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## 松乳菇多糖治疗原发性肝癌的细胞实验及机制

白瑞, 鲍中英, 段淑红, 苑晓东, 王硕

(首都医科大学附属北京世纪坛医院感染科, 北京 100038)

**[摘要]** 目的: 探讨松乳菇多糖(lactarius deliciosus gray polysaccharide, LDG-A)对原发性肝癌的治疗作用, 并分析其机制。方法: 人肝癌细胞株HepG2培养至对数期时, 以 $1.5 \times 10^6$ 个/孔接种至6孔板, 随机分为4组, 每组5个复孔, 细胞贴壁后, 空白组、实验1, 2, 3组分别用磷酸盐缓冲液(PBS), 和50, 150, 300  $\mu\text{g}/\text{mL}$  LDG-A干预。对比干预24, 48, 72 h细胞增殖抑制率和凋亡率; 对比干预72 h增殖相关基因血管内皮生长因子(vascular endothelial growth factor, VEGF), 磷脂酰肌醇3-激酶(phosphatidylinositol 3-kinase, PI3K), 肝细胞黏附分子1(hepatocyte adhesion molecule 1, hepaCAM1)和凋亡相关基因B淋巴细胞瘤-2基因(B lymphoma-2 gene, Bcl-2), Bcl-2相关X蛋白(Bcl-2 associated X protein, Bax), 活化型含半胱氨酸天冬氨酸蛋白水解酶-3(cleaved cysteinyl aspartate specific proteinase-3, cleaved-caspase-3) mRNA和蛋白相对表达量。结果: 实验2组增殖抑制率最高、实验3组其次、实验1组最低, 两两比较差异均有统计学意义( $P < 0.05$ ); 实验2组凋亡率最高、实验3组其次、实验1组更低、空白组最低, 两两比较差异均有统计学意义( $P < 0.05$ ); 3剂量组增殖抑制率、凋亡率均随时间延长呈显著升高趋势( $P < 0.05$ ), 空白组凋亡率随时间延长变化不明显( $P > 0.05$ ); 实验2组VEGF, PI3K, Bcl-2 mRNA和蛋白相对表达量最低、实验3组其次、实验1组更高、空白组最高, 两两比较差异均有统计学意义( $P < 0.05$ ); 实验2组HepaCAM1, Bax, Cleaved-caspase-3 mRNA和蛋白相对表达量最高、实验3组其次、实验1组更低、空白组最低, 每2组间比较差异均有统计学意义( $P < 0.05$ )。结论: LDG-A可抑制人肝癌细胞株HepG2的增殖、促进其凋亡, 其中浓度为150  $\mu\text{g}/\text{mL}$ 时效果最佳, 推测与下调VEGF, PI3K, Bcl-2 mRNA和蛋白表达、上调hepaCAM1, Bax, cleaved-caspase-3 mRNA和蛋白表达有关。

**[关键词]** 松乳菇多糖; 人肝癌细胞; 增殖; 凋亡

## Cell experiment and mechanism of lactarius deliciosus polysaccharide in the treatment of primary hepatocellular carcinoma

BAI Rui, BAO Zhongying, DUAN Shuhong, YUAN Xiaodong, WANG Shuo

(Department of Infection, Beijing Century Altar Hospital Affiliated to Capital Medical University, Beijing 100038, China)

**Abstract** **Objective:** To investigate of Lactarius deliciosus gray polysaccharide (LDG-A) therapeutic effect on primary

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通信作者 (Corresponding author): 鲍中英, Email: 1028878013@qq.com

