

Punicalagin



[Punicalagin promotes autophagy to protect](#)

Punicalagin promotes autophagy to protect



Punicalagin promotes autophagy to protect syncytiotrophoblasts from apoptosis

The following data support the hypothesis that punicalagin modulates the crosstalk between autophagy and apoptosis to promote survival in cultured syncytiotrophoblasts.

RESEARCH TITLE: [Punicalagin](#) promotes autophagy to protect primary human syncytiotrophoblasts from apoptosis

COUNTRIES: USA and China

CONDUCTED BY: Department of Obstetrics and Gynecology, Washington University School of Medicine, USA; Laboratory for Reproductive

Immunology, Hospital and Institute of Obstetrics and Gynecology, Fudan University Shanghai Medical College, China.

PUBLISHED ON: Reproduction. The journal of the Society for Reproduction and Fertility

RESEACH:

Abstract

Punicalagin is a prominent polyphenol in pomegranate juice that protects cultured syncytiotrophoblasts from stress-induced apoptosis.

Here, we test the hypothesis that punicalagin has this effect by inhibiting the mTOR kinase pathway to enhance autophagic turnover and limit apoptosis in cultured primary human syncytiotrophoblasts.

In syncytiotrophoblasts, starvation, rapamycin, or punicalagin all decreased the expression of phosphorylated ribosomal protein S6, a downstream target of the mTOR kinase, and of the autophagy markers, LC3-II and p62.

In contrast, in the presence of bafilomycin, an inhibitor of late stages of autophagy and degradation in the autophagolysosome, syncytiotrophoblasts exposed to starvation, rapamycin, or punicalagin all showed increased levels of LC3-II and p62.

The number of LC3-II punctae also increased in punicalagin-treated syncytiotrophoblasts exposed to chloroquine, another inhibitor of autophagic degradation, and punicalagin increased the number of lysosomes.

The apoptosis-reducing effect of punicalagin was attenuated by inhibition of autophagy using bafilomycin or knockdown of the autophagy related gene, *ATG16L1*. Collectively, these data support the hypothesis that punicalagin modulates the crosstalk between autophagy and apoptosis to promote survival in cultured syncytiotrophoblasts.

YEAR: 2015

<https://zumodegranada.com/en/punicalagin-promotes-autophagy/>



[Cardioameliorative effect of punicalagin](#)

Cardioameliorative effect of punicalagin



Cardioameliorative effect of punicalagin

The effect of [punicalagin](#) on metabolic risks, oxidative stress, inflammation, cardiac apoptosis and histopathological alterations in experimentally induced diabetes was addressed.

RESEARCH TITLE: Cardioameliorative effect of punicalagin against streptozotocin-induced apoptosis, redox imbalance, metabolic changes and inflammation

COUNTRIES: Egypt, Iraq

CONDUCTED BY: Zoology Department, Faculty of Science, Mansoura University, Mansoura, Egypt; Biology department, Pure Science Education Collage, Al-Anbar University, Al-Anbar, Iraq.

PUBLISHED ON: Elsevier

RESEACH:

The effect of punicalagin on metabolic risks, oxidative stress, inflammation, cardiac apoptosis and histopathological alterations in experimentally induced diabetes was addressed.

Diabetes was induced in male rats by a single injection of streptozotocin (STZ; 40 mg/kg, i.p.), and then punicalagin (1 mg/kg) was i.p. administered every other day for 15 days.

The diabetic rats treated with punicalagin exhibited ameliorated hyperglycemia and HbA1c; improved insulin levels, HOMA-IR levels and lipid profiles; and normalized levels of IL-1b, IL-6 and TNF-a. Punicalagin also reduced the increase in the MDA and H2O2 levels; normalized the levels of GSH, SOD and CAT in the heart; and improved serum markers of heart function including the levels of troponin T level and CK-MB and LDH activities.

Histopathological examinations of heart sections match these results, confirming the beneficial effect of punicalagin. It also modulated cardiomyocyte apoptosis via enhanced Bcl-2 expression; blocked the increases in P53, Bax and caspases-3, 8 and 9; and ameliorated DNA damage in the heart.

The current results suggest that punicalagin protected the heart against apoptosis, necrosis, inflammation and DNA damage by improving the redox state, suppressing caspases and P53 and increasing Bcl-2. **In conclusion, punicalagin possesses strong therapeutic potential in treating and regulating diabetes and attenuating its associated complications in the heart.**

YEAR: 2015

<https://zumodegranada.com/en/cardioameliorative-effect-of-punicalagin/>

[Punicalagin protective effect against high glucose and neural tube defects](#)

Punicalagin protective effect against high glucose and neural tube defects

Punicalagin is a primary polyphenol found in pomegranate juice, which possesses antioxidant, anti-inflammatory and anti-tumorigenic properties, suggesting a protective effect of punicalagin on diabetic embryopathy.

