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Magnolol protects against oxidative stress induced senscence of rat nucleus pulposus cells via SIRT1/PGC-1α signaling pathway

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Abstract

Background

In the context of intervertebral disc degeneration (IDD), the apoptosis of nucleus pulposus cells (NPCs) is a pivotal factor that contributes to disease progression. Magnolol, a natural compound extracted from the bark of Magnolia officinalis, has been extensively investigated for its potential to mitigate aging processes and function as a potent antioxidant. Consequently, our research aimed to elucidate the biological role of magnolol and to examine the potential mechanisms that may be associated with the progression of intervertebral disc degeneration, particularly concerning cellular senescence.

Material and Methods

To investigate the functions of magnolol in disc degeneration and elucidate its underlying mechanisms, a series of experiments were conducted to examine the impact of varying levels of hydrogen peroxide (H_2O_2) on rat neural progenitor cells. To explore the influence of magnolol at different concentrations, both magnolol alone and its combination with EX527 were introduced into the experimental culture. The survival of cells was assessed using the CCK-8 assay and cellular senescence was evaluated through immunohistochemical analysis utilising the β-galactosidase staining method. Cell death analysis was performed using Annexin V-EGEP/PI dual staining. The MitoSOTM Red assay kit was utilised to specifically measure mitochondrial reactive oxygen species (ROS), providing a targeted approach for assessing oxidative stress within cellular mitochondria. Mitochondrial membrane potential (MMP) was evaluated using a fluorescence microscope following JC-1 staining. Age-related indicators (P16, P21, P53, MMP-3, and P-Rb) and apoptosis-related proteins (Bax, Bcl-2) were analysed. Furthermore, the expression levels of the signalling pathways involving Caspase-3, PARP-1, SIRT1, and PGC-1α were comprehensively assessed using western blot techniques.

Results

The experimental results reveal that Magnolol exhibited no significant cytotoxic effects at concentrations up to 60 μM in rat NP cells after exposure for either 12 or 24 hours. The use of magnolol as a pre-treatment agent significantly alleviated the harmful effects of H_2O_2-induced apoptosis in various cellular models. Magnolol shows promise in mitigating the adverse consequences of H_2O_2-induced mitochondrial dysfunction by reducing elevated levels of reactive oxygen species (ROS) and enhancing mitochondrial membrane potential (MMP). Additionally, pre-treatment with magnolol significantly decreased the senescence rate in rat neuronal progenitor cells (NPCs), as indicated by a decline in senescence-related markers. Prior to exposing NPCs to 300 μM H_2O_2, the cells were treated with 10 μM EX527, a specific inhibitor of SIRT1. This study illustrated that the previously observed inhibitory effect of

magnolol on programmed cell death was effectively reversed, indicating a restoration of normal apoptotic pathways in the treated cells.

Conclusion

The findings of the study suggest that magnolol may protect mitochondrial integrity and diminish cellular senescence in rat nucleus pulposus (NPCs) subjected to hydrogen peroxide, through the SIRT1/PGC-1α signalling cascade. It is now clear that magnolol presents considerable potential as a novel therapeutic agent in the clinical setting, specifically aimed at addressing and alleviating the progression of disc degeneration.

INTRODUCTION

Low back pain is a common symptom of spinal disorders, with approximately 80% of the global population has experienced this issue, with the increasing age of the population leading to rising medical costs that strain both individuals and governments financially, thereby pressuring public resources.[1] The degeneration of intervertebral discs significantly contributes to lower back pain, supported by various scientific studies.[2] The disc consist of the annulus fibrosus, the fibrous outer layer, and the cartilaginous structures at the spinal column's ends.[3] The nucleus pulposus, a crucial component of the intervertebral disc, plays a vital role in maintaining the disc's internal environment. The progressive loss of the nucleus pulposus, a critical component of the intervertebral disc, is widely considered a defining characteristic of intervertebral disc degeneration (IVDD), particularly in the context of spinal disc disease. [4] The microenvironment of the nucleus pulposus undergoes significant alteration, contributing to the development and progression of intervertebral disc disease (IVDD). Oxidative stress serves as a fundamental driver of the alterations observed in microenvironmental conditions. Studies have demonstrated a close association between the progressive deterioration of disc structures in the spine and elevated levels of reactive oxygen species (ROS) within the surrounding tissues. [5] Mitochondria, which act as the primary energy producers in cells, are essential not only for cellular respiration but also as sites for the generation of reactive oxygen species (ROS). Under specific experimental conditions, the presence of reactive oxygen species (ROS) has been shown to result in a significant reduction of the mitochondrial membrane potential (MMP), a critical indicator of cellular health and energy production. [6] As organisms age, the process of senescence is marked by a prolonged and irreversible cessation of cell division, which substantially diminishes their capacity for further replication. Initial investigations have indicated that oxidative stress induces apoptosis in nucleus pulposus cells, as evidenced by our research.[7]

Silenced Transcription Factor 1 (SIRT1), enzyme in the NAD^+-dependent histone deacetylase family, is well-documented for its involvement in regulating histone acetylation and other non-histone substrates. [8] BThis enzyme deacetylates the protein peroxisome proliferator-activated receptor gamma coactivator-1α (PGC-1α), influencing its function and leading to a substantial upregulation of the PGC-1α

pathway.[9] The SIRT1/PGC-1α signalling network is a firmly established pathway that controls mitochondrial function and has been shown to be pivotal in both anti-ageing and antioxidant mechanisms.[10]

Magnolol (MG), a biphenolic lignan derived from Magnolia officinalis, exhibits diverse pharmacological effects, including potent antioxidant and anti-inflammatory properties, extensively researched in clinical trials.[11] Preclinical studies have demonstrated its efficacy in mitigating age-related pathologies such as osteoarthritis, neurodegenerative disorders, and osteoporosis. Notably, magnolol significantly enhances mitochondrial production in chondrocytes and osteoblasts, concurrently reducing oxidative stress and cellular damage in these specialised cells. Recent investigations propose its role as an antioxidant in cellular membranes and mitochondria, safeguarding these crucial components from oxidative stress. Furthermore, magnolol counteracts the detrimental impact of IL-1β on chondrocyte function by suppressing the SIRT1/AMPK/PGC-1a signalling pathway.[12] Nevertheless, further exploration is required to fully elucidate its function in IVDD) and NPCs senescence, with a dearth of studies investigating its potential in retarding disc degeneration or reinstating NPCs homeostasis. Therefore, this study was designed to investigate whether magnolol may ameliorate NPCs senescence through SIRT1/PGC-1α-mediated mitochondrial rescue and inhibit the expression of cell senescence markers. Our findings from this research indicate that magnolol could serve as a viable therapeutic strategy for the management of IVDD.

