PubMed Search

Search: (Berberine[MeSH]) AND (Aging[MeSH] OR Anti-Aging Agents[MeSH])

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2. Curr Med Chem. 2024;31(10):1214-1234. doi: 10.2174/0929867330666230207112539.

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Gasmi A(1), Asghar F(2), Zafar S(3), Oliinyk P(4)(5), Khavrona O(4)(5), Lysiuk R(4)(5), Peana M(6), Piscopo S(1), Antonyak H(7), Pen JJ(8)(9), Lozynska I(4)(5), Noor S(10), Lenchyk L(11)(12), Muhammad A(13), Vladimirova I(11)(12), Dub N(14), Antoniv O(4)(5), Tsal O(4)(5), Upyr T(11)(12), Bjørklund G(15).

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CONCLUSION: Berberine could serve as a potential candidate for the treatment of several diseases. Previous literature has provided a basis for scientists to establish clinical trials in humans. However, for obesity, the evidence appears to be sufficient for hands-on use.

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Heart aging is characterized by left ventricular hypertrophy and diastolic dysfunction, which in turn induces a variety of cardiovascular diseases. There is still no therapeutic drug to ameliorate cardiac abnormities in heart aging.

In this study we investigated the protective effects of berberine (BBR) and its derivative tetrahydroberberrubine (THBru) against heart aging process. Heart aging was induced in mice by injection of D-galactose (D-gal, 120?mg?·?kg-1?·?d-1, sc.) for 12 weeks. Meanwhile the mice were orally treated with berberine (50?mg?·?kg-1?·?d-1) or THBru (25, 50?mg?·?kg-1?·?d-1) for 12 weeks. We showed that BBR and THBru treatment significantly mitigated diastolic dysfunction and cardiac remodeling in D-gal-induced aging mice. Furthermore,

treatment with BBR (40??M) and THBru (20, 40??M) inhibited D-gal-induced senescence in primary neonatal mouse cardiomyocytes in vitro. Overall, THBru exhibited higher efficacy than BBR at the same dose. We found that the levels of mitophagy were significantly decreased during the aging process in vivo and in vitro, THBru and BBR promoted mitophagy with different potencies. We demonstrated that the mitophagy-inducing effects of THBru resulted from increased mRNA stability of prohibitin 2 (PHB2), a pivotal factor during mitophagy, thereby upregulating PHB2 protein expression. Knockdown of PHB2 effectively reversed the antisenescence effects of THBru in D-gal-treated cardiomyocytes. On the contrary, overexpression of PHB2 promoted mitophagy and retarded cardiomyocyte senescence, as THBru did. In conclusion, this study identifies THBru as a potent antiaging medicine that induces PHB2-mediated mitophagy and suggests its clinical application prospects.

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BACKGROUND: Accumulation of age-associated senescent cells accompanied with increased reactive oxygen species (ROS) and inflammatory factors contributes to the progression of age-related macular degeneration (AMD), the main cause of blindness in the elderly. Berberine (BBR) has shown efficacy in the treatment of age-related diseases including diabetes and obesity by decreasing ROS. However, the pharmacological effect of BBR on alleviating retinal aging remains largely unknown.

PURPOSE: Our study aimed to investigate the pharmacological effect of BBR as an anti-aging agent in retinal aging and its further molecular mechanisms.

METHODS: D-galactose (DG)-induced ARPE-19 cell senescence and retinal aging were employed to evaluate the anti-aging effect of BBR in vivo and in vitro. The

siRNA transfection, Western-Blot analyses, SA-?-Gal assay and immunofluorescence were performed to investigate the potential mechanisms of BBR on anti-aging of RPE.

RESULTS: In RPE-choroid of both natural aged and DG-induced accelerated aged mice, oxidative stress was increased along with the up-regulation of p21 expression, which was ameliorated by BBR treatment. BBR down-regulated the expression of REDD1 to decrease intracellular ROS content, attenuating DG-induced senescence in vitro and in vivo. Furthermore, p53 instead of HIF-1? was identified as the transcriptional regulator of REDD1 in DG-induced premature senescence. Importantly, NAC and BBR reversed the expression of p53 and the content of 8-OHdG, indicating that the positive feedback loop of ROS-DNA damage response (DDR) was formed, and BBR interrupted this feedback loop to alleviate DG-induced premature senescence by reducing REDD1 expression. In addition, BBR restored DG-damaged autophagy flux by up-regulating TFEB-mediated lysosomal biosynthesis by inhibiting REDD1 expression, thereby attenuating cellular senescence.

CONCLUSION: BBR down-regulates REDD1 expression to interrupt the ROS-DDR positive feedback loop and restore autophagic flux, thereby reducing premature senescence of RPE. Our findings elucidate the promising effects of REDD1 on cellular senescence and the great potential of BBR as a therapeutic approach.