hepatocellular carcinoma and to analyze its mechanism. **Methods:** When the human hepatocarcinoma cells HepG2 was cultured to the logarithmic phase,  $1.5 \times 10^6$ /well were subdivided into 6-well plates. The cells were randomly divided into 4 groups. Each group had 5 replicate wells. After adherent growth, the blank group, experiment 1, 2, 3 groups were treated with phosphate buffered saline (PBS), 50, 150, and 300  $\mu\text{g}/\text{mL}$  LDG-A, respectively. The rates of proliferation inhibition and apoptosis of the cells after 24, 48, and 72 hours of intervention were compared. The mRNA and protein relative expression of proliferation-related genes vascular endothelial growth factor (VEGF), phosphatidylinositol 3-kinase (PI3K), hepatocyte adhesion molecule 1 (hepaCAM1) and apoptosis-related genes B lymphoma-2 gene (Bcl-2), Bcl-2 associated X protein (Bax), cleaved cysteinyl aspartate specific proteinase-3 (cleaved-caspase-3), after 72 hours intervention were compared. **Results:** The proliferation inhibition rate of the experiment 2 group was the highest, the experiment 3 group was the second, the experiment 1 group was the lowest, and there were significant differences between each 2 groups ( $P < 0.05$ ). The apoptosis rate of the experiment 2 group was the highest, the experiment 3 group was the second, the experiment 1 group was slightly lower, the control group was the lowest, and there were significant differences between each 2 groups ( $P < 0.05$ ). The proliferation inhibition rates and the apoptosis rates of the 3 experiment groups were significantly increased with time ( $P < 0.05$ ). The apoptosis rate of the control group did not change significantly with time ( $P > 0.05$ ). The mRNA and protein relative expressions of VEGF, PI3K and Bcl-2 of the experiment 2 group were the lowest, the experiment 3 group was the second, the experiment 1 group was slightly higher, the blank group was the highest, and there were significant differences between each 2 groups ( $P < 0.05$ ). The mRNA and protein relative expressions of hepaCAM1, cleaved-caspase-3 and Bax of the experiment 2 group were the highest, the experiment 3 group was the second, the experiment 1 group was slightly lower, the blank group was the lowest, and there were significant differences between each 2 groups ( $P < 0.05$ ). **Conclusion:** LDG-A can inhibit the proliferation of human hepatocarcinoma cells HepG2 and promote its apoptosis, of which 150  $\mu\text{g}/\text{mL}$  LDG-A best, and it is presumed to be related to down-regulate the mRNA and protein expressions of VEGF, PI3K, Bcl-2 and up-regulate the mRNA and protein expressions of hepaCAM1, cleaved-caspase-3 and Bax.

**Keywords** lactarius deliciosus polysaccharide; human hepatocarcinoma cells; proliferation; apoptosis

肝癌是我国发病率高且危害严重的恶性肿瘤。据世界卫生组织统计<sup>[1]</sup>, 全球每年新发肝癌患者约100万例, 而我国约占50%以上, 全国每年死于肝癌的患者已超过10万人, 且随我国老龄化日益加剧, 肝癌的病死率逐年增加, 给人们的工作和生活造成严重影响。临床调查<sup>[2]</sup>发现: 肝癌根治术后1年复发率约30%, 而术后5年病死率高达95%, 对人们的生命造成严重威胁。目前, 肝癌放疗在控制病情发展、延长患者生命方面取得一定成效, 但同时也存在耐药性及副作用等诸多问题, 因此, 寻找有效治疗肝癌的药物至关重要。松乳菇多糖(lactarius deliciosus polysaccharide, LDG-A)是从松乳菇、红松菌等外生菌根菌种提取的一种多糖<sup>[3]</sup>。既往研究<sup>[4-5]</sup>表明: LDG-A具有抗菌、抗病毒、提高机体免疫力等多种药理学作用, 尤其是LDG-A的辅助抗肿瘤作用日益受到关注, 如具有抗喉癌、肝癌等恶性肿瘤作用, 但其具体的调控机制尚未完全清楚。因而本研究通过

观察LDG-A对人肝癌细胞株HepG2增殖和凋亡的影响, 对其调控机制进行初步探讨。

## 1 材料与方法

### 1.1 材料

人肝癌细胞株HepG2由中国医学科学院肿瘤医院细胞中心提供。LDG-A从松乳菇、红松菌中提取, 制备方法为水提醇析法<sup>[6]</sup>, 经纯化纯度为81.9%, 主要单糖组分为D-甘露糖、D-葡萄糖、D-半乳糖、D-岩藻糖、D-木糖、D-阿拉伯糖。二甲亚砜(dimethyl sulfoxide, DMSO)、二甲基噻唑(dimethylthiazole, MTT)为美国Sigma公司产品。RPMI-1640培养基、胎牛血清购自美国Hyclone公司; FITC-Anexin V/PI细胞凋亡试剂盒购自杭州联科生物技术股份有限公司; 反转录试剂盒、二喹啉甲酸(diquinolinecarboxylic acid, BCA)蛋白定量分析试剂盒购自美国Thermo公司; 兔抗人血管