MATERIALS AND METHODS

Magnolol (purity = 99.92%) was purchased from Med Chem Express (USA). Magnolol was dissolved in dimethyl sulfoxide (DMSO), with final DMSO concentrations ≤ 0.05%(V/V). H_2O_2 was acquired from Sigma (NJ, USA). EX527 (a selective inhibitor of SIRT1) was purchased from Med Chem Express (USA). The research project strictly adheres to the ethical guidelines established in the World Medical Association's Declaration of Helsinki, thereby prioritising the rights and well-being of all participants throughout the execution of the study.

Cell Culture.

The rat NPCs were purchased from iCell Bioscience Inc (Shanghai, China) and cultured in DMEM/F12 (Gibco, Rockville, MD, USA) with 10% fetal bovine serum (FBS) and 5% antibiotics. Each cell culture was maintained in a controlled environment, specifically within an incubator set at 37°C with a gas mixture of 5% CO_2. The medium was replaced at regular intervals, specifically every two days.

Cell Viability Analysis.

The cytotoxicity of magnolol on NP cells were assayed by cell counting kit-8 (CCK-8; Biosharp, China) according to the manufacturer’s protocol. Briefly, rat NPCs were cultured in 96-well plates (5×10^3 cells/well) and incubated with different concentrations (0, 2.5, 5, 10, 20, 40, 60, 80 and 100μM) of magnolol for an additional 12 or 24 h. At the indicated times, the cells were washed with phosphate-

buffered saline (PBS), and 100μl of DMEM containing10μl of CCK-8 solution was added to each well, followed by incubation at 37°C for 2 h. Then, the optical density at 450 nm was estimated in a microplate reader (Bio-Rad, USA). All assays were repeated three times.

Cell treatment.

According to the results of the CCK-8 assay, we treated rat NPCs with 5μM magnolol for 24h prior to exposure to 300μM H_2O_2 for 24h in the subsequent studies. To further determine whether the protective effects of magnolol were associated with SIRT1/PGC-1α activity, the rat NPCs were preconditioned with 10μM EX527 prior to exposure to 300μM H_2O_2 for 12h at room temperature. In this study, the rat NPCs were categorised into four distinct experimental groups: a control group, a group treated with H_2O_2, a magnolol-induced group (magnolol + H_2O_2), and a triple treatment group (H_2O_2 + magnolol + EX527).

Senescence-associated β-Galactosidase staining.

Cellular senescence was evaluated using the β-Galactosidase Staining Kit (C0602, Beyotime, Shanghai, China) in accordance with the manufacturer's instructions. Treated cells were first fixed in the supplied fixative for 15 minutes at room temperature, then washed with phosphate-buffered saline (PBS). One millilitre of β-Galactosidase Staining Solution was added and the cultures were incubated overnight at 37°C in a dry incubator without CO_2. Cells were finally examined with microscope (Nikon ECLIPSE Ts2) to identify blue-stained, β-galactosidase-positive cells.

Cell apoptosis analysis.

Rat neural progenitor cells (NPCs) were seeded into a 10 cm well at a density of 5 × 10^5 cells per well and maintained at 37°C in 5% CO2. When cultures reached 80% confluence, they received the experimental interventions specified in the study design. Cells were then washed with phosphate-buffered saline (PBS) and detached by trypsinisation. The collected rat NPCs were incubated with an Annexin V–EGFP/PI Apoptosis Detection Kit (Keygen Biotech, Wuhan, China) at room temperature in the dark for 30 minutes. Apoptotic cells were quantified by flow cytometry (BD Biosciences, San Jose, CA, USA).

TUNEL analysis.

Cells were seeded onto cover slips and processed according to the instructions for the TUNEL apoptosis detection kit. After treatment, cells were fixed with 4% paraformaldehyde, rinsed gently with PBS and permeabilised with 0.2% Triton X-100. Samples were incubated with freshly prepared TUNEL detection solution for 1 hour and then counterstained with DAPI in the dark for 5 minutes. Cells exhibiting bright red nuclear fluorescence were classified as TUNEL-positive and were observed by fluorescence microscopy. Three hundred cells were counted in random fields of view and the proportion of TUNEL-positive cells was calculated..

Determination of mitochondrial membrane potential.

Mitochondrial membrane potential was measured using the JC-1 assay kit (C2003S, Beyotime, Shanghai, China). Cells from each group were collected and suspended in the JC-1 staining working solution, then incubated at 37°C for 20 minutes. After centrifugation, cells were washed twice with JC-1 staining buffer. Following the final wash, cells were resuspended in JC-1 staining buffer, centrifuged and prepared for flow cytometry analysis.

Mitochondrial reactive oxygen species analysis.

MitoSO™ Red was used to measure mitochondrial reactive oxygen species (ROS) in accordance with the manufacturer's instructions. Cells were treated according to the experimental design and approximately 10^4 cells were collected. Samples were centrifuged at 600× g for 5 minutes and the supernatant discarded. Cells were then resuspended in MitoSO™ Red staining working solution to a density of 10^5/ml and incubated at 37℃ for 30 minutes. After incubation, samples were centrifuged at 600× g at 4ºC for 3–4 minutes, washed twice with PBS, resuspended in PBS and analysed by flow cytometry.

