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RESEARCH ARTICLE

The effects of Elgucare in a rat model of intervertebral disc degeneration

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Abstract

As an avascular tissue, the intervertebral disc (IVD) faces difficulties in obtaining nutrients and is prone to accumulating metabolic waste. The ensuing IVD degeneration (IVDD) causes symptoms such as low back pain. Traditional Chinese medicine has a millennia-long history of treating IVDD, with the advantages of safety and few adverse effects. Based on prior pharmacological research, the Chinese herbal formula Elgucare is abundant in the nutrients required by the IVD and can improve blood circulation, accelerating the removal of metabolic waste from the IVD. This study used a 23 G needle to surgically induce IVDD in a rat model. Thirty rats were randomly assigned to five groups: one that underwent sham surgery (Sham), one with IVDD that was not fed Elgucare (EGC-0), and three with IVDD that were fed Elgucare at different concentrations for six weeks (EGC-L, EGC-M, and EGC-H). Study parameters, including total body weight, plantar sensitivity to pain, gait analysis, IVD thickness, and IVD morphology, were used to assess the effects of Elgucare on IVDs. Our results showed that administering Elgucare to rats effectively reduced plantar tingling and improved swing speed during gait analysis. Elgucare also accelerated increases in IVD thickness and increased the proportion of IVD that returned to normal cellularity. The possible benefits of Elgucare include alleviating pain, improving mobility, and accelerating IVD repair, indicating its potential for use in IVD therapy.

Keywords Elgucare · Chinese herbal medicine · Intervertebral disc degeneration · Pain relief · Intervertebral disc repair

Introduction

Intervertebral discs (IVDs) are found between vertebrae and are flexible joints that provide mobility to the spine and absorb and transfer loads. IVDs are the largest avascular tissue and comprise three sections: the central nucleus pulposus (NP), the annulus fibrosus (AF) situated around the NP, and superior and inferior cartilage endplates (CEP) above and below the NP that connect the IVD to the vertebrae. The NP is highly hydrated and gelatinous, comprising type II collagen and proteoglycans. The CEPs act as conduits to supply nutrients and remove metabolic waste (Molladavoodi et al. 2020). Any restrictions limiting the transport of nutrients and metabolic waste through the CEP places the IVD at risk of degeneration (IVDD) (Hassan et al. 2021). A degenerated IVD diminishes in height and herniates outward (Oichi et al. 2020). The protrusion or extrusion caused by IVDD can result in the contact or compression of spinal nerves near the dorsal root ganglion, resulting in inflammation and nerve root pain with symptoms including low back pain (LBP) with or without sciatica (Ye et al. 2022). The most common first-line treatment for acute and chronic LBP is non-steroidal anti-inflammatory drugs. Skeletal muscle relaxants (SMRs) and acetaminophen are inconsistently recommended for acute LBP. Moreover, there is limited consensus on using acetaminophen and antidepressants as second-line treatments for chronic LBP. Antibiotics,

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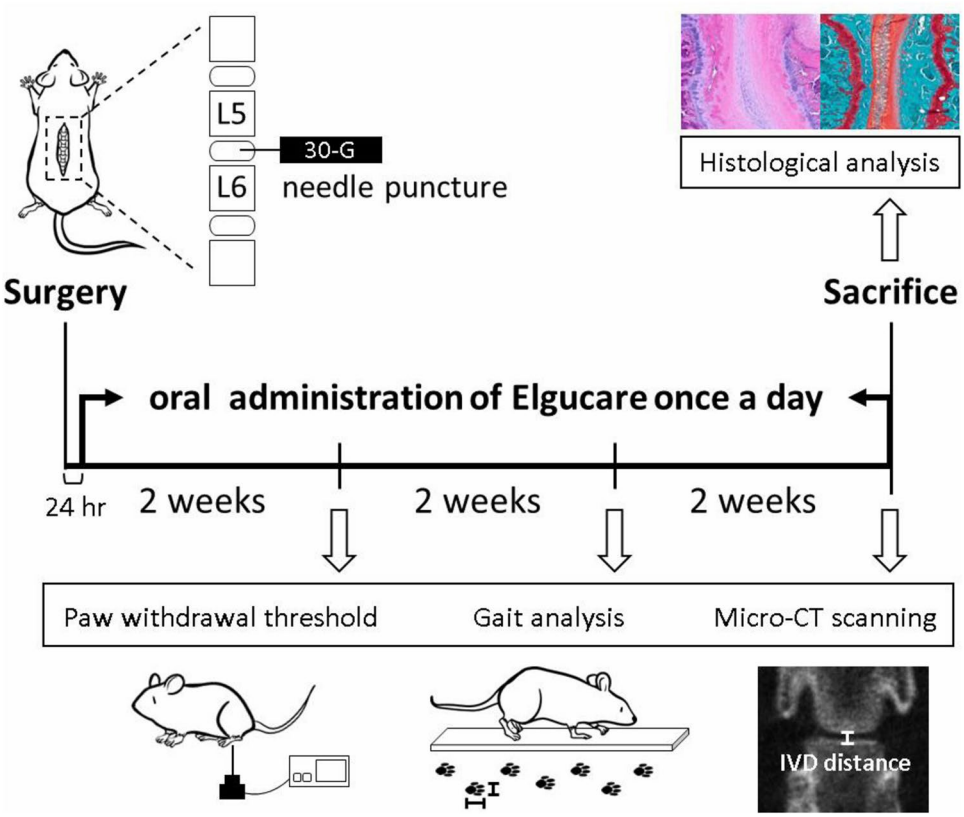


Fig. 1 Schematic of the study process

anticonvulsants, benzodiazepines, and oral corticosteroids are not recommended for acute and chronic LBP. SMRs for LBP are associated with an increased risk of adverse events (Price et al. 2022). Patients with severe disease and intractable pain require surgical management to remove the herniated portion of the IVD, preventing symptoms caused by persistent nerve compression.

