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RESEARCH ARTICLE

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Taurine alleviates endoplasmic reticulum stress in the chondrocytes from patients with osteoarthritis

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读书报告

田小平　2018-08-01

Abstract

Osteoarthritis (OA), characterized by pain and stiffness, swelling, deformity and dysfunction of joints,affects large numbers of population.The purpose of this study was to discover the effects of taurine in human OA chondrocytes and explore the underlying mechanisms.The mRNA and protein levels of Collagen II decreased as OA progressed, while the expressions of ER stress markers increased dramatically. H2O2 induced ER stress in chondrocytes, as shown by the significant increase in the expression of ER stress markers, inhibited chondrocyte viability and Collagen II synthesis, promoted apoptosis. However, taurine treatment inhibited these above phenomena.These results indicated that taurine exhibited anti-OA effect by alleviating H2O2 induced ER stress and subsequently inhibiting chondrocyte apoptosis.

● Introduction

Chondrocytes, the only cells existing in articular cartilage, can generate and maintain the articular cartilaginous matrix,which is composed mainly of collagen and proteoglycans.

Recent reports have demonstrated that elevated Chondrocytes loss caused by apoptosis is a major feature of OA.

Endoplasmic reticulum (**ER**) stress, which occurs due to an imbalance between the load of unfolded or misfolded proteins in the ER and the processing capacity of ER, participates in many disease pathologies . Recent studies have demonstrated that ER stress in chondrocytes is responsible for chondrocyte apoptosis along with the progression of OA.

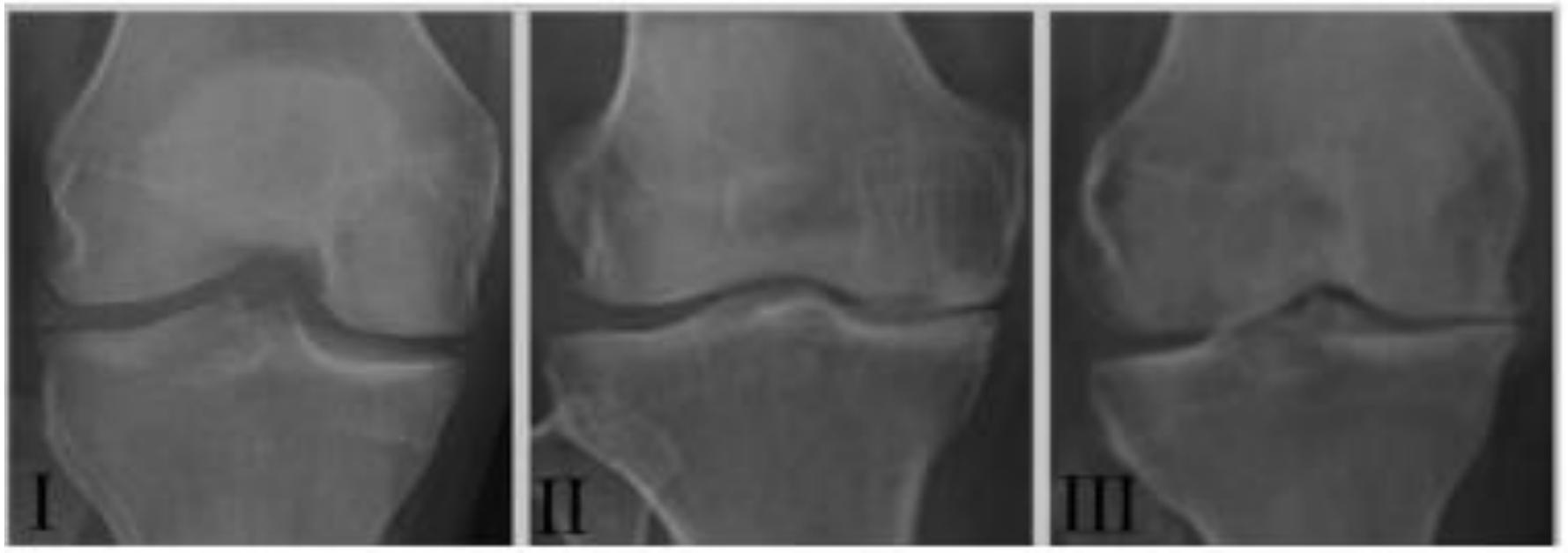
- Taurine, first isolated and characterized from the bile of the ox, is one of the most abundant endogenous free amino acids in humans.It has been implicated in several essential biological processes including bile acid conjugation, calcium modulation, osmoregulation, membrane stabilization and protein phosphorylation. Moreover, anti-apoptosis and anti-oxidant properties are essential for the cytoprotective functions of taurine.
- Previous studies have confirmed that taurine inhibits ER stress-induced apoptosis and protects against lung injury, stroke and neurodegenerative diseases.

