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# *Published clinical trials on the ingredients in Health Optimizing Impact-RX*

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## **Content of this document:**

Page 1 – 9: 17 publications on Delphinol's effect on anti-ageing, inflammation, immune system etc.

Page 10 - 13: 4 publications on Olive Leaf Extract's effect on anti-ageing, inflammation, cancer, etc.

Page 14: Main conclusions

## **Content of Health Optimizing Impact-RX:**

1-month supply in each bottle with a daily dose (2 capsules) of 200mg Delphinol® and 500mg Olive leaf extract (12% Oleuropein).

### **Plant Food Delphinidin-3-Glucoside Significantly Inhibits Platelet Activation and Thrombosis: Novel Protective Roles against Cardiovascular Diseases**

**Yan Yang<sup>1,2,3,4,\*</sup>, Zhenyin Shi<sup>2</sup>, Adili Reheeman<sup>3</sup>, Joseph W. Jin<sup>1,3</sup>, Conglei Li<sup>3,4</sup>, Yiming Wang<sup>1,3,4</sup>, Marc C. Andrews<sup>3,5</sup>, Pingguo Chen<sup>1,3</sup>, Guangheng Zhu<sup>3</sup>, Wenhua Ling<sup>2</sup>, Heyu Ni<sup>1,3,4,5,6,\*</sup>**

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#### **Abstract**

Delphinidin-3-glucoside (Dp-3-g) is one of the predominant bioactive compounds of anthocyanins in many plant foods. Although several anthocyanin compounds have been reported to be protective against cardiovascular diseases (CVDs), the direct effect of anthocyanins on platelets, the key players in atherothrombosis, has not been studied. The roles of Dp-3-g in platelet function are completely unknown. The present study investigated the effects of Dp-3-g on platelet activation and several thrombosis models *in vitro* and *in vivo*. We found that Dp-3-g significantly inhibited human and murine platelet aggregation in both platelet-rich plasma and purified platelets. It also markedly reduced thrombus growth in human and murine blood in perfusion chambers at both low and high shear rates. Using intravital microscopy, we observed that Dp-3-g decreased platelet deposition, destabilized thrombi, and prolonged the time required for vessel occlusion. Dp-3-g also significantly inhibited thrombus growth in a carotid artery thrombosis model. To elucidate the mechanisms, we examined platelet activation markers via flow cytometry and found that Dp-3-g significantly inhibited the expression of P-selectin, CD63, CD40L, which reflect platelet  $\alpha$ - and  $\delta$ -granule release, and cytosol protein secretion, respectively. We further demonstrated that Dp-3-g downregulated the expression of active integrin  $\alpha$ IIb $\beta$ 3 on platelets, and attenuated fibrinogen binding to platelets following agonist treatment, without interfering with the direct interaction between fibrinogen and integrin  $\alpha$ IIb $\beta$ 3. We found that Dp-3-g reduced phosphorylation of adenosine monophosphate-activated protein kinase, which may contribute to the observed inhibitory effects on platelet activation. Thus, Dp-3-g significantly inhibits platelet activation and attenuates thrombus growth at both arterial and venous shear stresses, which likely contributes to its protective roles against thrombosis and CVDs.

<https://doi.org/10.1371/journal.pone.0037323>

PDF: <https://drive.google.com/open?id=0B873BaXbiduNMUJwaHZKNW9FSFhiZXd6bUhOSnBzWVQ4UzM4>

## **Most important findings/conclusions:**

- Significantly inhibits platelet activation, thrombosis and clogging of carotid arteries.

- Through these specific findings, one can conclude there is a significant reduction in cardiovascular risk, especially those known to be associated with ageing.

## Delphinidin Chloride and Its Hydrolytic Metabolite Gallic Acid Promote Differentiation of Regulatory T cells and Have an Anti-inflammatory Effect on the Allograft Model

Ki Hyeob Hyun,\* Ki Cheol Gil,\* Sung Gun Kim, So-young Park, and Kwang Woo Hwang 



**Abstract:** Regulatory T cells (Tregs) control the reactivity of other T cells to prevent excessive inflammatory responses. They also play a role in preventing autoimmune diseases; but when they are overproduced, they decreased vital immunity, which can lead to invasion of external pathogens. Therefore, it is most important in preventing the development of immune diseases to maintain the homeostasis of these cells. Delphinidin chloride is an anthocyanidin and known to have anti-oxidant activities. However, its structure is very unstable and easily decomposed. One of these degradation products is gallic acid, which also has anti-oxidant effects. In this study, we examined the effect of these materials on Tregs in controlling immune response. It was found that these materials further promote differentiation into Tregs, and TGF- $\beta$  and IL-2 related signals are involved in this process. Furthermore, it was verified that a variety of immunosuppressive proteins were secreted more, and the function of induced Tregs was also increased. Finally, in the allograft model, we could find a decrease in activated T cells when these materials were treated because they increased differentiation into Tregs. Therefore, these two materials are expected to become new candidates for the treatment of diseases caused by excessive activation of immune cells, such as autoimmune diseases.

