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·基础研究·

姜黄素改善中波紫外线照射细胞损伤的机制研究

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[摘 要] **目的** 探讨姜黄素(CUR)通过Toll样受体4(TLR4)/核因子-κB(NF-κB)/核苷酸结合寡聚化结构域样受体蛋白3(NLRP3)信号通路对中波紫外线(UVB)诱导的角质形成细胞氧化损伤的影响。**方法** 体外正常培养人角质形成细胞HaCaT,以57 mJ/cm^{2}的UVB照射建立角质形成细胞氧化损伤模型,正常培养的细胞为Control组,建模后的细胞为UVB组,建模后经5 μmol/L CUR处理的细胞为CUR组,建模后经100 μg/L TLR4抑制剂TAK-242处理的细胞为TAK-242组,建模后经5 μmol/L CUR及100 nmol/L TLR4激活剂脂多糖(LPS)处理的细胞为CUR+LPS组。qRT-PCR检测各组细胞中TLR4、NF-κB、NLRP3 mRNA的表达水平;CCK-8检测各组细胞的增殖情况;根据试剂盒说明书采用荧光法检测各组细胞中活性氧(ROS)相对含量,超氧化物歧化酶(SOD)、过氧化氢酶(CAT)活力,丙二醛(MDA)、谷胱甘肽(GSH)浓度;ELISA检测各组细胞中肿瘤坏死因子-α(TNF-α)和白细胞介素-1β(IL-1β)等炎症因子的表达水平;流式细胞仪检测各组细胞的凋亡水平;Western blot检测各组细胞中增殖相关蛋白增殖细胞核抗原(PCNA)、凋亡相关蛋白[B淋巴细胞瘤-2(Bcl-2)、Bcl-2相关X蛋白(Bax)]及TLR4/NF-κB/NLRP3信号通路相关蛋白(TLR4、NF-κB、NLRP3)表达。**结果** 与Control组相比,UVB组细胞存活率,PCNA、Bcl-2蛋白表达水平,SOD、CAT活力,GSH浓度降低,而细胞凋亡率,Bax蛋白水平,ROS相对含量,MDA浓度,TNF-α、IL-1β水平,TLR4、NF-κB、NLRP3 mRNA和蛋白水平升高(P<0.05);与UVB组相比,TAK-242组、CUR组细胞存活率,PCNA、Bcl-2蛋白表达水平,SOD、CAT活力,GSH浓度升高,而细胞凋亡率,Bax蛋白水平,ROS相对含量,MDA浓度,TNF-α、IL-1β水平,TLR4、NF-κB、NLRP3 mRNA和蛋白水平降低(P<0.05);与CUR组相比,CUR+LPS组细胞存活率,PCNA、Bcl-2蛋白表达水平,SOD、CAT活力,GSH浓度降低,而细胞凋亡率,Bax蛋白表达水平,ROS相对含量,MDA浓度,TNF-α、IL-1β水平,TLR4、NF-κB、NLRP3 mRNA和蛋白水平升高(P<0.05)。**结论** CUR能够提高角质形成细胞的抗氧化应激水平,减轻炎症反应,促进细胞增殖,改善UVB照射引起的细胞损伤,其机制可能与抑制TLR4/NF-κB/NLRP3信号通路有关。

[关键词] 姜黄素;TLR4/NF-κB/NLRP3信号通路;中波紫外线;角质形成细胞;氧化损伤

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Mechanism of curcumin on improving cell damage induced by ultraviolet B irradiation