Traditional Chinese medicine (TCM) takes a dialectical approach to diagnosis, encompassing disease prevention, treatment, and health protection. IVDD is a Bi, or "painful obstruction," syndrome. TCM has been used to prevent and treat such syndromes for millennia. Often given as a multi-component and multi-targeted treatment, Chinese herbal medicine can produce synergistic effects to exert its efficacy (Zhu et al. 2020). For example, research has shown that the Chinese herbal formula Fufangqishe-Pill, containing ligustrazine, can slow IVDD progression in a rat model by inhibiting inflammatory factors such as cyclooxygenase

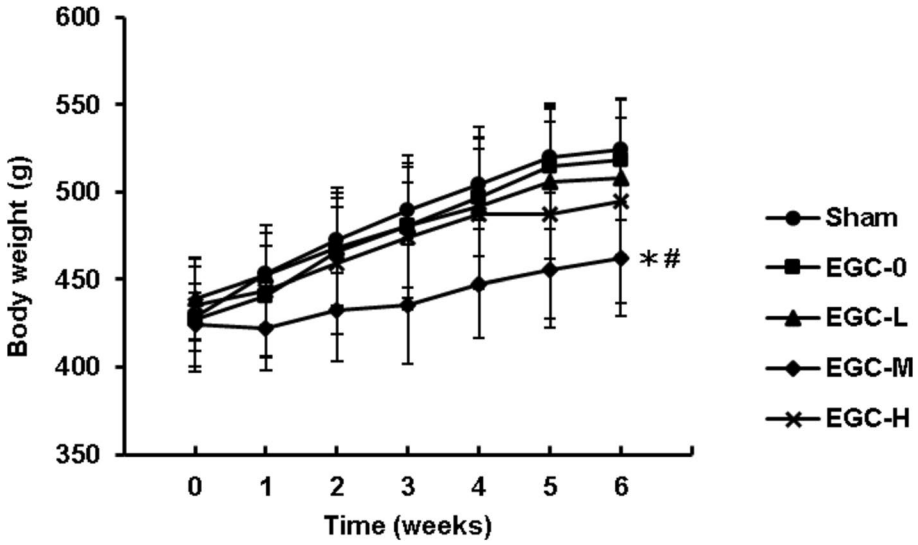


Fig. 2 Animal weight changes during postoperative weeks 0 to 6. Values are presented as mean ± SD ($n = 6$). Key: *, a significant difference ($p < 0.05$) compared to the EGC-0 group; #, a significant difference ($p < 0.05$) compared to the Sham group in a two-way ANOVA with Tukey's HSD test

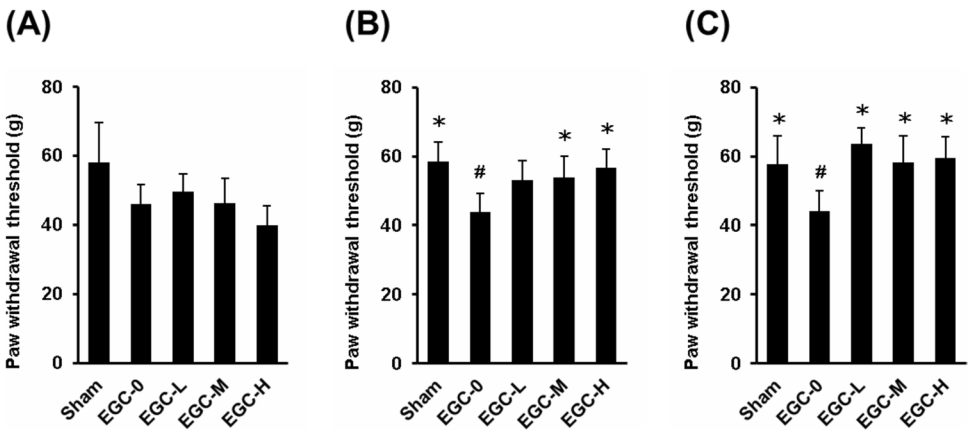


Fig. 3 Plantar tingling test results at postoperative weeks 2 (**A**), 4 (**B**), and 6 (**C**). Values are presented as mean ± SD ($n = 6$). Key: *, a significant difference ($p < 0.05$) compared to the EGC-0 group; #, a significant difference ($p < 0.05$) compared to the Sham group in a one-way ANOVA with Tukey's HSD test

2 (COX-2), interleukin (IL)-1β, and inducible nitric oxide synthase (iNOS) (Liu et al. 2019). TCM formulas can act to reduce inflammatory factors and mediators and reduce apoptosis and oxidative stress within NP cells. The treatment of IVDD using TCM is often combined with acupressure, acupuncture, Chinese manipulation, and physical therapy for greater effect (Zhu et al. 2020). A prospective observational study by Dai et al. (2020) reported that a Xiao Sui Hua He decoction could be an effective non-surgical treatment for lumbar disc herniation. They reported that 23 out of 69 patients showed significant resorption of NP protrusions. As described earlier, multiple studies have shown the potential of TCM in treating IVDD and herniated IVD. TCM offers the opportunity to reduce invasive surgical therapy and produces fewer adverse effects than Western medicine.

