

## • 文献综述 •

## 中药单体影响腰椎间盘突出炎性损伤的机制研究进展

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**[摘要]** 椎间盘退变机制复杂,近年来研究发现炎症反应通过诱导细胞外基质紊乱、氧化应激、调控细胞衰老和凋亡等途径参与椎间盘退变的病理过程,并可成为药物干预的重要靶点。目前研究提示活血化瘀、补益肝肾类中药单体可通过抑制炎症反应延缓椎间盘退变,减轻腰椎间盘突出症的临床症状,延缓病理过程。对中药单体影响腰椎间盘突出炎性损伤的机制进行深入研究,或可为腰椎间盘突出症的治疗提供新的方向。

**[关键词]** 腰椎间盘突出症;炎症反应;中药单体

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## Research Progress of Traditional Chinese Medicine Monomer in Inhibiting Inflammatory Injury of Lumbar Disc Herniation

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**Abstract** The mechanism of intervertebral disc degeneration (IVDD) is complex. Recent studies have shown that the inflammatory response drives the pathology of Lumbar disc herniation (LDH) by disrupting the extracellular matrix, inducing oxidative stress, and regulating cell senescence and apoptosis, which can be potential targets for drug intervention. Current research shows traditional Chinese medicine (TCM) monomers, which aim to activate blood circulation and tonify the liver and kidney, can inhibit inflammation. This inhibition can delay the progression of IVDD, alleviate the symptoms of LDH and slow the pathologic process. In-depth exploration of the mechanism by which TCM monomers influence the inflammatory injury of lumbar intervertebral discs may provide new directions for the treatment of LDH.

**Keywords:** lumbar disc herniation; inflammatory reaction; traditional Chinese medicine monomers

腰椎间盘突出症是常见疾病,全球患病率约为8%~25%,易发人群年龄为25~55岁<sup>[1]</sup>。保守治疗及手术干预可缓解症状,但未从根本上延缓椎间盘退变,且可能伴随残余神经症状。研究显示炎症与椎间盘退变密切相关,是潜在治疗途径<sup>[2]</sup>。抑制炎症及炎症因子释放,可调控细胞衰老、凋亡和氧化应激等过

程,改善腰椎间盘突出症及相关疼痛<sup>[3-5]</sup>。中药单体因其抗炎特性,在靶向炎症改善椎间盘退变上展现出独特潜力。现就近年来中药单体调控腰椎间盘突出炎性损伤机制影响腰椎间盘突出症的研究综述如下。

### 1 炎症与椎间盘退变

椎间盘内免疫炎症反应形成炎性微环境,导致微环境失调、细胞损伤,是椎间盘退变的关键因素<sup>[6]</sup>,主要表现在诱导细胞外基质紊乱,诱发氧化应激和调控细胞衰老、凋亡三方面。细胞外基质由胶原蛋白、蛋白多糖等构成,其合成分解平衡对于维持椎间盘功能和稳态至关重要<sup>[7]</sup>。异常机械负荷、炎症等因素会加剧基质分解,导致合成与降解失衡及细胞凋亡<sup>[8]</sup>。炎性

