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**Figure S1** The HPLC analysis of quality control indexes of LWDHD namely morroniside (A),

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loganin (B), and paeoniflorin (C), in plasma of IVDD mice after treatment with these LWDHD

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formulations for 1 and 8 weeks, using HPLC. Data are shown as mean  $\pm$  sem (n = 6). \*denotes

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a statistically significant difference in comparison to the LWDHD group (\*\* $p < 0.01$ ). \* indicates

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a significant difference compared with the LWDHD group (\* $p < 0.05$ , \*\* $p < 0.01$ ), while % signifies

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a significant difference compared with mice that received the same formulation for 1 week (% $p$

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< 0.01).

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**Abbreviations:** HPLC, High Performance Liquid Chromatography; LWDHD, Liuwei Dihuang

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Decoction; IVDD, Intervertebral disc degeneration.

11 **Table S1** Scoring criteria of the effect of LWDHD containing different doses of CO on IVD  
 12 tissues.

Item	Scoring criteria
Upright behavior (0-3)	Number of upright behaviors $\leq 25$ , score 0 point; $> 25$ and $\leq 30$ , score 1 point; $> 30$ and $\leq 35$ , score 2 points; $> 35$ , score 3 points.
Von-Frey test (0-3)	Von-Frey test $\leq 0.6$ , score 0 point; $> 0.6$ and $\leq 0.9$ , score 1 point; $> 0.9$ and $\leq 1.2$ , score 2 points; $> 1.2$ , score 3 points.
Total distance (0-3)	Total distance $> 32$ , score 0 point; $> 30$ and $\leq 32$ , score 1 point; $> 28$ and $\leq 30$ , score 2 points; $\leq 28$ , score 3 points.
Central motion time (0-3)	Central motion time $\leq 20$ , score 0 point; $> 20$ and $\leq 30$ , score 1 point; $> 30$ and $\leq 40$ , score 2 points; $> 40$ , score 3 points.
Distance relative to the center (0-3)	Distance relative to the center $> 2.5$ , score 0 point; $> 2$ and $\leq 2.5$ , score 1 point; $> 1.5$ and $\leq 2$ , score 2 points; $\leq 1.5$ , score 3 points.
Histological grading scale (0-3)	Histological grading scale $\leq 2.5$ , score 0 point; $> 2.5$ and $\leq 3$ , score 1 point; $> 3$ and $\leq 3.5$ , score 2 points; $> 3.5$ , score 3 points.
AGGRECAN (0-3)	AGGRECAN is a key element of the extracellular matrix found in AF. Tissues that contain elevated amounts of AGGRECAN tend to receive higher ratings. Relative optical density: $\leq 0.5$ , scores 0 point; $> 0.5$ and $\leq 1$ , scores 1 point; $> 1$ and $\leq 1.5$ , scores 2 points; $> 1.5$ , scores 3 points.
COL2 (0-3)	COL2 is the primary structural component found in medial AF. Tissues that contain elevated amounts of COL2 tend to receive higher ratings. Relative optical density: $\leq 0.3$ , score 0 point; $> 0.3$ and $\leq 0.6$ , score 1 point; $> 0.6$ and $\leq 0.9$ , score 2 points; $> 0.9$ , score 9 points.
MMP13 (0-3)	MMP13 is the most studied matrix metalloproteinase that cleaves COL2 in the AF. Tissues with higher levels of MMP13 have lower scores. Relative optical density: $> 1.2$ , scores 0 point; $> 0.8$ and $\leq 1.2$ , scores 1 point; $> 0.4$ and $\leq 0.8$ , scores 2 points; $\leq 0.4$ , scores 3 points.

