. 1173-1178.

YEAR:1992

ABSTRACT: Olea europaea leaves, oleuropein, hydroxytyrosol and tyrosol were compared with vitamin E and BHT, with regard to their antioxidative activities, by kinetic studies in model systems. The thermal initiated oxidation of methyl linoleate was performed in homogeneous solution at 60 degrees or 40 degrees with or without antioxidants. Olea europaea extracts, oleuropein and hydroxytyrosol were much more effective than BHT or vitamin E in extending the induction period. Assuming a stoichiometric factor $f=2$ for

BHT, this coefficient of inhibition reached 5 for hydroxytyrosol, 7 for oleuropein and 10 for *O. europaea* extracts. These extracts owe their antioxidative properties to their high oleuropein content (19% w/w) and also to a lesser amount of flavonoids (1.8% w/w with 0.8% of luteolin 7-glucoside). Tyrosol showed neither antioxidant nor pro-oxidant activity. No synergistic effect on the preservation of methyl linoleate was found when vitamin E was used together with tyrosol or *O. europaea* extracts.

TITLE:GC-MS evaluation of phenolic compounds in virgin olive oil.

AUTHOR: Angerosa,-F.; d'Alessandro,-N.; Konstantinou,-P.; Di-Giacinto,-L.

SOURCE: J-agric-food-chem. Washington, D.C. : American Chemical Society. July 1995. v. 43 (7) p. 1802-1807

YEAR:1995

ABSTRACT: A new gas chromatographic method for detection of phenolic compounds in virgin olive oils was developed. Identification of chromatographic peaks was made by mass selective detection. The presence of a main peak at m/z 192 or at m/z 280, related only to tyrosol and hydroxytyrosol, evident in the mass spectra of linked phenols, was very profitable for assigning the phenolic nature to minor polar compounds extracted by methanol from virgin olive oil. Twelve structures are possible, and some of them are deemed more likely on the basis of the chemical behavior of the compounds studied. The presence of a ligstrosid aglycon containing no carbomethoxy group and of oleuropein aglycon derivatives was evidenced. The levels of these substances is a very important parameter in the evaluation of virgin olive oil quality since phenols are strictly related both to the oil's resistance to oxidation because of their antioxidative properties (Montedoro, 192; Papadopoulos and Boskou, 1991) and to the typical bitter taste of olive oil (Angerosa and Solinas, 1990; Olias, 1992). Furthermore, some studies showed that the amount of phenolic substances present, just as the fatty acid composition, is related to the health beneficial effects that make virgin oil a very valuable and appreciated commodity (Panizzi et al., 1960; Galli et al., 1992).

TITLE: Antioxidant activity of virgin olive oil phenolic compounds in a micellar system.

AUTHOR: Fogliano,-V; Ritieni,-A.; Monti,-S.M.; Gallo,-M.; Della-Medaglia,-D.; Ambrosino,M.L.; Sacchi,-R

SOURCE: J-sci-food-agric. West Sussex: John Wiley & Sons Limited. Oct 1999. v. 79 (13) p. 1803-1808.

YEAR:1999

ABSTRACT: The antioxidant activity of two virgin olive oils, obtained from the same olive (*Olea europaea sativa*) batch but processed with different hammer crushing conditions, was evaluated by measuring their protective action towards linoleic acid peroxidation in a micellar system. The antioxidant efficiency (AE) of the oil phenolic fraction was higher when the olives were processed with a higher hammer crusher rotation rate. HPLC analysis demonstrated that one of the main derivatives of oleuropein, indicated as 3,4-DHPEA-EDA (the dialdehydic form of elenolic acid linked with 3,4-dihydroxyphenylethanol), is present only in the oil with higher AE. 3,4-DHPEA-EDA showed the greatest antioxidant ability among virgin olive oil phenols. Its greater efficiency in the micellar system in comparison with 3,4-dihydroxyphenylethanol (3,4DHPEA) is related to its greater lipophilicity. It is suggested that the behaviour in the watermicellar environment is representative of that in a real system such as tomato-based sauce with added virgin olive oil.

TITLE:Effect of virgin olive oil phenolic compounds on in vitro oxidation of human low density lipoproteins.

AUTHOR:Caruso,-D; Berra,-B; Giavarini,-F; Cortesi,-N; Fedeli,-E; Galli,-G

INSTITUTE:Institute of Pharmacological Sciences, University of Milan, Italy.

SOURCE:Nutr-Metab-Cardiovasc-Dis. 1999 Jun; 9(3): 102-7

YEAR:1999

ABSTRACT:BACKGROUND AND AIM: Substantial evidence suggests that oxidative modifications of low density lipoproteins (LDL) critically contribute to the pathogenesis and progression of human atherosclerosis. Oxidized LDL (oxLDL) are present in atherosclerotic plaques and contain oxysterols that exhibit a variety of adverse biological activities. Antioxidants have also been shown to prevent LDL modification. We have therefore assessed the efficacy of virgin olive oil phenolic compounds in preventing oxidative modifications of human LDL oxidized by UV light.

METHODS AND RESULTS: Cholesterol oxides formed during LDL photo-oxidation were determined by UV HPLC in the presence of different concentrations of phenolic compounds and their pure components (tyrosol and oleuropein), and probucol, a widely used synthetic antioxidant. Electrophoretic mobility was also assayed. The results demonstrate that phenolic compounds are much more potent in preventing cholesterol oxide formation and apoproteic moiety modification than their pure components and probucol.

CONCLUSIONS: The beneficial effects of a Mediterranean diet may be ascribable not only to the high unsaturated/saturated fatty acid ratio characteristic of olive oil, but also to the unique antioxidant properties of its phenolic compounds.

TITLE:Oleuropein, the bitter principle of olives, enhances nitric oxide production by mouse macrophages.

AUTHOR: Visioli,-F; Bellosta,-S; Galli,-C

INSTITUT: Institute of Pharmacological Sciences, Milan, Italy.Francesco.Visioli@unimi.it

SOURCE : Life-Sci. 1998; 62(6): 541-6

YEAR:1998

ABSTRACT: The Mediterranean diet, rich in fresh fruits and vegetables, has been associated with a lower incidence of cardiovascular disease and cancer, partly because of its high proportion of bioactive compounds such as vitamins, flavonoids and polyphenols. The major lipid component of such diet is the drupe-derived olive oil, that can be distinguished from other seed oils for the peculiar composition of its non-triglyceride fraction. In fact, several minor components, including polyphenols, grant the oil its particular taste and aroma. Oleuropein, the most abundant among these components, has been shown to be a potent antioxidant endowed with anti-inflammatory properties. We investigated the effects of oleuropein on NO release in cell culture and its activity toward nitric oxide synthase (iNOS) expression. The results show that oleuropein dose-dependently enhance nitrite production in LPS-challenged mouse macrophages. This effect was blocked by the iNOS inhibitor L-NAME, indicating increased iNOS activity. Also, Western blot analysis of cell homogenates show that oleuropein increases iNOS expression in such cells. Taken together, our data suggest that, during endotoxin challenge; oleuropein potentiates the macrophage-mediated response, resulting in higher NO production, currently believed to be beneficial for cellular and organismal protection.

TITLE: Olive-oil consumption and health: the possible role of antioxidants.

AUTHOR:Owen,-R-W; Giacosa,-A; Hull,-W-E; Haubner,-R; Wurtele,-G; Spiegelhalder,-B; Bartsch,-H

INSTITUTE:Division of Toxicology and Cancer Risk Factors, German Cancer Research Center, Heidelberg. R.Owen@DKFZ-Heidelberg. DE

SOURCE: Lancet-Oncol. 2000 Oct; 1: 107-12

YEAR: 2000

ABSTRACT: In the Mediterranean basin, olive oil, along with fruits, vegetables, and fish, is an important constituent of the diet, and is considered a major factor in preserving a healthy and relatively disease-free population. Epidemiological data show that the Mediterranean diet has significant protective effects against cancer and coronary heart disease. We present evidence that it is the unique profile of the phenolic fraction, along with high intakes of squalene and the monounsaturated fatty acid, oleic acid, which confer its health-promoting properties. The major phenolic compounds identified and quantified in olive oil belong to three

different classes: simple phenols (hydroxytyrosol, tyrosol); secoiridoids (oleuropein, the aglycone of ligstroside, and their respective decarboxylated dialdehyde derivatives); and the lignans [(+)-1-acetoxypinoresinol and pinoresinol]. All three classes have potent antioxidant properties. High consumption of extra-virgin olive oils, which are particularly rich in these phenolic antioxidants (as well as squalene and oleic acid), should afford considerable protection against cancer (colon, breast, skin), coronary heart disease, and ageing by inhibiting oxidative stress.

TITLE:The antioxidant anticancer potential of phenolic compounds isolated from olive oil

AUTHOR:Owen-RW; Giacosa-A; Hull-WE; Haubner-R; Spiegelhalter-B; Bartsch-H

INSTITUTE:Division of Toxicology, Cancer Research Centre, Im Neuenheimer Feld 280, D69120 Heidelberg

SOURCE:EUR-J-CANCER. European-Journal-of-Cancer. 2000; 36(10): 1235-1247

YEAR: 2000

ABSTRACT:In our ongoing studies on the chemoprevention of cancer we have a particular interest in the health benefits of the Mediterranean diet, of which olive oil is a major component. Recent studies have shown that extra virgin olive oil contains an abundance of phenolic antioxidants including simple phenols (hydroxytyrosol, tyrosol), aldehydic secoiridoids, flavonoids and lignans (acetoxypinoresinol, pinoresinol). All of these phenolic substances are potent inhibitors of reactive oxygen species attack on, e.g. salicylic acid, 2-deoxyguanosine. Currently there is growing evidence that reactive oxygen species are involved in the aetiology of fat-related neoplasms such as cancer of the breast and colorectum. A plausible mechanism is a high intake of ω -6 polyunsaturated fatty acids which are especially prone to lipid peroxidation initiated and propagated by reactive oxygen species, leading to the formation (via α , β -unsaturated aldehydes such as trans-4-hydroxy-2-nonenal) of highly pro mutagenic exocyclic DNA adducts. Previous studies have shown that the colonic mucosa of cancer patients and those suffering from predisposing inflammatory conditions such as ulcerative colitis and Crohn's disease generates appreciably higher quantities of reactive oxygen species compared with normal tissue. We have extended these studies by developing accurate high performance liquid chromatography (HPLC) methods for the quantitation of reactive oxygen species generated by the faecal matrix. The data shows that the faecal matrix supports the generation of reactive oxygen species in abundance. As yet, there is a dearth of evidence linking this capacity to actual components of the diet which may influence the colorectal milieu. However, using the newly developed methodology we can demonstrate that the antioxidant phenolic compounds present in olive oil are potent inhibitors of free radical generation by the faecal matrix. This indicates that the study of the inter-relation between reactive oxygen species and dietary antioxidants is an area of great promise for elucidating mechanisms of colorectal carcinogenesis and possible future chemopreventive strategies. Copyright (C) 2000 Elsevier Science Ltd.