内皮生长因子(vascular endothelial growth factor, VEGF)、磷脂酰肌醇3-激酶(phosphatidylinositol 3-kinase, PI3K)、肝细胞黏附分子1(hepatocyte adhesion molecule 1, hepaCAM1)、B淋巴细胞瘤-2基因(B lymphoma-2 gene, Bcl-2)、Bcl-2相关X蛋白(Bcl-2 related X protein, Bax)、活化型含半胱氨酸天冬氨酸蛋白水解酶-3(activated cysteine-containing aspartate proteolytic enzyme-3, cleaved-caspase-3)单抗(一抗)、羊抗兔VEGF, PI3K, HepaCAM1, Bax, Bcl-2, Caspase-3单抗(二抗)购自英国Abcam公司; DS-U3型成像系统购自日本尼康公司; Accuri C6流式细胞仪购自上海碧迪医疗器械有限公司; Model550酶标仪、CFX-96实时荧光定量PCR仪、PE2400电泳仪、GelDOC2000型凝胶成像分析系统购自美国Bio-rad公司; alphaEaseFC灰度值分析软件购自美国Alpha Innotech公司。

## 1.2 方法

### 1.2.1 分组及干预

人肝癌细胞株HepG2用RPMI-1640(10%胎牛血清)的培养液, 在37℃和5%CO<sub>2</sub>恒温箱培养。待细胞生长至对数期时, 调整细胞密度以1.5×10<sup>6</sup>个/孔分装后, 随机分为4组, 每组5个复孔, HepG2贴壁生长时, 空白组和实验组分别用磷酸盐缓冲液(phosphate buffered saline, PBS), 50, 150, 300 μg/mL LDG-A 20 μL进行干预, 相同条件下继续培养。

### 1.2.2 细胞增殖抑制率检测

收集培养24, 48, 72 h的HepG2细胞, 各孔加入现配MTT溶液20 μL, 继续培养4 h后弃去培养液, 加入DMSO溶液150 μL, 轻轻吹打至溶液澄清无结晶, 测定570 nm波长处OD值(A)。计算细胞增殖抑制率=[(A<sub>空白组</sub>-A<sub>实验组</sub>)/A<sub>空白组</sub>]×100%。

### 1.2.3 细胞凋亡水平检测

收集培养至24, 48, 72 h的HepG2细胞, 调整细胞浓度为1×10<sup>6</sup>个/mL, 离心后用含10%胎牛血清的PBS重悬, 然后用预冷70%酒精固定24 h(4℃), 然后再次离心后用PBS洗涤2次, 最后去沉淀细胞用RNase悬浮, 避光静置30 min, 加入染料缓冲液重悬(5 μL FITC-Anexin V, 10 μL PI), 于300目尼龙网过滤后, 采用流式细胞仪分析细胞凋亡率。

### 1.2.4 VEGF, PI3K, HepaCAM1, Bax, Bcl-2, cleaved-caspase-3 mRNA 相对表达量检测

收集培养72 h的HepG2细胞, 提取沉淀细胞中的总核糖核酸(ribonucleic acid, RNA), 反转录扩增为互补脱氧核糖核酸(complementary