Western Blot Analysis.

Briefly, the cell samples were lysed in the RIPA buffer, and the homogenate was centrifuged at 13,000 rpm for 10 min at 4˚C. Subsequently, proteins from the supernatant was extracted after centrifugation. The protein samples were separated by SDS-PAGE and transferred to a nitrocellulose membrane. Membranes were blocked by 1×TBST with milk powder and then incubated overnight at 4 ˚C with the following primary antibodies: SIRT1 (#8469, 1:1000, CST). PGC-1α (A20995, 1:1000, ABclonal), P53 (A5804, 1:1000, ABclonal), P16 (10883-1-AP, 1:2000, Proteintech), p-Rb (AP1362, 1:1000, ABclonal), Caspase-3 (A19664, 1:1000, ABclonal), Cyto-C (A4912, 1:1000, ABclonal), Bax (A19684, 1:1000, ABclonal) and Bcl-2 (A20777, 1:1000, ABclonal), followed by incubation with the HRP-labeled secondary antibody at RT for 90 min. Finally, the bands was detected by chemiluminescence method. In brief, Reagents A and B of the chemiluminescent reagent (BK0041-01, ECL Enhanced, ACE, Changzhou, China) were mixed 1:1 which further being used to incubate the membrane for 1 min. Then, the membrane was exposed under Gel imaging system (Tanon 5200 Multi, Shanghai, China) for protein signal detection. GADPH was used as an internal control.

Statistical Analysis

All data are presented as means ± SD from three independent experiments. Statistical analyses were performed with SPSS 25 (SPSS Inc., IL, U.S.A.). Results are shown as bar charts, and statistical differences were assessed by Student’s t-test or one-way ANOVA. $P < 0.05$ was considered statistically significant.

RESULTS

Effects of magnolol on H_2O_2-activated cell viability in rat NP cells

The molecular structure of Magnolol is shown in Fig. 1A. We first examined the safe dose range of magnolol that did not adversely affect the NP cells viability using the CCK-8 method. As demonstrated in Fig. 1B, NP Cells were treated with different concentrations (0, 2.5, 5, 10, 20, 40, 60, 80 and 100 μM) of magnolol for 12 and 24 h. Next, we calculated cell cytotoxicity as the percentage of the control group. CCK8 results illustrated that magnolol within 5μM was not cytotoxic to NP cells after 12 or 24 h (Figs. 1B,C). Based on previous literature and finding of the present study, the authors selected a 5μM concentration of magnolol and 300 μM concentration of H_2O_2 for further experiments.

Magnolol attenuates HO-induced nucleus pulposus cells degeneration

In our experimental analysis, we observed a significant upregulation of SIRT1 protein levels following treatment with Magnolol, as illustrated in the accompanying data visualisation (Fig. 2). Our research indicated that the Magnolol pretreatment group exhibited a marked reduction in cellular senescence when compared to the H_2O_2-treated group. This finding was supported by a decrease in the expression of senescence-associated proteins, including p53, p21, p16, MMP-3, and p-Rb. Conversely, fewer instances of hypertrophic and β-gal-positive cells were noted in this context, as depicted in Fig. 2A–D.

The application of Magnolol alleviates HO-induced mitochondrial dysfunction

A reduction in mitochondrial membrane potential (MMP), typically indicative of early apoptosis, serves as a marker of compromised mitochondrial function. JC-1, a fluorescent dye, is recognised for its selective binding to mitochondria under active metabolic conditions. In comparison to the control group, a significant decrease in mitochondrial membrane potential was observed following exposure to hydrogen peroxide (H_2O_2), a decline that was effectively reversed by the administration of magnolol. Furthermore, the presence of magnolol markedly reduced the elevated levels of mitochondrial reactive oxygen species (ROS) triggered by hydrogen peroxide (H_2O_2). In conclusion, these findings suggest that magnolol effectively mitigates both the apoptotic pathways initiated by hydrogen peroxide and the resultant mitochondrial dysfunction.

The impact of Magnolol on H_2O_2-activated apoptotic pathways in rat NP cells

To explore the influence of magnolol on NPCs apoptosis, a TUNEL assay was performed. The results revealed a notable increase in apoptotic NPCs in the H_2O_2-treated group compared to the control group. Interestingly, pre-treatment with magnolol led to a substantial reduction in the number of TUNEL-positive cells in the treated group, indicating its potential inhibitory effect. To confirm the preceding findings, Annexin V-FITC/PI assay was conducted as a subsequent experiment. In the control group, the apoptotic rate was 6.37 ± 0.21%, whereas post-treatment with hydrogen peroxide, this value significantly increased to 16.46 ± 0.38%. However, after pretreatment with magnolol, the apoptotic rate decreased to 7.14 ± 0.29%. he findings suggest that magnolol may mitigate hydrogen peroxide-induced programmed cell death in NP cells by regulating their intrinsic apoptotic signalling. Consistent with Western blot analysis, magnolol appears to attenuate the reduction in Bcl-2 protein levels induced by hydrogen peroxide (H_2O_2) and suppress the overabundance of critical mitochondrial apoptosis markers including BAX, PARP1, and caspase-3.

Magnolol attenuates HO-induced apoptosis in rat NPCs via the SIRT1/PGC-1α pathway

Western blot analysis indicated that the expression of apoptosis-associated proteins PARP-1 and BAX was significantly increased in the H_2O_2-treated group compared to the control group. Conversely, the levels of BCL-2 protein were markedly decreased relative to those in the control group. Compared to the H_2O_2 group, the MG group (Magnolol + H_2O_2) exhibited a significantly reduced increase in H_2O_2-induced apoptosis in NPCs. The incorporation of the compound EX-527 into the MG group effectively neutralised the previously observed inhibitory activity of magnolol. Consequently, the reduced levels of SIRT1 and PGC-1α, induced by hydrogen peroxide (H2O2), were restored following treatment with magnolol; however, the inhibitory effect of EX-527 counteracted this restoration. These findings suggest that magnolol provides a protective effect on nucleus pulposus cells against hydrogen peroxide-induced programmed cell death, primarily via the SIRT1/PGC-1α signalling pathway.

