Pharmaceutical Biology • Volume 61, Issue 1, Pages 1135 - 1151 • 2023

Document type
Article

Source type
Journal

ISSN
13880209

DOI
10.1080/13880209.2023.2230251

Publisher
Taylor and Francis Ltd.

CODEN
PHBIF

Original language
English

PubMed ID
37497554

View less

Cardioprotective effects of arjunolic acid in LPS-stimulated H9C2 and C2C12 myotubes via the My88-dependent TLR4 signaling pathway

Hasan, Md Mahmudul[a] ; Madhavan, Priya[b] ; Ahmad Noruddin, Nur Adelina[c]; Lau, Wai Kwan[c]; Ahmed, Qamar Uddin[d]; Arya, Aditya[b, c, e]; Zakaria, Zainul Amiruddin[f]

Save all to author list

[a] School of Biosciences, Faculty of Health and Medical Sciences, Taylor's University, Subang Jaya, Malaysia

[b] School of Medicine, Faculty of Health and Medical Sciences, Taylor's University, Subang Jaya, Malaysia

[c] National Institutes of Biotechnology Malaysia, Malaysian Institute of Pharmaceuticals and Nutraceuticals, Serdang, Malaysia

[d] Drug Discovery and Synthetic Chemistry Research Group, Department of Pharmaceutical Chemistry, Kulliyyah of Pharmacy, International Islamic University Malaysia, Kuantan, Malaysia

View additional affiliations

View PDF Full text options Export

Abstract

Author keywords

Indexed keywords

Sustainable Development Goals 2023

SciVal Topics

Chemicals and CAS Registry Numbers

Funding details

Abstract

Context: Arjunolic acid (AA) is a triterpenoid saponin found in Terminalia arjuna (Roxb.) Wight & Arn. (Combretaceae). It exerts cardiovascular protective effects as a phytomedicine. However, it is unclear how AA exerts the effects at the molecular level. Objective: This study investigates the cardioprotective effects of arjunolic acid (AA) via MyD88-dependant TLR4 downstream signaling marker expression. Materials and methods: The MTT viability assay was used to assess the cytotoxicity of AA. LPS induced invitro cardiovascular disease model was developed in H9C2 and C2C12 myotubes. The treatment groups were designed such as control (untreated), LPS control, positive control (LPS + pyrrolidine dithiocarbamate (PDTC)-25 µM), and treatment groups were co-treated with LPS and three concentrations of AA (50, 75, and 100 µM) for 24 h. The changes in the expression of TLR4 downstream signaling markers were evaluated through High Content Screening (HCS) and Western Blot (WB) analysis. Results: After 24 h of co-treatment, the expression of TLR4, MyD88, MAPK, JNK, and NF-κB markers were upregulated significantly (2-6 times) in the LPS-treated groups compared to the untreated control in both HCS and WB experiments. Evidently, the HCS analysis revealed that MyD88, NF-κB, p38, and JNK were significantly downregulated in the H9C2 myotube in the AA treated groups. In HCS, the expression of NF-κB was downregulated in C2C12. Additionally, TLR4 expression was downregulated in both H9C2 and C2C12 myotubes in the WB experiment. Discussion and conclusions: TLR4 marker expression in H9C2 and C2C12 myotubes was subsequently decreased by AA treatment, suggesting possible cardioprotective effects of AA. © 2023 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.

Author keywords

C2C12 myotube; cardiovascular disease; H9C2 myotube; high content screening; MyD88; skeletal muscle cell

Indexed keywords

Sustainable Development Goals 2023 New

SciVal Topics

Chemicals and CAS Registry Numbers

Funding details

References (39)

View in search results format >

All

Export Print E-mail Save to PDF Create bibliography

1 Al-Gayyar, M.M.H., Al Youssef, A., Sherif, I.O., Shams, M.E.E., Abbas, A.

Protective effects of arjunolic acid against cardiac toxicity induced by oral sodium nitrite: Effects on cytokine balance and apoptosis

(2014) *Life Sciences*, Part _2 111 (1), pp. 18-26. Cited 33 times.
www.elsevier.com/locate/lifescie
doi: 10.1016/j.lfs.2014.07.002