deoxyribonucleic acid, cDNA)。cDNA定量偶, 进行实时荧光定量PCR, 反应体系为2×qPCR Mix 12.5 μL, 7.5 μmol/L引物2 μL, cDNA 2.5 μL, ddH<sub>2</sub>O 8 μL; 反应条件为95℃预变性5 min; 95℃变性60 s, 61℃退火45 s, 60℃延伸2 min, 溶解曲线72℃至95℃, 每20 s升温1℃。以β-actin作为内参对照物。以凝胶成像系统分析VEGF, PI3K, HepaCAM1, Bax, Bcl-2, Cleaved-caspase-3 mRNA相对表达量, 2<sup>-ΔΔCt</sup>为目的基因的相对表达强度。VEGF正向引物5'-CTGATGCGTATCGTATGCTAGCTAGCT-3', 反向引物5'-ACGTGTACGTATCGTAGCTTACGTAGC-3'。PI3K正向引物5'-CGAGTGCTGATGCTGTAGCTGATCGTA-3', 反向引物5'-ACTGATGCGGTTTCGATCGTAGCTAGCT-3'。hepaCAM1正向引物5'-CTGATCGATCGACGACGAGCATCATC-3'; 反向引物5'-GTGCTATGCTACGATCGGCTATCGTCA-3'。Bax正向引物5'-GATGCTAGTGCCTAGCTAGCTAGTCA-3', 反向引物5'-AGCTAGTCGATGCTAGTACACACA-3'。Bcl-2正向引物5'-GCTAGCTATCAGCTAGCTAGAGCTAC-3', 反向引物5'-GTACGTAGCGATTTCGATCGGATCTCC-3'。Cleaved-caspase-3正向引物5'-CGTAGCTAGCTATGCATCGGCGATCAC-3', 反向引物5'-CGTAGCTAGTCGATCGTACGTATCGTA-3'。β-actin正向引物5'-GTCATCTATCATCGTATGAGCTACGATC-3', 反向引物5'-GTATCGTACAAAGTCGTATCGTATCGTA-3'。

### 1.2.5 VEGF, PI3K, hepaCAM1, Bax, Bcl-2, cleaved-caspase-3 蛋白相对表达量检测

收集培养72 h的HepG2细胞, 以蛋白提取试剂盒得到总蛋白, 然后BCA蛋白定量。每孔上样20 μL, 进行十二烷基硫酸钠聚丙烯酰胺凝胶电泳(sodium dodecyl sulfate polyacrylamide gel electrophoresis, SDS-PAGE)分离, 装配三明治, 然后进行转膜1.5 h。然后用脱脂奶粉摇床封闭24 h(4℃), 加入一抗(1:1 000), 室温摇床孵育2 h(室温), 洗涤后加入二抗(1:10 000), 孵育1 h(室温), 暗室中显色。拍照后用灰度值分析工具进行分析, 以VEGF, PI3K, hepaCAM1, Bax, Bcl-2, cleaved-caspase-3蛋白灰度值与内参β-actin灰度值比值表示蛋白相对表达量。

## 1.3 统计学处理

以SPSS 26.0作为数据分析工具, 用均数±标准差( $\bar{x} \pm s$ )表示计量资料并用LSD-t检验, 多样本计量

资料比较采用单因素方差分析。 $P < 0.05$ 为差异有统计学意义。

## 2 结果

### 2.1 不同时刻增殖抑制率比较

增殖抑制率组间比较: 实验2组最高、实验3组其次、实验1组最低, 2组间比较差异均有统计学意义( $P < 0.05$ ), 实验1~3组增殖抑制率均随时间延长呈显著升高趋势( $P < 0.05$ , 表1)。

### 2.2 不同时刻凋亡率比较

凋亡率组间比较, 实验2组最高、实验3组其次、实验1组更低、空白组最低, 2组间比较

差异均有统计学意义( $P < 0.05$ ), 实验1~3组凋亡率均随时间延长呈显著升高趋势( $P < 0.05$ ), 空白组凋亡率随时间延长变化不显著( $P > 0.05$ ; 表2, 图1)。

### 2.3 VEGF, PI3K, hepaCAM1, Bax, Bcl-2, cleaved-caspase-3 mRNA 相对表达量比较

实验2组VEGF, PI3K, Bcl-2 mRNA相对表达量最低, 实验3组其次, 实验1组更高, 空白组最高, 组间比较差异均有统计学意义( $P < 0.05$ ); 实验2组hepaCAM1, Bax, cleaved-caspase-3 mRNA相对表达量最高, 实验3组其次, 实验1组更低, 空白组最低, 每2组间比较差异均有统计学意义( $P < 0.05$ , 图2)。

表1 不同时刻增殖抑制率比较 ( $n=5, \bar{x} \pm s$ )

Table 1 Comparison of proliferation inhibition rates at different times ( $n=5, \bar{x} \pm s$ )