DISCUSSION

Degenerative disc disease is a common clinical manifestation linked to the advancement of spinal degeneration, frequently seen in individuals suffering from persistent back pain or limited mobility. Despite significant advancements in understanding its progression mechanisms and creating efficient treatment approaches, the underlying degenerative mechanisms remain essentially immutable.[13] Surgical intervention is generally considered the primary therapeutic approach in addressing degenerative disc disease.[14] This study investigates the potential protective effect of Magnolol in countering oxidative stress-induced degeneration of NPCs through the activation of the SIRT1/PGC-1α signalling pathway.

Hydrogen peroxide (H_2O_2) is a commonly employed agent that induces oxidative stress and interferes with cellular processes by raising intracellular reactive oxygen species (ROS) levels.[15] This elevation in

ROS levels contributes to the promotion of cellular senescence and programmed cell death in NPCs.[16] In the previous study, we found that H_2O_2 at the concentration of 300 μM promoted intracellular ROS generation, and indicates that the overproduction of ROS may play a pivotal role in H_2O_2-mediated apoptosis of NPCs and contribute to mitochondrial dysfunction. Magnolol was reported to lower apoptosis in MC3T3 cells exposed to oxidative stress suggests that it may help preserve disc function and integrity, potentially delaying the onset of degenerative disc disease.[17] In the current investigation, our study demonstrated that a concentration of 5 μM magnolol effectively neutralised the H_2O_2-mediated enhancement of mitochondrial ROS production and mitigated the inhibitory effect of H_2O_2 on the mitochondrial membrane potential.

SIRT1 regulates oxidative stress-related cellular damage and toxicity in mammalian systems by deacetylating crucial stress response proteins..[9] Specifically, SIRT1 has been shown to alleviate oxidative stress-induced senescence in rat NPCs. This process, primarily driven by SIRT1, is governed by the Akt-FoxO1 signalling pathway.[18] SIRT1 promotes PINK1/Parkin-mediated mitochondrial autophagy, mitigates IL-1β-induced mitochondrial dysfunction and reactive oxygen species accumulation, and inhibits NLRP3 inflammasome activation.[19] Magnolol, as a natural SIRT1 agonist, exhibits antioxidant properties among other functions.[11] In addition to its antioxidant properties, magnolol has been demonstrated to affect mitochondrial dysfunction via the PI3K/AKT signalling pathway.[20] By protecting neural cells from oxidative stress-related damage, this mechanism has been shown to mitigate neuronal injury.

The quantity of nucleus pulposus cells is a critical factor in the progression of intervertebral disc degeneration, as it directly affects the structural integrity of the discs. It is imperative to maintain the quantity of functional and operational intervertebral disc components during the repair process, as indicated in the referenced study.[21] agnolol, a compound derived from magnolia trees, exhibits potent antioxidant properties, effectively mitigates apoptosis, and aids in the restoration of mitochondrial function.[22] In this context, our research demonstrated that 5 μM magnolol significantly reduced oxidative stress-induced apoptosis in rat NPCs, as evidenced by the detection of key apoptosis markers.

The upregulation of SIRT1 and PGC-1α pathways diminishes oxidative stress and addresses metabolic disorders.[23] It has been reported that 4μM magnolol enhances SIRT1 activity, thereby mitigating IL-1β-induced chondrocyte damage via the SIRT1/AMPK/PGC-1α signal pathway.[12] In this study, we found that 5μM magnolol elevated SIRT1 and PGC-1α protein levels, whilst inactivation of the SIRT1/PGC-1α pathway reversed magnolol's inhibitory effects on apoptosis, cellular senescence and mitochondrial dysfunction. However, there are limitations to our study. Primarily, the lack of clinical validation and in vivo experimental data restricts the generalizability of our findings. While the in vitro model effectively elucidates the protective mechanisms of Magnolol against oxidative stress, the translation of these results to clinical settings remains unverified. A Furthermore, the investigation did not delve into the long-term effects of Magnolol administration, which is crucial for establishing its therapeutic potential.

In summary, the findings of this research demonstrate that magnolol effectively activates the SIRT1/PGC-1α signalling pathway in rat NPCs, thereby alleviating both H_2O_2-induced mitochondrial damage and oxidative stress. This conclusion is substantiated by the experimental evidence, which indicates that treatment significantly reduces the extent of cellular dysfunction under these conditions. The results suggest that magnolol may present a viable therapeutic option for managing diseases associated with neural progenitor cell dysfunction, as its potential efficacy in mitigating degenerative processes is evident. Future studies should prioritize the assessment of its effectiveness and safety in clinical applications. In addition to examining its functional impact across various cellular environments and tissue structures, we will investigate how these findings may differ depending on the specific cell type or tissue under consideration.

Declarations

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Date availability

The data that support the findings of this study are the property of the first author and the corresponding author. These data are not publicly available due to privacy and ownership restrictions, but are available from the corresponding author upon reasonable request.