- However, no study has been done to examine the possible protective functions of taurine on human OA yet. Therefore,we made a hypothesis that taurine treatment might protect against OA by attenuating ER stress-associated apoptosis.
- To identify that, cartilages were isolated from 24 OA patients who received total knee replacement.The mRNA and protein levels of type II collagen (Collagen II), glucose-regulated protein 78 (**GRP78**), growth arrest and DNA-damage inducible gene 153 (**GADD153**) and **Caspase-12** in cartilages from patients with different OA grades were quantified by qRT-PCR and Western blot analysis, respectively.

- OA patient-derived chondrocytes were cultured in three conditions including: No treatment (Control group), H2O2 treatment to induce ER stress (H2O2 group) and preincubation with taurine before H2O2 exposure (H2O2 + taurine group). The viability and apoptosis of cultured human OA chondrocytes were assessed by the CCK-8 assay and flow cytometry assay,respectively. Meanwhile, Western blot was also employed to evaluate the protein levels of Collagen II and ER stress markers in chondrocytes with different treatments.
- Our results illustrated that ER stress is highly involved in the H2O2-induced apoptosis in chondrocytes. Moreover, these results for the first time established that taurine alleviatedER stress in human OA chondrocytes as shown by the significant decrease in the expressions of ER stress markers, promoted chondrocyte viability and Collagen II synthesis, and inhibited chondrocyte apoptosis.