TITLE: Free radical-scavenging properties of olive oil polyphenols

AUTHOR:Visioli-F; Bellomo-G; Galli-C

INSTITUTE:Department of Biomedical Sciences, University of Torino, Novara

SOURCE: BIOCHEM-BIOPHYS-RES-COMMUN. Biochemical-and-Biophysical-ResearchCommunications. 1998; 247(1): 60-64

YEAR:1998

ABSTRACT:Plants in the Mediterranean basin, such as vine and olive trees, have developed an array of antioxidant defences to protect themselves from environmental stress. Accordingly, the incidence of coronary heart disease and certain cancers is lower in the Mediterranean area, where olive oil is the dietary fat of choice. As opposed to other vegetable oils, extra virgin olive oil, which is obtained by physical pressure from a whole fruit, is rich in phenolic components that are responsible for the particular stability of the oil. We have investigated the scavenging actions of some olive oil phenolics, namely hydroxytyrosol and oleuropein, with

respect to superoxide anion generation, neutrophils respiratory burst, and hypochlorous acid. The low EC₅₀s indicate that both compounds are potent scavengers of superoxide radicals and inhibitors of neutrophils respiratory burst: whenever demonstrated in vivo, these properties may partially explain the observed lower incidence of CHD and cancer associated with the Mediterranean diet.

TITLE: Olive oil and red wine antioxidant polyphenols inhibit endothelial activation: Antiatherogenic properties of Mediterranean diet phytochemicals

AUTHOR:Carluccio-MA; Siculella-L; Ancora-MA; Massaro-M; Scoditti-E; Storelli-C; Visioli-F; Distante-A; De-Caterina-R

INSTITUTE:C.N.R. Inst. of Clinical Physiology, Lecce

SOURCE:ARTERIOSCLER-THROMB-VASC-BIOL. Arteriosclerosis,-Thrombosis,-andVascular-Biology. 2003; 23(4): 622-629

YEAR:2003

ABSTRACT: Objective – Epidemiology suggests that Mediterranean diets are associated with reduced risk of cardiovascular disease. Because monocyte adhesion to the endothelium is crucial in early atherogenesis, we evaluated whether typical olive oil and red wine polyphenols affect endothelial-leukocyte adhesion molecule expression and monocyte adhesion. Methods and Results – Phytochemicals in olive oil and red wine, including oleuropein, hydroxytyrosol, tyrosol, elenolic acid, and resveratrol, with or without antioxidant activity, were incubated with human umbilical vein endothelial cells for 30 minutes, followed by co-incubation with bacterial lipopolysaccharide or cytokines to trigger adhesion molecule expression. At nutritionally relevant concentrations, only oleuropein, hydroxytyrosol, and resveratrol, possessing a marked antioxidant activity, reduced monocytoid cell adhesion to stimulated endothelium, as well as vascular cell adhesion molecule-1 (VCAM-1) mRNA and protein by Northern analysis and cell surface enzyme immunoassay. Reporter gene assays with deletional VCAM-1 promoter constructs indicated the relevance of nuclear factor- κ B, activator protein- 1, and possibly GATA binding sites in mediating VCAM- 1 transcriptional inhibition. The involvement of nuclear factor- κ B and activator protein-1 was finally demonstrated at electrophoretic mobility shift assays. Conclusions – Olive oil and red wine antioxidant polyphenols at nutritionally relevant concentrations transcriptionally inhibit endothelial adhesion molecule expression, thus partially explaining atheroprotection from Mediterranean diets.

ANTIVIRAL

TITLE: New applications of herbal extracts for functional food and pharmaceuticals. Part 2.

AUTHOR: Micol,-V; Estepa,-A; Caturla,-N; Perez-Fons,-L; Saura,-D; Ferrer-Montiel,-A; Cartagena,-V

INSTITUTE:[Inst. de Biol. Molecular y Cellular](#), Univ. Miguel Hernandez, E-03202 Elche (Alicante), Spain

SOURCE: Agro-Food-Industry-hi-tech. 2003; 14(6): 14-16 ; 15 ref.

YEAR: 2003

ABSTRACT: In this 2nd part of a 2-part article on use of plant extracts in functional foods and pharmaceuticals, application of natural antiviral supplements (especially olive leaf extract) in foods for animals and the role of polyphenols from herbal sources as neuroprotective agents in functional foods for humans are discussed.

TITLE: In vitro evaluation of secoiridoid glucosides from the fruits of Ligustrum lucidum as antiviral agents.

AUTHOR: Ma-Shuang-Cheng; He-Zhen-Dan; Deng-Xue-Long; But-Paul-Pui-Hay {a}; OoiVincent-Eng-Choon; Xu-Hong-Xi; Lee-Spencer-Hon-Sun; Lee-Song-Fong

INSTITUTE: {a} Department of Biology and Institute of Chinese Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong; [E-Mail: paulbut@cuhk.edu.hk](mailto:paulbut@cuhk.edu.hk), China

SOURCE: Chemical-and-Pharmaceutical-Bulletin-Tokyo. [print] November, 2001; 49 (11): 1471-1473.

YEAR: 2001

ABSTRACT: Six secoiridoid glucosides, lucidumoside C (1), oleoside dimethylester (2), neonuezhenide (3), oleuropein (4), ligustroside (5) and lucidumoside A (6), isolated from the fruits of *Ligustrum lucidum* (*Oleaceae*), were examined in vitro for their activities against four strains of pathogenic viruses, namely herpes simplex type 1 virus (HSV 1), influenza type A virus (Flu A), respiratory syncytial virus (RSV) and parainfluenza type 3 virus (Para 3). Antiviral activities were evaluated by the cytopathic effect (CPE) inhibitory assay. The purpose was to check if the anti-oxidative potency of these glucosides correlated with their antiviral potency. Results showed that none of the glucosides had any significant activity against HSV 1 and Flu A. Oleuropein, however, showed significant antiviral activities against RSV and Para 3 with IC50 value of 23.4 and 11.7 mug/ml, respectively. Lucidumoside C, oleoside dimethylester and ligustroside showed potent or moderate antiviral activities against Para 3 with IC50 values of 15.6-20.8 mug/ml. These results also documented that the anti-oxidative potency of these secoiridoid glucosides was not directly related to their antiviral effects.

TITLE: In Vitro Antiviral Activity of Calcium Elenolate

AUTHOR: Renis, H.

INSTITUTE: Department of Virology Research, The Upjohn Co., Kalamazoo, Michigan 49001

ABSTRACT: Calcium Elenolate [(C11H13O6)ZCa] is a multifunctional monoterpene which can be isolated from acid-hydrolyzed aqueous extracts of various parts of olive plants. This compound has been shown to be virucidal for all viruses against which it has been tested. No change in infectivity was noted when infectious ribonucleic acid (prepared from coxsackievirus A21) was incubated with calcium Elenolate. Incubation of calcium Elenolate with influenza A (PR8) virus resulted in loss of infectivity at concentrations which caused no observable change in hemagglutination titer or neuraminidase activity. The virucidal activity of this compound was shown to be greatest under alkaline conditions (pH 7.5). The quantity of virus inactivated was dependent on the calcium Elenolate concentration and the time of incubation. Incubation of calcium Elenolate with several nucleic acid constituents prior to the addition of virus caused no alteration in virucidal activity. However, when the incubation was carried out with amino acids prior to incubation with virus, losses in virucidal activity were detected with glycine, lysine, cysteine, and histidine, and to a lesser extent with phenylalanine, tryptophan, serine, and threonine. Pretreating cells with calcium eleolate did not alter coxsackievirus A21 attachment.

TITLE: Antiviral Activity of Calcium Elenolate of Parainfluenza Infection of Hamsters

AUTHOR: Soret, M. G.

SOURCE: Antimicrobial Agents and Chemotherapy – 1969, Copyright ©1970 American Society for Microbiology

INSTITUTE: Department of Virology Research, The Upjohn Co., Kalamazoo, Michigan 49001

ABSTRACT: The in vivo antiviral activity of calcium Elenolate was demonstrated in hamsters infected with parainfluenza 3 virus. The drug was virucidal when given within minutes of the viral inoculation. Calcium Elenolate also showed a "therapeutic" effect when given 8 hr after infection. This antiviral activity, after establishment of the infection, reduced the severity of the infectious process. The minimal effective dose of calcium Elenolate produced only minimal histological changes in the sensitive olfactory epithelium of the hamster while exerting significant therapeutic antiviral activity. The effects obtained suggest that calcium Elenolate may affect viral components of cellular origin in both free and cell-associated virus.

TITLE: Specificity of the Antiviral Agent Calcium Elenolate

AUTHOR: Heinze, J. E., Hale, &A., Carl, P.

ABSTRACT: Calcium elenolate, an antiviral agent which inhibits reverse transcriptases, inhibits the growth of chicken embryo fibroblast cells, as well as *Echerichia coli* and *Bacillus Subtilis* strains. The drug in vitro inhibits *E. coli* deoxyribonucleic acid (DNA) polymerase 111 holoenzyme, as well as several unrelated enzymes. The usual DNA polymerase assay components, with the exception of spermidine, have no effect on the observed inhibition. Inhibition of DNA polymerase 11 by the drug appears to be due to a direct and irreversible effect on the enzyme. However, DNA synthesis in *E. coli* is no more susceptible to the drug than is the increase in cell mass. These results suggest that calcium Elenolate is an inhibitor of rather low specificity.