View at Publisher

2 Abu Bakar, M.H., Tan, J.S.

Improvement of mitochondrial function by celastrol in palmitate-treated C2C12 myotubes via activation of PI3K-Akt signaling pathway

(2017) *Biomedicine and Pharmacotherapy*, 93, pp. 903-912. Cited 26 times.
www.elsevier.com/locate/biomedpharm
doi: 10.1016/j.biopha.2017.07.021

View at Publisher

3 Bansal, T., Chatterjee, E., Singh, J., Ray, A., Kundu, B., Thankamani, V., Sengupta, S., (...), Sarkar, S.

Arjunolic acid, a peroxisome proliferator-activated receptor agonist, regresses cardiac fibrosis by inhibiting non-canonical TGF- signaling

(2017) *Journal of Biological Chemistry*, 292 (40), pp. 16440-16462. Cited 38 times.
http://www.jbc.org/content/292/40/16440.full.pdf
doi: 10.1074/jbc.M117.788299

View at Publisher

4 Beiter, T., Hudemann, J., Burgstahler, C., Nieß, A.M., Munz, B.

Effects of extracellular orotic acid on acute contraction-induced adaptation patterns in C2C12 cells (Open Access)

(2018) *Molecular and Cellular Biochemistry*, 448 (1-2), pp. 251-263. Cited 10 times.
http://www.kluweronline.com/issn/0300-8177/
doi: 10.1007/s11010-018-3330-z

View at Publisher

5 Bode, A.M., Dong, Z.

The functional contrariety of JNK

(2007) *Molecular Carcinogenesis*, 46 (8), pp. 591-598. Cited 223 times.
doi: 10.1002/mc.20348

View at Publisher

6 Caso, J.R., Pradillo, J.M., Hurtado, O., Lorenzo, P., Moro, M.A., Lizasoain, I.

Toll-like receptor 4 is involved in brain damage and inflammation after experimental stroke

(2007) *Circulation*, 115 (12), pp. 1599-1608. Cited 493 times.
doi: 10.1161/CIRCULATIONAHA.106.603431

View at Publisher

7 Chao, W.

Toll-like receptor signaling: A critical modulator of cell survival and ischemic injury in the heart

(2009) *American Journal of Physiology - Heart and Circulatory Physiology*, 296 (1), pp. H1-H12. Cited 189 times.
http://ajpheart.physiology.org/cgi/reprint/296/1/H1
doi: 10.1152/ajpheart.00995.2008

View at Publisher

8 Chong, A.J., Shimamoto, A., Hampton, C.R., Takayama, H., Spring, D.J., Rothnie, C.L., Yada, M., (...), Verrier, E.D.

Toll-like receptor 4 mediates ischemia/reperfusion injury of the heart

(2004) *Journal of Thoracic and Cardiovascular Surgery*, 128 (2), pp. 170-179. Cited 211 times.
doi: 10.1016/j.jtcvs.2003.11.036

View at Publisher

9 Elsawy, H., Almalki, M., Elmenshawy, O., Abdel-Moneim, A.

In vivo evaluation of the protective effects of arjunolic acid against lipopolysaccharide-induced septic myocardial injury (Open Access)

(2022) *PeerJ*, 10, art. no. e12986. Cited 5 times.
https://peerj.com/articles/12986/
doi: 10.7717/peerj.12986

View at Publisher

10 Fan, X., Zhang, Y., Dong, H., Wang, B., Ji, H., Liu, X.

Trilobatin attenuates the LPS-mediated inflammatory response by suppressing the NF-κB signaling pathway (Open Access)

(2015) *Food Chemistry*, 166, pp. 609-615. Cited 72 times.
www.elsevier.com/locate/foodchem
doi: 10.1016/j.foodchem.2014.06.022

View at Publisher

11 Frantz, S., Kobzik, L., Kim, Y.-D., Fukazawa, R., Medzhitov, R., Lee, R.T., Kelly, R.A.

Toll4 (TLR4) expression in cardiac myocytes in normal and failing myocardium (Open Access)

(1999) *Journal of Clinical Investigation*, 104 (3), pp. 271-280. Cited 576 times.
http://www.jci.org
doi: 10.1172/JCI6709

