鸦胆子油乳注射液可能通过调节JAK2/STAT3信号通路抑制胰腺癌AsPC-1细胞上皮–间质转化

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摘要 该文旨在探讨鸦胆子油乳注射液(简称鸦胆子油乳)调节JAK2/STAT3信号通路对胰腺癌细胞上皮–间质转化(EMT)的影响。将胰腺癌AsPC-1细胞分为对照组、鸦胆子油乳低剂量组、鸦胆子油乳中剂量组、鸦胆子油乳高剂量组、鸦胆子油乳高剂量+Colivelin(JAK2/STAT3激活剂)组。该研究采用细胞划痕实验检测细胞迁移; Transwell实验检测细胞侵袭; MTT、EdU检测细胞增殖; 流式细胞术检测细胞凋亡率; qRT-PCR检测细胞*JAK2* mRNA、*STAT3* mRNA表达; Western blot检测细胞JAK2/STAT3通路、E-cadherin、N-cadherin、Vimentin蛋白表达水平。结果显示, 与对照组相比, 鸦胆子油乳低、中、高剂量组细胞活力、增殖率、细胞划痕愈合率、侵袭细胞个数、*JAK2* mRNA、*STAT3* mRNA、N-cadherin、Vimentin、p-JAK2/JAK2、p-STAT3/STAT3表达水平显著降低, 细胞凋亡率和细胞E-cadherin表达水平显著升高($P<0.05$)。与鸦胆子油乳高剂量组相比, 鸦胆子油乳高剂量+Colivelin组细胞活力和增殖率、细胞划痕愈合率与侵袭细胞个数、*JAK2* mRNA、*STAT3* mRNA基因表达水平、N-cadherin、Vimentin、p-JAK2/JAK2、p-STAT3/STAT3蛋白表达水平显著升高, 细胞凋亡率和E-cadherin表达水平显著下降($P<0.05$)。该研究得出鸦胆子油乳可以抑制AsPC-1细胞增殖、迁移、侵袭和EMT, 这可能是通过抑制JAK2/STAT3信号通路实现的。

关键词 鸦胆子油乳; JAK2/STAT3信号通路; 胰腺癌细胞; 上皮–间质转化

Impacts of Brucea Javanica Oil Emulsion Injection on Epithelial-Mesenchymal Transition of Pancreatic Cancer AsPC-1 Cells by Regulating JAK2/STAT3 Signaling Pathway

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Abstract The aim of this study was to investigate the impacts of Brucea javanica oil emulsion injection on EMT (epithelial-mesenchymal transition) of pancreatic cancer cells by regulating JAK2/STAT3 signaling pathway. AsPC-1 cells from pancreatic cancer were grouped into control group, low dose group, medium dose group, high dose group, and high dose+Colivelin (JAK2/STAT3 activator) group. Cell scratch test was applied to detect cell migration; Transwell experiment was applied to detect cell invasion; MTT and EdU were applied to detect cell proliferation; flow cytometry was applied to detect cell apoptosis rate; qRT-PCR was applied to detect the expression of *JAK2* mRNA and *STAT3* mRNA in cells; Western blot was applied to detect the expression levels of JAK2/STAT3 pathway, E-cadherin, N-cadherin, and Vimentin proteins in cells. Result display, compared

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with the control group, the cell viability and proliferation rate, scratch healing rate, the number of invasive cells, the expression of *JAK2* mRNA, *STAT3* mRNA, N-cadherin, Vimentin, p-JAK2/JAK2, p-STAT3/STAT3 proteins in the low, medium, and high dose Brucea javanica oil emulsion groups obviously reduced, the apoptosis rate and the expression of E-cadherin in cells obviously increased (P<0.05). Compared with the high-dose Brucea javanica oil emulsion group, the cell viability and proliferation rate, scratch healing rate, the number of invasive cells, thew expression of *JAK2* mRNA, *STAT3* mRNA, N-cadherin, Vimentin, p-JAK2/JAK2, p-STAT3/STAT3 proteins in the high-dose Brucea javanica oil emulsion+Colivelin group obviously increased, the apoptosis rate and the expression of E-cadherin in cells obviously decreased (P<0.05). The study concluded that Brucea javanica oil emulsion can reduce AsPC-1 cell proliferation, migration, invasion, and EMT, possibly by inhibiting the JAK2/STAT3 signaling pathway.