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因子如白细胞介素(IL)-6、肿瘤坏死因子- $\alpha$ (TNF- $\alpha$ )等会加剧这一失衡,并加速椎间盘结构改变<sup>[9-11]</sup>。另外,衰老细胞具有更强的基质降解能力,炎症反应不仅加速细胞衰老,还诱导细胞分泌更多的促炎因子及基质降解酶,进一步恶化细胞外基质环境<sup>[5]</sup>。氧化应激由活性氧(ROS)过量生成和抗氧化失衡引起,影响细胞信号转导、代谢调节、表型转化等过程<sup>[12]</sup>。在退变的椎间盘中,炎症和氧化应激相互促进,形成恶性循环。炎症刺激可诱导活性氧生成,活性氧的累积又能诱导炎症因子释放,如 TNF- $\alpha$ 、IL-1 $\beta$  等<sup>[13-14]</sup>。实际上细胞外基质代谢与炎症和氧化还原状态密切相关。IL-1 $\beta$  等炎症因子能诱导氧化应激,激活 NF- $\kappa$ B 和丝裂原活化蛋白激酶(MAPK)通路,降解细胞外基质成分,并通过促进细胞自噬和衰老来影响椎间盘<sup>[15-16]</sup>。长期的炎症和氧化应激还会触发细胞自噬和凋亡,降低细胞活性,改变细胞表型,影响椎间盘正常生理功能<sup>[5]</sup>。因此,炎症与氧化应激的交互作用是椎间盘退变的重要诱导因素。细胞衰老和凋亡是腰椎间盘突出症的关键驱动因素,常促进氧化应激、细胞外基质降解共同推动疾病发展。衰老信号会改变细胞表型,增加促炎和分解代谢因子分泌,并降低抗氧化剂水平,导致椎间盘组织降解<sup>[17]</sup>。IL-1 $\beta$  或 TNF- $\alpha$  能通过引发氧化应激驱动细胞凋亡,并增加衰老标志物如  $\beta$ -半乳糖苷酶和 p53 表达<sup>[18]</sup>。IL-1 $\beta$  还能通过 P38 MAPK 通路诱导细胞凋亡和细胞外基质减少<sup>[19]</sup>。此外,基因表达分析提示,炎症因子刺激后差异表达基因主要与细胞凋亡、细胞外基质降解等相关<sup>[20]</sup>。因此,针对性干预炎症对于延缓椎间盘退变具有重要意义。

## 2 中药单体调控炎症在改善腰椎间盘突出症中的应用

炎症是椎间盘退变的主要诱因,抑制炎症诱导的细胞外基质紊乱、氧化应激、细胞衰老及凋亡等过程对临床治疗意义深远。腰椎间盘突出症属“腰痹病”范畴,病位主要涉及肝肾筋骨,病因贯穿于肝肾亏虚、痰凝血瘀等方面。现代研究表明血瘀证与血栓类疾病在血小板功能和炎症方面存在密切联系<sup>[21]</sup>。炎症期间释放的细胞因子可激活血小板和凝血因子,形成血栓并加剧炎症,这为中药在靶向治疗腰椎间盘突出症过程中提供可靠依据<sup>[22]</sup>。中药单体因其成分单一、药理作用明确,在中医药疗法中具有独特优势,尤其在抑制炎症、改善腰椎间盘突出方面前景广阔。因此,运用中药单体靶向治疗椎间盘炎性损伤机制、改善椎间盘突出症,不仅有望提供更有效的治疗方案,还可以减少传统治疗伴随的弊端,对临床治疗意义深远。

### 2.1 淫羊藿苷

淫羊藿苷作为一类 8-异戊烯基黄酮苷类化合物,

通过抑制炎症介质、抵抗细胞凋亡和延缓基质降解等途径,在改善腰椎间盘突出症方面展现出显著潜力。IL-1 $\beta$  促进环氧合酶-2(COX-2)和诱导型一氧化氮合酶等炎症介质活性,刺激前列腺素  $E_2$  产生,并诱导基质金属蛋白酶和解聚蛋白样金属蛋白酶上调以加速椎间盘退变<sup>[23]</sup>。然而淫羊藿苷能显著降低细胞内这些炎症介质的水平,并抑制基质降解酶的表达,促进细胞外基质蛋白的表达和髓核细胞增殖<sup>[23-24]</sup>,由此可见淫羊藿苷具有抑制炎症及细胞外基质降解以延缓椎间盘退变的潜力。淫羊藿苷抑制髓核细胞凋亡和氧化应激以预防椎间盘退变与磷脂酰肌醇 3-激酶/蛋白激酶 B(PI3K/AKT)信号通路密切相关<sup>[25]</sup>。淫羊藿苷也能通过抑制 NF- $\kappa$ B 信号及后续 P56 因子、凋亡蛋白表达,抵抗细胞凋亡,减轻炎症反应<sup>[26]</sup>。此外,淫羊藿苷也能抑制炎症状态下软骨细胞的凋亡,并下调软骨细胞成骨标志物表达,抑制终板软骨的钙化和变性<sup>[27]</sup>。近年来,淫羊藿在改善椎间盘源性疼痛、干细胞迁移修复椎间盘等领域的研究不断扩展,对于寻找防治腰椎间盘突出症的靶点意义深远。