<https://onlinelibrary.wiley.com/doi/abs/10.1111/1750-3841.14490>

PDF: <https://drive.google.com/open?id=192YRqj3QLDsTc4N-ci9wxZQnIDPu3aAQ>

### Most important findings/conclusions:

- Increased function of Regulatory T Cells (Tregs), which often worsen with age.
- Thus better prevention of excessive activation of immune cells and inflammation.
- For that reason, it has significant anti-inflammatory and anti-autoimmune effects.

## Delphinidin, an Anthocyanidin in Pigmented Fruits and Vegetables, Protects Human HaCaT Keratinocytes and Mouse Skin Against UVB-Mediated Oxidative Stress and Apoptosis

Farrukh Afaq<sup>1</sup>, Deebea N. Syed<sup>1</sup>, Arshi Malik<sup>1</sup>, Naghma Hadi<sup>1</sup>, Sami Sarfaraz<sup>1</sup>, Mee-Hyang Kweon<sup>1</sup>, Naghma Khan<sup>1</sup>, Mohammad Abu Zaid<sup>1</sup> and Hasan Mukhtar<sup>1</sup>

Solar UV radiation, in particular its UVB component, is the primary cause of many adverse biological effects, the most damaging of which is skin cancer. Here, we assessed the photochemopreventive effect of delphinidin, a major anthocyanidin present in many pigmented fruits and vegetables, on UVB-mediated responses in human immortalized HaCaT keratinocytes and SKH-1 hairless mouse skin. We found that pretreatment of cells with delphinidin (1–20  $\mu$ M for 24 hours) protected against UVB (15–30 mJ/cm<sup>2</sup>, 24 hours)-mediated (i) decrease in cell viability and (ii) induction of apoptosis. Furthermore, we found that pretreatment of HaCaT cells with delphinidin inhibited UVB-mediated (i) increase in lipid peroxidation; (ii) formation of 8-hydroxy-2'-deoxyguanosine (8-OHdG); (iii) decrease in proliferating cell nuclear antigen expression; (iv) increase in poly(ADP-ribose) polymerase cleavage; (v) activation of caspases; (vi) increase in Bax; (vii) decrease in Bcl-2; (viii) upregulation of Bid and Bak; and (ix) downregulation of Bcl-xL. Topical application of delphinidin (1 mg/0.1 ml DMSO/mouse) to SKH-1 hairless mouse skin inhibited UVB-mediated apoptosis and markers of DNA damage such as cyclobutane pyrimidine dimers and 8-OHdG. Taken together our results suggest that treatment of HaCaT cells and mouse skin with delphinidin inhibited UVB-mediated oxidative stress and reduced DNA damage, thereby protecting the cells from UVB-induced apoptosis.