RESEARCH TITLE: [Punicalagin exerts protective effect against high glucose-induced cellular stress and neural tube defects](#)

COUNTRIES: USA

CONDUCTED BY: Department of Obstetrics, Gynecology & Reproductive Sciences, University of Maryland School of Medicine, Baltimore, USA; Department of Biochemistry and Molecular Biology, University of Maryland School of Medicine, Baltimore, USA

PUBLISHED ON: [Biochemical and Biophysical Research Communications](#)

RESEARCH:

Maternal diabetes-induced birth defects remain a significant health problem. Studying the effect of natural compounds with antioxidant properties and minimal toxicities on diabetic embryopathy may lead to the development of new and safe dietary supplements. Punicalagin is a primary polyphenol found in pomegranate juice, which possesses antioxidant, anti-inflammatory and anti-tumorigenic properties, suggesting a protective effect of punicalagin on diabetic embryopathy. Here, we examined whether punicalagin could reduce high glucose-induced neural tube defects (NTDs), and if this rescue occurs through blockage of cellular stress and caspase activation. Embryonic day 8.5 (E8.5) mouse embryos were cultured for 24 or 36 h with normal (5 mM) glucose or high glucose (16.7 mM), in presence or absence of 10 or 20 μ M punicalagin. 10 μ M punicalagin slightly reduced NTD formation under high glucose conditions; however, 20 μ M punicalagin significantly inhibited high glucose-induced neural tube defects formation. Punicalagin suppressed high glucose-induced lipid peroxidation marker 4-hydroxynonenal, nitrotyrosine-modified proteins, and lipid peroxides. Moreover, punicalagin abrogated endoplasmic reticulum stress by inhibiting phosphorylated protein kinase ribonucleic acid (RNA)-like ER kinase (p-PERK), phosphorylated inositol-requiring protein-1 α (p-IRE1 α), phosphorylated eukaryotic initiation factor 2 α (p-eIF2 α), C/EBP-homologous protein (CHOP), binding immunoglobulin protein (BiP) and x-box binding protein 1 (XBP1) mRNA splicing. Additionally, punicalagin suppressed high glucose-induced caspase 3

and caspase 8 cleavage. Punicalagin reduces high glucose-induced NTD formation by blocking cellular stress and caspase activation. These observations suggest punicalagin supplements could mitigate the teratogenic effects of hyperglycemia in the developing embryo, and possibly prevent diabetes-induced NTDs.

YEAR: 2015

<https://zumodegranada.com/en/punicalagin-protective-effect-against-high-glucose-and-neural-tube-defects/>

[Punicalagin exhibits negative regulatory effects on LPS-induced acute lung injury](#)

Punicalagin exhibits negative regulatory effects on LPS-induced acute lung injury

Punicalagin, mainly isolated from the fruit of Pomegranate (*Punica granatum* L.), is a natural polyphenolic compound. In the present study, we investigated the negative regulatory effect of punicalagin on acute lung injury (ALI) induced by Lipopolysaccharide (LPS).

This study offered a novel therapeutic strategy for improving clinical effects of acute lung injury (ALI)/acute respiratory distress syndrome and provided more evidence for the health benefits of pomegranate fruits.

RESEACH TITLE: Punicalagin exhibits negative regulatory effects on LPS-induced acute lung injury

COUNTRY: CHINA

CONDUCTED BY: Laboratory of Nutrition and Function Food, College of Light Industry Economics and Management, Jilin University, People's Republic of China; Key Laboratory of Zoonosis, Ministry of Education College of Veterinary Medicine, Jilin University, Changchun, People's Republic of China; Department of Chemical Engineering and Technology, College of Science and Technology, Yanbian University, Yanji, People's Republic of China.

PUBLISHED ON: European Food Reseach and Technology

RESEACH:

Punicalagin, mainly isolated from the fruit of Pomegranate (*Punica granatum* L.), is a natural polyphenolic compound. In the present study, we investigated the negative regulatory effect of punicalagin on acute lung injury (ALI) induced by Lipopolysaccharide (LPS). In the murine model of ALI, the data showed that punicalagin inhibited the production of TNF- [HYPERLINK](#) IL-1 β , and IL-6 and decreased protein concentration and myeloperoxidase activity with a single 4 mg/kg dose of punicalagin prior to the administration of intratracheal LPS in the bronchoalveolar lavage fluid. Furthermore, we investigated the effects of punicalagin how to modulate signal transduction. MAPK and activation were measured by Western blot and immunocytochemical analysis. The data showed that punicalagin significantly inhibited phosphorylated p38 MAPK protein expression and shocked p65-NF- [HYPERLINK](#) translocation into the nucleus. These results indicated punicalagin may exert negative regulatory effects on ALI partly through suppressing p38 MAPKs or/and pathways. This study offered a novel

therapeutic strategy for improving clinical effects of acute lung injury (ALI)/acute respiratory distress syndrome and provided more evidence for the health benefits of pomegranate fruits.