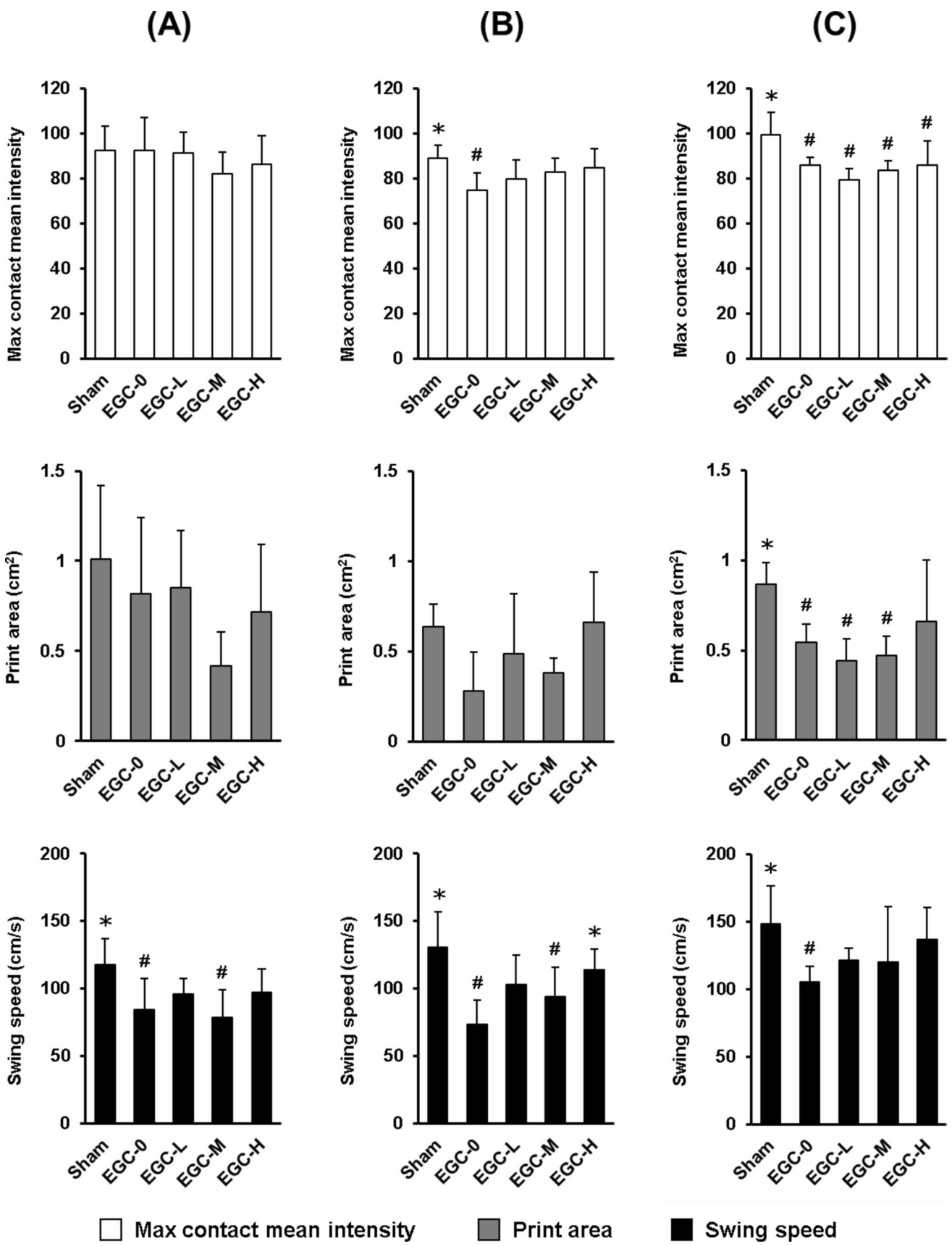
This study focuses on Elgucare, a Chinese herbal formula created by D.C. Botanical Biotechnology Co., Ltd. (New Taipei City, Taiwan). Prior clinical research has shown that this formula maintains IVD hydration, increases IVD height, reduces LBP, and improves quality of life (Lo et al. 2021). Jujubae Fructus (Da Zao) and Polygonati Odorati Rhizoma (Yu Zhu) contain abundant polysaccharides and proteoglycans (Li et al. 2007; Liu et al. 2021; Wang et al. 2023). While Da Zao's effect on collagen content remains to be determined, existing literature indicates that vitamin C and traumatic acid in Da Zao are associated with collagen synthesis (Gonzalez et al. 2023; Jabłońska-Trypuć et al. 2016; Liu et al. 2021). Salviae Miltiorrhizae Radix (Dan Shen) and Paederiae Herba (Ji Shi Teng) are commonly used to improve blood circulation and dispel blood stasis. Furthermore, a review by Shan et al. (2021) suggests that Dan Shen has benefits such as enhancing microcirculation; promoting vasodilation; preventing atherosclerosis; and anti-inflammatory, anti-tumor, blood pressure-lowering, and lipid-lowering activities. In the traditional theory of TCM, Lycopodii Herba (Shen Jin Cao) can be used to treat contusions and clots, relax muscles, relieve pain, dilate blood vessels, and improves blood circulation.

Its critical active component, lycopodium alkaloids, has been shown to have neuroprotective effects (Wang et al. 2021). Rhodiola Herba (Hong Jin Tian) can inhibit the degradation of hypoxia-inducible factor 1 (HIF-1) in the body (Liang et al. 2018), facilitating the maintenance of erythrocyte oxygen transport and promoting physiological functions. Astragali Radix (Huang Qi) and Glycyrrhizae Radix (Gan Cao) have anti-inflammatory, antioxidant, and neuroprotective properties (Guo et al. 2019; Sharifi-Rad et al. 2021). In addition, Gan Cao has traditionally been used to harmonize the effects of other ingredients. The aforementioned pharmacological research has shown that Elgucare's herbal formula is rich in the nutrients needed by IVDs and can promote blood circulation. By improving the CEPs' transport function, Elgucare enables nutrients to enter IVDs successfully and metabolic waste to be carried away. Both of these processes are believed to improve IVD health. This study uses a surgically-induced rat model of IVDD to evaluate Elgucare's effects on pain, motor ability, and IVD repair.

Methods and materials

Animal model

Thirty 8-week-old male Sprague-Dawley rats underwent 1–2 weeks of adaptive feeding before random group assignment for the testing process (Fig. 1). IVD damage was surgically induced in the rats. After anesthetization, the site of the L5–L6 vertebrae on the rat's dorsal spine was located, and a 1.5–2 cm incision was made. Laminotomy exposed the IVD, which was then destroyed with a 23 G needle. Finally, the wound was closed by suturing the muscles and skin. After antisepsis, the rat was left until it regained consciousness. Twenty-four hours after the operation, Elgucare was administered daily by tube feeding for six weeks, at which point the rats were sacrificed. The rats were permitted to eat and drink freely. Their clinical symptoms were observed


(A)
(B)
(C)
Max contact mean intensity
Print area (cm²)
Swing speed (cm/s)
Sham
EGC-0
EGC-L
EGC-M
EGC-H
*
#
Max contact mean intensity
Print area
Swing speed

◂**Fig. 4** Gait analysis results at postoperative weeks 2 (column **A**), 4 (column **B**), and 6 (column **C**). Values are presented as mean ± SD ($n = 6$). Key: *, a significant difference ($p < 0.05$) compared to the EGC-0 group; #, a significant difference ($p < 0.05$) compared to the Sham group in a one-way ANOVA with Tukey's HSD test

daily, and their weight was measured weekly. Plantar tingling tests, gait analysis, and micro-computed tomography scans were performed at weeks 2, 4, and 6. After the rats were sacrificed, vertebrae specimens were collected for histopathological analysis.