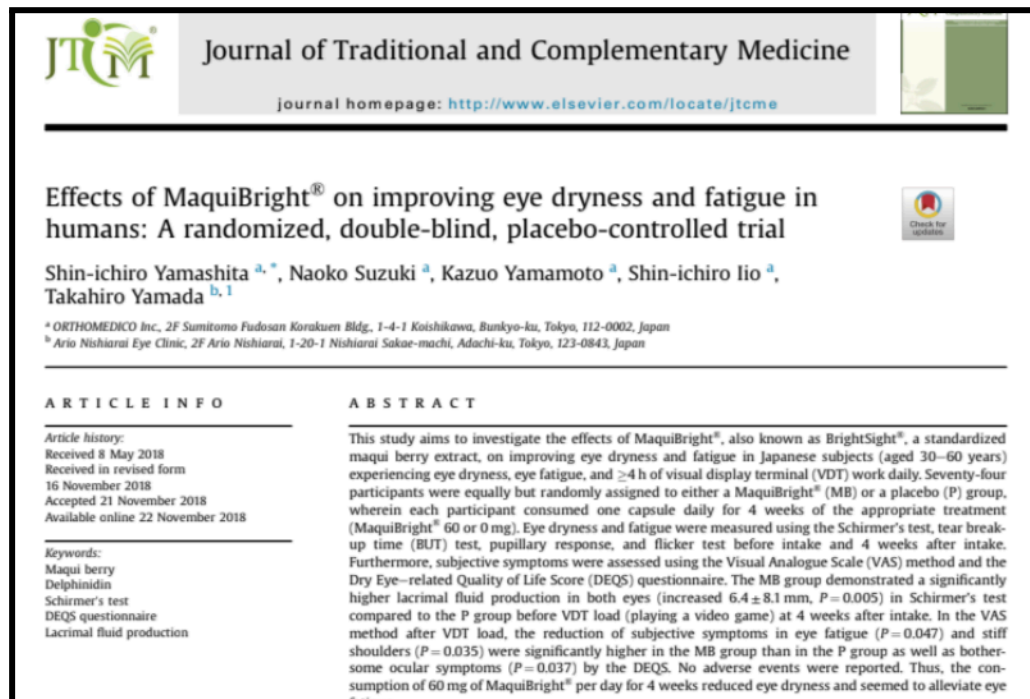
*Journal of Investigative Dermatology* (2007) **127**, 222–232. doi:10.1038/sj.jid.5700510; published online 10 August 2006

<https://doi.org/10.1038/sj.jid.5700510>

PDF: <https://drive.google.com/open?id=1gRa-E9H3OqIFiQRa8WJWalZ7Xc9aMyeP>

### Most important findings/conclusions:

- Reduced damage and cell death of the skin cells from UVB exposure.
- As a consequence, the skin will develop fewer signs of ageing from sun exposure.

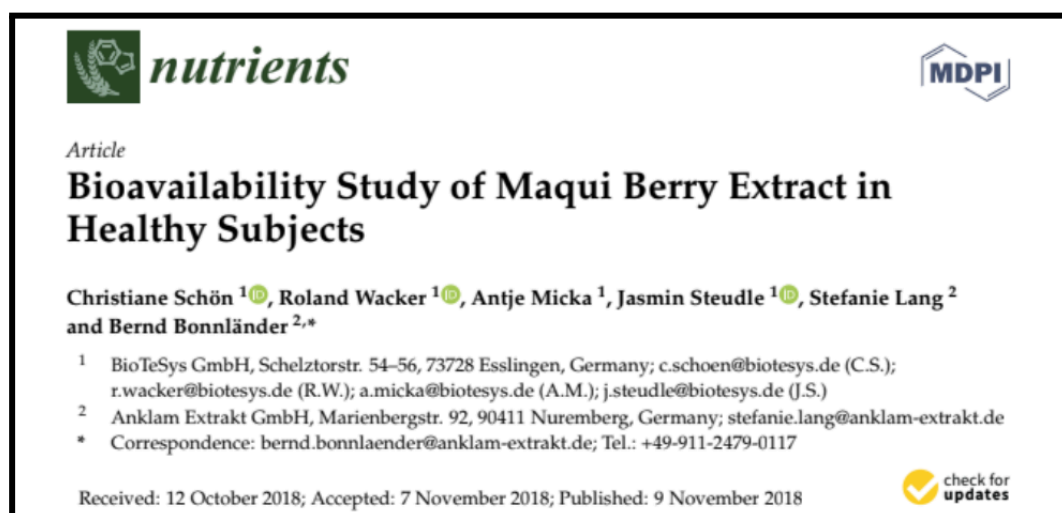


<https://doi.org/10.1016/j.jtcme.2018.11.001>

PDF: <https://drive.google.com/open?id=1UJWT1KCDJSte6dfv3LgKQ7PrGUTEDC6H>

#### Most important finding/conclusion:

- Significant effect on eye fatigue and dry eyes in dosage of only 30% of the daily intake of Health Optimizing Impact-RX.



<https://doi.org/10.3390/nu10111720>

PDF: <https://drive.google.com/open?id=0B873BaXbiduNelh0WnZmeGMtR1JYUzYzVvY01VDZKNXhWOWUw>

#### Most important findings/conclusions:

- Extremely good bioavailability of the main active ingredients.
- Just 1 dose gives high concentrations in blood for several hours.