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Berberine (BBR), an isoquinoline alkaloid, exerts protective effects on various

cardiac injuries, and also extends the lifespan of individuals. However, the cardioprotective effect of BBR on cardiac senescence remains unknown. This study investigated the effects of BBR on cardiac senescence and its underlying mechanism. Senescent H9c2 cells induced by doxorubicin (DOX) and naturally aged rats were used to evaluate the protective effects of BBR on cardiac senescence. The results showed that BBR protected H9c2 cells against DOX-induced senescence. Exogenous Klotho (KL) exerts similar effects to those of BBR. BBR significantly increased in protein expression of KL, while transfection with KL-specific siRNA (siKL) inhibited the protective effect of BBR against senescence. Both BBR and exogenous KL decreased the levels of reactive oxygen species, inhibited apoptosis, and alleviated mitochondrial dysfunction in these cells; and transfection with siKL attenuated these effects of BBR. In naturally aged rats, BBR indeed protected the animals from cardiac aging, at least partially, through lowering the levels of cardiac hypertrophy markers, and increased the expression of KL in cardiac tissue. Additionally, BBR markedly reversed downregulation of sirtuin1 (SIRTI) in the aged heart. In vitro experiments revealed that BBR and exogenous KL also increased the expression of SIRT1, whereas siKL limited this effect of BBR in senescent H9c2 cell. In summary, BBR upregulated KL expression and prevented heart from cardiac senescence through anti-oxidative and anti-apoptotic effects, as well as alleviation of mitochondrial dysfunction. These effects may be mediated via regulation of the Klotho/SIRT1 signaling pathway.

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PURPOSE: Our study aimed to investigate the pharmacological effect of BBR as an anti-aging agent in retinal aging and its further molecular mechanisms.

METHODS: D-galactose (DG)-induced ARPE-19 cell senescence and retinal aging were employed to evaluate the anti-aging effect of BBR in vivo and in vitro. The siRNA transfection, Western-Blot analyses, SA-?-Gal assay and immunofluorescence were performed to investigate the potential mechanisms of BBR on anti-aging of RPE.

RESULTS: In RPE-choroid of both natural aged and DG-induced accelerated aged mice, oxidative stress was increased along with the up-regulation of p21 expression, which was ameliorated by BBR treatment. BBR down-regulated the expression of REDD1 to decrease intracellular ROS content, attenuating DG-induced senescence in vitro and in vivo. Furthermore, p53 instead of HIF-1? was identified as the transcriptional regulator of REDD1 in DG-induced premature senescence. Importantly, NAC and BBR reversed the expression of p53 and the content of 8-OHdG, indicating that the positive feedback loop of ROS-DNA damage response (DDR) was formed, and BBR interrupted this feedback loop to alleviate DG-induced premature senescence by reducing REDD1 expression. In addition, BBR restored DG-damaged autophagy flux by up-regulating TFEB-mediated lysosomal biosynthesis by inhibiting REDD1 expression, thereby attenuating cellular senescence.

CONCLUSION: BBR down-regulates REDD1 expression to interrupt the ROS-DDR positive feedback loop and restore autophagic flux, thereby reducing premature senescence of RPE. Our findings elucidate the promising effects of REDD1 on cellular senescence and the great potential of BBR as a therapeutic approach.

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Berberine (BBR), an isoquinoline alkaloid, exerts protective effects on various cardiac injuries, and also extends the lifespan of individuals. However, the cardioprotective effect of BBR on cardiac senescence remains unknown. This study investigated the effects of BBR on cardiac senescence and its underlying mechanism. Senescent H9c2 cells induced by doxorubicin (DOX) and naturally aged rats were used to evaluate the protective effects of BBR on cardiac senescence. The results showed that BBR protected H9c2 cells against DOX-induced senescence. Exogenous Klotho (KL) exerts similar effects to those of BBR. BBR significantly increased in protein expression of KL, while transfection with KL-specific siRNA (siKL) inhibited the protective effect of BBR against senescence. Both BBR and exogenous KL decreased the levels of reactive oxygen species, inhibited apoptosis, and alleviated mitochondrial dysfunction in these cells; and transfection with siKL attenuated these effects of BBR. In naturally aged rats, BBR indeed protected the animals from cardiac aging, at least partially, through lowering the levels of cardiac hypertrophy markers, and increased the expression of KL in cardiac tissue. Additionally, BBR markedly reversed downregulation of sirtuin1 (SIRTI) in the aged heart. In vitro experiments revealed that BBR and exogenous KL also increased the expression of SIRT1, whereas siKL limited this effect of BBR in senescent H9c2 cell. In summary, BBR upregulated KL expression and prevented heart from cardiac senescence through anti-oxidative and anti-apoptotic effects, as well as alleviation of mitochondrial dysfunction. These effects may be mediated via regulation of the Klotho/SIRT1 signaling pathway.

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