The study divided the test animals into five groups of six rats. The Sham (control) group underwent sham surgery with no IVD destruction. Rats with surgically induced IVD damage were divided into the EGC-0 group, which received no Elgucare feeding, and the EGC-L, EGC-M, and EGC-H groups, which received a daily feeding dose of Elgucare of 210 mg/kg body weight (low concentration), 315 mg/kg body weight (moderate concentration), and 470 mg/kg body weight (high concentration), respectively. This dose is 6.25 times the daily recommended dose for humans. The animal testing procedure fully complied with the Institutional Animal Care Use Committee guidelines and was performed by the Scientific Integration Design Service Corporation (Kaohsiung, Taiwan).

Plantar tingling assessment

A Plantar Test Unit (Ugo Basile, Italy) was used to analyze the response of the left hind paw to mechanical stimulation. Plantar tingling tests used a needle testing method, gradually increasing the pressure in grams applied to the plantar surface by the needle apparatus. An aesthesiometer automatically recorded the pressure eliciting paw withdrawal. The test animal was tested for plantar tingling sensitivity four times at each time point, with the mean value used as study data.

Gait analysis

The gait pattern of the left hind paw was analyzed at postoperative weeks 2, 4, and 6. As a rat traversed the glass walkway of the fully automated rat gait analysis system CatWalk XT (Noldus, The Netherlands), the system automatically captured the footprints and assessed motor ability. This study analyzed three parameters: the maximum contact mean intensity, which is defined as the average pressure when the plantar surface is in maximal contact with the glass walkway as the rat walks; the print area, which is the area calculated by multiplying the length and width of the footprint; and the swing speed, which measures the speed from the time that the test animal lifts its foot to the next time that the foot is on the ground.

IVD thickness

A μCT-100 micro-computed tomography system DELPet-μCT (DELBio, Taiwan) was used to assess IVD morphology at postoperative weeks 2, 4, and 6. At weeks 2 and 4, imaging was performed in vivo after anesthetization; at week 6, vertebral columns collected after sacrifice were imaged. IVD thickness was measured in μCT images as the distance at its center between the vertebrae above and below it.

Histopathological analysis

The rats were sacrificed at postoperative week 6, and their vertebrae were collected, fixed in 10% neutral buffered formalin, and embedded in paraffin. Three-micrometer sections were cut using a microtome, mounted on a mounting slide, and stained with either hematoxylin and eosin (H&E) or safranin O/fast green. Histologic and cartilage tissue morphology were observed using a whole slide scanner and interpreted for results. H&E staining results were interpreted according to cellularity, whereas safranin O staining results follow the Ohnishi et al. (2016) system.

Statistical analysis

Data are represented as mean ± standard deviation (SD). Statistical analysis used one-way or two-way analysis of variance (ANOVA) as the data required. Post-hoc analyses used Tukey's honestly significant difference (HSD) test to compare means between the experimental and control groups. A $p < 0.05$ indicates a significant difference between groups.

Results

Weight changes

Rats were weighed weekly during postoperative weeks 0–6 (Fig. 2). No significant differences were observed between the Sham, EGC-0, EGC-L, and EGC-H groups. The EGC-M group showed significantly reduced weight accumulation ($p < 0.05$) compared to the Sham and EGC-0 groups. Despite the EGC-M rats weighing between 400 and 550 g by week 6, they showed an increasing trend in weight gain over time. After sacrifice, the organs appeared grossly normal,

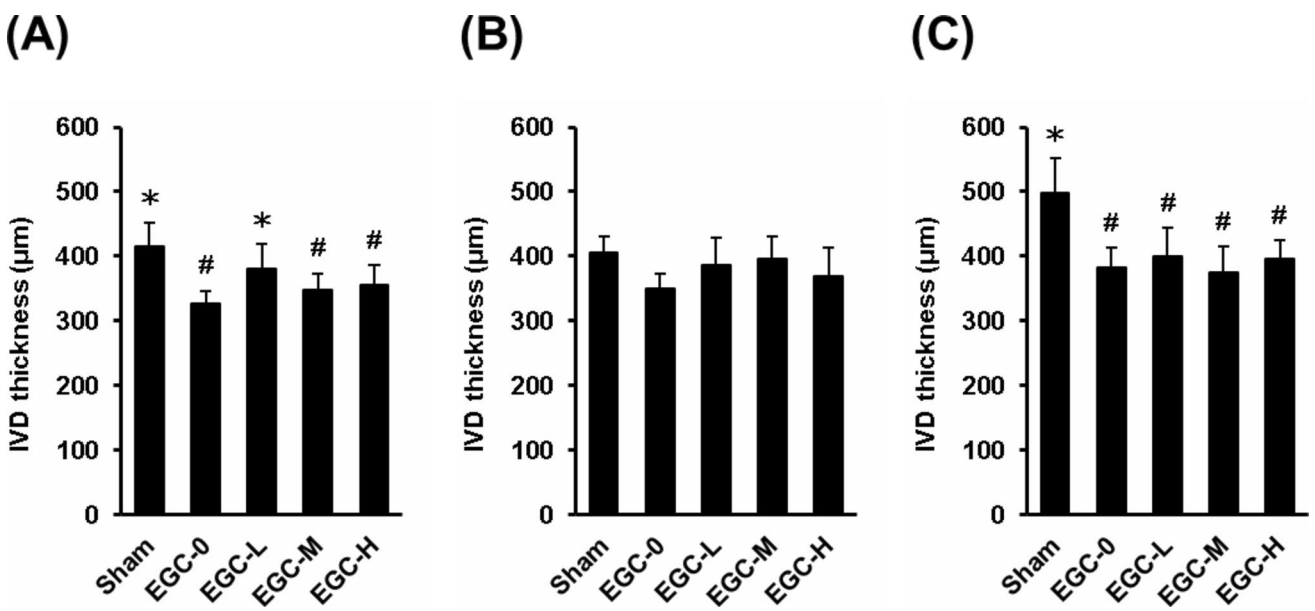


Fig. 5 IVD thicknesses at postoperative weeks 2 (**A**), 4 (**B**), and 6 (**C**). Values are presented as mean ± SD ($n = 6$). Key: *, a significant difference ($p < 0.05$) compared to the EGC-0 group; #, a significant difference ($p < 0.05$) compared to the Sham group in a one-way ANOVA with Tukey's HSD test

suggesting that Elgucare feeding had no adverse effects on growth.