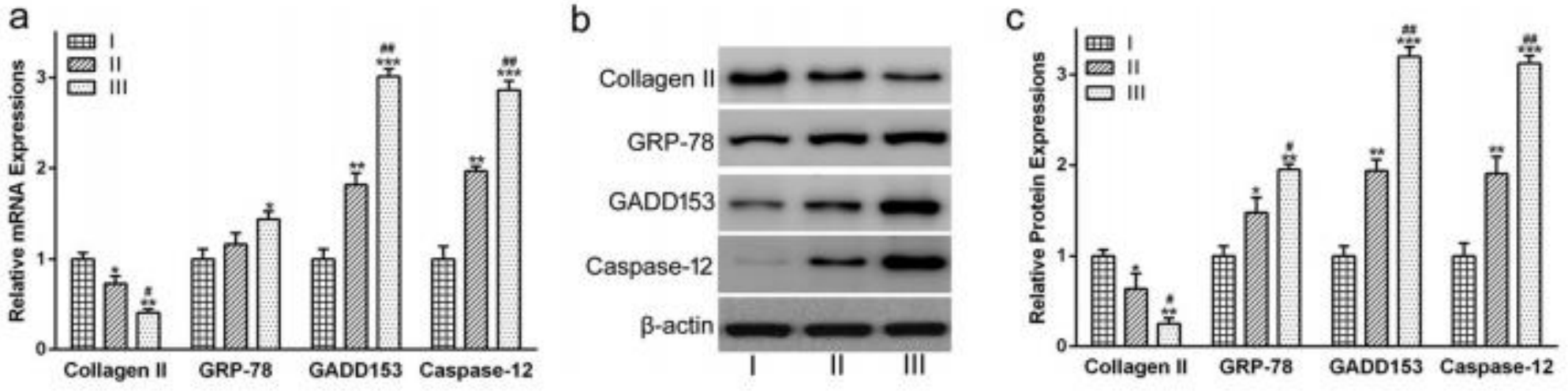
● Methods and materials

- **Patients**
- **Specimen processing**

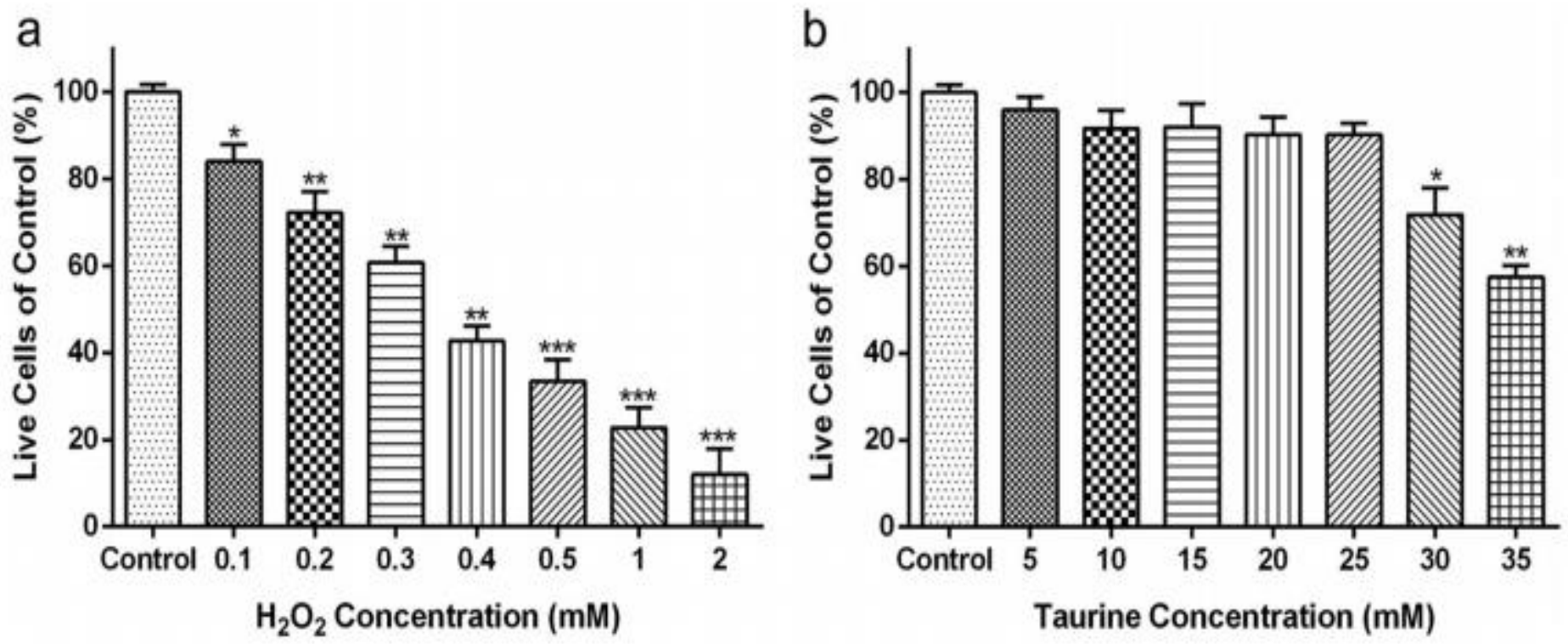


- **OA patient-derived chondrocyte culture**
- **Western blot analysis**
- **RNA extraction and real-time quantitative PCR (qRT-PCR) analysis**
- **CCK-8 assay**
- **Flow cytometry assay**
- **Statistical analysis**