BLOOD PRESSURE (HYPERTENSION)

TITLE: Anti hypertensive, antiatherosclerotic and antioxidant activity of triterpenoids isolated from *Olea europaea*, subspecies *africana* leaves

AUTHOR: Somova, -LI; Shode, -FO; Ramnanan, -P; Nadar, -A

SOURCE: J-Ethnopharmacol. 2003 Feb; 84(2-3): 299-305,

YEAR: 2003

ABSTRACT: For the first time a bioassay-directed study of triterpenoids isolated from the leaves of *Olea europaea* from Greece, from wild African olive and from a cultivar of *O. europaea* grown in Cape Town was reported. The experiment was undertaken since our preliminary analyses showed that the African wild olive leaf is rich in triterpenoids and contain only traces of the glycoside oleuropein, which is typical for the European olive leaves. The isolate of the African wild olive leaves (AO) used in the experiments was found to contain 0.27% 1:1 mixture of oleanolic acid and ursolic acid, named oleuafricein. The isolate of Greek olive leaves (GO) was found to contain 0.71% oleanolic acid, and the Cape Town cultivar (CT) contained 2.47% oleanolic acid. No ursolic acid was found in either GO or CT. The anti hypertensive, diuretic, antiatherosclerotic, antioxidant and hypoglycemic effects of authentic oleanolic and ursolic acid and the three isolates (GO, AO and CT) were studied on Dahl salt-sensitive (DSS), insulinresistant rat genetic model of hypertension. All three isolates, in a dose 60 mg/kg b.w. for 6 weeks treatment, prevented the development of severe hypertension and atherosclerosis and improved the insulin resistance of the experimental animals. GO, OA and CT isolates could provide an effective and cheap treatment of this particular, most common type of salt-sensitive hypertension in the African population.

TITLE: Blood pressure lowering effect of an olive leaf extract (*Olea europaea*) in L-NAME induced hypertension in rats.

AUTHOR: Khayyal, -M-T; el-Ghazaly, -M-A; Abdallah, -D-M; Nassar, -N-N; Okpanyi, -S-N; Kreuter, -M-H

INSTITUTE: Department of Pharmacology, Faculty of Pharmacy, Cairo University, Cairo, [Egypt](mailto:mtkhayyal@hotmail.com), mtkhayyal@hotmail.com

SOURCE: Arzneimittelforschung. 2002; 52(11): 797-802,

YEAR: 2002

ABSTRACT: A specially prepared olive leaf extract (EFLA 943) has been tested for its blood pressure lowering activity in rats rendered hypertensive by daily oral doses of L-NAME (NGnitro-L-arginine methyl ester, 50 mg/kg) for at least 4 weeks. Oral administration of the extract at different dose levels at the same time as L-NAME for a period of 8 weeks showed a dose dependent prophylactic effect against the rise in blood pressure induced by L-NAME, best effects being induced by a dose of 100 mg/kg of the extract. In rats previously rendered hypertensive by L-NAME for 6 weeks and then treated with that dose of the extract for a further 6 weeks without discontinuation of L-NAME, normalisation of the blood pressure was observed. The findings confirm previous reports on the hypotensive effects of olive leaf. The special extract, EFLA 943, was

shown to give consistent results with little individual variability. The anti hypertensive effect of the extract may be related to a variety of factors involving reversal of vascular changes involved in the L-NAME induced hypertension.

TITLE: Vasodilator effect of olive leaf.

AUTHOR:Zaruelo A, Duarte J, Jimenez J, Gonzalez M, Utrilla MP.

INSTITUTE:Department of Pharmacology, School of Pharmacy, University of Granada, Spain.

ABSTRACT: We studied the importance of the smooth vascular muscle endothelium in the vasodilator action of the decoction of olive (*Olea europaea*) leaf. The decoction caused relaxation of isolated rat aorta preparations both in the presence (IC₅₀ 1.12 +/- 0.33 mg/ml) and in the absence (IC₅₀ 1.67 +/- 0.16 mg/ml) of endothelium. The results indicate that the relaxant activity of the lyophilized decoction is independent of the integrity of the vascular endothelium. We also showed that oleuropein is a component responsible for vasodilator activity but, from the results, it seems likely that at least one other principle is to be found in the olive leaf which is either a vasodilator itself or else potentiates the relaxant effect of oleuropein.

TITLE: Pharmaco-chemical studies of Olea in the Azerbaijan Soviet Socialist Republic

AUTHOR:Movsumov-IS; Aliev-AM; Tagieva-ZD

SOURCE:Farmatsiya-Moscow (Farmatsiya); 1987; 36(2); 32-34

YEAR:1987

ABSTRACT:The hypotensive effects of flavonoids extracted from the leaves and fruits of varieties of *Olea europaea* found in the Azerbaijan Soviet Socialist Republic were studied. The pharmacological effects of the extracts were largely ascribed to oleuropein. Leaves and fruits of *Olea* varieties "Azerbaijan" and "Baku" have been found to contain p-mannitol, phenylcarboxylic acid, apigenin, luteolin and quercetin derivatives flavonoids. Studies of separate fractions suggested that hypotensive effect of the extracts produced from leaves and fruits of the *Olea* varieties mentioned is mainly related to oleuropein.

TITLE: Investigation on the extraction and concentration of oleuropein and flavonoids in Olea europaea L. based products.

AUTHOR:De-Laurentis-N {a}; Crescenzo-G; Lai-O-R; Milillo-M-A

INSTITUTE:{a} Dep. Med. Chem., Fac. Pharm., Univ. Bari, Via Orabona 4, 70126 Bari, Italy

SOURCE: Pharmaceutical-and-Pharmacological-Letters. 1997; 7 (1) 27-30.

YEAR: 1997

ABSTRACT: HPLC reversed phase (RP) is the technique used for the identification and dosage of the secoiridoid oleuropein, of flavonoids (apigenin, quercetin, kaempferol), of glycosyl flavonoids (hesperidin, rutin, the leaves and buds of *Olea europaea* L. This luteolin-7-O-glucoside, apigenin-7-O-glucoside), present in chromatographic method, which is simple and easy to use, presents a high reproducibility. Quantitative results and pharmacological considerations are reported here. Several studies have been carried out on the isolation and therapeutic activities of the flavonoids and secoiridoids contained in *Olea europaea* L.. These works report data related to the influence of oleuropein on heart activity and on arterial pressure (Messrli, F.H. Ed. 1996)), to the antispasmodic action and the calcium-antagonism of quercetin on smooth muscles of ileum in guinea pig (Ganten D. & Mulrow P. J., 1990) and to the hypocholesterolemic activity of hesperidin in rats kept on a hyperlipidic diet (Timmermans P.B.M.W.M, et al. 1993).

TITLE: Pharmacological analysis of the iridoid oleuropein.

AUTHOR:Petkov,-V; Manolov,-P

SOURCE:Arzneimittelforschung. 1972 Sep; 22(9): 1476-86

YEAR:1972

ABSTRACT: Empirical clinical data about a healing effect of the olive leaves in the case of hypertensive disease stimulated searching for the active component. In 1960 Panizzi et al. (20) succeeded in isolating a bitter glucoside which was given the name of oleuropein and its empirical formula was found to be $C_{25}H_{42}O_{11}$. This glucoside belongs to the iridoid group. Recently (1970) Inouye et al, (9) cast light upon the structure of oleuropein. Iridoids represent a new structural-chemical class. The majority of the compounds included in this group are glucosides in which carbohydrate component appears most frequently as D-glucose (occasionally as disaccharide, too). Though the first iridoid found in nature, verbenalin, was isolated as early as 1835 (24), successful investigations into the chemical structure of this group were only commenced in the recent fifteen years. The cause of this delay lies in the extremely great instability of the majority of compounds in this group. Characteristic feature of the aglycons of iridoids is the presence of cyclopentane-pyrane system. In some of them, the so called secoiridoids, the cyclopentane ring is open. This group of compounds was given the name of iridoids by Briggs et al. (2) in 1963. Very interesting data were recently obtained to show the presence of biogenetic correlations between iridoids and alkaloids as well as their ability of principle to transform one into another. Thus it has been established by the radioisotope studies of Popov (22) that the alkaloid gentioflavine isolated from some species of *Gentiana* might be obtained through a particular transformation of the molecule of the iridoid gentiopicroside. Further the alkaloids gentianidine and gentianadine are obtained by transforming the molecule of gentioflavine. The latter appears to be a precursor also of the alkaloids of the gentiane-structure type (genianine, etc.) through a would-be intermediate formation of a compound similar in structure to the iridoid gentioflavoside. It has been shown by way of isotopic studies, too, that the new-isolated iridoid gentioside represents an intermediate phase of the iridoid step in the biosynthesis pathway that leads to the formation of alkaloids in the gentiane plants. Oleuropein is water soluble and unstable against acids. When subjected to tentative studies (personal communication of Dr. Kloss [12]) oleuropein displays the following effects: it provokes an increase of coronary blood stream (experiments with heart after Langendorff), produces an elevation of blood-stream in the guinea pig limb, exerts a spasmolytic effect in case of histamine spasm. A 2% solution of oleuropein applied in a dose of 0.1 ml decreases by 22% the blood pressure of the rat, while administered in a dose of 1.0 ml by 31%. These scarce data about the pharmacodynamics of oleuropein gave us grounds to study in more details its pharmacology. Our investigations into the iridoid of the olive leaves were largely stimulated by the encouraging results obtained from studies of iridoids isolated from valerian (*Valeriana officinalis* L). For a long time the importance of valerian as a sedative drug has been discussed and even contested. However this problem was considered differently after Thies [25-29], Mannestatter et al. [13], Wagner et al. [30] and some others succeeded in isolating from the valerian root a new group of active substances, reckoned amount the iridoid group. These new substances were determined quantitatively and studied under experimental and clinical conditions. Iridoids called valepotriases (the most important of which are valtratum, didrovaltratum and acevaltratum) contained in a relatively high concentration (0.5 to 2%) in the valerian root displayed a clear-cut activity as sedative drugs [5, 69].