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Abstract: Objective To explore the effect of curcumin (CUR) on oxidative damage of keratinocytes induced by ultraviolet B (UVB) irradiation through Toll-like receptor 4 (TLR4)/nuclear factor-kappa B (NF-κB)/nucleotide-binding oligomerization domain-containing protein 3 (NLRP3) signaling pathway. **Methods** Human keratinocytes of HaCaT were cultured normally in vitro, and the keratinocyte oxidative damage model was established by the irradiation of 57 mJ/cm^2 UVB. The cells with normal culture were as the control group, the cells treated after modeling were as the UVB group, the cells treated with 5 μmol/L CUR after modeling were as the CUR group, the cells treated with 100 μg/L TLR4 inhibitor of TAK-242 after modeling were as the TAK-242 group, and the cells treated with 5 μmol/L CUR and 100 nmol/L TLR4 activator of lipopolysaccharide(LPS) were as the CUR+LPS group. qRT-PCR was applied to detect the relative expression levels of TLR4, NF-κB, and NLRP3 mRNAs of cells in each group. CCK-8 was applied to detect the cell proliferation in each group. The relative content of reactive oxygen species (ROS), the viabilities of superoxide dismutase (SOD) and catalase (CAT), and the concentrations of glutathione (MDA) and glutathione (GSH) of cells in each group were detected by fluorescence assay according to the kit instruction. ELISA kit was used to detect the expression of inflammatory factors of tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β) of cells in each group. Flow cytometry was applied to detect the cell apoptosis in each group. Western blot was applied to detect the expression of proliferation related protein of proliferating cell nuclear antigen (PCNA), apoptosis related proteins [B-cell lymphoma-2(Bcl-2) and Bcl-2-associated X protein (Bax)], and TLR4/NF-κB/NLRP3 signaling pathway related proteins (TLR4, NF-κB and NLRP3) of cells in each group. **Results** Compared with the Control group, the cell survival rate, the expression levels of PCNA and Bcl-2 proteins, the viabilities of SOD and CAT, and the GSH concentration in the UVB group decreased, while the apoptosis rate, the level of Bax protein, the relative content of ROS, the concentration of MDA, the levels of TNF-α and IL-1β, and the mRNA and protein levels of TLR4, NF-κB and NLRP3 increased (P<0.05). Compared with the UVB group, the cell survival rate, the expression levels of PCNA and Bcl-2 proteins, the viabilities of SOD and CAT, and the GSH concentration in the TAK-242 group and CUR group increased, while the apoptosis rate, the level of Bax protein, the relative content of ROS, the concentration of MDA, the levels of TNF-α and IL-1β, and the mRNA and protein levels of TLR4, NF-κB and NLRP3 decreased (P<0.05). Compared with the CUR group, the cell survival rate, the expression levels of PCNA and Bcl-2 proteins, the viabilities of SOD and CAT, and the GSH concentration in the CUR+LPS group decreased, while the apoptosis rate, the level of Bax protein, the relative content of ROS, the concentration of MDA, the levels of TNF-α and IL-1β, and the mRNA and protein levels of TLR4, NF-κB and NLRP3 increased (P<0.05). **Conclusion** CUR can increase the antioxidant stress level of keratinocytes, alleviate inflammatory response, promote cell proliferation, and improve cell damage caused by UVB irradiation, which may be related to the inhibition of TLR4/NF-κB/NLRP3 signaling pathway.

Keywords: curcumin; TLR4/NF-κB/NLRP3 signaling pathway; ultraviolet B; keratinocytes; oxidative damage

角质形成细胞是构成人表皮的主要细胞，当中波（波长280~320 nm）紫外线（ultraviolet B,UVB）作用于皮肤表皮时会引起角质形成细胞氧化损伤和细胞凋亡，影响细胞内超氧化物歧化酶（superoxide dismutase, SOD）、谷胱甘肽（glutathione, GSH）和过氧化氢酶（catalase,CAT）所构成的抗氧化酶系统，导致活性氧（reactive oxygen species, ROS）、丙二醛（malondialdehyde,MDA）水平升高，引起细胞膜脂质过氧化、蛋白变性和DNA断裂，进而引发急性效应，如晒伤、光老化和皮肤癌[1-3]。因此，探寻能够缓解UVB诱导的角质形成细胞氧化损伤的药物及相关靶点具有重要意义。姜黄素（curcumin,CUR）是一种从姜黄根茎中提取的多酚化合物，其抗炎、抗氧化特性有利于银屑病、硬皮病等皮肤病的治疗[4-5]。有学者研究发现，CUR能够通过减轻UVB照射诱导的急性炎症和光老化来抑制紫外线诱导的皮肤癌变[6]，由此推测其对UVB诱导的角质形成细胞氧化损伤也具有一定的治疗作用。Toll样受体4（Toll-like receptor 4, TLR4）、核因子-κB（nuclear factor-kappa B,NF-κB）及核苷酸结合寡聚化结构域样受体蛋白3（nucleotide-binding oligomerization domain-containing protein 3,NLRP3）炎症小体所构成的信号通路已被证实在氧化损伤和炎症的调节中发挥关键作用[7-8]。不仅如此，TLR4/NF-κB/NLRP3信号通路还能够通过调控炎症细胞因子的产生和释放，影响皮肤细胞的增殖、分化和凋亡等过程，抑制该信号通路可减轻氧化应激和炎症反应，延缓组织损伤[9]。因此，本研究旨在探讨CUR能否通过调控TLR4/NF-κB/NLRP3信号通路减轻UVB诱导的角质形成细胞氧化应激及炎