Keywords Brucea javanica oil emulsion; JAK2/STAT3 signaling pathway; pancreatic cancer cells; epithelial-mesenchymal transition

胰腺癌是一种常见的消化道肿瘤疾病, 经过治疗之后, 5年生存率仍然较低[1]。胰腺癌早期诊断较为困难, 不易被发现, 病发时肿瘤细胞已发生转移进入晚期, 治愈率低, 死亡率很高, 放疗和化疗效果有限, 预后很差[2]。研究表明上皮–间质转化(epithelial-mesenchymal transition, EMT)是导致肿瘤迁移和侵袭的主要原因[3], 因此探究胰腺癌细胞EMT的分子机制并寻找有效的临床药物对胰腺癌患者的治疗具有重要意义。鸦胆子油乳(Brucea javanica oil emulsion)是从苦木科植物种子中提取出来的, 具有多种药理活性成分[4], 研究表明鸦胆子油乳具有抑制癌细胞DNA合成的功效, 可诱导癌细胞死亡, 促进机体对癌细胞的免疫反应[5]。秦丽娟等[6]研究表明, 鸦胆子油乳注射液可通过阻断PI3K/AKT信号通路来抑制胶质瘤细胞增殖和侵袭。耿国军等[7]研究表明, 鸦胆子油乳可抑制肺腺癌细胞增殖, 促进其凋亡, 将其阻滞于G_0/G_1期。研究表明, JAK2/STAT3信号通路参与多种肿瘤的发生发展[8]。黎敏航等[9]研究表明阻断JAK2/STAT3信号通路可以抑制肝癌HepG2细胞的增殖、迁移、侵袭和EMT过程, 并促进其凋亡。赵海林等[10]研究表明, 阿魏酸钠可以抑制JAK2/STAT3信号通路从而抑制胶质瘤细胞增殖、迁移和侵袭, 并促进其凋亡。猜测JAK2/STAT3信号通路在肿瘤细胞增殖、迁移和侵袭过程中发挥重要作用。鸦胆子油乳已被证实具有抑制肿瘤生长的作用, 但其是否通过抑制癌细胞EMT过程来实现其对癌细胞的抑制作用, 尚无定论。因此本研究探讨鸦胆子油乳注射液调节JAK2/STAT3信号通路对胰腺癌细胞EMT的影响, 以期为临床用药提供科学依据。

1 材料与方法

1.1 细胞与试剂

胰腺癌AsPC-1细胞购自浙江美森细胞科技有限公司; JAK2/STAT3激活剂Colivelin购自南京肽业生物科技有限公司; 鸦胆子油乳注射液购自沈阳药科大学集琦药业; RPMI 1640培养基购自江西江蓝纯生物试剂有限公司; 胎牛血清购自赛业生物科技有限公司; qRT-PCR反转录试剂盒购自北京智杰方远科技有限公司; Trizol试剂购自郑州霖恩生物科技有限公司; 胰蛋白酶购自上海晶抗生物工程有限公司; 总RNA提取试剂盒购自上海海方生物技术有限公司; MTT试剂盒购自江苏麦格生物科技有限公司; Transwell小室购自上海北诺生物科技有限公司; JAK2、STAT3、p-JAK2、p-STAT3、E-cadherin、Vimentin一抗及二抗均购自英国Abcam公司。

1.2 细胞培养及分组

培养: 将AsPC-1细胞接种于RPMI 1640培养基中, 在37 °C、5% CO_2的条件下恒温培养, 待细胞融合度达到85%左右时, 加入酶制剂进行消化传代, 收集传代细胞。

分组: 将对数生长期的AsPC-1细胞分为对照组、鸦胆子油乳低剂量组(5 ml/L)、鸦胆子油乳中剂量组(10 ml/L)、鸦胆子油乳高剂量组(20 ml/L)[11]、鸦胆子油乳高剂量(20 ml/L)+Colivelin组(0.5 μmol/L Colivelin溶于DMSO中)[12]。将各组细胞接种于96孔培养板中, 分别添加相应药物处理细胞, 培养48 h。

1.3 MTT法、EdU染色检测细胞增殖

MTT法: 将各组细胞接种于96孔板中培养, 分别在24 h、48 h时向每孔中加入MTT溶液, 37 °C孵育4 h

之后, 再加入150 μL的DMSO, 振荡至完全溶解后, 用酶标仪检测各孔吸光度(*D*)值(490 nm波长)。计算抑制率, 抑制率=[(*D*空白组−*D*实验组)/*D*空白组]×100%。

EdU染色: 将各组细胞接种于96孔板中培养48 h, 然后向每孔中加入适量EdU于37 ℃孵育2 h, 按照EdU-555细胞增殖检测试剂盒说明书指导进行EdU及DAPI染色。以荧光显微镜采集各组细胞图像, 采用ImageJ软件定量各组EdU阳性细胞数及总细胞数, 计算各组细胞增殖率, 公式为: 增殖率=(EdU阳性细胞数/总细胞数)×100%。