TITLE: Essai Clinique D'Un Extrait Titre de Feuilles D'Olivier Dans Le Traitement De L'Hypertension Arterielle Essentielle [Clinical Assay of *Olea europaea* Aqueous Extract in Hypertension Arterial Treatment.]

AUTHOR: Cherif, S., Rahal, N., Haouala, M., Hizaoui, B., Dargouth, F., Gueddiche, M., Kallel, Z., Balansard, G., & Boukef, K..

SOURCE: J. Pharm. Belg., 1996, 51, 2, 69-71

YEAR: 1996

ABSTRACT: A clinical assay of *Olea europaea* L. aqueous extract was carried on two groups of patients suffering with essential hypertension. 12 patients consulting for the first time, 18 patients with anti hypertensive treatment. Treatment based on *Olea europaea* L. leaf aqueous extract was given (400mg x 4/24h) during 3 months, after 15 days treatment based on placebo. We note for all patients a statistically significant decrease of blood pressure ($p < 0,001$), we didn't find any modification of biological parameters, excepted a significant little decrease of glycemia and calcemia $p < 0,01$ and $p < 0,001$ respectively. We didn't find any side effect in the two groups.

CANCER

TITLE:The inhibitory effects of compounds from olive leaf on tumor necrosis factor production and on beta-hexosaminidase release.

AUTHOR: Nishibe-Sansei {a}; Han-Yingmei {a}; Noguchi-Yukari {a}; Ueda-Hiroshi; YamazakiMasatoshi; Mizutani-Kenji; Kambara-Toshimitsu; Kishida-Naoko

INSTITUTE: {a} Faculty of Pharmaceutical Sciences, Health Sciences University of Hokkaido, Ishikari-Tobetsu, Hokkaido, 061-0293, Japan

SOURCE: Natural-Medicines. [print] August, 2001; 55 (4): 205-208.

YEAR: 2001

ABSTRACT: The extraction and isolation of olive leaf gave luteolin 7-O-glucoside, luteolin 4'-Oglucoside and oleuropein as the major components. The inhibitory effects of these compounds on tumor necrosis factor (TNF-alpha) production and on beta-hexosaminidase release from rat basophilic leukemia (RBL-2H3) cells, which were both recently found to be linked to allergic reaction, were examined. Oleuropein showed a potent inhibitory effect on TNF-alpha production. Luteolin 4'-O-glucoside showed a strong inhibitory effect on beta-hexosaminidase release (IC50: 17.1 mug/ml).

TITLE:The antioxidant/anticancer potential of phenolic compounds isolated from olive oil

AUTHOR: Owen-RW; Giacosa-A; Hull-WE; Haubner-R; Spiegelhalder-B; Bartsch-H

INSTITUTE:Division of Toxicology, Cancer Research Centre, Im Neuenheimer Feld 280, D69120 Heidelberg

SOURCE: EUR-J-CANCER. European-Journal-of-Cancer. 2000; 36(10): 1235-1247

YEAR:2000

ABSTRACT: In our ongoing studies on the chemoprevention of cancer we have a particular interest in the health benefits of the Mediterranean diet, of which olive oil is a major component. Recent studies have shown that extravirgin olive oil contains an abundance of phenolic antioxidants including simple phenols (hydroxytyrosol, tyrosol), aldehydic secoiridoids, flavonoids and lignans (acetoxypinoresinol, pinoresinol). All of these phenolic substances are potent inhibitors of reactive oxygen species attack on, e.g. salicylic acid, 2-deoxyguanosine. Currently there is growing evidence that reactive oxygen species are involved in the aetiology of fat-related neoplasms such as cancer of the breast and colorectum. A plausible mechanism is a high intake of < omega >-6 polyunsaturated fatty acids which are especially prone to lipid peroxidation initiated and propagated by reactive oxygen species, leading to the formation (via < alpha >,< beta >-unsaturated aldehydes such as trans-4-hydroxy-2-nonenal) of highly promutagenic exocyclic DNA adducts. Previous studies have shown that the colonic mucosa of cancer patients and those suffering from predisposing inflammatory conditions such as ulcerative colitis and Crohn's disease generates appreciably higher quantities of reactive oxygen species compared with normal tissue. We have extended these studies by developing accurate high performance liquid chromatography (HPLC) methods for the quantitation of reactive oxygen species generated by the faecal matrix. The data shows that the faecal matrix supports the generation of reactive oxygen species in abundance. As yet, there is a dearth of evidence linking this capacity to actual components of the diet which may influence the colorectal milieu. However, using the newly developed methodology we can demonstrate that the antioxidant phenolic compounds present in olive oil are potent inhibitors of free radical generation by the faecal matrix. This indicates that the study of the inter-relation between reactive oxygen species and dietary antioxidants is an area of great promise for elucidating mechanisms of colorectal carcinogenesis and possible future chemopreventive strategies.

TITLE: Antiatherogenic components of olive oil.

AUTHOR:Visioli,-F; Galli,-C

INSTITUTE:nstitute of Pharmacological Sciences, University of Milan, Via Balzaretti 9, Milan 20133, [Italy. francesco.visioli@unimi.it](http://francesco.visioli@unimi.it)

SOURCE:Curr-Atheroscler-Rep. 2001 Jan; 3(1): 64-7

YEAR: 2001

ABSTRACT: Olive oil is the principal source of fat in the Mediterranean diet, which has been associated with a **lower incidence of coronary heart disease and certain cancers**. Olive oil is characterized by a high proportion of monounsaturated oleic acid, but the main peculiarity of extra-virgin oil is the presence of remarkable quantities of phenolic compounds, notably hydroxytyrosol and oleuropein, that provide high **stability and strong taste**. Recently, several studies have demonstrated that olive oil phenolics are powerful antioxidants, both in vitro and in vivo, and exert additional potent biologic activities that could partially account for the observed cardioprotective effects of the Mediterranean diet.

CHOLESTEROL, CORONARY & HEART PROBLEMS

TITLE: Anti hypertensive, antiatherosclerotic and antioxidant activity of triterpenoids isolated from *Olea europaea*, subspecies *africana* leaves.

AUTHOR: Somova,-LI; Shode,-FO; Ramnanan,-P; Nadar,-A

SOURCE: J-Ethnopharmacol. 2003 Feb; 84(2-3): 299-305,

YEAR:2003

ABSTRACT: For the first time a bioassay-directed study of triterpenoids isolated from the leaves of *Olea europaea* from Greece, from wild African olive and from a cultivar of *O.europaea* grown in Cape Town was reported. The experiment was undertaken since our preliminary analyses showed that the African wild olive leaf is rich in triterpenoids and contain only traces of the glycoside oleuropein, which is typical for the European olive leaves. The isolate of the African wild olive leaves (AO) used in the experiments was found to contain 0.27% 1:1 mixture of oleanolic acid and ursolic acid, named oleuafricein. The isolate of Greek olive leaves (GO) was found to contain 0.71% oleanolic acid, and the Cape Town cultivar (CT) contained 2.47% oleanolic acid. No ursolic acid was found in either GO or CT. The antihypertensive, diuretic, antiatherosclerotic, antioxidant and hypoglycemic effects of **authentic oleanolic and ursolic acid** and the three isolates (GO, AO and CT) were studied on Dahl salt-sensitive (DSS), insulinresistant rat genetic model of hypertension. All three isolates, in a dose 60 mg/kg b.w. for **6 weeks treatment, prevented the development of severe hypertension and atherosclerosis and improved the insulin resistance of the experimental animals**.

TITLE: HPLC analysis of oleuropein and some flavonoids in leaf and bud of *Olea europaea* L.

AUTHOR:Ficarra-P; Ficarra-R; De-Pasquale-A; Monforte-MT; Calabro-ML

INSTITUTE: Dipartimento Farmaco Chimico, Univ. di Messina, Viale Annunziata, 98168 Messina, Italy

SOURCE:Farmaco-Ed-Sci; 1991; 46(Jun); 803-815

YEAR:1991

ABSTRACT: A rapid, precise and reproducible reversed phase HPLC method is described for the quantitative determination of oleuropein and some flavonoids from the leaves and buds of *Olea europaea* in order to determine which constituents are responsible for the antilipemic effects of the plant.

TITLE: Protective effect of oleuropein, an olive oil biophenol, on low density lipoprotein oxidizability in rabbits.

AUTHOR:Coni,-E; Di-Benedetto,-R; Di-Pasquale,-M; Masella,-R; Modesti,-D; Mattei,-R; Carlini,-E-A

INSTITUTE: Food Department, Istituto Superiore di Sanita, Rome, Italy_e.coni@iss.it

SOURCE: Lipids. 2000 Jan; 35(1): 45-54

YEAR:2000

ABSTRACT: On the basis of the results obtained with pilot studies conducted in vitro on human low density lipoprotein (LDL) and on cell cultures (Caco-2), which had indicated the ability of certain molecules present in olive oil to inhibit pro-oxidative processes, an in vivo study was made of laboratory rabbits fed special diets. Three different diets were prepared: a standard diet for rabbits (diet A), a standard diet for rabbits modified by the addition of 10% (w/w) extra virgin olive oil (diet B), a modified standard diet for rabbits (diet C) differing from diet B only in the addition of 7 mg kg⁻¹ of oleuropein. A series of biochemical parameters was therefore identified, both in the rabbit plasma and the related isolated LDL, before and after Cu-induced oxidation. The following, in particular, were selected: (i) biophenols, vitamins E and C, uric acid, and total, free, and ester cholesterol in the plasma; (ii) proteins, triglycerides, phospholipids, and total, free, and ester cholesterol in the native LDL (for the latter, the dimensions were also measured); (iii) lipid hydroperoxides, aldehydes, conjugated dienes, and relative electrophoretic mobility (REM) in the oxidized LDL (ox-LDL). In an attempt to summarize the results obtained, it can be said that this investigation has not only verified the antioxidant efficacy of extra virgin olive oil biophenols and, in particular, of oleuropein, but has also revealed a series of thus far unknown effects of the latter on the plasmatic lipid situation. In fact, the addition of oleuropein in diet C increased the ability of LDL to resist oxidation (less conjugated diene formation) and, at the same time, reduced the plasmatic levels of total, free, and ester cholesterol (-15, -12, and -17%, respectively), giving rise to a redistribution of the lipidic components of LDL (greater phospholipid and cholesterol amounts) with an indirect effect on their dimensions (bigger by about 12%).