View at Publisher

12 Frost, R.A., Nystrom, G.J., Lang, C.H.

Lipopolysaccharide stimulates nitric oxide synthase-2 expression in murine skeletal muscle and C_2C_{12} myoblasts via Toll-like receptor-4 and c-Jun NH_2-terminal kinase pathways

(2004) *American Journal of Physiology - Cell Physiology*, 287 (6 56-6), pp. C1605-C1615. Cited 48 times.
doi: 10.1152/ajpcell.00010.2004

View at Publisher

13 Ghosh, J., Das, J., Manna, P., Sil, P.C.

The protective role of arjunolic acid against doxorubicin induced intracellular ROS dependent JNK-p38 and p53-mediated cardiac apoptosis

(2011) *Biomaterials*, 32 (21), pp. 4857-4866. Cited 135 times.
doi: 10.1016/j.biomaterials.2011.03.048

View at Publisher

14 Gilde, A.J., Van der Lee, K.A.J.M., Willemsen, P.H.M., Chinetti, G., Van der Leij, F.R., Van der Vusse, G.J., Staels, B., (...), Van Bilsen, M.

Peroxisome proliferator-activated receptor (PPAR) α and PPARβ/δ, but not PPARγ, modulate the expression of genes involved in cardiac lipid metabolism

(2003) *Circulation Research*, 92 (5), pp. 518-524. Cited 357 times.
http://circres.ahajournals.org
doi: 10.1161/01.RES.0000060700.55247.7C

View at Publisher

15 Hazarika, L., Sen, S., Doshi, J.
Molecular docking analysis of arjunolic acid from Terminalia arjuna with a coronary artery disease target APOE4
(2021) *Bioinformation*, 17 (11), pp. 949-958.

16 Hemalatha, T., Pulavendran, S., Balachandran, C., Manohar, B.M., Puvanakrishnan, R.
Arjunolic acid: A novel phytomedicine with multifunctional therapeutic applications
(2010) *Indian Journal of Experimental Biology*, 48 (3), pp. 237-248. Cited 55 times.
http://nopr.niscair.res.in/bitstream/123456789/7399/1/IJEB%2048%283%29%20238-247.pdf

17 Ikebe, M., Kitaura, Y., Nakamura, M., Tanaka, H., Yamasaki, A., Nagai, S., Wada, J., (...), Katano, M.
Lipopolysaccharide (LPS) increases the invasive ability of pancreatic cancer cells through the TLR4/MyD88 signaling pathway
(2009) *Journal of Surgical Oncology*, 100 (8), pp. 725-731. Cited 130 times.
http://www3.interscience.wiley.com/cgi-bin/fulltext/122580901/PDFSTART
doi: 10.1002/jso.21392
View at Publisher

18 Kalyanavenkataraman, S., Nanjan, P., Banerji, A., Nair, B.G., Kumar, G.B.
Discovery of arjunolic acid as a novel non-zinc binding carbonic anhydrase II inhibitor (Open Access)
(2016) *Bioorganic Chemistry*, 66, pp. 72-79. Cited 6 times.
http://www.elsevier.com/inca/publications/store/6/2/2/7/9/4/index.htt
doi: 10.1016/j.bioorg.2016.03.009
View at Publisher

19 Kawai, T., Adachi, O., Ogawa, T., Takeda, K., Akira, S.
Unresponsiveness of MyD88-deficient mice to endotoxin (Open Access)
(1999) *Immunity*, 11 (1), pp. 115-122. Cited 1741 times.
www.immunity.com
doi: 10.1016/S1074-7613(00)80086-2
View at Publisher

20 Knuefermann, P., Sakata, Y., Baker, J.S., Huang, C.-H., Sekiguchi, K., Hardarson, H.S., Takeuchi, O., (...), Vallejo, J.G.
Toll-like receptor 2 mediates Staphylococcus aureus-induced myocardial dysfunction and cytokine production in the heart (Open Access)
(2004) *Circulation*, 110 (24), pp. 3693-3698. Cited 86 times.
doi: 10.1161/01.CIR.0000143081.13042.04
View at Publisher