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Ethics approval and consent to participate

Clinical trial number: not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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Figures

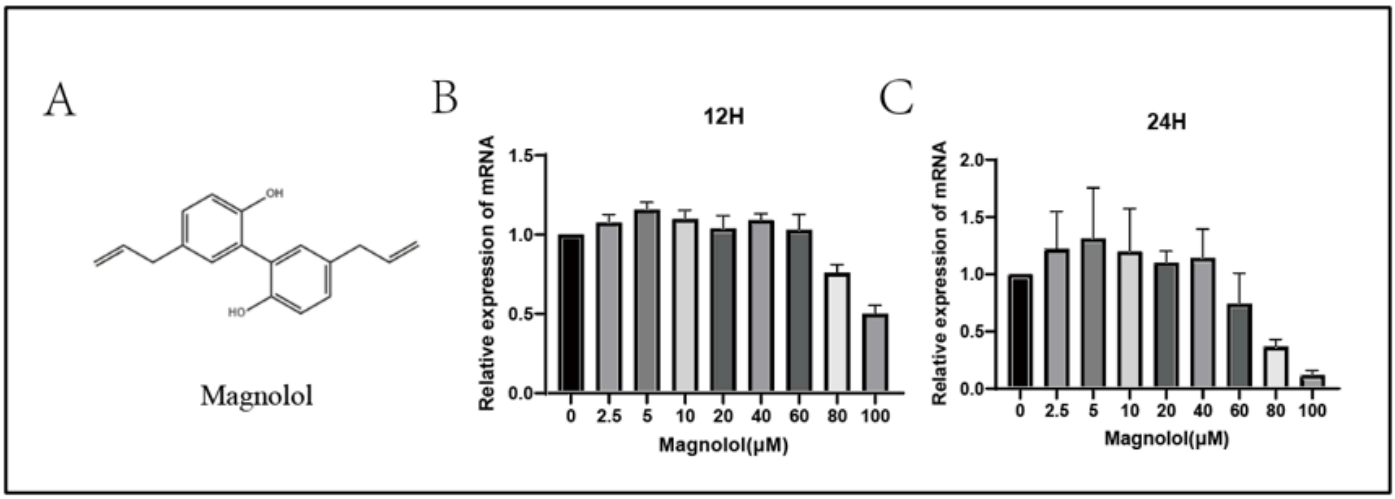


Figure 1

Effects of magnolol on the cell viability of chondrocytes. (A) Chemical structure of magnolol. (B,C) The cytotoxic effect of magnolol on was determined at various concentrations for 12 and 24 h using a CCK8 assay. The values presented are the means ± SD.

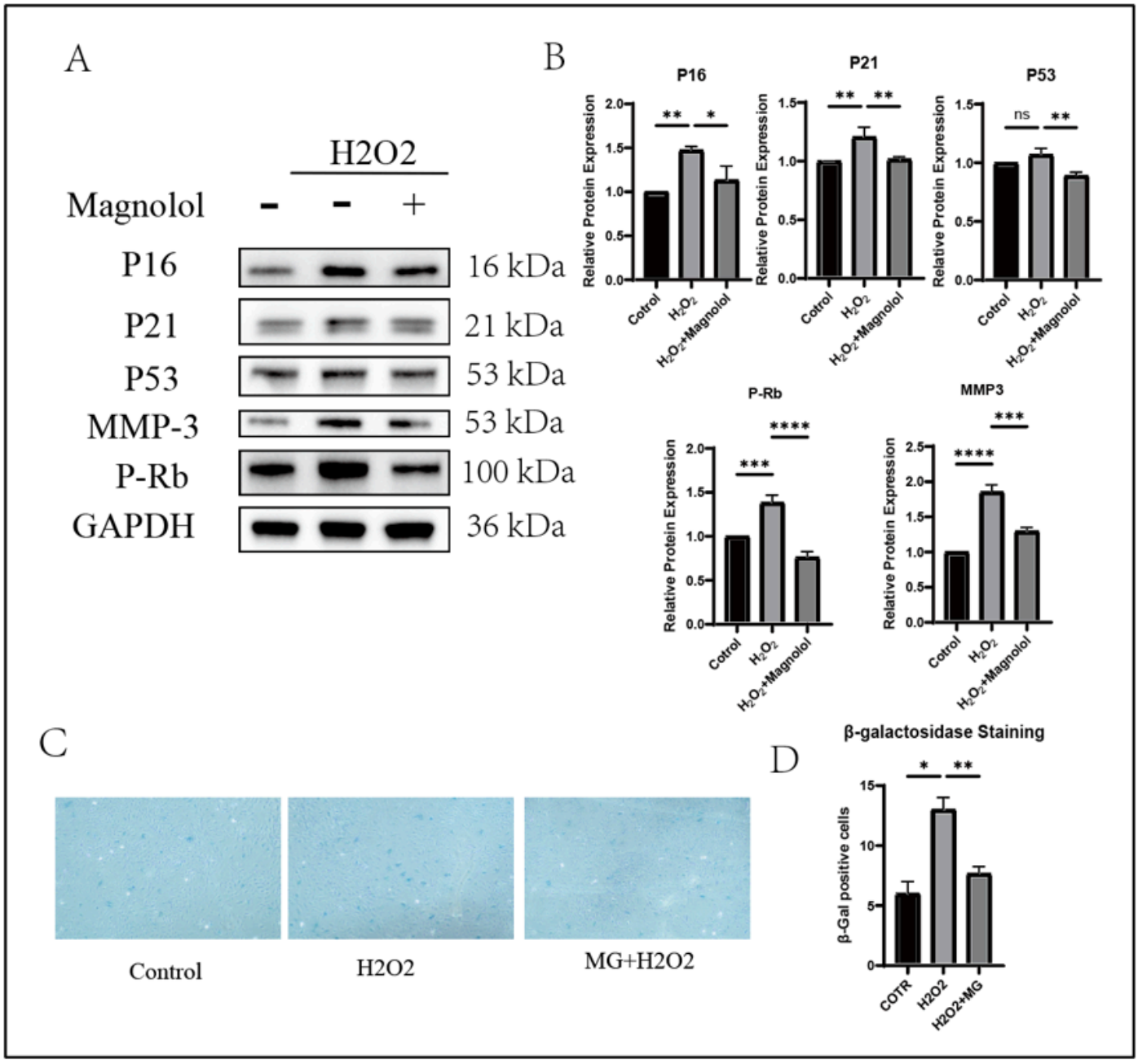


Figure 2

Magnolol activated SIRT1 to rescue oxidative stress-induced rat NP cells senescence The rat NP cells were divided into control, H_2O_2 treatment group and Magnolol pretreatment group. The expression of SIRT1 and some senescence relative proteins (p53, p21, p16, MMP-3 and p-Rb) were detected using Western blot showed in (A)and (B). GAPDH was used as an internal control. β-galactosidase staining was used to detect senescent rat NP cells.(C,D). (*P<0.05, **P<0.01, ***P<0.001 vs H_2O_2 treatment group)