Plantar tingling

This study used a needle testing method to assess the rat's response to mechanical stimulation of their plantar surface by applying weight to the plantar surface of the left hind paw and recording the force that elicited the paw withdrawal reflex (Fig. 3). At postoperative week 2, there were no significant differences between groups. At weeks 4 and 6, paw withdrawal occurred at a stimulus of approximately 44 g for rats in the EGC-0 group compared to approximately 58 g for the Sham group. This difference reflects significantly greater pain severity in the EGC-0 group ($p < 0.05$). At week 4, paw withdrawal thresholds of the EGC-M and EGC-H groups were 54 ± 6 g and 57 ± 5 g, respectively, significantly higher than the EGC-0 group ($p < 0.05$).

After feeding for six weeks, all three EGC-fed groups differed significantly from the EGC-0 group ($p < 0.05$) in the paw withdrawal threshold, which had increased to 63 ± 5 (EGC-L), 58 ± 8 (EGC-M), and 60 ± 6 g (EGC-H). There was no difference between the EGC-fed groups and the Sham group. According to the plantar tingling data, the pain in EGC-fed groups showed substantial relief as feeding duration increased and even approached that of the Sham group after administering Elgucare for six weeks. These findings indicate the effectiveness of Elgucare in alleviating pain.

Gait analysis

A fully automated rat gait analysis system was used to analyze the max contact mean intensity, print area, and swing speed of the left hind paw while walking (Fig. 4). At postoperative week 2, there were no significant differences in the maximum contact mean intensities between groups. At week 4, the mean intensity of the EGC-0 group was significantly lower than that of the Sham group ($p < 0.05$). At week 6, the mean intensities of the EGC-0, EGC-L, EGC-M, and EGC-H groups were all significantly lower than that of the Sham group ($p < 0.05$).

There were no significant differences in the print area across groups at postoperative weeks 2 and 4. At postoperative week 6, the print areas of the EGC-0, EGC-L, and EGC-M groups were significantly lower than that of the Sham group ($p < 0.05$). The study data showed no improvement in rat maximum contact mean intensity and print area after administering Elgucare.

Swing speed analysis showed that the EGC-0 group differed significantly from the Sham group at postoperative weeks 2, 4, and 6 (all $p < 0.05$). At postoperative weeks 2 and 4, swing speed was significantly lower for the EGC-M group than for the Sham group ($p < 0.05$). However, at week 4, the high-dose EGC-H group's swing speed was 114 ± 16 cm/s, significantly higher than the EGC-0 group's 74 ± 18 cm/s ($p < 0.05$), indicating that Elgucare aids improvement in swing speed.

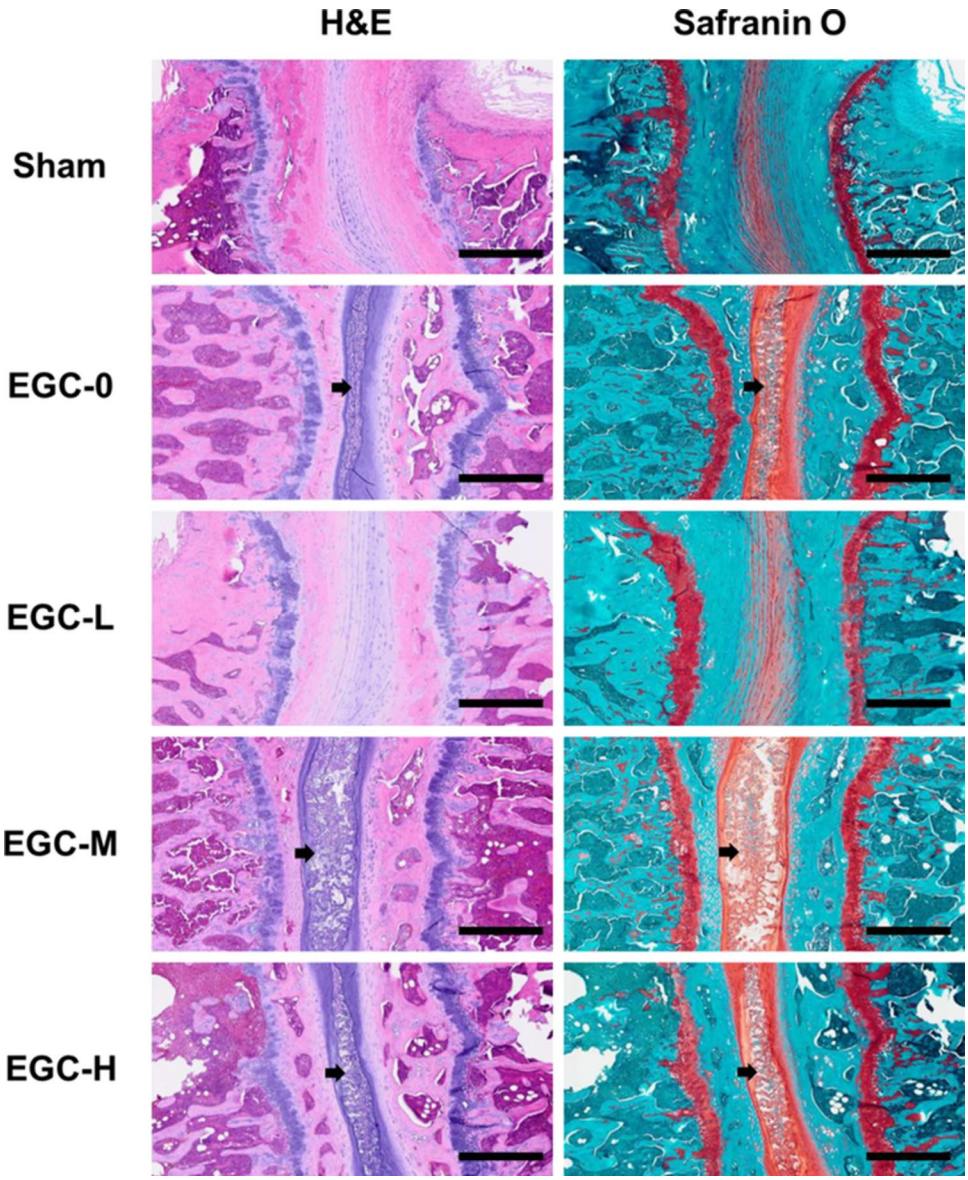


Fig. 6 Histopathological analysis results at postoperative week 6. Arrows indicate sites of cell aggregation. Scale bars = 500 μm