1.4 细胞划痕实验检测细胞迁移

将各组AsPC-1细胞制成细胞悬液, 稀释浓度达到1×10^{5}个/mL, 取2 mL加入6孔板中, 待细胞生长融合60%左右时, 用10 μL移液枪头在细胞层上进行划痕, 记录此时划痕宽度, PBS洗去不贴壁的细胞, 更换无血清培养基培养24 h, 记录24 h划痕宽度, 计算细胞迁移率。

1.5 Transwell实验检测细胞侵袭

将各组AsPC-1细胞制备成细胞悬液, 用Matrigel基质胶包被Transwell小室上室, 待胶干后, 上室中加入200 μL制备的细胞悬液, 下室中加入600 μL含血清的RPMI 1640培养基, 置于培养箱内培养24 h后, 使用多聚甲醛室温固定10 min, 结晶紫染色10 min, 显微镜下观察侵袭细胞数。

1.6 流式细胞术检测细胞凋亡

将各组细胞以每孔1×10^{5}个细胞接种于96孔板中, 37 ℃、5% CO_2培养过夜, 然后根据凋亡试剂盒说明书步骤进行后续处理, 之后再加入Annexin V-FITC与PI试剂, 室温避光反应15 min, 最后用流式细胞仪检测各组细胞凋亡情况。

1.7 qRT-PCR检测*JAK2* mRNA、*STAT3* mRNA的表达水平

使用Trizol试剂提取各组细胞中的总RNA, 将RNA逆转录为cDNA后, 荧光定量PCR对cDNA进行扩增。以*GAPDH*为内参, 使用$2^{-\Delta\Delta Ct}$方法计算*JAK2* mRNA、*STAT3* mRNA的相对表达量。引物*JAK2* mRNA: 正向5′-AGA CAA CAC TGG GGA GGT GGT-3′, 反向5′-TCA TGC TGC AAG GAT TTA AGG A-3′; *STAT3* mRNA: 正向5′-ACC AGC AGT ATA GCC GCT TC-3′, 反向5′-GCC ACA ATC CGG GCA ATC T-3′; *GAPDH*: 正向5′ -CTG GGC TAC ACT GAG CAC C-3′, 反向5′-AAT GGT CGT TGA GGG CAA TG-3′。

1.8 Western blot检测细胞JAK2、STAT3、E-cadherin、N-cadherin、Vimentin蛋白表达水平

裂解各组细胞, 蛋白提取试剂盒提取各组细胞总蛋白质, 检测细胞中蛋白含量, SDS-PAGE电泳分离蛋白并转膜, 5%的脱脂奶粉封闭液中室温封闭2 h, 加入p-JAK2、p-STAT3、JAK2、STAT3、E-cadherin、N-cadherin、Vimentin(1:2 000稀释)一抗4 ℃摇床过夜, 洗膜后再分别加入相应的二抗(1:5 000稀释)常温下孵育2 h, 使用ECL发光液显影, 用Image-Pro Plus进行定量分析。

1.9 统计分析

用SPSS 25.0软件分析实验数据, 以均数±标准差($\bar{x}\pm s$)的形式来表示统计数据, 多组间比较采用单因素方差分析, 组内两两比较用SNK-q检验; P<0.05表示差异有统计学意义。

2 结果

2.1 各组AsPC-1细胞增殖能力比较

与对照组相比, 鸦胆子油乳低、中、高剂量组细胞活力和增殖率均显著性降低, 呈剂量依赖性(P<0.05); 与鸦胆子油乳高剂量组比较, 鸦胆子油乳高剂量+Colivelin组细胞活力和增殖率均显著升高(P<0.05)(图1和表1)。