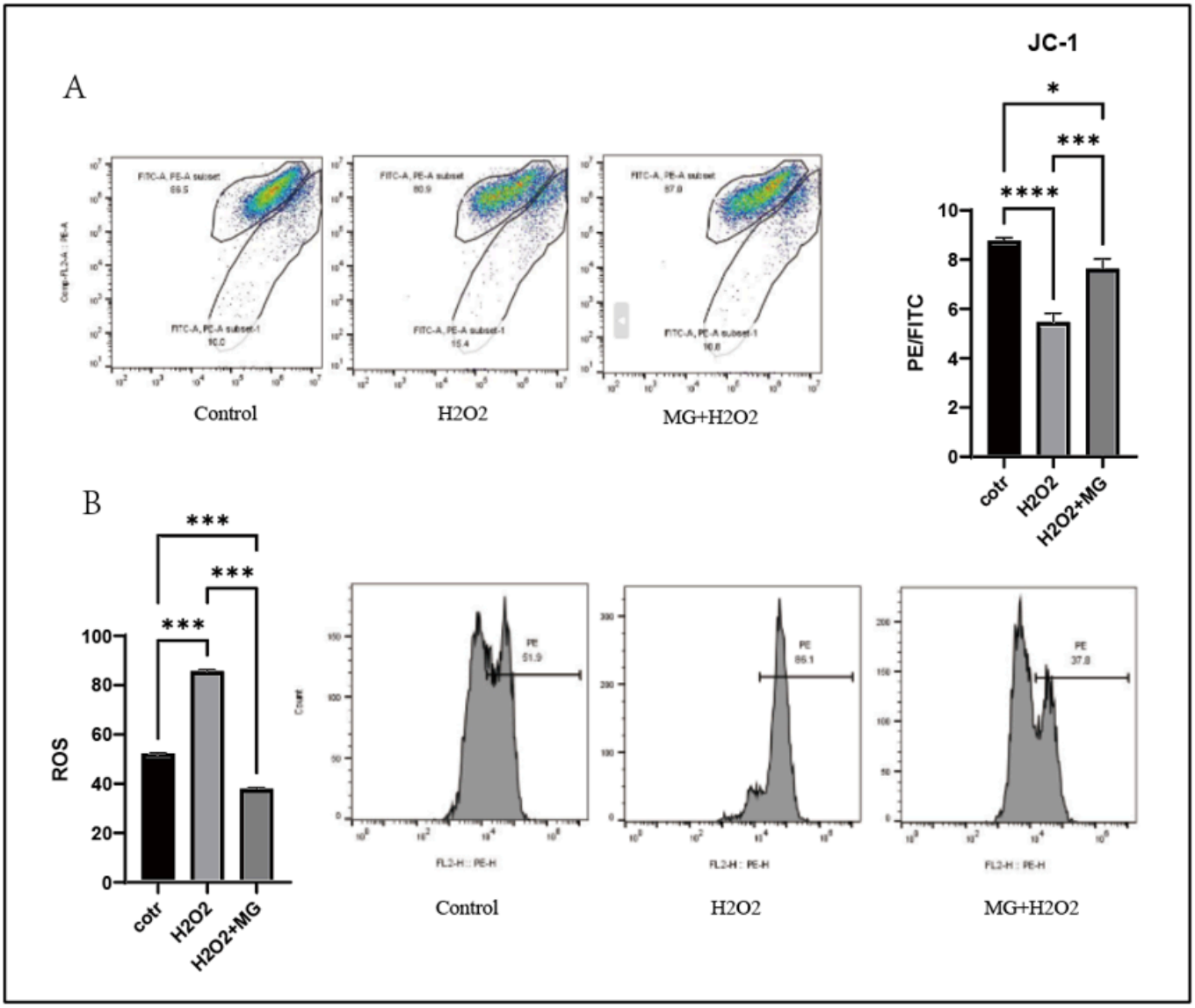


Figure 3

Magnolol at 5μM alleviates H_2O_2-induced cell mitochondrial dysfunction. Flow cytometer revealed mitochondrial membrane potential (MMP) changes after JC-1 staining of NPCs as described in Methods.(A) The mitochondrial ROS levels in rat NPCs were examined by MitoSOX staining as described in Methods.(B) **P < 0.01, ***P < 0.001 vs. H_2O_2 treatment group.