组别	增殖抑制率 /%		
	24 h	48 h	72 h
实验1组	12.50 ± 1.23	21.37 ± 2.08 <sup>&amp;</sup>	32.85 ± 3.14 <sup>&amp; §</sup>
实验2组	27.36 ± 3.05*	33.30 ± 3.24* <sup>&amp;</sup>	58.36 ± 5.70* <sup>&amp; §</sup>
实验3组	19.46 ± 1.81* <sup>#</sup>	26.22 ± 3.13* <sup>#&amp;</sup>	38.41 ± 3.62* <sup>#&amp; §</sup>
F	58.842	28.208	48.674
P	<0.001	<0.001	<0.001

与实验1组比, \* $P < 0.05$ ; 与实验2组比, <sup>#</sup> $P < 0.05$ ; 与24 h比, <sup>&</sup> $P < 0.05$ ; 与48 h比, <sup>§</sup> $P < 0.05$ 。

Compared with the experimental group 1, \* $P < 0.05$ ; compared with the experimental group 2, <sup>#</sup> $P < 0.05$ ; compared with 24 hours, <sup>&</sup> $P < 0.05$ ; compared with 48 hours, <sup>§</sup> $P < 0.05$ .

表2 对比不同时刻凋亡率( $n=5, \bar{x} \pm s$ )

Table 2 Comparison apoptosis rates at different times ( $n=5, \bar{x} \pm s$ )

组别	凋亡率/%		
	24 h	48 h	72 h
空白组	1.06 ± 0.11	1.21 ± 0.12	1.35 ± 0.13
实验1组	8.20 ± 0.83*	13.36 ± 1.32* <sup>§</sup>	19.91 ± 2.49* <sup>§ †</sup>
实验2组	23.37 ± 2.55* <sup>#</sup>	35.52 ± 3.65* <sup># §</sup>	42.45 ± 4.97* <sup># § †</sup>
实验3组	17.44 ± 1.83* <sup>#&amp;</sup>	22.06 ± 2.47* <sup>#&amp; §</sup>	28.87 ± 2.86* <sup>#&amp; § †</sup>
F	184.427	197.311	151.919
P	<0.001	<0.001	<0.001

与空白组比较, \* $P < 0.05$ ; 与实验1组比, <sup>#</sup> $P < 0.05$ ; 与实验2组比, <sup>&</sup> $P < 0.05$ ; 与24 h比, <sup>§</sup> $P < 0.05$ ; 与48 h比, <sup>†</sup> $P < 0.05$ 。

Compared with the blank group, \* $P < 0.05$ ; compared with the experimental group 1, <sup>#</sup> $P < 0.05$ ; compared with the experimental group 2, <sup>&</sup> $P < 0.05$ ; compared with 24 hours, <sup>§</sup> $P < 0.05$ ; compared with 48 hours, <sup>†</sup> $P < 0.05$ .