2.2 各组AsPC-1细胞迁移和侵袭比较

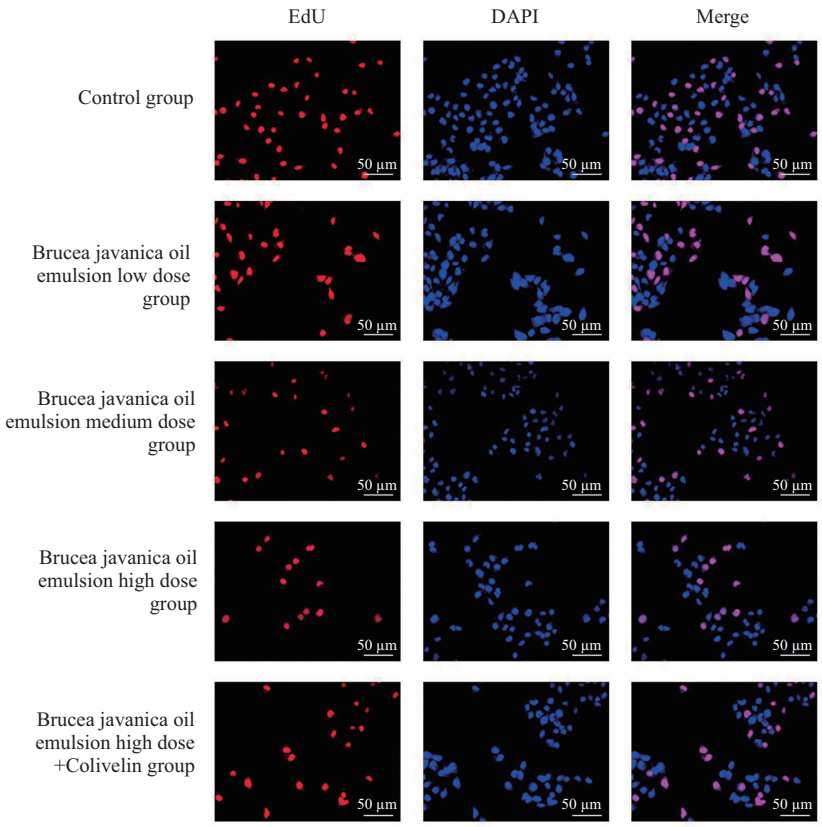
与对照组相比, 鸦胆子油乳低、中、高剂量组细胞划痕愈合率与侵袭细胞个数显著降低, 且呈剂量依赖性(P<0.05); 与鸦胆子油乳高剂量组比较, 鸦胆子油乳高剂量+Colivelin组划痕愈合率与侵袭细胞个数显著升高(P<0.05)(图2~图5)。

2.3 各组AsPC-1细胞凋亡率比较

与对照组(14.58±1.72)%相比, 鸦胆子油乳低、中、高剂量组细胞凋亡率[(21.36±2.13)%、(27.42±2.42)%、(38.74±2.83)%]显著升高, 呈剂量依赖性(P<0.05); 与鸦胆子油乳高剂量组比较, 鸦胆子油乳高剂量+Colivelin组细胞凋亡率(26.67±2.28)%显著降低(P<0.05)(图6)。

2.4 各组AsPC-1细胞*JAK2* mRNA、*STAT3* mRNA表达比较

与对照组相比, 鸦胆子油乳低、中、高剂量组细胞*JAK2* mRNA、*STAT3* mRNA表达水平显著降低, 呈剂量依赖性(P<0.05); 与鸦胆子油乳高剂量组比



EdU阳性呈红色, DAPI呈蓝色。

EdU positive was red, DAPI was blue.

图1 EdU染色检测各组AsPC-1细胞增殖

Fig.1 EdU staining to detect the proliferation of AsPC-1 cells in each group

表1 各组AsPC-1细胞增殖能力比较

Table 1 Comparison of the proliferation capacity of AsPC-1 cells in each group

分组 Group	抑制率/% Inhibition ratio /%		增殖率/% Proliferation rate /%
	24 h	48 h	
Control group	0	0	63.47±5.82
Brucea javanica oil emulsion low dose group	15.56±1.38$^{@}$	11.53±1.24$^{@}$	52.18±4.37$^{@}$
Brucea javanica oil emulsion medium dose group	35.56±2.43$^{@¥}$	28.21±2.53$^{@¥}$	41.54±3.26$^{@¥}$
Brucea javanica oil emulsion high dose group	62.27±5.64$^{@¥\#}$	44.87±3.86$^{@¥\#}$	28.76±1.84$^{@¥\#}$
Brucea javanica oil emulsion high dose+Colivelin group	26.67±2.13$^{\&}$	20.51±1.87$^{\&}$	45.74±2.38$^{\&}$

n=6。$^{@}P$<0.05, 与对照组比较; $^{¥}P$<0.05, 与鸦胆子油乳低剂量组比较; $^{\#}P$<0.05, 与鸦胆子油乳中剂量组比较; $^{\&}P$<0.05, 与鸦胆子油乳高剂量组比较。

n=6. $^{@}P$<0.05 compared with control group; $^{¥}P$<0.05 compared with Brucea javanica oil emulsion low dose group; $^{\#}P$<0.05 compared with Brucea javanica oil emulsion medium dose group; $^{\&}P$<0.05 compared with Brucea javanica oil emulsion high dose group.