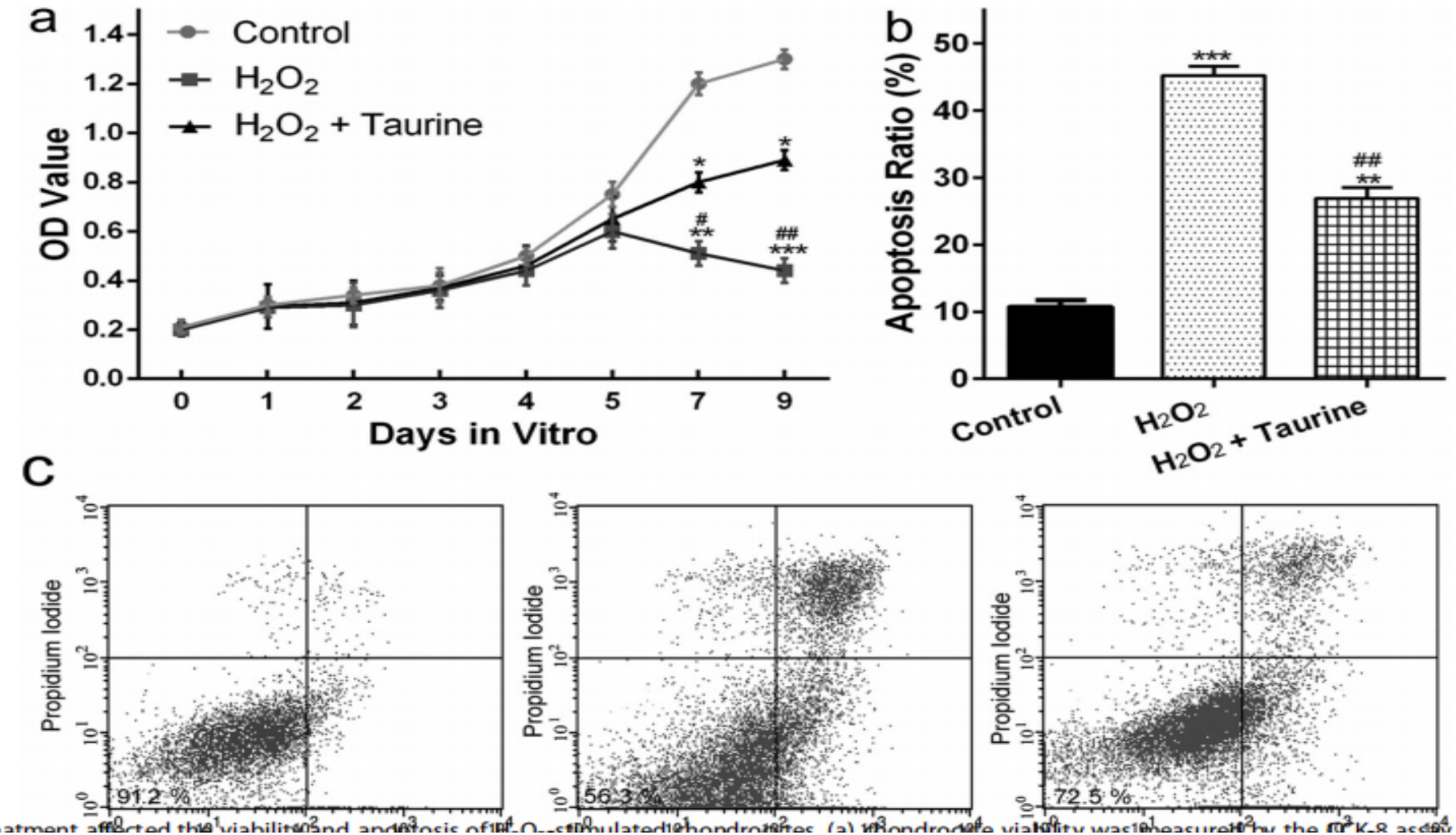
● Results



The expressions of Collagen II and ER stress markers in the cartilage of OA patients associated with the severity of OA progression.