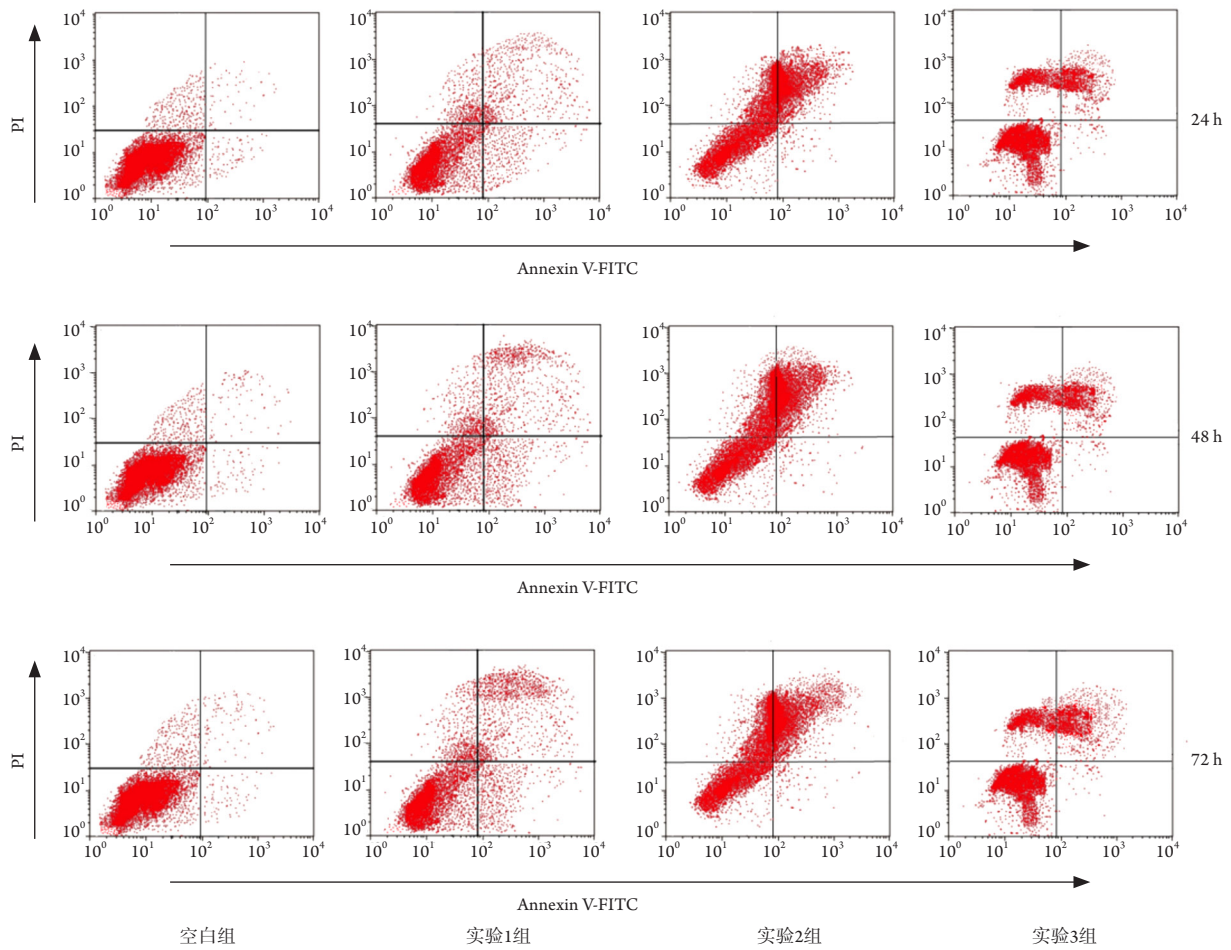


图1 不同时刻细胞凋亡率

Figure 1 Apoptosis rate at different times

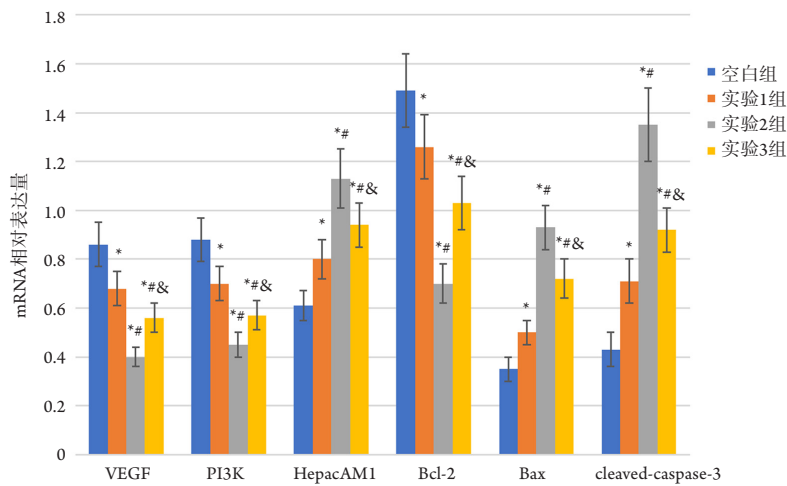


图2 VEGF, PI3K, hepaCAM1, Bax, Bcl-2, cleaved-caspase-3 mRNA相对表达量比较

Figure 2 Comparison of relative expressions of VEGF, PI3K, hepaCAM1, Bax, Bcl-2 and cleaved-caspase-3 mRNA

与空白组比较, \* $P < 0.05$ ; 与实验1组比较, # $P < 0.05$ ; 与实验2组比较, & $P < 0.05$ 。

Compared with the blank group, \* $P < 0.05$ ; compared with the experimental group 1, # $P < 0.05$ ; compared with the experimental group 2, & $P < 0.05$ .