## Delphinidin attenuates pathological cardiac hypertrophy via the AMPK/NOX/MAPK signaling pathway

Youming Chen<sup>1,\*</sup>, Zhuowang Ge<sup>1,\*</sup>, Shixing Huang<sup>2,\*</sup>, Lei Zhou<sup>3</sup>, Changlin Zhai<sup>4</sup>, Yuhan Chen<sup>1</sup>, Qiuyue Hu<sup>5</sup>, Wei Cao<sup>1</sup>, Yuteng Weng<sup>6</sup>, Yanyan Li<sup>1</sup>

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Keywords: delphinidin, cardiac hypertrophy, AMPK, NADPH oxidase, oxidative stress

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<https://www.impactaging.com/full/12/5362>

PDF: <https://drive.google.com/open?id=1styZ15O-TTDRMp6wU75Z44uA2PLG7UGX>

### Most important finding/conclusion:

- Delphinidin was conclusively shown to repress pathological cardiac hypertrophy by modulating oxidative stress through the AMPK/NADPH oxidase (NOX)/mitogen-activated protein kinase (MAPK) signalling pathway.

**Avaliação da atividade anti-inflamatória *in vitro* de um produto de administração oral contendo peptídeos de colágeno, delphinol® vitamina C e hibiscus**

*In vitro evaluation of the anti-inflammatory activity of an oral administration product containing collagen peptides, Delphinol®, vitamin c and hibiscus*

DOI: <http://www.dx.doi.org/10.5935/scd1984-8773.201810311004>

**Artigo Original**

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<http://www.surgicalcosmetic.org.br/detalhe-artigo/665/Avaliacao-da-atividade-anti-inflamatoria-in-vitro-de-um-produto-de-administracao-oral-contendo-peptideos-de-colageno--delphinol%C2%AE-vitamina-C-e-hibiscus>

PDF: <https://drive.google.com/open?id=0B873BaXbiduNaJJY2h4X0FLMm9pbE1uSWRITFRSa2dGbm1z>

### Most important findings/conclusions:

- Effect on inflammaging (the increase of the inflammatory response due to ageing), by modulating the inflammatory cytokines interleukin-1 alpha, interleukin-6, interleukin-8 and tumour necrosis factor-alpha.
- Reduction of cellular oxidative stress and irreversible cellular damage.





## Article

# A Delphinidin-Enriched Maqui Berry Extract Improves Bone Metabolism and Protects against Bone Loss in Osteopenic Mouse Models

Masahiro Nagaoka <sup>1</sup>, Toyonobu Maeda <sup>2</sup>, Masahiro Chatani <sup>3</sup>, Kazuaki Handa <sup>3</sup>, Tomoyuki Yamakawa <sup>3</sup>, Shuichi Kiyohara <sup>3</sup>, Takako Negishi-Koga <sup>3</sup>, Yasumasa Kato <sup>2</sup> , Masamichi Takami <sup>3</sup>, Shumpei Niida <sup>4</sup>, Stefanie C. Lang <sup>5</sup>, Marlena C. Kruger <sup>6</sup> and Keiko Suzuki <sup>1,\*†</sup>

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<https://doi.org/10.3390/antiox8090386>

PDF: <https://drive.google.com/open?id=1J3bFJaohnpSQ37E5UNvNOv2cRTmT0I3r>

## Most important findings/conclusions:

- Promising natural agent for the prevention of bone loss in osteopenic conditions by not only inhibiting bone resorption but also stimulating bone formation.
- Therefore profound anti-aging effects for age-related degeneration of the skeleton.



# A Combined Regimen of Dietary Supplements Containing Omega-3 Fish Oil and Standardized Maqui Berry Extract Improves Dry Eye Related Symptoms in a Pilot Randomized Interventional Clinical Study

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<sup>2</sup>Southern College of Optometry, Memphis, TN, USA

<sup>3</sup>Paragon BioTech Inc., Portland, OR, USA

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<https://www.longdom.org/abstract/a-combined-regimen-of-dietary-supplements-containing-omega3-fish-oil-and-standardized-maqui-berry-extract-improves-dry-e-52530.html>

PDF: [https://drive.google.com/open?id=1zgIE-XDX5yXxEh8nCVt1tAw5ri3\\_ijgQ](https://drive.google.com/open?id=1zgIE-XDX5yXxEh8nCVt1tAw5ri3_ijgQ)

## Most important finding/conclusion:

- The ingredients in Health Optimizing Impact-RX combined with Health Optimizing Omega-EPA are effective for DED (evaluated by assessing corneal staining, changes in tear osmolarity values and matrix metalloproteinase-9 (MMP-9) levels), and the combination outperforms each ingredient alone.