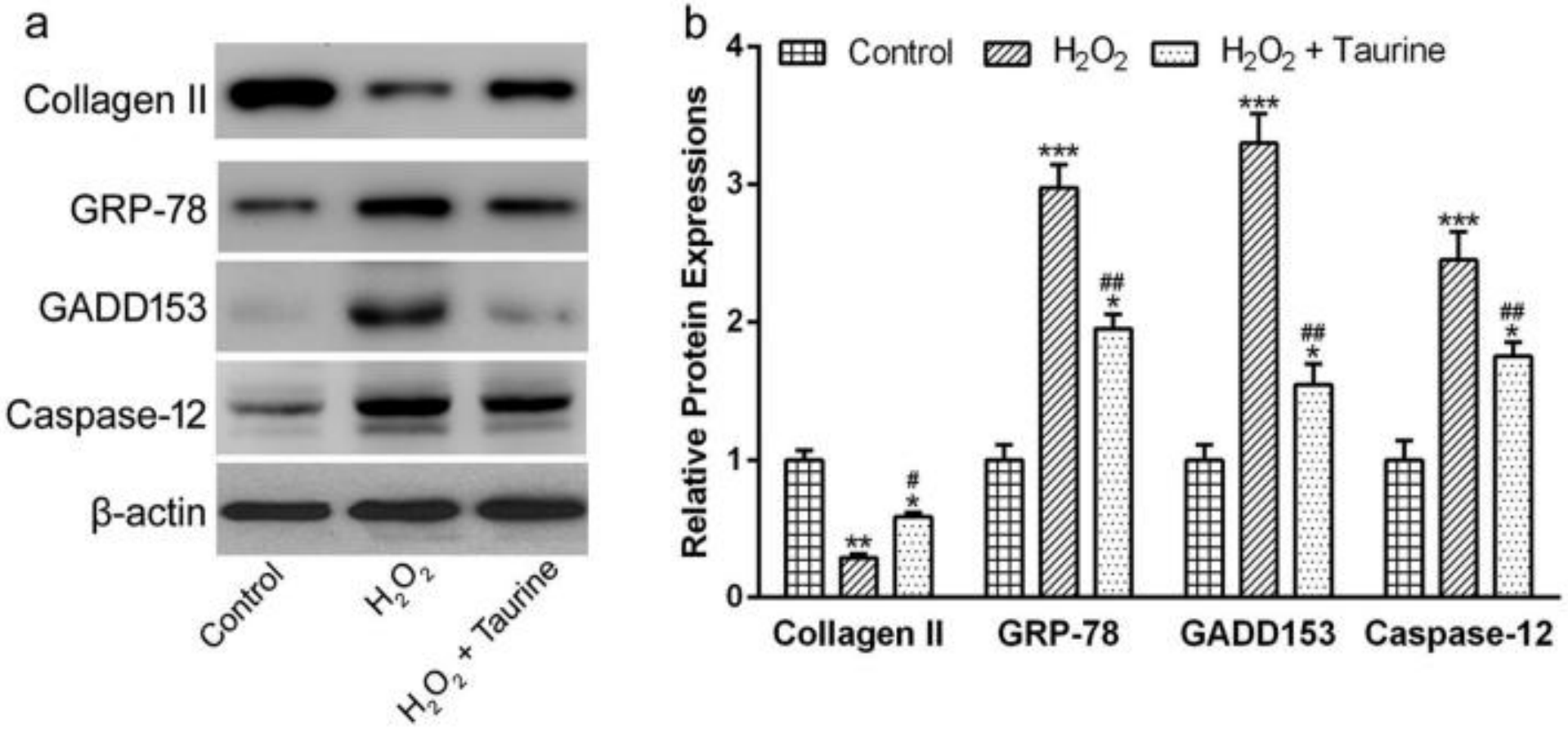


0.3 mM H2O2 and 25 mM taurine were chosen for the subsequent experiments.



rine treatment affected the viability and apoptosis of H2O2-stimulated chondrocytes. (a) Chondrocyte viability was measured by the CCK-8 assay. (b)

Taurine protected chondrocytes against damage induced by H2O2 in vitro.



Taurine inhibited ER stress induced by H2O2 stimulation in human OA chondrocytes

● Discussion

- Previous studies have indicated that elevated chondrocyte apoptosis, which is associated with the degradation of cartilage matrix, is the hallmark of OA and chondrocyte apoptosis inhibition is vital for the treatment of OA.
- In addition, a large number of studies have proved that ER stress is also associated with chondrocyte death by apoptosis in vivo and in vitro.
- the mRNA and protein levels of Collagen II gradually decreased as OA progressed. Furthermore,the mRNA and protein expressions of the above ER markers ,which were specific for ER stress, increased dramatically as cartilage degeneration worsened. Thus, the above results indicated that ER stress played a crucial role in the development of OA, which was consisted with previous reports.

- Taurine could not only promote cell growth and maintain phenotype of human articular chondrocytes , but also ameliorate ROS-induced cartilage damage through its antioxidant property.
- According to the results, H2O2 stimulation significantly enhanced the protein abundances of ER stress markers, which indicated the induction of ER stress by H2O2-stimulated oxidative stress, and
- taurine administration significantly inhibited these phenomena.In addition, taurine administration also prevented the decrease in Collagen II protein level by H2O2 treatment.
- Taken together,the above data provided compelling evidence that taurine had cytoprotective effects against H2O2 induced ER stress by promoting chondrocyte viability and inhibiting apoptosis.

- In conclusion, our study demonstrated that the use of taurine had anti-apoptotic effects on OA patient-derived chondrocytes stimulated with H2O2.
- Taurine treatment promoted chondrocyte viability and inhibited chondrocyte apoptosis by suppressing the ER stress pathway, as evidenced by the up-regulation of the expression of Collagen II and the down-regulation of the expressions of ER stress markers. Thus, our results illustrated that taurine was a promising OA therapeutic agent.

● Conclusion

This study provided solid evidence that taurine treatment exhibited anti-OA roles by suppressing H2O2-induced apoptosis in cultured chondrocytes of OA patients. The possible mechanism was that preincubation with 25 mM taurine alleviated H2O2-induced ER stress in chondrocytes by significantly inhibiting the expression of three ER stress markers and increasing Collagen II synthesis. Thus, our study showed that taurine was a promising OA therapeutic agent.

Thanks