症反应,从而减缓皮肤紫外线照射损伤。

1 材料与方法

1.1 主要试剂与仪器

人角质形成细胞HaCaT购自美国ATCC细胞库;DMEM培养基(批号:20220305)、胎牛血清(批号:20220506)购自德国Sigma-Aldrich公司;CUR(批号:20210609)购自上海麦克林生化科技股份公司;脂多糖(lipopolysaccharide,LPS)(批号:20210907)、TAK-242(批号:20221011)购自美国MCE公司;CCK-8试剂盒(批号:20210629)购自上海翌圣生物技术股份有限公司;ROS试剂盒(批号:20220806)、MDA试剂盒(批号:20220907)、SOD试剂盒(批号:20221005)、CAT试剂盒(批号:20210509)、GSH试剂盒(批号:20220109)、肿瘤坏死因子-α(tumor necrosis factor-α,TNF-α)试剂盒(批号:20220618)、白细胞介素-1β(interleukin-1β,IL-1β)试剂盒(批号:20221121)及Annexin V-FITC/PI细胞凋亡检测试剂盒(批号:20220608)购自南京建成生物工程研究所;SDS-PAGE凝胶制备试剂盒(批号:20210907)购自江苏康为世纪生物科技有限公司;增殖细胞核抗原(proliferating cell nuclear antigen,PCNA)(批号:20221014)、B淋巴细胞瘤-2(B-cell lymphoma-2,Bcl-2)(批号:20220305)、Bcl-2相关X蛋白(Bcl-2-associated X protein,Bax)(批号:20211205)、TLR4(批号:20220605)、NF-κB(批号:20211216)、NLRP3(批号:20220306)一抗购自美国Affinity公司;GAPDH(批号:20220206)及二抗山羊抗兔(批号:20221105)、山羊抗鼠(批号:20200908)购自英国Abcam公司。多功能酶标仪(型号:SpectraMax iD5)购自北京悦昌行科技有限公司;凝胶成像系统(型号:Tanon 1600)购自上海天能生命科学有限公司;流式细胞仪(型号:CyFlow Cube 6)购自广州吉源生物科技有限公司。

1.2 方法

1.2.1 细胞培养及分组 使用含10%胎牛血清、1%青霉素-链霉素的DMEM完全培养基培养HaCaT细胞,再以57 mJ/cm^{2}的UVB照射24 h建立角质形成细胞氧化损伤模型[10],正常培养的细胞为Control组,建模后的细胞为UVB组,建模后经5 μmol/L CUR[10]处理的细胞为CUR组,建模后经100 μg/L TLR4抑制剂TAK-242[11]处理的细胞为TAK-242组,建模后经5 μmol/L CUR及100 nmol/L TLR4激活剂LPS[12]处理的细胞为CUR+LPS组。

1.2.2 qRT-PCR检测mRNA的相对表达水平 提取各组细胞中总RNA,进行qRT-PCR。以β-actin为内参,采用$2^{-\triangle\triangle Ct}$法计算TLR4、NF-κB、NLRP3 mRNA的相对表达水平。引物序列见表1。