较, 鸦胆子油乳高剂量+Colivelin组细胞*JAK2* mRNA、*STAT3* mRNA表达水平显著升高(P<0.05)(图7)。

2.5 各组AsPC-1细胞EMT相关蛋白表达比较

与对照组相比, 鸦胆子油乳低、中、高剂量组细胞E-cadherin表达水平显著升高, N-cadherin和Vimentin表达水平显著下降, 呈剂量依赖性(P<0.05); 与鸦胆子油乳高剂量组比较, 鸦胆子油乳高剂量+Colivelin组细胞E-cadherin表达水平显著下降, N-cadherin、和Vimentin表达水平显著升高(P<0.05)(图8和图9)。

2.6 各组AsPC-1细胞JAK2/STAT3通路相关蛋白表达比较

与对照组相比, 鸦胆子油乳低、中、高剂量

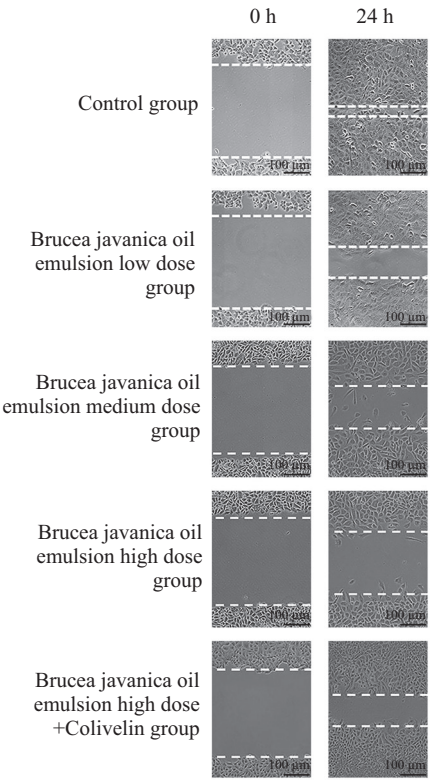


图2　划痕实验检测各组细胞迁移

Fig.2　Cell migration was detected by scratch test

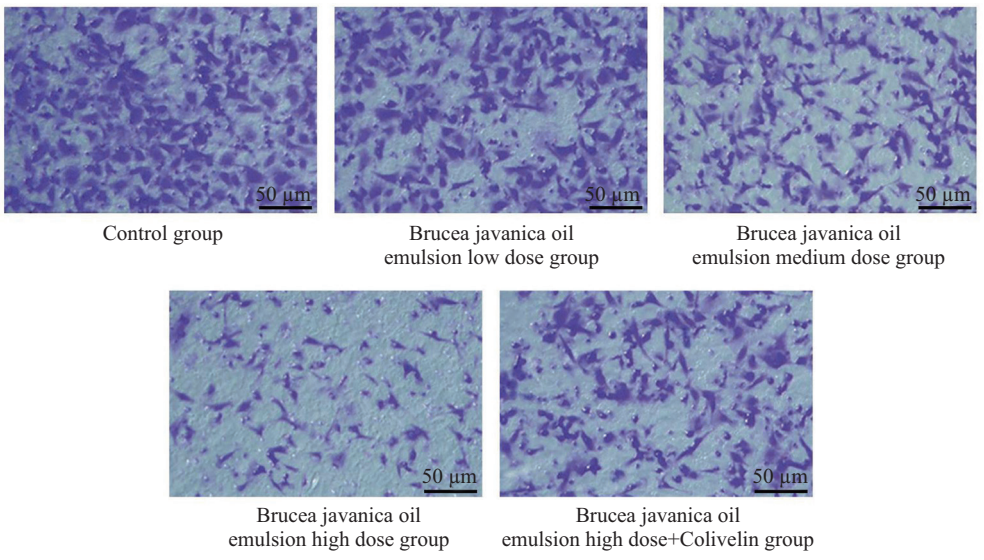


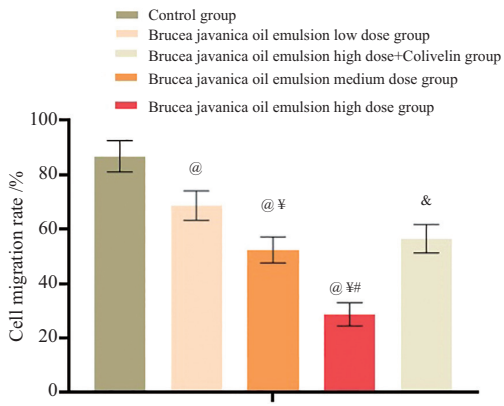
图3　Transwell实验检测细胞侵袭结果图

Fig.3　Cell invasion results of Transwell cell assay

组细胞p-JAK2/JAK2、p-STAT3/STAT3表达水平显著降低, 呈剂量依赖性(P<0.05); 与鸦胆子油乳高剂量组比较, 鸦胆子油乳高剂量+Colivelin组细胞p-JAK2/JAK2、p-STAT3/STAT3表达水平显著显著升高(P<0.05)(图10和图11)。