21 Li, H., Li, Y., Liu, D., Liu, J.
LPS promotes epithelial–mesenchymal transition and activation of TLR4/JNK signaling (Open Access)
(2014) *Tumor Biology*, 35 (10), pp. 10429-10435. Cited 46 times.
http://journals.sagepub.com/loi/tub
doi: 10.1007/s13277-014-2347-5
View at Publisher

22 Manna, P., Sil, P.C.

Impaired redox signaling and mitochondrial uncoupling contributes vascular inflammation and cardiac dysfunction in type 1 diabetes: Protective role of arjunolic acid

(2012) *Biochimie*, 94 (3), pp. 786-797. Cited 36 times.
doi: 10.1016/j.biochi.2011.11.010

View at Publisher

23 Manna, P., Sinha, M., Sil, P.C.

Arsenic-induced oxidative myocardial injury: Protective role of arjunolic acid

(2008) *Archives of Toxicology*, 82 (3), pp. 137-149. Cited 188 times.
doi: 10.1007/s00204-007-0272-8

View at Publisher

24 Meng, Z., Yan, C., Deng, Q., Gao, D.-F., Niu, X.-L.

Curcumin inhibits LPS-induced inflammation in rat vascular smooth muscle cells in vitro via ROS-relative TLR4-MAPK/NF-κB pathways

(2013) *Acta Pharmacologica Sinica*, 34 (7), pp. 901-911. Cited 155 times.
doi: 10.1038/aps.2013.24

View at Publisher

25 Miriyala, S., Chandra, M., Maxey, B., Day, A., St. Clair, D.K., Panchatcharam, M.

Arjunolic acid ameliorates reactive oxygen species via inhibition of $p47^{phox}$-serine phosphorylation and mitochondrial dysfunction

(2015) *International Journal of Biochemistry and Cell Biology*, 68, pp. 70-77. Cited 7 times.
http://www.elsevier.com/locate/biocel
doi: 10.1016/j.biocel.2015.08.015

View at Publisher

26 Mishra, S., Chatterjee, S.

Lactosylceramide promotes hypertrophy through ROS generation and activation of ERK1/2 in cardiomyocytes

(2014) *Glycobiology*, 24 (6), pp. 518-531. Cited 16 times.
http://glycob.oxfordjournals.org/
doi: 10.1093/glycob/cwu020

View at Publisher

27 Morabito, C., Rovetta, F., Bizzarri, M., Mazzoleni, G., Fanò, G., Mariggiò, M.A.

Modulation of redox status and calcium handling by extremely low frequency electromagnetic fields in C2C12 muscle cells: A real-time, single-cell approach

(2010) *Free Radical Biology and Medicine*, 48 (4), pp. 579-589. Cited 81 times.
doi: 10.1016/j.freeradbiomed.2009.12.005

View at Publisher

28 Oyama, J.-I., Blais Jr., C., Liu, X., Pu, M., Kobzik, L., Kelly, R.A., Bourcier, T.

Reduced Myocardial Ischemia-Reperfusion Injury in Toll-Like Receptor 4-Deficient Mice (Open Access)

(2004) *Circulation*, 109 (6), pp. 784-789. Cited 546 times.
doi: 10.1161/01.CIR.0000112575.66565.84

View at Publisher

29 Park, B.S., Song, D.H., Kim, H.M., Choi, B.-S., Lee, H., Lee, J.-O.

The structural basis of lipopolysaccharide recognition by the TLR4-MD-2 complex (Open Access)

(2009) *Nature*, 458 (7242), pp. 1191-1195. Cited 1672 times.
doi: 10.1038/nature07830

View at Publisher

30 Proszynski, T.J., Gingras, J., Valdez, G., Krzewski, K., Sanes, J.R.

Podosomes are present in a postsynaptic apparatus and participate in its maturation (Open Access)

(2009) *Proceedings of the National Academy of Sciences of the United States of America*, 106 (43), pp. 18373-18378. Cited 61 times.
http://www.pnas.org/content/106/43/18373.full.pdf
doi: 10.1073/pnas.0910391106

View at Publisher

31 Rahiman, S.S.F., Morgan, M., Gray, P., Shaw, P.N., Cabot, P.J.

Inhibitory effects of dynorphin 3-14 on the lipopolysaccharide-induced toll-like receptor 4 signalling pathway