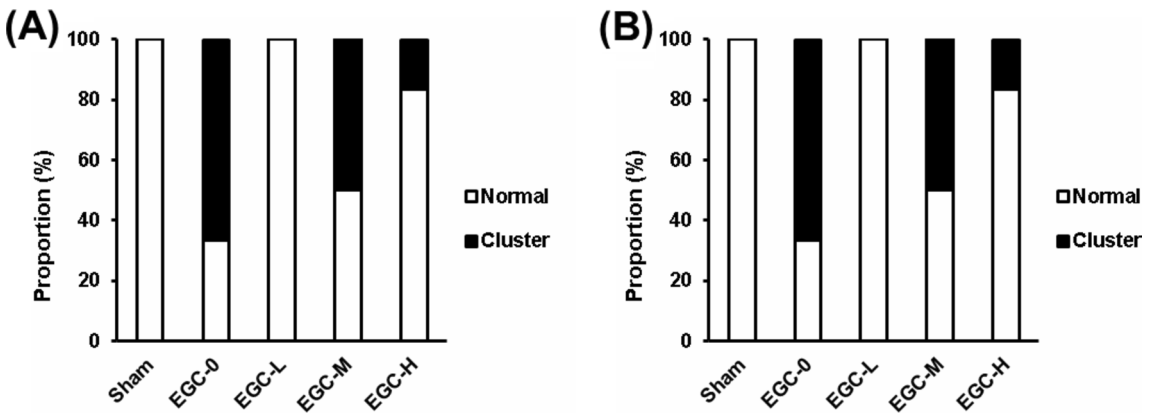


Fig. 7 Proportions of H&E (**A**) and safranin O/fast green (**B**) staining interpretations at postoperative week 6

IVD thickness

Micro-computed tomography was used to scan and record images of the vertebral column and measure the IVD thickness (Fig. 5). At week 2, IVDs were significantly narrower in the EGC-0, ECG-M, and EGC-H groups than in the Sham group ($p < 0.05$). However, the IVD thickness for the EGC-L group was approximately 381 ± 38 μm, significantly higher than the EGC-0 group's 328 ± 19 μm ($p < 0.05$) but not significantly different from the Sham group. At week 4, there were no significant differences among groups. At week 6, the IVD thicknesses of the EGC-0, EGC-L, EGC-M, and EGC-H groups were significantly narrower than that of the Sham group. The Sham group's IVD thickness was approximately 498 ± 53 μm by week 6, thicker than in weeks 2 and 4, which is believed to reflect growth in rat body habitus with time. At postoperative weeks 2, 4, and 6, IVD thicknesses in the EGC-0 group were 328 ± 19, 349 ± 24, and 382 ± 33 μm, respectively, indicating that the IVD thickens with time, a phenomenon attributed to intrinsic repair after damage. However, by week 2, the IVDs of the EGC-L, EGC-M, and EGC-H groups had already reached thicknesses of approximately 350–400 μm, approaching that of the EGC-0 group at week 6.

Histopathological analysis

The rats were sacrificed at postoperative week 6, and their vertebrae were collected for histopathological examination. H&E staining was used to observe histopathological morphology, while safranin O/fast green staining was used to observe the cartilage's histopathological morphology (Fig. 6). For the EGC-0 group, the H&E stained sections showed many aggregated cells, primarily within cartilage vaults. Further examination using the safranin O stain showed chondrocyte aggregation in the NP. For the EGC-M and EGC-H groups, cell aggregation was also noted in several rats. However, no cell aggregation was observed in the stained sections of the Sham and EGC-L groups, which showed normal IVD histological morphology.

This study destroyed the IVD by needle puncture, and the results showed that histological morphology remained normal in the AF. Therefore, we will elaborate only on the NP findings. H&E and safranin O staining results are shown in Fig. 7; both sets of findings agree after interpretation. All IVDs showed normal histology in the Sham group. Cell aggregation was observed in 67% of the EGC-0 specimens; only 33% showed normal morphology. The proportions of rats with normal histology in the EGC-L, EGC-M, and EGC-H groups were 100%, 50%, and 83%, respectively, indicating that administering Elgucare increased the likelihood that IVD histology returned to normal.

Discussion

Research has shown that puncturing and destroying rat IVDs using a 0.8 mm external needle width (21 G) results in acute to moderate degeneration of the IVD one week after surgery. In contrast, a 0.5 mm exterior needle width (25 G) induces progressive IVD degeneration (Elmounedi et al. 2022; Glaeser et al. 2020). This study used a 0.6 mm (23 G) external needle width to puncture and destroy the IVD. Since the needle diameter measured 0.6 mm, the nociceptive effects should occur more slowly, modeling chronic pain caused by degeneration. Therefore, the plantar tingling findings at postoperative week 2 did not differ from those of the Sham group (Fig. 3). In the published literature, a human clinical trial of Elgucare asked IVDD patients to record pain scores on a survey scale. Its results showed a significant improvement in pain after taking Elgucare (Lo et al. 2021). However, pain scores in clinical research are easily influenced by age, sex, psychological state, and other such factors, with correspondingly larger discrepancies in data. This study used scientific methodology to measure pain data in rats, finding that after 4–6 weeks of Elgucare administration, the pain experienced by the rats was relieved. These findings are consistent with those of the clinical trial. In addition, many studies have shown that Ji Shi Teng, Shen Jin Cao, and Gan Cao have analgesic effects (Hasan et al. 2021; Wang et al. 2021; Xiao et al. 2019), suggesting that Elgucare has great potential as an analgesic.