3　讨论

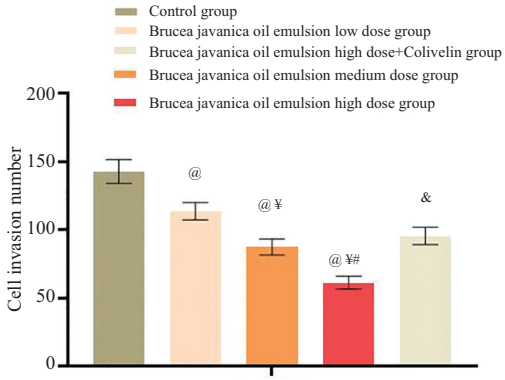
胰腺癌是一种高发病率高死亡率的恶性肿瘤, 近几十年间, 其发病率也呈逐年升高趋势[13]。世界卫生部门统计, 胰腺癌死亡人数占所有癌症的4.5%[14]。胰腺癌患者死亡率高发原因之一是其具有



[@]*P*<0.05, 与对照组比较; [¥]*P*<0.05, 与鸦胆子油乳低剂量组比较; [#]*P*<0.05, 与鸦胆子油乳中剂量组比较; [&]*P*<0.05, 与鸦胆子油乳高剂量组比较。
[@]*P*<0.05 compared with control group; [¥]*P*<0.05 compared with Brucea javanica oil emulsion low dose group; [#]*P*<0.05 compared with Brucea javanica oil emulsion medium dose group; [&]*P*<0.05 compared with Brucea javanica oil emulsion high dose group.

图4 划痕愈合率

Fig.4 Scratch healing rate



[@]*P*<0.05, 与对照组比较; [¥]*P*<0.05, 与鸦胆子油乳低剂量组比较; [#]*P*<0.05, 与鸦胆子油乳中剂量组比较; [&]*P*<0.05, 与鸦胆子油乳高剂量组比较。
[@]*P*<0.05 compared with control group; [¥]*P*<0.05 compared with Brucea javanica oil emulsion low dose group; [#]*P*<0.05 compared with Brucea javanica oil emulsion medium dose group; [&]*P*<0.05 compared with Brucea javanica oil emulsion high dose group.

图5 细胞侵袭个数

Fig.5 Number of invaded cells

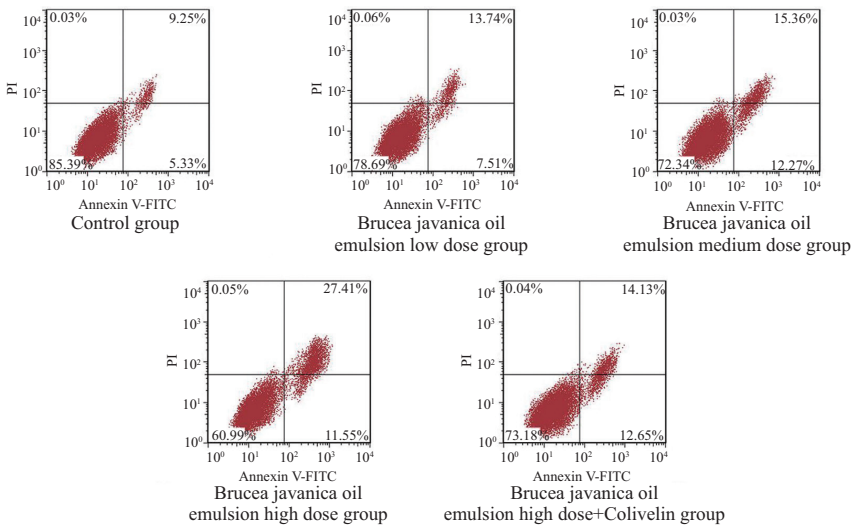
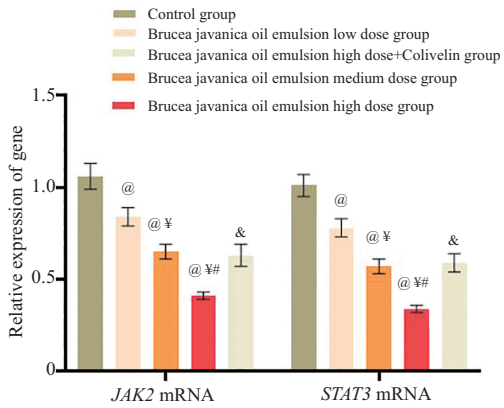


图6 细胞凋亡结果图

Fig.6 Results of apoptosis



$^{@}P$<0.05, 与对照组比较; $^{¥}P$<0.05, 与鸦胆子油乳低剂量组比较; $^{\#}P$<0.05, 与鸦胆子油乳中剂量组比较; $^{\&}P$<0.05, 与鸦胆子油乳高剂量组比较。
$^{@}P$<0.05 compared with control group; $^{¥}P$<0.05 compared with brucea javanica oil emulsion low dose group; $^{\#}P$<0.05 compared with brucea javanica oil emulsion medium dose group; $^{\&}P$<0.05 compared with Brucea javanica oil emulsion high dose group.