表1 qRT-PCR引物序列

基因	正向引物(5′-3′)	反向引物(5′-3′)
TLR4	TCAATCTCTCTTTAGACCTGTC	TGAACTCATCAATGCTCAC
NF-κB	GCCATAGCCATAGTTGC	GCTGGTTATTCTGGAAGTC
NLRP3	CAGCCAGAGTGGAATGATGC	TTGCTTGGATGCTCCTTGAC
β-actin	TGTCACCAACTGGGACGATA	GGGGTGTTGAAGGTCTCAAA

1.2.3 CCK-8检测各组细胞增殖情况 将HaCaT细胞接种在96孔板中,并按1.2.1进行相应细胞分组处理。24 h后加入10 μL的CCK-8溶液再次培养2 h。采用酶标仪测定450 nm波长处的吸光度,并计算各组细胞存活率。

1.2.4 各组细胞中ROS、MDA、SOD、CAT、GSH测定 在细胞分组处理后,收集细胞,然后参照试剂盒说明书检测各组HaCaT细胞中ROS相对含量,SOD、CAT活力及MDA、GSH浓度。

1.2.5 ELISA检测各组细胞中TNF-α、IL-1β水平 取各组HaCaT细胞培养液,离心,取上清。依据ELISA试剂盒说明书步骤进行检测,并计算TNF-α、IL-1β水平。

1.2.6 流式细胞仪检测各组细胞凋亡水平 收集各组HaCaT细胞,用PBS重悬。根据Annexin V-FITC/PI细胞凋亡检测试剂盒说明书进行染色,然后在流式细胞仪中测定细胞凋亡率。

1.2.7 Western blot检测各组细胞中相关蛋白表达 各组细胞加入裂解液后置于冰上裂解,提取HaCaT细胞总蛋白。使用BCA蛋白测定试剂盒测定蛋白浓度。SDS-PAGE凝胶电泳分离蛋白,并转移至PVDF膜,然后将膜在5%脱脂奶粉中孵育2 h,再与PCNA(1∶1 000)、Bcl-2(1∶1 000)、Bax(1∶3 000)、TLR4(1∶2 000)、NF-κB(1∶1 000)、NLRP3(1∶1 000)、GAPDH(1∶8 000)一抗在4 ℃孵育过夜,之后与二抗(1∶5 000)于37 ℃孵育2 h。在凝胶成像系统中观察并拍照,用Image J软件进行蛋白定量分析。

1.3 统计学分析

数据采用SPSS 26.0软件进行统计学分析,结果以均数±标准差($\bar{x}\pm s$)表示,采用单因素方差分析进行多组间比较,进一步两两比较采用*SNK-q*检验。$P<0.05$表示差异有统计学意义。

2 结果

2.1 各组细胞中TLR4、NF-κB、NLRP3 mRNA的表达 与Control组相比,UVB组细胞的TLR4、NF-κB、

NLRP3 mRNA水平升高($P<0.05$);与UVB组相比,TAK-242组、CUR组细胞的TLR4、NF-κB、NLRP3 mRNA水平降低($P<0.05$);与CUR组相比,CUR+LPS组细胞的TLR4、NF-κB、NLRP3 mRNA水平升高($P<0.05$),见表2。

表2 HaCaT细胞中TLR4、NF-κB、NLRP3 mRNA的相对表达水平($\bar{x}\pm s$)

组别	TLR4	NF-κB	NLRP3
Control组	1.00±0.12	0.99±0.10	1.01±0.11
UVB组	2.03±0.23*	1.89±0.20*	2.11±0.22*
CUR组	1.34±0.14#	1.26±0.13#	1.48±0.15#
TAK-242组	1.53±0.16#	1.41±0.14#	1.62±0.17#
CUR+LPS组	1.95±0.20△	1.73±0.17△	2.01±0.20△

*:与Control组比较,$P<0.05$;#:与UVB组比较,$P<0.05$;△:与CUR组比较,$P<0.05$

2.2 CUR对细胞增殖的影响

与Control组相比,UVB组细胞存活率、PCNA蛋白表达水平降低($P<0.05$);与UVB组相比,TAK-242组、CUR组细胞存活率、PCNA蛋白表达水平升高($P<0.05$);与CUR组相比,CUR+LPS组细胞存活率、PCNA蛋白表达水平降低($P<0.05$),见图1、表3。