TITLE: Simultaneous determination of oleuropein and its metabolites in plasma by high-performance liquid chromatography.

AUTHOR: Tsarbopoulos,-A; Gikas,-E; Papadopoulos,-N; Aligiannis,-N; Kafatos,

INSTITUTE: GAIA Research Center, Bioanalytical Department, The Goulandris Natural History Museum, 13 Levidou street, Kifissia, GR-145 62, [Greece. atsarbop@gnhm.gr](mailto:atsarbop@gnhm.gr)

SOURCE: J-Chromatogr-B-Analyt-Technol-Biomed-Life-Sci. 2003 Feb 25; 785(1): 157-64,

YEAR: 2003

ABSTRACT: A method based on high-performance liquid chromatography (HPLC) with a diode array detection system was developed and validated aiming at the simultaneous determination of oleuropein (OE) and its metabolites, hydroxytyrosol (HT) and tyrosol (T), in human plasma. These phenolic components are believed to play a vital role in the prevention of coronary artery disease and atherosclerosis. The proposed method includes a clean-up solid-phase extraction procedure (using a C(18) column) with high recovery efficiency (85-100%). The statistical evaluation of the method reveals good linearity, accuracy and reproducibility for all the compounds analyzed with RSD values less than 6.5%, while the detection limit is 50 ng/ml for both OE and T and 75 ng/ml for HT. This assay can be employed in bioavailability studies of olive oil phenolic compounds, thus assisting the evaluation of their pharmacological role.

TITLE: Effect of phenolic compounds of virgin olive oil on LDL oxidation resistance.

AUTHOR: Moreno-JA; Lopez-Miranda-J; Gomez-P; Fatiha-Benkhalti; El-Boustani-E; PerezJimenez-F

INSTITUTE: Unidad de Lipidos y Arteriosclerosis, Hospital Universitario Reina Sofia, Avda. Menendez Pidal, s/n. 14004 Cordoba, Spain.

SOURCE: Medicina-Clinica-Barcelona. 2003, 120: 4, 128-131; 41 ref.

YEAR: 2003

ABSTRACT: Background and objective: Several epidemiological and experimental studies have associated the intake of antioxidants, which are abundant in the Mediterranean diet, with a low incidence of cardiovascular disease. One possible mechanism of this action is the oxidative protection in low density lipoproteins (LDL). The aim of our study was to compare the antioxidative activity of diverse phenolic compounds present in virgin olive oil on these lipoproteins. Subjects and method: LDL was isolated from

blood plasma of healthy volunteers by sequential ultracentrifugation. This was followed by oxidation with CuCl₂ in the presence of different concentrations of phenolic compounds and virgin olive oil extract. Production of conjugated dienes was determined by the continuous monitoring of increased absorbency at 234 nm as an indicator of LDL oxidation. Results: Virgin olive oil extract prolonged the latency 000 Elsevier Science Ltd phase and significantly lowered the progression rate ($p < 0.05$) at low concentrations (2 µg/ml). This antioxidative effect was also observed with low concentrations (2 nM) of caffeic acid and oleuropein ($p < 0.05$). However, it was necessary to increase the concentration of flavone up to 50 times to observe a similar effect ($p < 0.05$). Conclusion: Both virgin olive oil extract enriched in phenolic compounds and phenolic compounds present in olive oil (caffeic acid and oleuropein) are potent antioxidants at very low concentrations. Thus, the beneficial effects of a Mediterranean diet may be partly due to the protective action of these compounds.

TITLE: Investigation on the extraction and concentration of oleuropein and flavonoids in *Olea europaea* L. based products.

AUTHOR: De-Laurentis-N {a}; Crescenzo-G; Lai-O-R; Milillo-M-A

INSTITUTE:{a} Dep. Med. Chem., Fac. Pharm., Univ. Bari, Via Orabona 4, 70126 Bari, Italy

SOURCE: Pharmaceutical-and-Pharmacological-Letters. 1997; 7 (1) 27-30.

YEAR:1997

ABSTRACT: HPLC reversed phase (RP) is the technique used for the identification and dosage of the secoiridoid oleuropein, of flavonoids (apigenin, quercetin, kaempferol), of glycosyl flavonoids (hesperidin, rutin, the leaves and buds of *Olea europaea* L. This luteolin-7-0glucoside, apigenin-7-0-glucoside), present in chromatographic method, which is simple and easy to use, presents a high reproducibility. Quantitative results and pharmacological considerations are reported here. Several studies have been carried out on the isolation and therapeutic activities of the flavonoids and secoiridoids contained in *Olea europaea* L. These works report data related to the influence of oleuropein on heart activity and on arterial pressure (Messrli, F.H. Ed. 1996)), to the antispasmodic action and the calcium-antagonism of quercetin on smooth muscles of ileum in guinea pig (Ganten D. & Mulrow P. J., 1990) and to the hypocholesterolemic activity of hesperidin in rats kept on a hyperlipidic diet (Timmermans P.B.M.W.M, et al. 1993).

TITLE:Effect of virgin olive oil phenolic compounds on in vitro oxidation of human low density lipoproteins.

AUTHOR: Caruso,-D; Berra,-B; Giavarini,-F; Cortesi,-N; Fedeli,-E; Galli,-G

INSTITUTE:Institute of Pharmacological Sciences, University of Milan, Italy.

SOURCE:Nutr-Metab-Cardiovasc-Dis. 1999 Jun; 9(3): 102-7

YEAR:1999

ABSTRACT:BACKGROUND AND AIM: Substantial evidence suggests that oxidative modifications of low density lipoproteins (LDL) critically contribute to the pathogenesis and progression of human atherosclerosis. Oxidized LDL (oxLDL) are present in atherosclerotic plaques and contain oxysterols that exhibit a variety of adverse biological activities. Antioxidants have also been shown to prevent LDL modification. We have therefore assessed the efficacy of virgin olive oil phenolic compounds in preventing oxidative modifications of human LDL oxidized. by UV light.

METHODS AND RESULTS: Cholesterol oxides formed during LDL photo-oxidation were determined by UV-HPLC in the presence of different concentrations of phenolic compounds and their pure components (tyrosol and oleuropein), and probucol, a widely used synthetic antioxidant. Electrophoretic mobility was also assayed. The results demonstrate that phenolic compounds are much more potent in preventing cholesterol oxide formation and apoproteic moiety modification than their pure components and probucol.

CONCLUSIONS: The beneficial effects of a Mediterranean diet may be ascribable not only to the high

unsaturated/saturated fatty acid ratio characteristic of olive oil, but also to the unique antioxidant properties of its phenolic compounds.

TITLE: Oleuropein, the bitter principle of olives, enhances nitric oxide production by mouse macrophages.

AUTHOR: Visioli,-F; Bellosta,-S; Galli,-C

INSTITUTE:Institute of Pharmacological Sciences, Milan, [Italy. Francesco.Visioli@unimi.it](mailto:Francesco.Visioli@unimi.it)

SOURCE: Life-Sci. 1998; 62(6): 541-6

YEAR:1998

ABSTRACT:The Mediterranean diet, rich in fresh fruits and vegetables, has been associated with a lower incidence of cardiovascular disease and cancer, partly because of its high proportion of bioactive compounds such as vitamins, flavonoids and polyphenols. The major lipid component of such diet is the drupe-derived olive oil, which can be distinguished from other seed oils for the peculiar composition of its non-triglyceride fraction. In fact, several minor components, including polyphenols, grant the oil its particular taste and aroma. Oleuropein, the most abundant among these components, has been shown to be a potent antioxidant endowed with anti-inflammatory properties. We investigated the effects of oleuropein on NO release in cell culture and its activity toward nitric oxide synthase (iNOS) expression. The results show that oleuropein dose-dependently enhance nitrite production in LPS-challenged mouse macrophages. This effect was blocked by the iNOS inhibitor L-NAME, indicating increased iNOS activity. Also, Western blot analysis of cell homogenates show that oleuropein increases iNOS expression in such cells. Taken together, our data suggest that, during endotoxin challenge, oleuropein potentiates the macrophage-mediated response, resulting in higher NO production, currently believed to be beneficial for cellular and organismal protection.

TITLE: Olive oil and red wine antioxidant polyphenols inhibit endothelial activation: Antiatherogenic properties of Mediterranean diet phytochemicals

AUTHOR:Carluccio-MA; Siculella-L; Ancora-MA; Massaro-M; Scoditti-E; Storelli-C; Visioli-F; Distante-A;De-Caterina-R

INSTITUTE: C.N.R. Inst. of Clinical Physiology, Lecce

SOURCE: Arteriosclerosis,-Thrombosis,-and-Vascular-Biology. 2003; 23(4): 622-629

YEAR:2003

ABSTRACT:Objective – Epidemiology suggests that Mediterranean diets are associated with reduced risk of cardiovascular disease. Because monocyte adhesion to the endothelium is crucial in early atherogenesis, we evaluated whether typical olive oil and red wine polyphenols affect endothelial-leukocyte adhesion molecule expression and monocyte adhesion. Methods and Results – Phytochemicals in olive oil and red wine, including oleuropein, hydroxytyrosol, tyrosol, elenolic acid, and resveratrol, with or without antioxidant activity, were incubated with human umbilical vein endothelial cells for 30 minutes, followed by co-incubation with bacterial lipopolysaccharide or cytokines to trigger adhesion molecule expression. At nutritionally relevant concentrations, only oleuropein, hydroxytyrosol, and resveratrol, possessing a marked antioxidant activity, reduced monocytoid cell adhesion to stimulated endothelium, as well as vascular cell adhesion molecule-1 (VCAM-1) mRNA and protein by Northern analysis and cell surface enzyme immunoassay. Reporter gene assays with deletional VCAM-1 promoter constructs indicated the relevance of nuclear factor- κ B, activator protein-1, and possibly GATA binding sites in mediating VCAM-1 transcriptional inhibition. The involvement of nuclear factor- κ B and activator protein-1 was finally demonstrated at electrophoretic mobility shift assays. Conclusions – Olive oil and red wine antioxidant polyphenols at nutritionally relevant concentrations transcriptionally inhibit endothelial adhesion molecule expression, thus partially explaining atheroprotection from Mediterranean diets.