图7 各组AsPC-1细胞*JAK2* mRNA、*STAT3* mRNA表达

Fig.7 Expression of *JAK2* mRNA and *STAT3* mRNA in AsPC-1 cells of each group

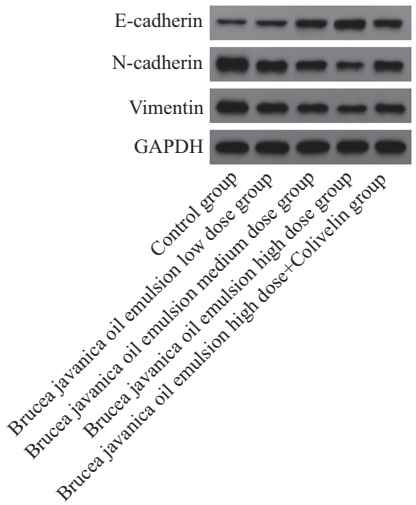
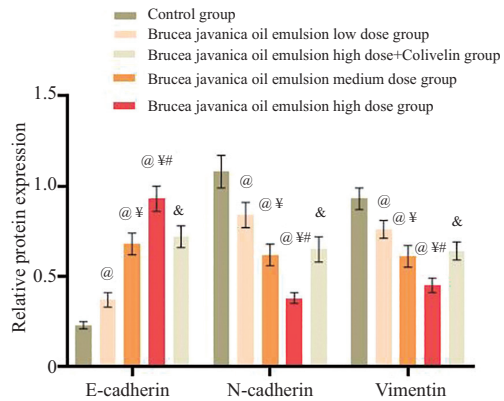


图8 各组细胞E-cadherin、N-cadherin、Vimentin蛋白表达

Fig.8 Expression of E-cadherin, N-cadherin and Vimentin in cells of each group



$^{@}P$<0.05, 与对照组比较; $^{¥}P$<0.05, 与鸦胆子油乳低剂量组比较; $^{\#}P$<0.05, 与鸦胆子油乳中剂量组比较; $^{\&}P$<0.05, 与鸦胆子油乳高剂量组比较。
$^{@}P$<0.05 compared with control group; $^{¥}P$<0.05 compared with Brucea javanica oil emulsion low dose group; $^{\#}P$<0.05 compared with Brucea javanica oil emulsion medium dose group; $^{\&}P$<0.05 compared with Brucea javanica oil emulsion high dose group.

图9 鸦胆子油乳对各组细胞E-cadherin、N-cadherin、Vimentin蛋白表达的影响

Fig.9 Effects of Brucea javanica oil emulsion on expression of E-cadherin, N-cadherin and Vimentin in cells of each group

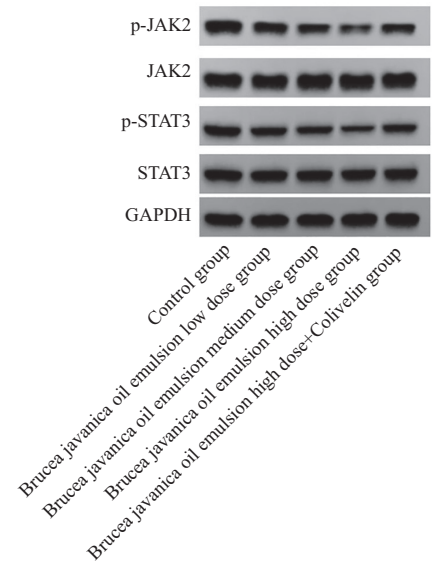
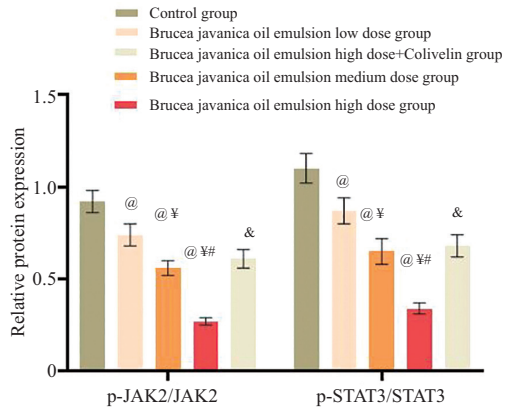