2.3 CUR对细胞中ROS、MDA、SOD、CAT、GSH的影响

与Control组相比,UVB组细胞的SOD、CAT活力及GSH浓度降低,而ROS相对含量、MDA浓度升高($P<0.05$);与UVB组相比,TAK-242组、CUR组细胞的SOD、CAT活力及GSH浓度升高,而ROS相对含量、MDA浓度降低($P<0.05$);与CUR组相比,CUR+LPS组细胞的SOD、CAT活力及GSH浓度降低,而ROS相对含量、MDA浓度升高($P<0.05$),见表4。

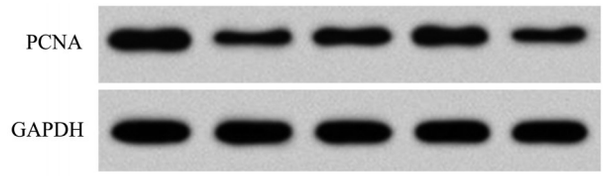


图1 Western blot检测各组细胞中PCNA蛋白表达

表3 CUR对细胞增殖的影响($\bar{x}\pm s$)

组别	存活率(%)	PCNA蛋白
Control组	100.00±0.00	1.00±0.11
UVB组	50.99±6.02*	0.46±0.05*
CUR组	73.51±7.43#	0.72±0.08#
TAK-242组	79.78±7.99#	0.80±0.09#
CUR+LPS组	59.63±5.65△	0.55±0.06△

*:与Control组比较,$P<0.05$;#:与UVB组比较,$P<0.05$;△:与CUR组比较,$P<0.05$

2.4 CUR对细胞中炎症因子TNF-α、IL-1β表达的影响

与Control组相比,UVB组细胞的TNF-α、IL-1β水平升高($P<0.05$);与UVB组相比,TAK-242组、CUR组细胞的TNF-α、IL-1β水平降低($P<0.05$);与CUR组相比,CUR+LPS组细胞的TNF-α、IL-1β水平升高($P<0.05$),见表5。

2.5 CUR对细胞凋亡的影响

与Control组相比,UVB组细胞的Bcl-2蛋白水平降低,而细胞凋亡率、Bax蛋白水平升高($P<0.05$);与UVB组相比,TAK-242组、CUR组细胞的Bcl-2蛋白水平升高,而细胞凋亡率、Bax蛋白水平降低($P<0.05$);与CUR组相比,CUR+LPS组细胞的Bcl-2蛋白水平降低,而细胞凋亡率、Bax蛋白水平升高($P<0.05$),见图2~3、表6。

表4 CUR对细胞中ROS、MDA、SOD、CAT、GSH水平的影响($\bar{x}\pm s$)

组别	ROS相对含量(%)	MDA(mmol/mg)	SOD(U/mg)	CAT(U/mg)	GSH(mmol/mg)
Control组	85.45±7.97	5.34±0.65	30.32±3.11	15.41±1.55	38.67±3.87
UVB组	213.46±20.12*	13.98±1.48*	11.98±1.20*	5.02±0.51*	9.74±1.00*
CUR组	154.21±13.65#	10.52±1.03#	21.34±2.15#	10.30±1.11#	22.02±2.45#
TAK-242组	149.39±11.34#	9.07±0.90#	23.17±2.52#	12.56±1.28#	25.99±2.30#
CUR+LPS组	190.01±16.01△	12.51±1.25△	15.01±1.51△	6.98±0.70△	16.36±1.72△

*:与Control组比较,$P<0.05$;#:与UVB组比较,$P<0.05$;△:与CUR组比较,$P<0.05$

表5 CUR对细胞中TNF-α、IL-1β表达的影响($\bar{x}\pm s$,pg/mL)

组别	TNF-α	IL-1β
Control组	41.72±4.17	33.82±3.28
UVB组	95.26±9.53*	74.19±7.32*
CUR组	69.04±6.96#	55.33±5.53#
TAK-242组	67.81±6.48#	53.47±4.97#
CUR+LPS组	84.55±8.02△	68.55±5.90△