TITLE:Antiatherogenic components of olive oil.

AUTHOR:Visioli,-F; Galli,-C

INSTITUTE: Institute of Pharmacological Sciences, University of Milan, Via Balzaretti 9, Milan 20133, [Italy. francesco.visioli@unimi.it](http://italy.francesco.visioli@unimi.it)

SOURCE:Curr-Atheroscler-Rep. 2001 Jan; 3(1): 64-7

YEAR:2001

ABSTRACT: Olive oil is the principal source of fat in the Mediterranean diet, which has been associated with a lower incidence of coronary heart disease and certain cancers. Olive oil is characterized by a high proportion of monounsaturated oleic acid, but the main peculiarity of extra-virgin oil is the presence of remarkable quantities of phenolic compounds, notably hydroxytyrosol and oleuropein, that provide high stability and strong taste. Recently, several studies have demonstrated that olive oil phenolics are powerful antioxidants, both in vitro and in vivo, and exert additional potent biologic activities that could partially account for the observed cardioprotective effects of the Mediterranean diet.

TITLE: Effects of leaves and shoots of *Olea europaea* L. and oleuropein on experimental hypercholesterolemia in rat

AUTHOR:De-Pasquale-R; Monforte-MT; Trozzi-A; Raccuia-A; Tommasini-S; Ragusa-S

INSTITUTE:Pharmaco-Biological Department, School of Pharmacy, Vill. ss. Annunziata, 98168 Messina

SOURCE:PLANT-MED-PHYTOTHER. Plantes-Medicinales-et-Phytotherapie. 1991; 25(2-3): 134-140

YEAR:1991

ABSTRACT:The effects of glycerol-alcoholic extracts of shoots and leaves of *Olea europaea* L. and oleuropein on diet and triton hypercholesterolemia were studied in Wistar rats. It was found that the hypocholesterolemic effects of the *Olea* extracts can be ascribed to a synergic action of oleuropein and polyunsaturated fatty acids contained in the drugs.

TITLE:Oleuropein Protects Low Density Lipoprotein from Oxidation

AUTHOR:Visoli, F. & Galli, C.

SOURCE:Life Sciences, Vol. 55, No. 24, pp. 1965-1971

YEAR:1994

ABSTRACT:The Mediterranean diet, rich in fruit, vegetables, grain, and vegetable oil (mainly olive oil) is correlated with a lower incidence of coronary heart disease (CHD). Natural antioxidants contained in the Mediterranean diet might also play a role in the prevention of cardiovascular diseases, through inhibition of LDL oxidation. We tested this hypothesis "in vitro" by inducing LDL oxidation with copper sulphate and preincubating the samples with oleuropein, the bitter principle of olives, that is one of the major components of the polyphenolic fraction of olive oil. Oleuropein 10⁻⁵ M effectively inhibited CuSO₄-induced LDL oxidation, as assessed by various parameters. We demonstrate in this investigation that polyphenolic components of the Mediterranean diet interfere with biochemical events that are implicated in atherogenic disease, thus proposing a new link between the Mediterranean diet and prevention of CHD.

TITLE: Pharmacological analysis of the iridoid oleuropein.

AUTHOR:Petkov,-V; Manolov,-P

SOURCE:Arzneimittelforschung. 1972 Sep; 22(9): 1476-86

YEAR:1972

ABSTRACT:Empirical clinical data about a healing effect of the olive leaves in the case of hypertensive disease stimulated searching for the active component. In 1960 Panizzi et al. (20) succeeded in isolating a bitter glucoside which was given the name of oleuropein and its empirical formula was found to be C₂₇H₄₂O₁₀. This glucoside belongs to the iridoid group. Recently (1970) Inouye et al. (9) cast light upon the structure of oleuropein. Iridoids represent a new structural-chemical class. The majority of the compounds included in this group are glucosides in which carbohydrate component appears most frequently as D-glucose (occasionally as disaccharide, too). Though the first iridoid found in nature, verbenaalin, was isolated as early as 1835 (24), successful investigations into the chemical structure of this group were only commenced in the recent fifteen years. The cause of this delay lies in the extremely great instability of the

majority of compounds in this group. Characteristic feature of the aglycons of iridoids is the presence of cyclopentane-pyrane system. In some of them, the so called secoiridoids, the cyclopentane ring is open. This group of compounds was given the name of iridoids by Briggs et al. (2) in 1963. Very interesting data were recently obtained to show the presence of biogenetic correlations between iridoids and alkaloids as well as their ability of principle to transform one into another. Thus it has been established by the radioisotope studies of Popov (22) that the alkaloid gentioflavine isolated from some species of *Gentiana* might be obtained through a particular transformation of the molecule of the iridoid gentiopicroside. Further the alkaloids gentianidine and gentianadine are obtained by transforming the molecule of gentioflavine. The latter appears to be a precursor also of the alkaloids of the gentiane-structure type (genianine, etc.) through a would-be intermediate formation of a compound similar in structure to the iridoid gentioflavoside. It has been shown by way of isotopic studies, too, that the new-isolated iridoid gentioside represents an intermediate phase of the iridoid step in the biosynthesis pathway that leads to the formation of alkaloids in the gentiane plants. Oleuropein is water soluble and unstable against acids. When subjected to tentative studies (personal communication of Dr. Kloss [12]) oleuropein displays the following effects: it provokes an increase of coronary blood stream (experiments with heart after Langendorf), produces an elevation of blood-stream in the guinea pig limb, exerts a spasmolytic effect in case of histamine spasm. A 2% solution of oleuropein applied in a dose of 0.1 ml decreases by 22% the blood pressure of the rat, while administered in a dose of 1.0 ml by 31%. These scarce data about the pharmacodynamics of oleuropein gave us grounds to study in more details its pharmacology. Our investigations into the iridoid of the olive leaves were largely stimulated by the encouraging results obtained from studies of iridoids isolated from valerian (*Valeriana officinalis* L). For a long time the importance of valerian as a sedative drug has been discussed and even contested. However this problem was considered differently after Thies [25-29], Mannetstatter et al. [13], Wagner et al. [30] and some others succeeded in isolating from the valerian root a new group of active substances, reckoned amount the iridoid group. These new substances were determined quantitatively and studied under experimental and clinical conditions. Iridoids called valepotriases (the most important of which are valtratum, didrovaltratum and acevaltratum) contained in a relatively high concentration (0.5 to 2%) in the valerian root displayed a clear-cut activity as sedative drugs [5, 69].

COSMETIC

TITLE: Natural actives for cosmetics

AUTHOR:Ziolkowsky-B

SOURCE:Seifen-Oele-Fette-Wachse (Seifen-Oele-Fette-Wachse); 2002; 128(1-2); 19-23,

YEAR:2002

ABSTRACT:Today many raw materials and actives are won from natural products, to be used in cosmetic preparations, which support the body's natural process. These natural actives can effectively be used in preventing negative external and internal processes such as anti-aging, anti-irritants, antioxidants or as moisturizers, thighteners and cell activators.

TITLE: Dietetic and/or cosmetic preparation comprising a mixture of lycopene and olive leaf extract

AUTHOR:Coll,-D; Mathonnet,-J-P; Zannini,-G

YEAR:2000

ABSTRACT:A dietetic or cosmetic preparation comprises an active mixture of lycopene with an olive leaf extract; the olive leaf extract aids solubilization of the lycopene. It is claimed that the lipid regulation action of the olive leaf extract associates with the cell preservation action of the lycopene.

DIABETES (HYPOGLYCEMIA)

TITLE: Hypoglycemic Activity of Olive Leaf

AUTHOR:Gonzalez, M., Zarzuelo, A., Gomez, M. J., Utrilla, M. P., Jimenez, J., and Osuna I.

INSTITUTE:Department of Farmacologia, Facultad de Farmacia, Universidad de Granada, Granada,Spain.

SOURCE:Planta Med. 58 (1992) 513-515

YEAR:1992

ABSTRACT:The hypoglycemic activity of olive leaf was studied. Maximum hypoglycemic activity was obtained from samples collected in the winter months, especially in February. One of the compounds responsible for this activity was oleuropeoside, which showed activity at a dose of 16mg/kg. The compound also demonstrated antidiabetic activity in animals with alloxan-induced diabetes. The hypoglycemic activity of this compound may result from two mechanisms (a) potentiation of glucose-induced insulin release, and (b) increased peripheral uptake of glucose.

TITLE: The Evaluation of Long-term Effects of Cinnamon Bark and Olive Leaf on Toxicity Induced by Streptozotocin Administration to Rats.

AUTHOR:Onderoglu, S., Sozer, S., Mine Erbil, K., Ortac, R. & Lermioglu, F.

SOURCE:J. Pharm. Pharmacol. 1999, 51: 1305-1312

YEAR:1999

ABSTRACT:The effects of cinnamon bark and olive leaf have been investigated on streptozotocin-induced tissue injury, and some biochemical and haematological changes in rats. The effects on glycaemia were also evaluated. Long term administration of olive leaf caused significant improvement in tissue injury induced by streptozotocin treatment; the effect of cinnamon bark was less extent. No effects on blood glucose levels were detected. However, significant decreases in some increased biochemical and haematological parameters of streptozotocin-treated rats were observed. Aspartate aminotransferase, urea and cholesterol levels were significantly decreased by treatment with both plant materials, and alanine aminotransferase by treatment with olive leaf. Cinnamon bark also caused a significant decrease in platelet counts. In addition, any visible toxicity, except decrease in body weight gain, attributable to the long term use of plant materials was not established in normal rats. The data indicate that long term use of olive leaf and cinnamon bark may provide benefit against diabetic conditions. Determination of underlying mechanism(s) of beneficial effects, toxicity to other systems and clinical assessments of related plant materials are major topics requiring further studies.

TITLE:Essai Clinique D'Un Extrait Titre de Feuilles D'Olivier Dans Le Traitement De L'Hypertension Arterielle Essentielle [Clinical Assay of Olea europaea Aqueous Extract in Hypertension Arterial Treatment.]

AUTHOR: Cherif, S., Rahal, N., Haouala, M., Hizaoui, B., Dargouth, F., Gueddiche, M., Kallel, Z., Balansard, G., & Boukef, K..