The gait cycle is typically divided into two distinct phases, one in which the plantar surface presses against the ground in support (stance phase), the other in which the plantar surface of the paw is lifted into the air to stride forward (swing phase) (Lai et al. 2009). Of the parameters assessed in this study, maximum contact mean intensity and print area belong to the former category, and swing speed to the latter. Past studies have shown no significant differences in gait analysis parameters related to stepping (such as average and minimal intensity) after puncture and destruction of the L5–L6 IVD in rats. The groups with damaged IVDs showed significant decreases in stride length and swing speed compared to the Sham group (Miyagi et al. 2013), indicating that stride-related parameters may be more suitable for assessing motor ability in rats with IVD damage. Swing speed is the speed of the striding paw as it swings forward until it steps on the ground again. This study found that swing speed significantly increased after administering Elgucare. Elgucare may improve IVD elasticity and spine stability and might, therefore, improve back pain. Therefore, Elgucare can aid in improving motor ability in IVDD

animals. Gait analysis comprises many parameters, such as stride length, stand time, and duty cycle (Miyagi et al. 2011). Future research may examine the other parameters more broadly to assess the effectiveness of Elgucare in improving motor ability.

Rats administered Elgucare required only two weeks to achieve an IVD thickness comparable to that of non-Elgucare rats at week 6. It is believed that initiating Elgucare administration 24 h after surgery accelerates the growth in IVD thickness within the initial two weeks. This data suggests that ingesting Elgucare can increase the rate of rat IVD repair. Since this study did not observe IVD thickness changes during the initial two weeks among rats administered Elgucare, it is difficult to assess the potential of Elgucare for accelerating repair. This aspect could be an avenue for future research.

In histopathological analysis, cell aggregation is commonly observed in degenerating IVD tissue, and the cells involved are primarily those associated with immune function or proliferation (Tamang 2017). Therefore, we may infer that cell aggregation reflects a response in which the body attempts to repair the IVD tissue. In this study, when IVDD rats did not receive any therapeutic intervention, 33% ($n=6$, comprising EGC-0) of rat IVDs showed no cell aggregation at postoperative week 6. In contrast, the proportion of IVDs without cell aggregation reached 78% among rats administered Elgucare ($n=18$, comprising ECG-L, EGC-M, and EGC-H). While the principles behind cell aggregation remain unclear, many studies have already used it to determine the extent of IVD damage (Johnson et al. 2001; Masuda et al. 2005; Ohnishi et al. 2016; Yang et al. 2009). Because the IVD is an avascular tissue, it must rely on diffusion through the CEP to transport nutrients and metabolites. When oxygen and nutrition are insufficient and metabolic waste accumulates, the IVD is limited in regenerating and repairing itself after damage(Ma et al. 2019). However, Elgucare can accelerate injury repair, indicating its potential for maintaining IVD health.

Reviewing published literature shows that laboratory research has primarily focused on IVD repair, with pain suppression being comparatively overlooked. In contrast, clinical research emphasized urgent pain relief for the patient, focusing less on methods for IVD repair(Lyu et al. 2021). While basic research and clinical applications have different emphases, it is evident that relieving pain and promoting repair are both issues that require attention in IVDD. This study showed that Elgucare could assist in pain relief and repair and, therefore, has potential as a therapeutic option for IVDD.

While this study found that the Chinese herbal formula of interest can benefit the IVDD patient, certain limitations still exist. Firstly, this is an animal study using a rat model. The impact on a vertebral column in the rat differs from the stresses on human IVDs in the upright posture but may serve as a basis for comparison. Secondly, this study used white male rats without considering hormonal influences on IVD damage and repair. Nevertheless, studying animals of one sex allows for understanding trends within a homogenous group. Thirdly, each group in this study contained only six test animals. Therefore, findings still require validation from large-scale trials in the future.

Conclusions

This study used a surgically induced rat IVDD model to evaluate the effectiveness of the Chinese herbal formula Elgucare. Its results show that Elgucare could provide pain relief, improve motor ability, and, most importantly, accelerate IVD damage repair in rats with IVDD. These findings indicate that Elgucare can effectively maintain IVD health. Future research may further investigate how Elgucare repairs the IVD, which will undoubtedly benefit IVD therapy.

Author contributions TKC conceived the study, acquired and analyzed the data, drafted and revised the manuscript, and validated the data; YCL conceived the study, acquired and analyzed the data, drafted and revised the manuscript, and validated the data; TYC acquired and analyzed the data, drafted the manuscript, and validated the data; YTC conceived the study, acquired and analyzed the data, and drafted the manuscript; CCC conceived the study, acquired and analyzed the data, drafted and revised the manuscript, validated the data, and supervised the study. All authors read and approved the final manuscript.

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Declarations

Ethical approval The animal testing procedure fully complied with the Institutional Animal Care Use Committee guidelines and was performed by the Scientific Integration Design Service Corporation (Kaohsiung, Taiwan).

Conflict of interest Ting-Kuo Chang has no conflict of interest. Yueh-Ching Liu has no conflict of interest. Tzu-Yun Chien has no conflict of interest. Yu-Ting Chen has no conflict of interest. Ching-Chen Chen has no conflict of interest.

Informed consent Consent was not required because this study involved no human subjects.

References

Dai F, Dai YX, Jiang H, Yu PF, Liu JT (2020) Non-surgical treatment with XSHHD for ruptured lumbar disc herniation: a 3-year prospective observational study. BMC Musculoskelet Disord 21:1–8

Elmounedi N, Bahloul W, Turki M, Amri R, Aoui M, Elbaya W, Keskes H (2022) Impact of needle size on the onset and the progression of disc degeneration in rats. Pain Physician 25:509–517

Guo Z, Lou Y, Kong M, Luo Q, Liu Z, Wu J (2019) A systematic review of phytochemistry, pharmacology and pharmacokinetics on astragali radix: implications for astragali radix as a personalized medicine. Int J Mol Sci 20:1463

Glaeser JD, Tawackoli W, Ju DG et al (2020) Optimization of a rat lumbar IVD degeneration model for low back pain. JOR Spine 3:e1092