## Healthy property of maqui berry extract

Giovanni Scapagnini, Sergio Davinelli, Armando Zarrelli

a) Department of Health Sciences, University of Molise, Campobasso, Italy

b) InterUniversity Consortium SannioTech, Piazza San G. Moscati, 82030 Apollosa (BN), Italy

c) Department of Chemical Sciences, University Federico II, Complesso Universitario Monte S. Angelo, Via Cintia 4, 80126 Napoli, Italy

PDF: <https://drive.google.com/open?id=1UAxeRD6x-9EAKRUKctwoEwYQyNGIXVCs>

### **Most important finding/conclusion:**

- A valuable tool to combat oxidative stress and cellular inflammation, and thus lowers the risk of age-associated diseases as oxidative stress and inflammation are associated with faster ageing.

## Nutraceutical and antioxidant effects of a delphinidin-rich maqui berry extract Delphinol®: a review

R. R. WATSON, F. SCHÖNLAU

Anthocyanins represent water-soluble flavonoid species, commonly found in higher plants, the richest plant source representing berries. While all anthocyanins present with antioxidant activity, the delphinidins represent the most potent antioxidant anthocyanins.

Mel and Enid Zuckerman,  
College of Public Health, and School of Medicine,  
University of Arizona Health Science Center,  
Tucson, AZ, USA

<https://www.semanticscholar.org/paper/Nutraceutical-and-antioxidant-effects-of-a-maqui-a-Watson-Sch%C3%B6nlauf/f6926c356f173cc841d7043189ca181767ca556c>

PDF: [https://drive.google.com/open?id=1SsTMfkzNovG1YAIXkwb3jzYY\\_BKZ46F2](https://drive.google.com/open?id=1SsTMfkzNovG1YAIXkwb3jzYY_BKZ46F2)

### **Most important findings/conclusions:**

- Significantly reduces oxidative stress and blood glucose.
- Counteracts vascular inflammatory situations and thrombosis.
- Elevated endothelial NO, lowered platelet aggregability, anti-inflammatory effects.
- Counteracts skin ageing due to inhibition of UV-induced challenges.
- Inhibit differentiation of osteoclasts and bone demineralisation.

# A Randomized Clinical Trial Evaluating the Efficacy of an Anthocyanin–Maqui Berry Extract (Delphinol®) on Oxidative Stress Biomarkers

Sergio Davinelli, PhD, Juan Carlos Bertoglio, MD, PhD, Armando Zarrelli, PhD, Riccardo Pina, PhD, Giovanni Scapagnini, MD, PhD

Department of Medicine and Health Sciences, University of Molise, Campobasso, ITALY (S.D., G.S.); Department of Medicine, Hospital Clinico Regional de Valdivia, Valdivia, CHILE (J.C.B.); Department of Chemical Sciences, University of Napoli 'Federico II, Napoli, ITALY (A.Z.); Equipe Enervit Srl, Scientific Unit of Enervit Spa, Milano, ITALY (R.P.); Inter-University Consortium "SannioTech", Apollonia (BN), ITALY (G.S., A.Z.)

**Key words:** berry, anthocyanin, oxidative stress, oxidized LDL, F<sub>2</sub>-isoprostanes

<https://doi.org/10.1080/07315724.2015.1080108>

## Most important finding/conclusion:

- Improved oxidative status (Ox-LDL and F<sub>2</sub>-isoprostanes) in healthy adults, overweight adults, and adult smokers.

Food Science and Human Wellness 8 (2019) 264–267

Contents lists available at ScienceDirect

**Food Science and Human Wellness**

journal homepage: [www.elsevier.com/locate/fshw](http://www.elsevier.com/locate/fshw)

**Hyperinsulinemia, cancer and maqui berry: The promise of nutritional supplementation**

Brett Deters, Mir Saleem\*

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**ARTICLE INFO**

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**Keywords:**  
Hyperinsulinemia  
Cardiovascular disease  
Diabetes  
Insulin  
Maqui berry  
Cancer

**ABSTRACT**

Nutritional supplementation has long been studied as a possible treatment alternative or as an adjunct to the standard treatments for common ailments and diseases. According to the latest research, the Chilean maqui berry, *Aristotelia chilensis*, has been shown to reduce postprandial insulin levels by as much as fifty percent. The berry, which has been shown to be as effective as metformin at increasing insulin sensitivity and controlling blood glucose levels, follows a simple mechanism of action that involves the inhibition of sodium dependent glucose transporters in the small intestine, slowing the rate at which sugars enter the bloodstream and thereby decreasing blood sugar spikes and the corresponding increase in insulin levels. Chronically high blood glucose levels have been proven to play a significant role in the development of cancers, as diabetics and prediabetics have been proven to have elevated risk of developing cancerous growth. Consistent dietary supplementation with maqui berry may therefore indirectly reduce the risk of cancer, as well as other diseases which respond negatively to hyperglycemia and hyperinsulinemia.