### 2.2 白藜芦醇

白藜芦醇是中药虎杖的活性成分,通过其抗氧化、抗炎特性影响细胞凋亡、自噬等多途径防治腰椎间盘突出症。研究发现白藜芦醇可降低髓核细胞中炎症因子水平(如 IL-6 和 IL-8 等),从而缓解背根神经节疼痛,并通过靶向沉默信息调节因子 1 抑制 Wnt/ $\beta$ -连环蛋白信号通路,减少 IL-1 $\beta$  介导的细胞外基质降解,从而维持椎间盘的功能完整性<sup>[28-29]</sup>。在神经根病自体髓核模型中,白藜芦醇能减轻背根神经节的水肿和炎症,并改善细胞形态,表明其对背根神经节疼痛和损伤具有良好的改善效果<sup>[30]</sup>。除了改善髓核细胞功能外,白藜芦醇还能调节纤维环细胞和终板软骨细胞的功能,进一步促进椎间盘的整体作用。白藜芦醇能降低炎症状态下椎间盘终板软骨细胞内对高迁移率蛋白 1 的表达,增加终板软骨细胞的活性,抑制凋亡率,并升高抗炎因子 IL-10 的含量<sup>[31]</sup>。炎症因子处理后纤维环细胞内凋亡参数及胞内活性氧水平的降低进一步支持其改善椎间盘退变的作用<sup>[32]</sup>。这种抗炎减轻椎间盘的破坏效应是通过调控 Janus 激酶/信号转导和转录激活因子 3(JAK/STAT3)信号通路实现的<sup>[33]</sup>。这些作用机制揭示了白藜芦醇在调节炎症反应及相关信号通路,防治腰椎间盘突出症中发挥了关键作用,为腰椎间盘突出症的治疗提供了新的方向。

### 2.3 黄芩素

黄芩素是中药黄芩的重要活性成分,是一类具有抑制炎症、改善氧化应激、调控铁死亡等生物活性的黄酮类化合物,主要通过抑制炎症和细胞衰老改善椎间盘退变状态。黄芩素能够抑制一氧化氮、前列腺素

$E_2$ 、TNF- $\alpha$ 、IL-6 及 COX-2 等炎症因子的表达,并以剂量依赖性方式抑制基质降解酶的表达,防止细胞外基质的恶性降解,维持基质良性平衡状态<sup>[34]</sup>,这类效应从机制上主要是通过激活 NF- $\kappa$ B 和 MAPK 通路实现。黄芩素还可以调控 PI3K/Akt 通路,抑制 TNF- $\alpha$  激活的人髓核细胞凋亡<sup>[35]</sup>。此外,黄芩苷能够抑制衰老髓核细胞表型中炎症因子的分泌,逆转细胞衰老进程,抑制炎症反应,从而延缓椎间盘退变<sup>[36]</sup>。以上研究均提示黄芩素是临床上调控炎症防治腰椎间盘突出症的潜在药物选择。

## 2.4 姜黄素

姜黄素是中药姜黄的主要活性成分,以其抗炎、抗氧化特性影响多个信号通路,在缓解腰椎间盘突出症疼痛症状、延缓椎间盘退变方面显示出显著的效果。多项研究表明姜黄素能调控 Akt、NF- $\kappa$ B、细胞外信号调节激酶信号通路,抑制椎间盘内的神经炎症,降低 IL-6 和 COX-2 的表达,发挥抗炎镇痛作用<sup>[37-38]</sup>。姜黄素还能调节转化生长因子  $\beta 1/2$  (TGF- $\beta 1/2$ )、MMP-9、COX-2、脑源性神经营养因子和一氧化氮合酶水平,发挥抗炎镇痛功效,以达到防治腰椎间盘突出症的作用<sup>[39]</sup>。此外,联合负载姜黄素的介孔二氧化硅纳米粒的局部注射,进一步优化了姜黄素的释放和生物活性,并增强了姜黄素通过抑制炎症来延缓椎间盘退变的疗效<sup>[40]</sup>。该系统的研究成果不仅展示了姜黄素在抑制炎症和修复椎间盘方面的作用,也为单体药物联合组织工程医学用于腰椎间盘突出症的治疗提供了新的视角和手段。