TUNEL	TUNEL assay is used to detect apoptosis, with higher scores resulting in higher degrees of apoptosis.
(0-3)	Positive cell rate: > 15%, score 0 point; > 10% and ≤ 15%, score 1 point; > 5% and ≤ 10%, score 2 points; ≤ 5%, score 3 points.
Ki-67	Ki-67 is a nuclear protein that is associated with the activity of cell proliferation. Tissues containing high amounts of Ki-67 tend to receive higher ratings.
(0-3)	Relative optical density: ≤ 0.25, score 0 point; > 0.25 and ≤ 0.5, score 1 point; > 0.5 and ≤ 0.75, score 2 points; > 0.75, score 3 points.
TrkA	TrkA is one of the cell surface receptors for NGF and is associated with pain. The more TrkA-containing tissue, the lower the score.
(0-3)	Relative optical density: > 30, scores 0 point; > 20 and ≤ 30, scores 1 point; > 10 and ≤ 20, scores 2 points; ≤ 10, scores 3 points.
CASPASE1	Caspase1 is a cysteine protease that induces pyroptosis after its activation by various inflammasomes. Tissues with higher levels of Caspase1 have lower scores.
(0-3)	Relative optical density: > 15, scores 0 point; > 10 and ≤ 15, scores 1 point; > 5 and ≤ 10, scores 2 points; ≤ 5, scores 3 points.
GSDMD	GSDMD is a pore-forming protein that mediates pyroptosis. Tissues with higher levels of GSDMD have lower scores.
(0-3)	Relative optical density: > 15, scores 0 point; > 10 and ≤ 15, scores 1 point; > 5 and ≤ 10, scores 2 points; ≤ 5, scores 3 points.
IL-1β	IL-1β is a member of the IL-1 cytokine family and is involved in pyroptosis. Tissues with higher levels of IL-1β have lower scores.
(0-3)	Relative optical density: > 2, scores 0 point; > 1.5 and ≤ 2, scores 1 point; > 1 and ≤ 1.5, scores 2 points; ≤ 1, scores 3 points.
NRF2 (S40)	NRF2 (S40) is a transcription factor that regulates the expression of many antioxidant enzymes. NRF2 (S40) can play an important role in adaptive responses to oxidative stress. Tissues that contain elevated amounts of NRF2 (S40) tend to receive higher ratings.
(0-3)	

	Relative optical density: $\leq 0.5$ , score 0 point; $> 0.5$ and $\leq 1$ , score 1 point; $> 1$ and $\leq 1.5$ , score 2 points; $> 1.5$ , score 3 points.
KEAP1 (0-3)	KEAP1 is an important regulator of antioxidant stress response. Tissues with higher levels of KEAP1 have lower scores. Relative optical density: $> 2$ , scores 0 point; $> 1.5$ and $\leq 2$ , scores 1 point; $> 1$ and $\leq 1.5$ , scores 2 points; $\leq 1$ , scores 3 points.
p-I- $\kappa$ B (0-3)	I- $\kappa$ B is an inhibitor of NF- $\kappa$ B that remains inactive in the resting state. I- $\kappa$ B is phosphorylated and loses its inhibitory effect on NF- $\kappa$ B, thereby allowing it to enter the nucleus to regulate gene expression. Tissues with higher levels of p-I- $\kappa$ B have lower scores. Relative optical density: $> 1.5$ , scores 0 point; $> 1$ and $\leq 1.5$ , scores 1 point; $> 0.5$ and $\leq 1$ , scores 2 points; $\leq 0.5$ , scores 3 points.
p-P65 (0-3)	P65 is an important component of the NF- $\kappa$ B signaling pathway and p-P65 can be used as a marker of NF- $\kappa$ B signaling pathway activation. Tissues with higher levels of p-P65 have lower scores. Relative optical density: $> 6$ , scores 0 point; $> 4$ and $\leq 6$ , scores 1 point; $> 2$ and $\leq 4$ , scores 2 points; $\leq 2$ , scores 3 points.

13 **Abbreviations:** LWDHD, Liuwei Dihuang Decoction; CO, *Cornus officinalis*; IVD,  
14 Intervertebral disc; AF, Annulus fibrosus; COL2, Collagen 2; MMP13, matrix metalloproteinase  
15 13; TrkA, Tyrosine kinase A; NGF, Nerve growth factor; GSDMD, Gasdermin D; IL-1 $\beta$ ,  
16 Interleukin-1 $\beta$ ; NRF2, E2-related factor 2; KEAP1, Kelch-like ECH-associated protein 1; p-I- $\kappa$ B;  
17 phospho-I- $\kappa$ B; NF- $\kappa$ B, Nuclear factor- $\kappa$ B; p-P65, phospho-P65.

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