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<https://doi.org/10.1016/j.fshw.2019.07.001>

PDF: <https://drive.google.com/open?id=19oKigj4FryFb6vWlqvAT77UzytQ18Oo>

## Most important findings/conclusions:

- As effective as metformin at improving insulin sensitivity and blood glucose levels, but without the side effects (lactic acidosis, diarrhoea, nausea, vomiting, flatulence, asthenia/fatigue, etc.).
- May reduce the risk of cancer and other diseases which respond negatively to hyperglycemia and hyperinsulinemia.

ORIGINAL ARTICLE

## Delphinol<sup>®</sup> standardized maqui berry extract significantly lowers blood glucose and improves blood lipid profile in prediabetic individuals in three-month clinical trial

Jorge ALVARADO, Frank SCHOENLAU, Andrés LESCHOT, Ana M. SALGADO, Pilar VIGIL PORTALES\*

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<https://www.minervamedica.it/en/journals/panminerva-medica/article.php?cod=R41Y2016S01A0001>

PDF: <https://drive.google.com/open?id=0B873BaXbiduNR0k4MlI0OTlpRFMxOUowVjBHVTY5UDhHWjhy>

### Most important findings/conclusions:

- Greatly reduced HbA1c (a marker for insulin resistance / pre-diabetes / diabetes).
- Greatly improved LDL/HDL ratio (= Greatly improved cholesterol balance).

PANMINERVA MED 2014;56(Suppl. 3 to No. 2):1-7

## Delphinol<sup>®</sup> standardized maqui berry extract reduces postprandial blood glucose increase in individuals with impaired glucose regulation by novel mechanism of sodium glucose cotransporter inhibition

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A. YAÑEZ<sup>3</sup>, L. QUIÑONES<sup>4</sup>, D. D. CACERES<sup>5</sup>, R. A. BURGOS<sup>1</sup>

**Aim.** The impetus of our study was to investigate the effects of a nutritional supplement Delphinol<sup>®</sup>, an extract of maqui berries (*Aristotelia chilensis*) standardised to ≥25% delphinidins and ≥35% total anthocyanins, on postprandial blood glucose and insulin levels and identify the physiologic mechanism involved.

**Methods.** Postprandial blood glucose and insulin were investigated in double-blind, placebo-controlled, cross-over fashion in ten volunteers with moderate glucose intolerance. Longer term effects on blood sugar levels were investigated in streptozotocin-diabetic rats over a four months period. Effects of maqui berry delphinidins on sodium-glucose symport were examined in rodent jejunum of the small intestine.

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<sup>3</sup>Instituto de Bioquímica y Microbiología, Universidad Austral de Chile, Valdivia, Chile

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<https://www.minervamedica.it/en/journals/panminerva-medica/article.php?cod=R41Y2014S01A0001>

PDF: <https://drive.google.com/open?id=0B873BaXbiduNbVNkSXZUaUJ1UlhwQnFDOHkzMkRBdWppaUZZ>

### Most important finding/conclusion:

- Greatly reduced glucose spike (postprandial blood glucose) after eating rice.





Article

# Delphinidin Reduces Glucose Uptake in Mice Jejunal Tissue and Human Intestinal Cells Lines through FFA1/GPR40

Jorge Hidalgo <sup>1</sup>, Stefanie Teuber <sup>1</sup>, Francisco J. Morera <sup>1</sup>, Camila Ojeda <sup>1</sup>, Carlos A. Flores <sup>2</sup>, María A. Hidalgo <sup>1</sup>, Lucía Núñez <sup>3,4</sup>, Carlos Villalobos <sup>3,4</sup> and Rafael A. Burgos <sup>1,\*</sup>

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<https://www.mdpi.com/1422-0067/18/4/750>

PDF: <https://drive.google.com/open?id=0B873BaXbiduNYkhMS3g4Yl8teFZqb2Q5NUlJT2Jsc1IHRWxr>

## Most important finding/conclusion:

- The antidiabetic effect through inhibiting glucose uptake in the intestines.