*:与Control组比较,$P<0.05$;#:与UVB组比较,$P<0.05$;△:与CUR组比较,$P<0.05$

2.6 CUR对细胞TLR4/NF-κB/NLRP3信号通路相关蛋白表达的影响

与Control组相比,UVB组细胞的TLR4、NF-κB、NLRP3蛋白水平升高($P<0.05$);与UVB组相比,TAK-242组、CUR组细胞的TLR4、NF-κB、NLRP3蛋白水平降低($P<0.05$);与CUR组相比,CUR+LPS组细胞的TLR4、NF-κB、NLRP3蛋白水平升高($P<0.05$),见图4、表7。

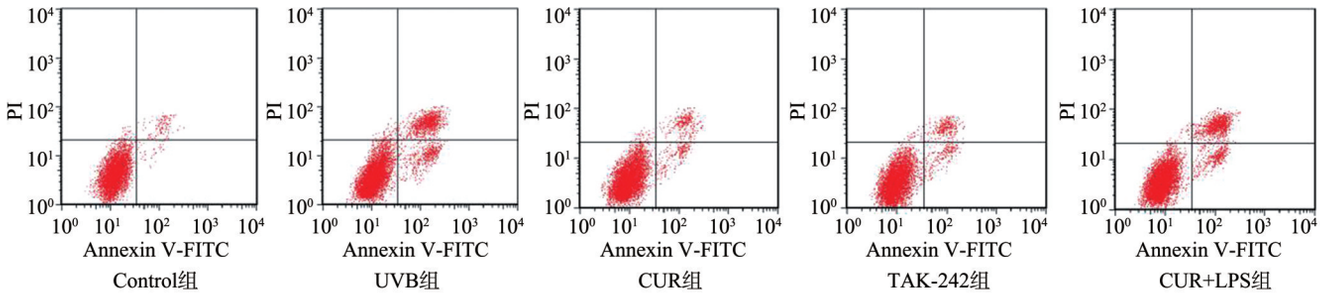


图2 流式细胞仪检测细胞的凋亡率

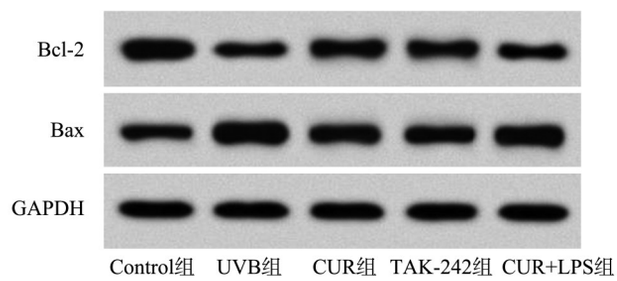


图3 Western blot检测细胞中Bcl-2、Bax蛋白的表达

表6 CUR对细胞凋亡的影响($\bar{x}\pm s$)

组别	细胞凋亡率(%)	Bcl-2蛋白	Bax蛋白
Control组	2.49±0.26	1.76±0.18	1.00±0.13
UVB组	36.57±3.66*	0.90±0.10*	2.07±0.21*
CUR组	20.02±2.00#	1.31±0.14#	1.55±0.16#
TAK-242组	18.68±1.59#	1.39±0.15#	1.41±0.14#
CUR+LPS组	31.33±3.12△	1.09±0.12△	1.83±0.18△

*:与Control组比较,$P<0.05$;#:与UVB组比较,$P<0.05$;△:与CUR组比较,$P<0.05$

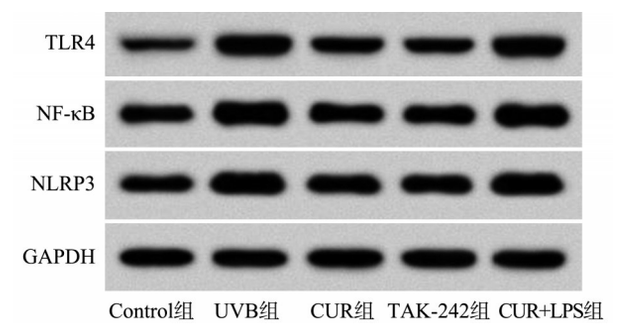


图4 Western blot检测细胞中TLR4、NF-κB、NLRP3蛋白表达

表7 CUR对细胞中TLR4/NF-κB/NLRP3信号通路相关蛋白表达的影响($\bar{x}\pm s$)