SOURCE:J. Pharm. Belg., 1996, 51, 2, 69-71

YEAR: 1996

ABSTRACT:A clinical assay of *Olea europaea* L. aqueous extract was carried on two groups of patients suffering with essential hypertension. 12 patients consulting for the first time, 18 patients with anti hypertensive treatment. Treatment based on *Olea europaea* L. leaf aqueous extract was given (400mg x 4/24h) during 3 months, after 15 days treatment based on placebo. We note for all patients a statistically significant decrease of blood pressure ($p < 0,001$), we didn't find any modification of biological parameters, excepted a significant little decrease of glycemia and calcemia $p < 0,01$ and $p < 0,0$

FEVER

TITLE:A Modern Herbal

AUTHOR:Grieve, M.

SOURCE:Jonathan Cape Ltd, London

YEAR:1931, Reprinted 1974, 1975, 1977, 1979.

EXTRACT:Medicinal Action & Uses: The olive leaves are astringent and antiseptic. Internally a decoction of 2 handfuls boiled in a quart of water until reduced to half a pint has been used in Levant in obstinate fevers. Both leaves and bark have valuable febrifugal qualities.

GENERAL

TITLE: Olive oil phenols are absorbed in humans.

AUTHOR:Vissers,-M-N; Zock,-P-L; Roodenburg,-A-J; Leenen,-R; Katan,-M-B

INSTITUTE:Division of Human Nutrition and Epidemiology, Wageningen University, Wageningen, The Netherlands

SOURCE:J-Nutr. 2002 Mar; 132(3): 409-17,

YEAR:2002

ABSTRACT:Animal and in vitro studies suggest that olive oil phenols are effective antioxidants. The most abundant phenols in olive oil are the nonpolar oleuropein- and ligstroside-aglycones and the polar hydroxytyrosol and tyrosol. The aim of this study was to gain more insight into the metabolism of those phenols in humans. We measured their absorption in eight healthy ileostomy subjects. We also measured urinary excretion in the ileostomy subjects and in 12 volunteers with a colon. Subjects consumed three different supplements containing 100 mg of olive oil phenols on separate days in random order. Ileostomy subjects consumed a supplement with mainly nonpolar phenols, one with mainly polar phenols and one with the parent compound oleuropein-glycoside. Subjects with a colon consumed a supplement without phenols (placebo) instead of the supplement with oleuropein-glycoside. Ileostomy effluent and urine were collected for 24 h after supplement intake. Tyrosol and hydroxytyrosol concentrations were low (< 4 mol/100 mol of intake) in the ileostomy effluent, and no aglycones were detected. We estimated that the apparent absorption of phenols was at least 55-66% of the ingested dose. Absorption was confirmed by the excretion of tyrosol and hydroxytyrosol in urine. In ileostomy subjects, 12 mol/100 mol and in subjects with a colon, 6 mol/100 mol of the phenols from the nonpolar supplement were recovered in urine as tyrosol or hydroxytyrosol. In both subject groups, 5-6 mol/100 mol of the phenols was recovered from the polar supplement. When ileostomy subjects were given oleuropein-glycoside, 16 mol/100 mol was recovered in 24-h urine, mainly in the form of hydroxytyrosol. Thus, humans absorb a large part of ingested olive oil phenols and absorbed olive oil phenols are extensively modified in the body.

TITLE: The blessing from the mount of olives

AUTHOR: Hardelius-M

SOURCE: FIP-World-Congress (International-Pharmaceutical-Federation-World-Congress); 2002;62,152,

YEAR:2002

ABSTRACT:The olive-tree appears in many fundamental myths of our culture and the Mount of Olives is the theatre of several essential scenes from the life of Jesus."Olive oil frightens away all suffering" according to the old proverb and you get the following recommendations on the web: "Research from Europe shows how olive leaf extract can help fight 137 different diseases, including ear infections; hepatitis and pneumonia" The antiquity praised the medical qualities of the olive leaf but even before the 5th century B.C. Hippocrates did advise them in case of ulcer or cholera. Pliny the Elder reminded of the Anecdote "There are two liquids delightful for the human body for internal use the wine and for external use olive oil " Olive oil is the only vegetable oil to be extracted by cold pressure and it is an ingredient in several preparations such as ointments and plasters in the ancient Pharmacopeias. The olive-tree is since the Neolithic period considered present all around the Mediterranean Sea. Two thirds of the trees are concentrated in the European part of

the Mediterranean areas and only 3% in the New World. The consumption is highest in Greece with 20 kg per inhabitant and year. In an International Consensus Statement from EU this year you can read "There is increasing scientific evidence that there are positive health effects from the Traditional Mediterranean Diet where olive oil is the principal source of fat."

TITLE: In vitro anti-complementary activity of flavonoids from olive (*Olea europaea* L.) leaves

AUTHOR: Pieroni-A; Heimler-D; Pieters-L; Van-Poel-B; Vlietinck-AJ

INSTITUTE: Pharmazeutisches Institut, Rheinische-Friedrich-Wilhelms-Univ., Kreuzbergweg 26, D-53115 Bonn

SOURCE: PHARMAZIE. Pharmazie-. 1996; 51(10):765-768

YEAR: 1996

ABSTRACT: From extracts of olive (*Olea europaea* L., Oleaceae) leaves showing anticomplementary activity, the flavonoids apigenin, apigenin-4'-O-rhamnosylglucoside, apigenin-7-O-glucoside, luteolin, luteolin-4'-O-glucoside, luteolin-7-O-glucoside, chrysoeriol, chrysoeriol-7-O-glucoside and quercetin-3-O-rhamnoside were isolated.

TITLE: Natural substance based agent

AUTHOR: Stueckler,-F,

YEAR: 1999

ABSTRACT: A food supplement with advantageous physiological effects contains lecithin, red wine extract and D-alpha-tocopherol at concn. of 0.05-10.00 parts by [wt. in](#) a support material (e.g. dairy products, margarine, fruit juice, vegetable juice, yeast, pectin or olive oil). One or more other ingredients may optionally be incorporated at concn. of 0.01-1.00 parts by wt., including: squalene, beta-carotene, lycopene, green tea extract, garlic extract, genistein, Dlimonene, bisabolol (levomenol), leucocianidol (pynkogenol), Ginkgo biloba leaf extract, hawthorn extract, artichoke extract, our lady's thistle fruit extract, ascorbic acid, B group vitamins, olive leaf extract, diosmin, escin, troxerutin, anguarate extract, pectin, salmon oil concentrate, shiitake (*Lentinus edodes*) extract, incense (*Boswellia*) extract and *Uncaria tomentosa* root extract.

HIVI/AIDS

TITLE: Anti-HIV activity of olive leaf extract (OLE) and modulation of host cell gene expression by HIV -1 infection and OLE treatment

AUTHOR: Lee-Huang-S; Zhang-L; Huang-PL; Chang-Y T; Huang-PL

INSTITUTE: department of Biochemistry, NY University School of Medicine, New York, NY 10016

SOURCE: Biochemical-and-Biophysical-Research-Communications. 2003; 307(4): 1029-1037,

YEAR: 2003

ABSTRACT: We investigated the antiviral activity of olive leaf extract (OLE) preparations standardized by liquid chromatography-coupled mass spectrometry (LC-MS) against HIV-1 infection and replication. We find that OLE inhibits acute infection and cell-to-cell transmission of HIV -1 as assayed by syncytia formation using uninfected MT2 cells co-cultured with HIV-1 infected H9 T lymphocytes. OLE also inhibits HIV-1 replication as assayed by p24 expression in infected H9 cells. These anti-HIV effects of OLE are dose dependent, with EC₅₀s of around 0.2 µg/ml. In the effective dose range, no cytotoxicity on uninfected target cells was detected. The therapeutic index of OLE is above 5000. To identify viral and host targets for OLE, we characterized gene expression profiles associated with HIV-1 infection and OLE treatment using cDNA microarrays. HIV-1 infection modulates the expression patterns of cellular genes involved in apoptosis, stress, cytokine, protein kinase C, and hedgehog signaling. HIV-1 infection up-

regulates the expression of the heat-shock proteins hsp27 and hsp90, the DNA damage inducible transcript 1 gadd45, the p53-binding protein mdm2, and the hedgehog signal protein patched 1, while it down-regulates the expression of the anti-apoptotic BCL2-associated X protein Bax. Treatment with OLE reverses many of these HIV A infection-associated changes. Treatment of HIV-1-infected cells with OLE also up-regulates the expression of the apoptosis inhibitor proteins IAP1 and 2, as well as the calcium and protein kinase C pathway signaling molecules IL-2, IL-2R< alpha >, and ornithine decarboxylase ODC1.

TITLE:A new triple combination therapy

AUTHOR: Konlee,-M

SOURCE:Posit-Health-News. 1998 Fall; (No 17): 12-4,

YEAR:1998

ABSTRACT: Elderberry, chondroitin, and glucosamine sulfate have been found to block HIV replication at three distinct points in the replication cycle. For quadruple therapy, a reverse transcriptase inhibitor such as olive leaf extract or Eпивir (3TC) could be added. In one case, a female, taking no HIV drugs, used an elderberry extract, called Sambucol, with olive leaf extract and experienced a viral load drop from 17,000 to 4,000. Instructions are given for making both alcohol-free and alcohol-based elderberry extracts. In 1993, researchers at Jerusalem's Hebrew University Medical School found in a placebo-controlled double-blind study that Sambucol led to a rapid recovery from influenza and inhibited replication of nine other strains of the flu virus. A theory is that elderberry renders viruses nonfunctional by staining and coating them. Another promising treatment is soil based organisms, which improved Natural Killer cell function in a person with CFIDS.

IMMUNE SYSTEM

TITLE: Replenishing your immune system with nature's antibiotic apothecary

AUTHOR:Wellman-T

SOURCE:Total Health Magazine (TOTAL HEALTH -MAG) 2001 Nov-Dec; 23(6): 76-8,

YEAR: 2001

ABSTRACT:In a world of superbugs that are resistant to antibiotics and the coming plague" of new viruses, scientific research shows that olive leaf extract kills germs and infections of all kinds and that power comes from its active agent, elenolic acid with its salt compound, calcium d-elenolate.