## 2.4 VEGF, PI3K, hepaCAM1, Bax, Bcl-2, cleaved-caspase-3 蛋白相对表达量比较

实验2组VEGF, PI3K, Bcl-2蛋白相对表达量最低, 实验3组其次, 实验1组更高, 空白组最高, 每2组间比较差异均有统计学意义( $P<0.05$ );

实验2组hepaCAM1, Bax, cleaved-caspase-3蛋白相对表达量最高, 实验3组其次, 实验1组更低, 空白组最低, 每2组间比较差异均有统计学意义( $P<0.05$ , 图3~4)。

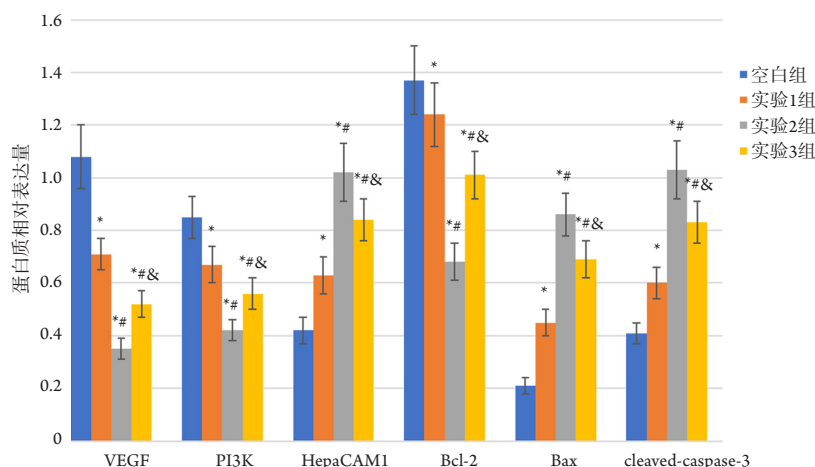


图3 VEGF, PI3K, hepaCAM1, Bax, Bcl-2, cleaved-caspase-3蛋白相对表达量比较

Figure 3 Comparison of relative expression levels of VEGF, PI3K, hepaCAM1, Bax, Bcl-2 and cleaved-caspase-3 proteins

与空白组比较,  $*P<0.05$ ; 与实验1组比较,  $^{\#}P<0.05$ ; 与实验2组比较,  $^{\&}P<0.05$ 。

Compared with the blank group,  $*P<0.05$ ; compared with the experimental group 1,  $^{\#}P<0.05$ ; compared with the experimental group 2,  $^{\&}P<0.05$ .

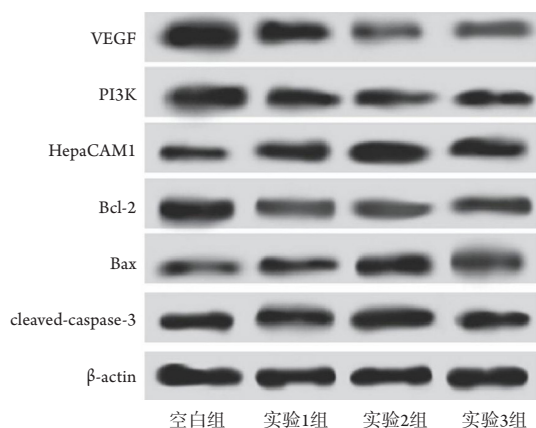


图4 蛋白质免疫印迹图

Figure 4 Photos of Western immunoblotting

## 3 讨论

肝癌是我国高发恶性肿瘤之一, 肝病、环境因素、遗传因素等均是导致肝癌发病的危险因素; 此外, 病毒感染、饮酒等原因所致的肝炎也是肝癌发生的危险因素, 且病毒性肝炎并肝癌的

发生人数越来越多<sup>[7]</sup>。近年来, 随着医疗技术的不断发展, 癌症的治疗取得了丰硕成果, 但是肝癌患者的病死率依然处于较高水平<sup>[8]</sup>。当前, 肝癌的主要治疗手段包括手术切除、放疗、化疗等综合治疗, 但是由于病灶切除不彻底、化疗药物靶向性差及耐药性等原因, 导致癌细胞扩散复发, 最终导致治疗以失败告终<sup>[9-10]</sup>。因此, 寻找靶向性强且可有效杀伤肝癌细胞的药物, 对遏制肿瘤恶性进展、提高肝癌患者生存率十分重要。