YEAR: 2014

<https://zumodegranada.com/en/punicalagin-exhibits-negative-regulatory-effects-on-lps-induced-acute-lung-injury-2/>

[The bioactive properties of pomegranate polyphenol \(Punicalagin\)](#)

The bioactive properties of pomegranate polyphenol (Punicalagin)

Plant polyphenols are reported to have bioactive properties, which may be used for protection against diseases. Therefore, the aim of this research was to investigate the bioactive activities of a pomegranate tannin polyphenol compound, punicalagin.

RESEARCH TITLE: The bioactive properties of pomegranate polyphenol (Punicalagin)

COUNTRY: UK

CONDUCTED BY: University of Surrey

PUBLISHED ON:ETHOS

RESEARCH:

Plant polyphenols are reported to have bioactive properties, which may be used for protection against diseases. Therefore, the aim of this research was to investigate the bioactive activities of a pomegranate tannin polyphenol compound, punicalagin. In particular, the antioxidant, antihypertensive and anticancer mechanisms were investigated. Punicalagin was found in pomegranate husk but not in pomegranate juice when analysed by HPLC and LC-MS. Antioxidant mechanisms involved hydrogen peroxide scavenging, ferrous chelating and reducing ability. Higher hydrogen peroxide scavenging activity was achieved by 0.1 mg/ml from both punicalagin and pomegranate juice when compared with butylated hydroxytoluene (BHT) or trolox ($p < 0.05$). Punicalagin and pomegranate juice exhibited ferrous chelating ability significantly lower than Ethylenediaminetetraacetic acid. Cell toxicity induced by tert-butylhydroperoxide (3 mM) was significantly inhibited by punicalagin (5 and 10 μ M) in Caco-2 cells; these results were confirmed by cell morphology. Punicalagin protection was achieved by inhibiting cellular reactive oxygen species (ROS) as well as malondialdehyde levels. Glutathione level was significantly increased in stressed cells pretreated with both concentration of punicalagin, indicating good antioxidant activity for punicalagin. Punicalagin (1-60 μ M) increased nitric oxide production in endothelial cells (EA.hy926) through decreased ROS levels and increased endothelial nitric oxide synthase enzyme (eNOS) activation. Activation of eNOS enzyme was achieved by an increase of cellular calcium concentration. At the same concentration of punicalagin (1-60 μ M), the activity of angiotensin converting enzyme (ACE) was significantly inhibited. The dual action of punicalagin as nitric

oxide synthase inducer and ACE inhibitor showed antihypertensive effect. Punicalagin (50 and 75 μ M) showed toxic effects on the colon cancer cell line (Caco-2) but not on a normal colon cell line (HCEC); both results were confirmed by morphological studies. In the presence of punicalagin, cytoplasmic ROS production decreased, indicating antioxidant activity whereas superoxide radicals released from mitochondria increased due to mitochondrial dysfunction. Annexin V and caspase family (caspase 9, 8 and 3) activation confirmed that cell death occurred via apoptosis pathway by both concentrations of punicalagin. The cell cycle was arrested by punicalagin in the G₁S-phase at the concentrations tested. The above findings indicating that punicalagin has antioxidant, antihypertensive and anticarcinogenic activity.

YEAR: 2014

<https://zumodegranada.com/en/the-bioactive-properties-of-pomegranate-polyphenol-punicalagin/>

[Anti-inflammatory properties of a pomegranate extract and its metabolite urolithin-A in a colitis rat model and the effect of colon inflammation on phenolic metabolism](#)

Anti-inflammatory properties of a pomegranate extract and its metabolite urolithin-A in a colitis rat model and the effect of colon inflammation on phenolic metabolism

The effect of pomegranate juice (PJ) or grapefruit juice (GFJ) on CYP3A activity was studied in vitro and in healthy human volunteers.

Thus, pomegranate juice does not alter clearance of intravenous or oral midazolam, whereas grapefruit juice (GFJ) impairs clearance and elevates plasma levels of oral midazolam.

J Clin Pharmacol March 2007 vol. 47

<https://zumodegranada.com/en/anti-inflammatory-properties-of-a-pomegranate-extract-and-its-metabolite-urolithin-a-in-a-colitis-rat-model-and-the-effect-of-colon-inflammation-on-phenolic-metabolism-2/>