组别	TLR4	NF-κB	NLRP3
Control组	0.67±0.08	1.00±0.09	0.88±0.09
UVB组	1.40±0.15*	2.10±0.21*	1.72±0.17*
CUR组	1.13±0.11#	1.56±0.16#	1.34±0.14#
TAK-242组	0.98±0.10#	1.47±0.15#	1.26±0.13#
CUR+LPS组	1.35±0.14△	1.92±0.19△	1.62±0.16△

*:与Control组比较,$P<0.05$;#:与UVB组比较,$P<0.05$;△:与CUR组比较,$P<0.05$

3 讨论

长时间UVB照射会导致皮肤氧化损伤,产生的ROS会猛烈攻击DNA、蛋白质和生物膜系统,引发一系列炎症、氧化应激等病理反应,从而导致角质细胞凋亡,皮肤屏障功能受损,显著增加感染和致癌风险[13-15]。因此,探讨UVB照射与皮肤损伤所引发的级联反应对于寻找有效的干预措施具有重要意义。

CUR由于其显著的抗炎、抗氧化及抗菌特性,成为了预防和治疗皮肤炎症、延缓老化的潜在药物[16]。CUR还能够有效抵御因长期UVB照射导致的皮肤损伤,加速伤口愈合进程,改善胶原沉积,并促进创面成纤维细胞和血管密度的增加[8]。此外,CUR还能提升机体内SOD、GSH等抗氧化酶的含量,进而有效清除ROS自由基,减轻炎症反应[17]。CUR还可以通过调节凋亡相关蛋白(如Bcl-2、Bax)的表达,为机体提供全面的保护[18]。本研究亦显示,CUR减少了角质形成细胞中炎症因子TNF-α、IL-1β及ROS、MDA的产生,并增加了抗氧化酶SOD、GSH、CAT的活性,从而抑制细胞凋亡,促进细胞增殖。这提示,CUR能够减少UVB照射诱导的炎症和氧化应激反应,增强抗氧化酶活性,从而保护细胞免受氧化损伤,但CUR发挥作用的途径尚不清楚。

TLR4/NF-κB/NLRP3信号通路与多种疾病的发生发展密切相关。TLR4会先识别并结合相应配体,激活NF-κB信号通路,并转移至细胞核内,调控TNF-α、IL-1β等炎症相关基因以及炎症小体NLRP3的表达,进而激活Caspase-1等效应分子,促进炎症因子释放[19]。Li等[20]研究证明,通过抑制TLR4/NF-κB/NLRP3信号通过能够减轻皮肤炎症反应,缓解皮肤损伤。Zhang等[21]进一步研究表明,通过使TLR4/NF-κB介导的NLRP3炎症小体失活能够调控心肌细胞氧化损伤、巨噬细胞极化等进程,从而减轻心肌缺血再灌注损伤。本研究结果显示,CUR可显著抑制UVB照射上调的TLR4/NF-κB/NLRP3信号通路相关蛋白(TLR4、NF-κB、NLRP3)的表达,从而减少炎症因子TNF-α、IL-1β及ROS、MDA

的产生,并促进SOD、GSH、CAT所构成的抗氧化酶系统的激活,从而抑制细胞凋亡;然而,添加LSP逆转了上述指标的变化趋势,与王慧等[22]研究结果相似。这表明,CUR可通过抑制TLR4/NF-κB/NLRP3信号通路,减轻炎症及氧化应激反应,抑制细胞凋亡,从而缓解细胞损伤。

综上所述,CUR能够提高角质形成细胞的抗氧化应激水平,减轻炎症反应,促进细胞增殖,缓解UVB照射引起的细胞损伤,其作用机制可能与抑制TLR4/NF-κB/NLRP3信号通路有关。但本研究仅为体外初步实验,其在体内的生物利用度和代谢等问题,仍需要大量的动物或临床试验数据证实。

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