本研究发现: LDG-A可抑制人肝癌细胞株 HepG2的增殖, 促进其凋亡, 浓度为150  $\mu\text{g}/\text{mL}$ 时效果最佳。肝癌细胞的过度增殖及凋亡失衡是肝癌发展和恶化的重要原因<sup>[11]</sup>。钱叶等<sup>[12]</sup>研究发现: LDG-A可诱导肺癌细胞株A549的凋亡, 并在12.5~50  $\mu\text{g}/\text{mL}$ 浓度范围内表现出剂量依赖性, 与本研究150  $\mu\text{g}/\text{mL}$ 诱导凋亡的剂量略有不同, 可能与细胞来源不同有关。LDG-A是一类聚氨基葡萄糖类活性物质, 经纯化后得到水溶性LDG-A, 此类多糖有真菌菌丝体产生, 是真菌储藏能量的重要物质, 同时又有很高药用价值<sup>[13]</sup>。构效分析研究<sup>[14]</sup>发现: 多糖的分子质量和结构与

抗肿瘤活性关系密切, LDG-A分子质量多集中于60 kD, 而当分子质量>16 kD时, 多糖的侧链分支和结构功能单位增多, 抗肿瘤活性较强。由此, LDG-A对人肝癌细胞株HepG2具有增殖抑制和促凋亡作用。

此外, 本研究发现: LDG-A对人肝癌细胞株HepG2的增殖抑制和促凋亡作用与下调VEGF, PI3K, Bcl-2 mRNA和蛋白表达, 上调HepaCAM1, Bax, cleaved-caspase-3 mRNA和蛋白表达有关。VEGF是一种特异性有丝分裂原, 通过与酪氨酸受体结合发挥促血管内皮细胞增殖作用, 与肿瘤细胞的增殖、生长密切相关<sup>[15]</sup>。PI3K是VEGF下游重要效应分子<sup>[16]</sup>, VEGF与相应受体结合后, 可激活PI3K, 进而激活下游血管生成相关因子, 诱导细胞异常增殖过程。HepaCAM1是近年来新发现的一种免疫球蛋白样细胞黏附分子<sup>[17]</sup>, 该蛋白可通过提高细胞与基质间的黏附作用而降低细胞增殖能力, 进而抑制肿瘤细胞的发生、发展。Bcl-2主要分布于线粒体中, 通过增强线粒体膜电位, 进而阻止Ca<sup>2+</sup>的释放及相关酶的激活而发挥抗凋亡作用。Bax是与Bcl-2高度同源的一种蛋白, 该蛋白不仅可激活死亡效应级联反应, 同时可竞争性抑制Bcl-2活性, 发挥凋亡促进作用<sup>[18]</sup>。Caspase-3是一种重要的凋亡促进关键酶, 一旦被激活, 可激活细胞表面死亡受体途径进而诱导细胞凋亡发生<sup>[19]</sup>。本研究应用LDG-A对人肝癌细胞株HepG2干预后, 增殖促进基因VEGF, PI3K表达降低, 增殖抑制基因HepaCAM1表达增加, 说明LDG-A对HepG细胞具有增殖抑制作用, 另一方面, 凋亡促进基因Bax, cleaved-caspase-3表达增加, 凋亡抑制基因Bcl-2表达降低, 调节Bcl-2/Bax凋亡通路, 发挥凋亡促进作用。由此, LDG-A可通过抑制VEGF/PI3K信号通路而抑制肝癌细胞的增殖, 通过调控Bax/Bcl-2信号通路而促进肝癌细胞凋亡, 发挥多靶点共同杀伤肝癌细胞的作用。

综上所述, LDG-A可抑制人肝癌细胞株HepG2的增殖、促进其凋亡, 其中浓度为150 μg/mL时效果最佳, 推测与下调VEGF, PI3K, Bcl-2 mRNA和蛋白表达、上调hepaCAM1, Bax, cleaved-caspase-3 mRNA和蛋白表达有关。

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