图10 各组AsPC-1细胞p-JAK2、JAK2、p-STAT3、STAT3蛋白表达

Fig.10 Expression of p-JAK2, JAK2, p-STAT3 and STAT3 proteins in AsPC-1 cells of each group



$^{@}P$<0.05, 与对照组比较; $^{¥}P$<0.05, 与鸦胆子油乳低剂量组比较; $^{\#}P$<0.05, 与鸦胆子油乳中剂量组比较; $^{\&}P$<0.05, 与鸦胆子油乳高剂量组比较。

$^{@}P$<0.05 compared with control group; $^{¥}P$<0.05 compared with Brucea javanica oil emulsion low dose group; $^{\#}P$<0.05 compared with Brucea javanica oil emulsion medium dose group; $^{\&}P$<0.05 compared with Brucea javanica oil emulsion high dose group.

图11 鸦胆子油乳对各组AsPC-1细胞JAK2/STAT3通路相关蛋白的影响

Fig.11 Effects of Brucea javanica oil emulsion on JAK2/STAT3 pathway related proteins in AsPC-1 cells of each group

较强的迁移和侵袭能力, 导致癌细胞在体内易发生转移, 导致预后差复发率高[15]。EMT是上皮细胞失去极性向间质细胞转化, 其特点是细胞黏附性下降, 细胞运动迁移和侵袭能力增强, 是胰腺癌细胞发生转移和侵袭的重要机制之一[16]。因此探究如何抑制EMT过程对治疗胰腺癌具有重要意义。

鸦胆子油乳是从鸦胆子中提取的, 主要成分为不饱和脂肪酸。研究表明鸦胆子油乳具有抗癌活性, 可抑制肿瘤生长[17]。朱湘亮等[18]研究表明, 鸦胆子油乳可以诱导非小细胞肺癌A549细胞自噬, 抑制细胞增殖和迁移。罗琦等[19]研究表明, 鸦胆子油乳可以抑制宫颈癌HeLa细胞增殖, 并诱导其凋亡, 使其阻滞于S期。推测鸦胆子油乳也可以抑制胰腺癌的发生发展。本研究用不同浓度的鸦胆子油乳处理AsPC-1细胞, 结果表明, 鸦胆子油乳低、中、高剂量组AsPC-1细胞活力、增殖率、细胞划痕愈合率与侵袭细胞个数较对照组显著降低, 表明鸦胆子油乳可以抑制AsPC-1细胞的恶性生物学行为发展。N-cadherin、Vimentin、E-cadherin是EMT标志物, E-cadherin可维持细胞间黏附作用, N-cadherin可促进上皮–间质细胞的迁移, Vimentin为间质细胞特异性蛋白, EMT发生时N-cadherin、Vimentin表达上调,

E-cadherin表达下调。本研究结果表明, 鸦胆子油乳处理AsPC-1细胞可显著上调E-cadherin表达, 降低N-cadherin、Vimentin表达, 提示鸦胆子油乳可抑制胰腺癌细胞的EMT过程。

研究表明, JAK2/STAT3信号通路参与人类多种肿瘤的发生过程, 激活该通路导致肿瘤细胞恶性增殖, 抑制该通路可降低肿瘤细胞的恶性发展[20]。张薇等[12]研究表明, 青蒿琥酯通过阻断JAK2/STAT3信号通路可以抑制淋巴瘤Raji细胞增殖, 并促进其凋亡。邓雪松[21]研究表明, 阻断JAK2/STAT3信号通路可以抑制早期胃癌的生物学行为发生。本研究实验结果表明, 与对照组相比, 鸦胆子油乳低、中、高剂量组细胞*JAK2*、*STAT3*基因和磷酸化蛋白表达量显著降低, EMT过程受到抑制, 提示鸦胆子油乳可以抑制JAK2/STAT3信号通路。与鸦胆子油乳单独处理相比, 鸦胆子油乳和Colivelin共同处理可提高细胞活力、增殖率、细胞划痕愈合率、侵袭细胞个数、*JAK2*、*STAT3*基因和磷酸化蛋白表达水平, 促进EMT过程。这提示Colivelin可逆转鸦胆子油乳对胰腺癌细胞的抑制作用, 促进细胞增殖、迁移、侵袭和EMT。

综上所述, 鸦胆子油乳可通过抑制JAK2/STAT3信号通路进而抑制AsPC-1细胞增殖、迁移、侵袭和EMT。但本实验仅在一种细胞水平进行探究, 后续还需进行多种细胞以及动物实验验证。

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