Hindawi Publishing Corporation  
BioMed Research International  
Volume 2016, Article ID 9070537, 10 pages  
<http://dx.doi.org/10.1155/2016/9070537>



## Research Article

# Delphinidin-Rich Maqui Berry Extract (Delphinol®) Lowers Fasting and Postprandial Glycemia and Insulinemia in Prediabetic Individuals during Oral Glucose Tolerance Tests

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<https://www.hindawi.com/journals/bmri/2016/9070537/>

PDF: <https://drive.google.com/open?id=0B873BaXbiduNMVRkTEpPWWUwR1FMylIFNS1FUlJ0TUlKQ0Zz>

## Most important findings/conclusions:

- Reduced fasting blood sugar, blood sugar spikes after eating, and insulinemia.
- For pre-diabetics, a highly significant effect was achieved at 180mg Delphinol.

Nutrients

[Nutrients](#). 2016 Aug; 8(8): 513.  
Published online 2016 Aug 19. doi: [10.3390/nu8080513](https://doi.org/10.3390/nu8080513)

PMCID: PMC4997426  
PMID: [27548217](https://pubmed.ncbi.nlm.nih.gov/27548217/)

## Evidence to Support the Anti-Cancer Effect of Olive Leaf Extract and Future Directions

[Anna Boss](#),<sup>1,\*</sup> [Karen S. Bishop](#),<sup>2</sup> [Gareth Marlow](#),<sup>1</sup> [Matthew P. G. Barnett](#),<sup>3</sup> and [Lynnette R. Ferguson](#)<sup>1,2</sup>

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This article has been [cited by](#) other articles in PMC.

### Associated Data

▶ Supplementary Materials

### Abstract

[Go to:](#)

The traditional Mediterranean diet (MD) is associated with long life and lower prevalence of cardiovascular disease and cancers. The main components of this diet include high intake of fruit, vegetables, red wine, extra virgin olive oil (EVOO) and fish, low intake of dairy and red meat. Olive oil has gained support as a key effector of health benefits and there is evidence that this relates to the polyphenol content. Olive leaf extract (OLE) contains a higher quantity and variety of polyphenols than those found in EVOO. There are also important structural differences between polyphenols from olive leaf and those from olive fruit that may improve the capacity of OLE to enhance health outcomes. Olive

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4997426/>

PDF: <https://drive.google.com/file/d/1AD6Opp0w8YZoxf79E6SjgqlzjmYowsCT/view?usp=sharing>

### Most important findings/conclusions:

- Olive polyphenols have been claimed to play an important protective role in cancer and other inflammation-related diseases.
- Protect against DNA damage initiated by free radicals.
- The pathways and signalling cascades manipulated include the NF-κB inflammatory response and the oxidative stress response.
- This review aims to amalgamate the current literature regarding bioavailability and mechanisms involved in the potential anti-cancer action of olive leaf polyphenols.



Scientia  
Pharmaceutica

Sci Pharm. 2010 Apr-Jun; 78(2): 133–154.

Published online 2010 Apr 23. doi: [10.3797/scipharm.0912-18](https://doi.org/10.3797/scipharm.0912-18)

PMCID: PMC3002804

PMID: [21179340](https://pubmed.ncbi.nlm.nih.gov/21179340/)

## Oleuropein in Olive and its Pharmacological Effects

Syed Haris Omar

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This article has been [cited by](#) other articles in PMC.

### Abstract

Go to:

Olive from *Olea europaea* is native to the Mediterranean region and, both the oil and the fruit are some of the main components of the Mediterranean diet. The main active constituents of olive oil include oleic acid, phenolic constituents, and squalene. The main phenolic compounds, hydroxytyrosol and oleuropein, give extra-virgin olive oil its bitter, pungent taste. The present review focuses on recent works that have analyzed the relationship between the major phenolic compound oleuropein and its pharmacological activities including antioxidant, anti-inflammatory, anti-atherogenic, anti-cancer activities, antimicrobial activity, antiviral activity, hypolipidemic and hypoglycemic effect.

**Keywords:** Mediterranean diet, Olive, Phenolic compound, Oleuropein

### 1. Introduction

Go to:

Several species within the olive family, botanically known as *Olea europaea*, provide commercial products such as food, lumber, cosmetics and medicine. Olive oil is a component of the Mediterranean diet, containing variable amounts of triacylglycerols and small quantities of free fatty acids, glycerol, pigments, aroma compounds, sterols, tocopherols, phenols, unidentified resinous components and others [1]. The

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3002804/>

PDF: <https://drive.google.com/file/d/1FHLk8rCKck5uF3mqbUffQJL9iKoKbE80/view?usp=sharing>

### Most important findings/conclusions:

- The major phenolic compound oleuropein has pharmacological activities, including antioxidant, anti-inflammatory, anti-atherogenic, anti-ageing, skin protectant, anti-cancer activities, antimicrobial activity, antiviral activity, hypolipidemic and hypoglycemic effects.