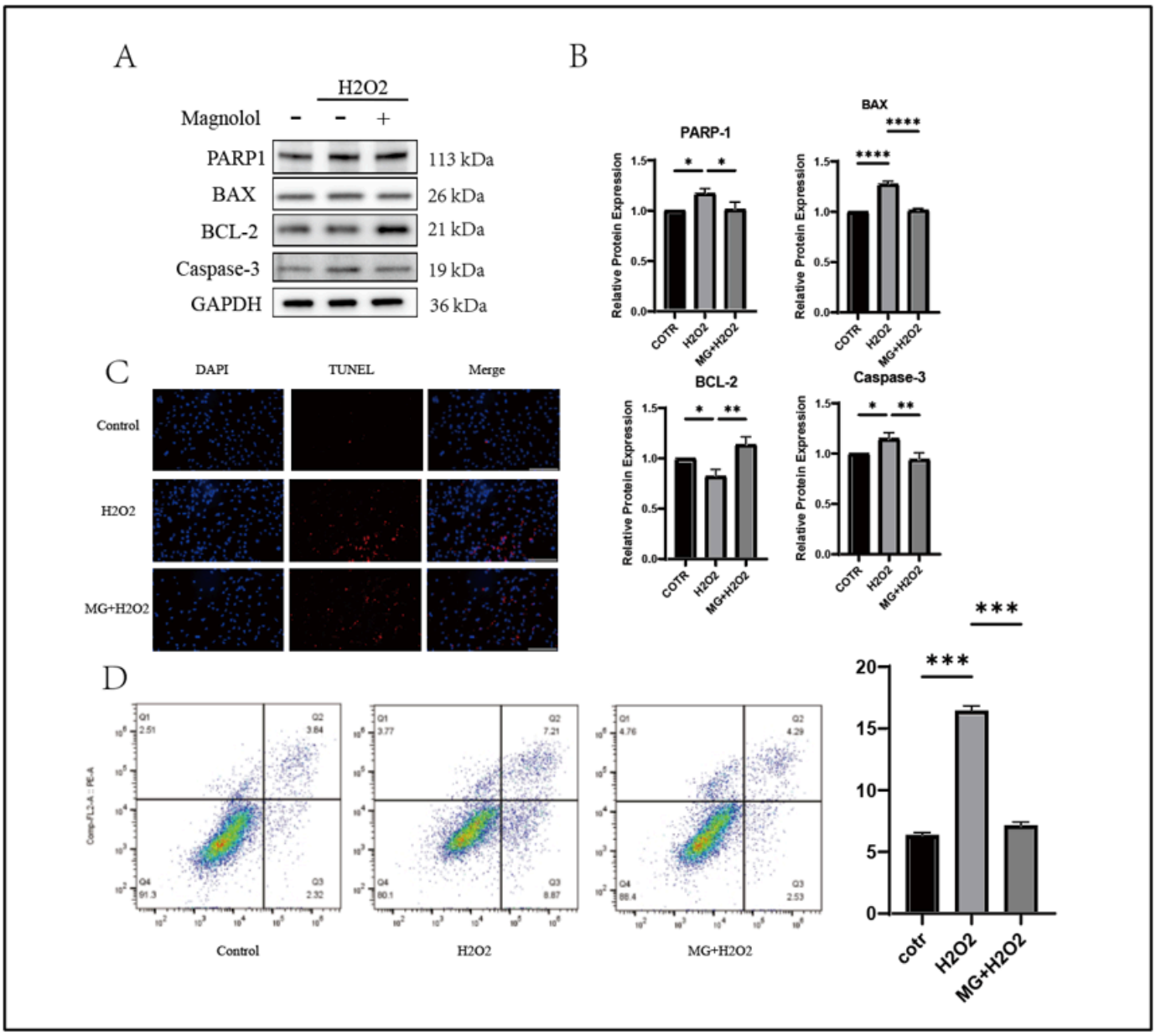


Figure 4

Effect of Magnolol on H_2O_2-induced apoptosis levels in rat NP cells. Western blot analysis shows the expression of BCL-2, BAX, caspase-3 and PARP1, genes associated with NP apoptosis. The relative expression of BCL-2, BAX, and caspase-3 was quantified via normalization to GAPDH. (A,B) : TUNEL shows red fluorescence and nuclei show DAPI-stained blue fluorescence. Scale bars: 200 μM. (C) All data are presented as the mean ± SD (n = 3), *p < 0.05; **p < 0.01; ***p < 0.001; ****p < 0.0001.