## 2.5 黄芪甲苷

黄芪甲苷是从中药黄芪中提取的一种皂苷类化合物,具有抗炎和免疫调节作用,有助于改善椎间盘退变。黄芪甲苷和丹参酮 II A 能够在体外靶向抑制 JAK2/STAT1 相关的微小 RNA-233,减少髓核细胞的凋亡和炎症反应<sup>[41]</sup>。同时,黄芪甲苷在调控 NF- $\kappa$ B、PI3K/Akt 信号通路,抑制盘内炎症、细胞外基质降解等方面也具有良好治疗效果<sup>[42-43]</sup>。黄芪甲苷治疗腰椎间盘突出症的机制还涉及上调 IL-10/ $\beta$ -内啡肽通路以减轻炎症反应和细胞凋亡,缓解神经根损伤,及上调微小 RNA-125a-5p 表达,抑制核苷酸寡聚化结构域样受体蛋白 1 的表达和 NF- $\kappa$ B/MAPK 信号通路,减少 IL-1 $\beta$  诱导的髓核细胞损伤和炎症反应<sup>[44-45]</sup>,提示黄芪甲苷可能通过抑制炎症反应及细胞损伤在治疗腰椎间盘突出症过程中发挥积极效应。

## 2.6 人参皂苷

人参皂苷是中药人参的主要活性成分,其中人参皂苷 Re 和 Rg 类主要通过抑制炎症、凋亡等途径参与延缓椎间盘退变并维持其生物学特性的过程。研究显示小鼠腹腔注射人参皂苷 Re 后,髓核的脱水程度降

低。在细胞层面,人参皂苷 Re 能抑制炎症因子诱导的 NF- $\kappa$ B 通路激活,维持细胞外基质分解代谢的平衡,从而延缓椎间盘退变<sup>[46]</sup>。类似地,人参皂苷 Rg3 也通过抑制 NF- $\kappa$ B 和 MAPK 信号通路,并保护细胞免受炎症和氧化应激损伤<sup>[47-48]</sup>。其他亚型如人参皂苷 Rg1 也通过调控 NF- $\kappa$ B、YAP1/TAZ、Wnt/ $\beta$ -连环蛋白信号通路,展现出较好的抗炎、抗凋亡和基质保护作用<sup>[49-50]</sup>。因此,人参皂苷或可作为延缓椎间盘退变、防治腰椎间盘突出症的药物选择之一。

## 2.7 其他中药提取物

其他中药提取物(如小檗碱、雷公藤红素及三七皂苷等)也因其显著的抗炎和细胞外基质修复作用,在延缓椎间盘退变过程中发挥重要作用。小檗碱是存在于黄柏、厚朴中的异喹啉类生物碱物质,具有抗炎和抗氧化特性,对骨关节炎等多种炎症性疾病有良好治疗效果。小檗碱通过抑制 NF- $\kappa$ B 途径活化以维持细胞外基质分解代谢酶和活性氧平衡,并抑制微环境炎症导致的细胞凋亡<sup>[51]</sup>。雷公藤红素是雷公藤中的天然活性成分,具有显著的抗炎活性,能够降低椎间盘内炎症因子和氧化应激,抑制软骨终板退变,并促进椎间盘细胞外基质的修复<sup>[52]</sup>。三七皂苷是中药三七的活性成分,大鼠椎间盘退变模型显示其能促进细胞外基质的生成,抑制体内炎症因子,并通过抑制 NF- $\kappa$ B/NOD 样受体蛋白 3 通路预防椎间盘退变<sup>[53]</sup>。此外,芒果苷、柚皮苷、牛膝总皂苷、乌药碱等中药提取物也显示出调控炎症、防治腰椎间盘突出症的潜力,但其效果和调控机制仍需进一步探索。

## 3 总结与展望

中药单体能通过调控炎症、氧化应激和细胞衰老等延缓椎间盘退变、抑制疼痛,改善腰椎间盘突出症。相关研究也存在局限性:1)缺乏系统的药物代谢动力学研究和个体用药指导;2)动物模型与人体生物力学差异导致研究的局限性;3)中药单体靶向炎症的适配性及长期应用的毒副作用需要特别重视。未来研究需加强基础研究与临床治疗结合,综合分析细胞及通路间的协同效应,并明确长期用药的剂量及生物毒性,以使疗效最大化,减少副作用。

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(上接第 91 页)

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