Oncotarget. 2017 Mar 14; 8(11): 17409.

PMCID: PMC5392257

Published online 2017 Feb 20. doi: [10.18632/oncotarget.15538](https://doi.org/10.18632/oncotarget.15538)

PMID: [28407695](https://pubmed.ncbi.nlm.nih.gov/28407695/)

## Oleuropein, unexpected benefits!

Wenyan Sun, Bess Frost, and Jiankang Liu

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A “Mediterranean diet” rich in plant-based foods, fish, and olive oil, is associated with reduced risk of most aging-related diseases including metabolic syndrome and neurodegenerative disorders. Oleuropein, a polyphenolic compound enriched in olive oil and leaves of the olive tree, has attracted scientific attention in recent years because of a variety of reported health benefits. While the mechanisms by which oleuropein functions *in vivo* and *in vitro* have been investigated [1], more studies are needed to better understand oleuropein's protective mechanism of action and to develop oleuropein as a therapeutic. Oleuropein and its metabolite, hydroxytyrosol, have powerful antioxidant activity, which might be responsible for some of olive oil's antioxidant, anti-inflammatory, and disease-fighting activities.

Oleuropein is best known for its blood pressure-lowering effect. When administered via intraperitoneal or intravenous injections, oleuropein significantly reduces systolic and diastolic blood pressure in animal models. The ability of oleuropein to lower blood pressure may justify the traditional use of olive leaf in the treatment of mild to moderate hypertension. Our recent study provides significant insight into the mechanism whereby oleuropein reduces blood pressure. We find that oleuropein protects the hypothalamus

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5392257/>

PDF: <https://drive.google.com/file/d/1FHLk8rCKck5uF3mqbUffQJL9iKoKbE80/view?usp=sharing>

### Most important findings/conclusions:

- Oleuropein reduces oxidative damage in the substantia nigra of aged rats, a region of the brain that is most affected by neurodegeneration in Parkinson's disease. Oleuropein prevents the toxic aggregation of both amyloid beta and tau, proteins that are involved in Alzheimer's disease.
- Oxidative stress and deregulation of the mTOR pathway is a common theme among neurodegeneration, cancer, diabetes, and physiological ageing, suggesting that the protective effects of oleuropein in various disorders may occur through a shared molecular mechanism.

Human Nutrition: Review Article

# Olive Leaf (*Olea europaea* L. *folium*): Potential Effects on Glycemia and Lipidemia

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Keywords: > Olive leaf > Diabetes > Glycemia > Lipidemia > Cardiovascular effects

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<https://www.karger.com/Article/FullText/505508>

PDF: <https://drive.google.com/file/d/1VHZmAUqaPYOH9GZ93MG0FtPE-0VJzu6W/view?usp=sharing>

## **Most important findings/conclusions:**

- Toxicity studies suggest that olive leaf is generally safe, even at high doses.
- Results of the study showed that diabetic patients had lower HbA1c and fasting plasma insulin levels.
- According to these results, olive leaf extract can be used as an adjunct treatment for the normalisation of glucose homeostasis in diabetic patients.
- According to dose in mouse macrophages, another study found that oleuropein increased inducible nitric oxide synthase expression and nitric oxide production.
- Studies in the literature prove that olive leaf extract decreases endoplasmic reticulum stress, and thus it may also decrease myocardial infarction rate.



## **Main conclusions:**

- Delphinol® is by far the most effective anti-ageing substance ever researched, and combined with Olive Leaf Extract which has additional anti-inflammatory, antioxidant and anti-ageing properties, it creates truly transformational results. The Health Optimizing Impact-RX supplement contains both of these two ingredients in effective dosages.
- Most ageing processes start early in adulthood and continue throughout life at an ever-increasing rate. These processes are significantly slowed down by the ingredients in Health Optimizing Impact-RX. Starting the supplement in one's 20s will impact the lifespan and quality of life (especially the last half). Starting the supplement after retirement age will significantly slow down further ageing, but cannot fully reverse the prior 50 years. Measurable effects emerge already after a few days or weeks, and daily intake over time is the key to the greatest benefits.