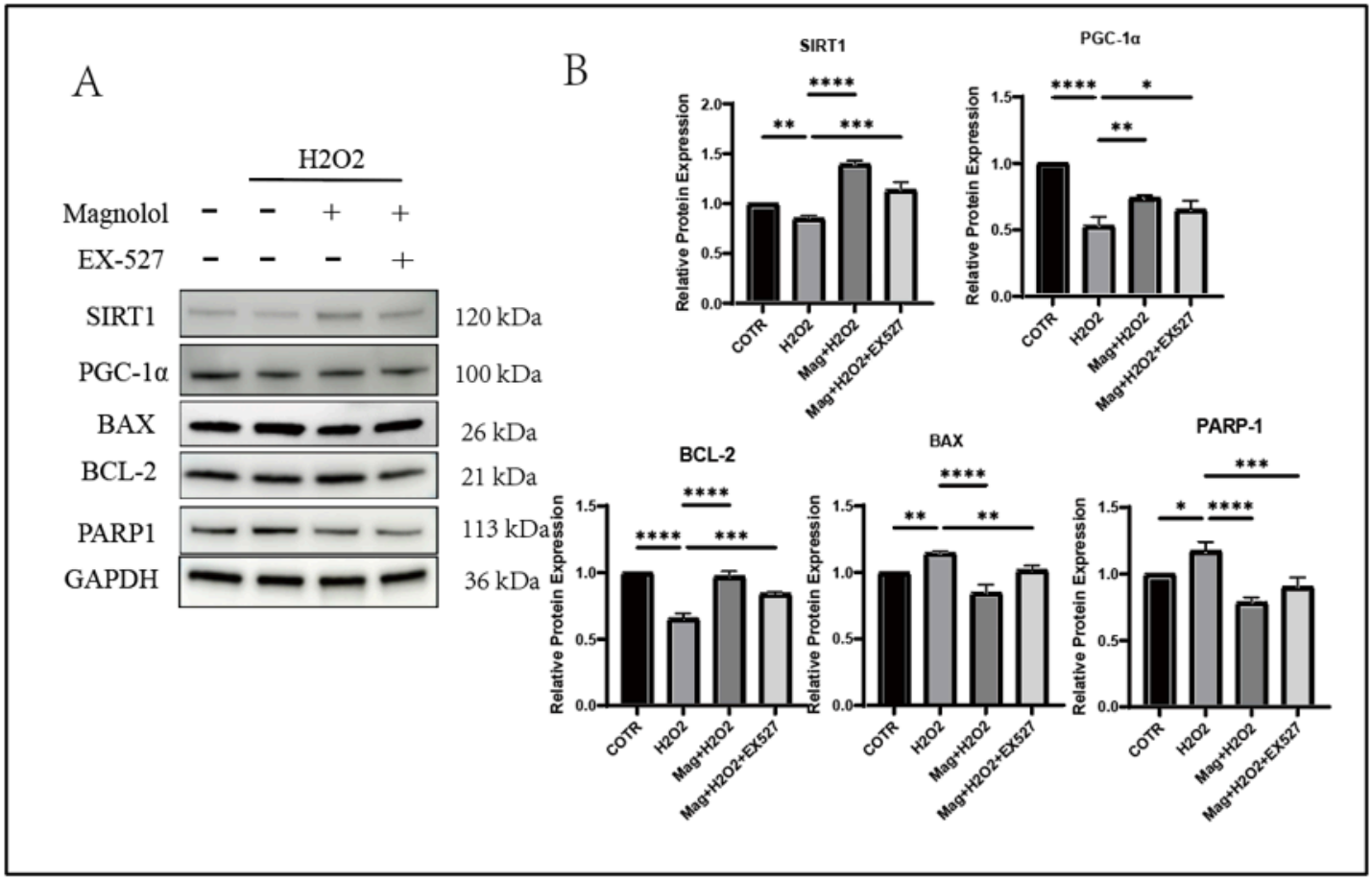


Figure 5

Effect of Mag on H_2O_2-induced apoptosis levels in rat NP cells. Western blot analysis shows the expression of BCL-2, BAX, caspase-3 and PARP1, genes associated with NP apoptosis. (A) The relative expression of BCL-2, BAX, and caspase-3 was quantified via normalization to GAPDH. (B) All data are presented as the mean ± SD (n = 3), *p < 0.05; **p < 0.01; ***p < 0.001; ****p < 0.0001

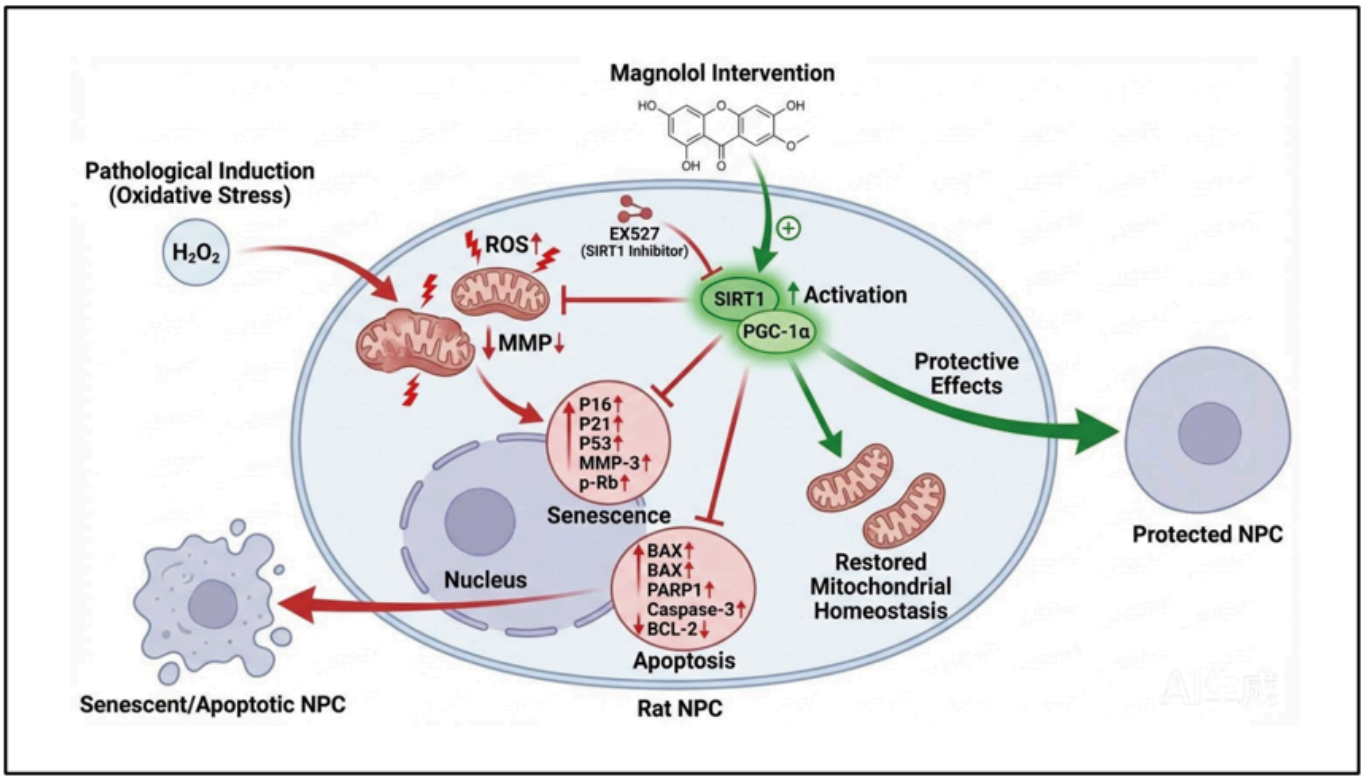


Figure 6

depicts the molecular pathways by which magnolol alleviates oxidative stress-induced cellular senescence initiated by hydrogen peroxide (H2O2). Magnolol's modulation of the SIRT1/PGC-1α signalling pathway provides antioxidant defence, enhances mitochondrial equilibrium, and reduces cellular senescence in rat nuclear pore complex (NPC) cells, thereby potentially retarding the advancement of intervertebral disc degeneration..

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- FIG21.pdf
- FIG4.pdf
- FIG5.pdf