TITLE: Transfer factor.

AUTHOR:Anonymous

SOURCE:Posit-Health-News. 1998 Fall; (No 17): 21,

YEAR:1998

ABSTRACT:

Transfer factor, a natural substance of the immune system, was discovered in 1949. More than 3,000 scientific articles have established it as an effective treatment for many diseases, usually those related to the immune system. In China, more than six million people have used transfer factor as a prophylaxis for hepatitis. Information on ordering articles on transfer factor, olive leaf extract, and coconut oil is included.

RADIO-PROTECTIVE

TITLE: Radioprotective effects in vivo of phenolics extracted from *Olea europaea* L. leaves against X-ray-induced chromosomal damage: comparative study versus several flavonoids and sulfur-containing compounds.

AUTHOR:Benavente-Garcia O, Castillo J, Lorente J, Alcaraz M.

INSTITUTE:Research and Development Department, Furfural Espanol S.A., Camino Viejo de Pliego s/n, 80320 Alcantarilla, Murcia, [Spain. laboratorio@furesa.es](mailto:laboratorio@furesa.es)

ABSTRACT:The radioprotective effects of a polyphenolic extract of *Olea europaea* L. leaves (OL); the flavonoids diosmin and rutin, which are widely used as pharmaceuticals; and the sulfur-containing compounds dimethylsulfoxide (DMSO) and 6-n-propyl-2-thiouracil (PTU) were determined by using the micronucleus test for anticlastogenic activity, evaluating the reduction of the frequency of micronucleated polychromatic erythrocytes (MnPCEs) in bone marrow of mouse before and after X-ray irradiation. With treatment before X-irradiation, the most effective compounds were, in order, rutin > DMSO > OL > PTU > diosmin. These results showed, for the polyphenols studied, a linear correlation ($r(2) = 0.965$) between anticlastogenic activity and antioxidant capacity. The magnitude of protection with treatment after X-irradiation were lower, and the most effective compounds were, in order, OL > diosmin > rutin; DMSO and PTU lacked radioprotective activity. Therefore, OL is the only substance that showed a significant anticlastogenic activity both before and after X-ray irradiation treatments. Structurally, the free oxygen radicals and lipoperoxyradicals scavenging capacity and, consequently, the anticlastogenic activity of these polyphenolic compounds are based principally on the presence of specific functional groups, mainly catechol groups (rutin, oleuropein, hydroxytyrosol, verbascoside, luteolin), that also increase the stability of the aroxyl-polyphenol radical generated in the above processes.

RESPIRATORY (INFLUENZA, PNEUMONIA ETC)

TITLE: In vitro evaluation of secoiridoid glucosides from the fruits of *Ligustrum lucidum* as antiviral agents.

AUTHOR:Ma-Shuang-Cheng; He-Zhen-Dan; Deng-Xue-Long; But-Paul-Pui-Hay {a}; OoiVincent-Eng-Choon; Xu-Hong-Xi; Lee-Spencer-Hon-Sun; Lee-Song-Fong

INSTITUTE: {a} Department of Biology and Institute of Chinese Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong; [E-Mail: paulbut@cuhk.edu.hk](mailto:paulbut@cuhk.edu.hk), China

SOURCE:Chemical-and-Pharmaceutical-Bulletin-Tokyo. [print] November, 2001; 49 (11): 1471-1473.

YEAR:2001

ABSTRACT:Six secoiridoid glucosides, lucidumoside C (1), oleoside dimethylester (2), neonuezhenide (3), oleuropein (4), ligustroside (5) and lucidumoside A (6), isolated from the fruits of *Ligustrum lucidum* (*Oleaceae*), were examined in vitro for their activities against four strains of pathogenic viruses, namely herpes simplex type 1 virus (HSV-1), influenza type A virus (Flu A), respiratory syncytial virus (RSV) and parainfluenza type 3 virus (Para 3). Antiviral activities were evaluated by the cytopathic effect (CPE) inhibitory assay. The purpose was to check if the anti-oxidative potency of these glucosides correlated with their antiviral potency. Results showed that none of the glucosides had any significant activity against HSV-1 and Flu A. Oleuropein, however, showed significant antiviral activities against RSV and Para 3 with IC50 value of 23.4 and 11.7 mug/ml, respectively. Lucidumoside C, oleoside dimethylester and ligustroside showed potent or moderate antiviral activities against Para 3 with IC50 values of 15.6-20.8 mug/ml. These results also documented that the anti-oxidative potency of these secoiridoid glucosides was not directly related to their antiviral effects.

TITLE: On the in-vitro antimicrobial activity of oleuropein and hydroxytyrosol.

AUTHOR:Bisignano,-G; Tomaino,-A; Lo-Cascio,-R; Crisafi,-G; Uccella,-N; Saija,-A

INSTITUTE:Department Farmaco-Biologico, University of Messina, Italy.

SOURCE:J-Pharm-Pharmacol. 1999 Aug; 51(8): 971-4

YEAR:1999

ABSTRACT:Secoiridoides (oleuropein and derivatives), one of the major classes of polyphenol contained in olives and olive oil, have recently been shown to inhibit or delay the rate of growth of a range of bacteria and microfungi but there are no data in the literature concerning the possible employment of these secoiridoides as antimicrobial agents against pathogenic bacteria in man. In this study five ATCC standard bacterial strains (*Haemophilus influenzae* ATCC 9006, *Moraxella catarrhalis* ATCC 8176, *Salmonella typhi* ATCC 6539, *Vibrio parahaemolyticus* ATCC 17802 and *Staphylococcus aureus* ATCC 25923) and 44 fresh clinical isolates (*Haemophilus influenzae*, eight strains, *Moraxella catarrhalis*, six strains, *Salmonella* species, 15 strains, *Vibrio cholerae*, one strain, *Vibrio alginolyticus*, two strains, *Vibrio parahaemolyticus*, one strain, *Staphylococcus aureus*, five penicillin-susceptible strains and six penicillin-resistant strains), causal agents of intestinal or respiratory tract infections in man, were tested for in-vitro susceptibility to two olive (*Olea europaea*) secoiridoides, oleuropein (the bitter principle of olives) and hydroxytyrosol (derived from oleuropein by enzymatic hydrolysis and responsible for the high stability of olive oil). The minimum inhibitory concentrations (MICs) calculated in our study are evidence of the broad antimicrobial activity of hydroxytyrosol against these bacterial strains (MIC values between 0.24 and 7.85 microg mL⁻¹) for ATCC strains and between 0.97 and 31.25 microg mL⁻¹ for clinically isolated strains). Furthermore oleuropein also inhibited (although to a much lesser extent) the growth of several bacterial strains (MIC values between 62.5 and 500 microg mL⁻¹) for ATCC strains and between 31.25 and 250 microg mL⁻¹ for clinical isolates); oleuropein was ineffective against *Haemophilus influenzae* and *Moraxella catarrhalis*. These data indicate that in addition to the potential employment of its active principles as food additives or in integrated pest-management programs, *Olea europaea* can be considered a potential source of promising antimicrobial agents for treatment of intestinal or respiratory tract infections in man.

TITLE:In vitro evaluation of secoiridoid glucosides from the fruits of *Ligustrum lucidum* as antiviral agents.

AUTHOR:Ma-Shuang-Cheng; He-Zhen-Dan; Deng-Xue-Long; But-Paul-Pui-Hay {a}; OoiVincent-Eng-Choon; Xu-Hong-Xi; Lee-Spencer-Hon-Sun; Lee-Song-Fong

INSTITUTE:{a} Department of Biology and Institute of Chinese Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong; [E-Mail: paulbut@cuhk.edu.hk](mailto:paulbut@cuhk.edu.hk), China

SOURCE: Chemical-and-Pharmaceutical-Bulletin-Tokyo. [print] November, 2001; 49 (11): 1471-1473.

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ULCERS

TITLE: *Olea europaea* L.: stimulant, anti-ulcer and anti-inflammatory effects

AUTHOR: Fehri-B; Aiache-JM; Mrad-S; Korbi-S; Lamaison-JL

INSTITUTE: Dept. of Pharmacol. and Toxicol., Soc. of Pharm. Industries of Tunisia Fondouk Choucha, Rades 2040, Tunisia

SOURCE: Boll-Chim-Farm (Bollettino-Chimico-Farmaceutico); 1996; 135(Jan); 42-49,

YEAR: 1996

ABSTRACT: The dried aqueous extract of the leaf of *Olea europaea* containing 3.25% oleuropein was studied for pharmacological effects using the hole board, open field, rota rod, and automatic reflex conditioner tests. At low doses, the preparation stimulated the CNS, but at high doses it caused CNS depression. The extract induced dose dependent and significant anti-inflammatory effects on carrageenin induced edema in rats. It also provided pronounced protection against aspirin induced gastric ulcers.

TITLE: The blessing from the mount of olives (HP-S-004)

AUTHOR: Hardelius-M

SOURCE: FIP-World-Congress (International-Pharmaceutical-Federation-World-Congress); 2002;62,152,

YEAR: 2002

ABSTRACT: The olive-tree appears in many fundamental myths of our culture and the Mount of Olives is the theatre of several essential scenes from the life of Jesus. "Olive oil frightens away all suffering" according to the old proverb and you get the following recommendations on the web: "Research from Europe shows how olive leaf extract can help fight 137 different diseases, including ear infections; hepatitis and pneumonia" The antiquity praised the medical qualities of the olive leaf but even before the 5th century B.C. Hippocrates did advise them in case of ulcer or cholera. Pliny the Elder reminded of the Anecdote "There are two liquids delightful for the human body for internal use the wine and for external use olive oil " Olive oil is the only vegetable oil to be extracted by cold pressure and it is an ingredient in several preparations such as ointments and plasters in the ancient Pharmacopeias. The olive-tree is since the Neolithic period considered present all around the Mediterranean Sea. Two thirds of the trees are concentrated in the European part of the Mediterranean areas and only 3% in the New World. The consumption is highest in Greece with 20 kg per inhabitant and year. In an International Consensus Statement from EU this year you can read "There is increasing scientific evidence that there are positive health effects from the Traditional Mediterranean Diet."

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