Gonzalez MJ, Miranda-Massari JR, Olalde J (2023) Vitamin C and mitochondrial function in health and exercise. In: Ostojic SM (ed) Molecular nutrition and mitochondria. Academic Press, pp 225–242

Hasan MK, Ara I, Mondal MSA, Kabir Y (2021) Phytochemistry, pharmacological activity, and potential health benefits of *Glycyrrhiza glabra*. Heliyon 7:e07240

Hassan CR, Lee W, Komatsu DE, Qin YX (2021) Evaluation of nucleus pulposus fluid velocity and pressure alteration induced by cartilage endplate sclerosis using a poro-elastic finite element analysis. Biomech Model Mechanobiol 20:281–291

Johnson WE, Eisenstein SM, Roberts S (2001) Cell cluster formation in degenerate lumbar intervertebral discs is associated with increased disc cell proliferation. Connect Tissue Res 42:197–207

Jabłońska-Trypuć A, Pankiewicz W, Czerpak R (2016) Traumatic acid reduces oxidative stress and enhances collagen biosynthesis in cultured human skin fibroblasts. Lipids 51:1021–1035

Lai DT, Begg RK, Palaniswami M (2009) Computational intelligence in gait research: a perspective on current applications and future challenges. IEEE Trans Inf Technol Biomed 13:687–702

Li J-W, Chen Y-Y, Ding S-D, Zhang LF (2007) Isolation and analysis of a novel protoglycan from *Zizyphus jujuba* cv. Jinsixiaozao. J Food Drug Anal 15:9

Liang ZL, Zhang XY, Wang F, Zhang K, Liu HF, Liu HL (2018) Understanding molecular mechanisms of *Rhodiola rosea* for the treatment of acute mountain sickness through computational approaches (a STROBE-compliant article). Medicine 97:e11886

Liu S, Cheng Y, Tan Y, Dong J, Bian Q (2019) Ligustrazine prevents intervertebral disc degeneration via suppression of aberrant TGFβ activation in nucleus pulposus cells. Biomed Res Int 2019:5601734

Liu S-J, Lv Y-P, Tang Z-S, Zhang Y (2021) *Ziziphus jujuba* Mill., a plant used as medicinal food: a review of its phytochemistry, pharmacology, quality control and future research. Phytochem Rev 20:507–541

Lo W-C, Chen YT, Chen CC (2021) The effects of Elgucare on degenerated intervertebral disc-induced low back pain and disc regeneration: a clinical trial. Comput Math Methods Med

Lyu F-J, Cui H, Pan H, Mc Cheung K, Cao X, Iatridis JC, Zheng Z (2021) Painful intervertebral disc degeneration and inflammation:from laboratory evidence to clinical interventions. Bone Res 9:7

Ma K, Chen S, Li Z, Deng X, Huang D, Xiong L, Shao Z (2019) Mechanisms of endogenous repair failure during intervertebral disc degeneration. Osteoarthr Cartil 27:41–48

Masuda K, Aota Y, Muehleman C, Imai Y, Okuma M, Thonar EJ, Andersson GB, An HS (2005) A novel rabbit model of mild, reproducible disc degeneration by an anulus needle puncture: correlation between the degree of disc injury and radiological and histological appearances of disc degeneration. Spine 30:5–14

Miyagi M, Ishikawa T, Kamoda H et al (2011) Assessment of gait in a rat model of myofascial inflammation using the CatWalk system. Spine 36:1760–1764

Miyagi M, Ishikawa T, Kamoda H et al (2013) Assessment of pain behavior in a rat model of intervertebral disc injury using the CatWalk gait analysis system. Spine 38:1459–1465

Molladavoodi S, McMorran J, Gregory D (2020) Mechanobiology of annulus fibrosus and nucleus pulposus cells in intervertebral discs. Cell Tissue Res 379:429–444

Ohnishi T, Sudo H, Iwasaki K, Tsujimoto T, Ito YM, Iwasaki N (2016) In vivo mouse intervertebral disc degeneration model based on a new histological classification. PLoS One 11:e0160486

Oichi T, Taniguchi Y, Oshima Y, Tanaka S, Saito T (2020) Pathomechanism of intervertebral disc degeneration. JOR Spine 3:e1076

Price MR, Cupler ZA, Hawk C, Bednarz EM, Walters SA, Daniels CJ (2022) Systematic review of guideline-recommended medications prescribed for treatment of low back pain. Chiropr Man Ther 30:26

Shan X-X, Hong B-Z, Liu J, Wang GK, Chen WD, Yu NJ, Peng DY, Wang L, Zhang CY (2021) Review of chemical composition, pharmacological effects, and clinical application of Salviae Miltiorrhizae Radix et rhizoma and prediction of its Q-markers. China J Chin Mater Med 46:5496–5511

Sharifi-Rad J, Quispe C, Herrera-Bravo J et al (2021) Glycyrrhiza genus: enlightening phytochemical components for pharmacological and health-promoting abilities. Oxid Med Cell Longev 2021:1–20

Tamang BK (2017) The role of cell clusters in intervertebral disc degeneration and its relevance behind repair. Arch Med 3:15

Wang B, Guan C, Fu Q (2021) The traditional uses, secondary metabolites, and pharmacology of Lycopodium species. Phytochem Rev 21:1–79

Wang S, He F, Wu H, Xiang F, Zheng H, Wu W, Li S (2023) Health-promoting activities and associated mechanisms of Polygonati rhizoma polysaccharides. Molecules 28:1350

Xiao M, Ying L, Li S, Fu X, Du G (2019) Progress on research and development of Paederia scandens as a natural medicine. Int J Clin Exp Med 12:158–167

Yang F, Leung VY, Luk KD, Chan D, Cheung KM (2009) Mesenchymal stem cells arrest intervertebral disc degeneration through chondrocytic differentiation and stimulation of endogenous cells. Mol Ther 17:1959–1966

Ye F, Lyu FJ, Wang H, Zheng Z (2022) The involvement of immune system in intervertebral disc herniation and degeneration. JOR Spine 5:e1196

Zhu L, Yu C, Zhang X, Yu Z, Zhan F, Yu X, Wang S, He F, Han Y, Zhao H (2020) The treatment of intervertebral disc degeneration using traditional Chinese Medicine. J Ethnopharmacol 263:113117