(2017) *Peptides*, 90, pp. 48-54. Cited 11 times.
www.elsevier.com/locate/peptides
doi: 10.1016/j.peptides.2017.02.004

View at Publisher

32 Ranneh, Y., Akim, A.M., Hamid, H.A., Khazaai, H., Fadel, A., Zakaria, Z.A., Albujja, M., (...), Bakar, M.F.A.

Honey and its nutritional and anti-inflammatory value

(2021) *BMC Complementary Medicine and Therapies*, 21 (1), art. no. 30. Cited 72 times.
https://link.springer.com/journal/12906/volumes-and-issues
doi: 10.1186/s12906-020-03170-5

View at Publisher

33 Seneviratne, A.N., Sivagurunathan, B., Monaco, C.

Toll-like receptors and macrophage activation in atherosclerosis (Open Access)

(2012) *Clinica Chimica Acta*, 413 (1-2), pp. 3-14. Cited 80 times.
doi: 10.1016/j.cca.2011.08.021

View at Publisher

34 Sharifi-Rad, M., Varoni, E.M., Salehi, B., Sharifi-Rad, J., Matthews, K.R., Ayatollahi, S.A., Kobarfard, F., (...), Rigano, D.

Plants of the genus zingiber as a source of bioactive phytochemicals: From tradition to pharmacy (Open Access)

(2017) *Molecules*, 22 (12), art. no. 2145. Cited 181 times.
http://www.mdpi.com/1420-3049/22/12/2145/pdf
doi: 10.3390/molecules22122145

View at Publisher

35 Shen, X.-D., Ke, B., Zhai, Y., Gao, F., Busuttil, R.W., Cheng, G., Kupiec-Weglinski, J.W.

Toll-like receptor and heme oxygenase-1 signaling in hepatic ischemia/reperfusion injury (Open Access)

(2005) *American Journal of Transplantation*, 5 (8), pp. 1793-1800. Cited 153 times.
doi: 10.1111/j.1600-6143.2005.00932.x

View at Publisher

36 Shimamoto, A., Chong, A.J., Yada, M., Shomura, S., Takayama, H., Fleisig, A.J., Agnew, M.L., (...), Verrier, E.D.

Inhibition of toll-like receptor 4 with eritoran attenuates myocardial ischemia-reperfusion injury (Open Access)

(2006) *Circulation*, 114 (SUPPL. 1), pp. I270-I274. Cited 246 times.
doi: 10.1161/CIRCULATIONAHA.105.000901

View at Publisher

37 Sumitra, M., Manikandan, P., Kumar, D.A., Arutselvan, N., Balakrishna, K., Manohar, B.M., Puvanakrishnan, R.

Experimental myocardial necrosis in rats: Role of arjunolic acid on platelet aggregation, coagulation and antioxidant status (Open Access)

(2001) *Molecular and Cellular Biochemistry*, 224 (1-2), pp. 135-142. Cited 122 times.
doi: 10.1023/A:1011927812753

View at Publisher

38 Takeda, K., Akira, S.

Toll-like receptors in innate immunity (Open Access)

(2005) *International Immunology*, 17 (1), pp. 1-14. Cited 2759 times.
doi: 10.1093/intimm/dxh186

View at Publisher

39 Wu, H.-S., Zhang, J.-X., Wang, L., Tian, Y., Wang, H., Rotstein, O.

Toll-like receptor 4 involvement in hepatic ischemia/reperfusion injury in mice (Open Access)

(2004) *Hepatobiliary and Pancreatic Diseases International*, 3 (2), pp. 250-253. Cited 94 times.

Hasan, M.M.; School of Biosciences, Faculty of Health and Medical Sciences, Taylor's University, Subang Jaya, Malaysia; email:mhasan222@gmail.com

Madhavan, P.; School of Medicine, Faculty of Health and Medical Sciences, Taylor's University, Subang Jaya, Malaysia; email:priya.madhavan@taylors.edu.my

About Scopus

What is Scopus

Content coverage

Scopus blog

Scopus API

Privacy matters

Language

日本語版を表示する

查看简体中文版本

查看繁體中文版本

Просмотр версии на русском языке

Customer Service

Help

Tutorials

Contact us