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## 中医药调控 VEGF 信号通路抗血管生成干预乳腺癌前病变的研究进展

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**[摘要]** 乳腺癌防治已成为全球公共卫生领域亟待解决的重大问题,其癌前病变(PBC)作为乳腺癌演变进程中的关键病理过渡期,具有显著的临床转化风险,有效干预PBC进展对遏制乳腺癌的发生具有重要临床意义。病理研究表明,异常血管生成是驱动PBC向乳腺癌转化的关键病理机制,而血管内皮生长因子(VEGF)作为促血管生成的核心调控分子,在该过程中起枢纽作用。PBC的恶性转化进程与VEGF介导的促血管生成网络的异常激活密切相关。现代医学虽通过手术及内分泌等治疗取得一定疗效,但尚存在创伤性、耐药性及不良反应等临床局限。近年研究发现,VEGF信号系统通过介导磷脂酰肌醇3-激酶/蛋白激酶B(PI3K/Akt)和丝裂原活化蛋白激酶(MAPK)信号通路,缺氧诱导因子-1 $\alpha$ (HIF-1 $\alpha$ )/VEGF信号通路与 $\delta$ 样蛋白4(DLL4)/缺口受体1(Notch1)等多条信号通路形成复杂的调控网络,在PBC血管新生过程中发挥核心作用。中医药凭借其多组分协同、多通路调控及安全性高等特性,在通过靶向抑制VEGF信号通路干预病理性血管生成、阻断PBC进展方面呈现显著优势。该文基于VEGF信号通路调控视角,系统梳理中医药抑制血管新生干预PBC的最新研究进展,探讨中医药用于早期防治PBC的应用机制及价值,以期临床干预PBC策略的优化提供借鉴与参考。

**[关键词]** 中医药; 乳腺癌前病变; 血管内皮生长因子(VEGF); 血管生成; 研究进展

**[中图分类号]** R273;R287;R285 **[文献标识码]** A **[文章编号]** 1005-9903(XXXX)XX-0001-08

**[doi]** 10.13422/j.cnki.syfjx.20251524

**[网络出版地址]**

**[网络出版日期]** XXXX-XX-XX **[增强出版附件]** 内容详见 <http://www.syfjxzz.com> 或 <http://cnki.net>



### Traditional Chinese Medicine Regulates VEGF Signaling Pathway for Anti-angiogenic Intervention in Preneoplastic Breast Cancer: A Review

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**[Abstract]** Breast cancer prevention and treatment have become major issues that urgently need to be addressed in the field of global public health. As a key pathological transitional stage in the progression of breast cancer, preneoplastic breast cancer (PBC) carries a significant risk of clinical transformation. Effective intervention in the progression of PBC is of great clinical significance in preventing the occurrence of breast cancer. Pathological studies have shown that abnormal angiogenesis is a key mechanism driving the transformation of PBC into breast cancer. Vascular endothelial growth factor (VEGF), as a core regulatory molecule that promotes angiogenesis, plays a pivotal role in this process. The malignant transformation of PBC is closely associated with the abnormal activation of the VEGF-mediated pro-angiogenic network. Although modern medicine has achieved certain therapeutic effects through surgery and endocrine therapy, clinical limitations such as invasiveness, drug resistance, and adverse

**[收稿日期]** 2025-04-08

**[基金项目]** 国家自然科学基金项目(81760896);云南省科技厅中医药基础研究联合专项青年项目(202101A070001-300);云南省科技厅基础研究计划面上项目(202101AZ070001-033)

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reactions still exist. Recent studies have demonstrated that the VEGF signaling system mediates the phosphatidylinositol 3-kinase-protein kinase B (PI3K/Akt) signaling pathway and the mitogen-activated protein kinase (MAPK) pathway. In addition, the hypoxia-inducible factor-1 $\alpha$  (HIF-1 $\alpha$ )/VEGF signaling pathway and the delta-like ligand 4 (DLL4)/Notch receptor 1 (Notch1) signaling pathway, together with other pathways, form a complex regulatory network that plays a central role in angiogenesis during PBC. Traditional Chinese medicine (TCM), characterized by multi-component synergy, multi-pathway regulation, and high safety, demonstrates significant advantages in inhibiting pathological angiogenesis and blocking PBC progression by targeting the VEGF signaling pathway. From the perspective of VEGF pathway regulation, this paper systematically reviews the latest research progress on TCM in inhibiting angiogenesis and intervening in PBC, and discusses its mechanisms and application value in the early prevention and treatment of PBC, with the aim of providing references for optimizing clinical intervention strategies for PBC.

**[Keywords]** traditional Chinese medicine; preneoplastic breast cancer; vascular endothelial growth factor (VEGF); angiogenesis; research advances

乳腺癌防治已成为全球公共卫生领域的重要议题。世界卫生组织《2020全球癌症统计报告》显示,乳腺癌发病率首次超越肺癌成为全球最高发的恶性肿瘤<sup>[1]</sup>。近年来乳腺癌的发病年龄日益呈现出年轻化的趋势<sup>[2]</sup>。据统计,2022年我国乳腺癌发病总人数达35.7万,占全球发病率的15.6%,严重威胁着女性的生命健康<sup>[3]</sup>。该疾病遵循“正常腺体—增生性病变—非典型增生—原位癌—浸润癌”的渐进式演变规律,其中乳腺癌前病变(PBC)作为癌变必经阶段,临床数据显示其未干预病例的浸润性转化率可达40%以上,这使得PBC的早期阻断与病理逆转成为乳腺癌二级预防的关键突破口<sup>[4]</sup>。早期阻断PBC、逆转乳腺癌变进程成为临床治疗的难点与热点,具有重要意义。目前现代医学对于PBC的治疗变主要采用手术和内分泌调节治疗,但手术创伤性及内分泌治疗引发的耐药性和不良反应等问题亟待解决。血管生成是恶性肿瘤发生、进展、和侵袭的关键途径,哈佛大学Folkman教授于1971年首次揭示了血管生成在恶性肿瘤生长和转移过程中的关键作用<sup>[5]</sup>。分子病理学研究证实,异常血管新生是PBC恶性转化的关键病理基础,其中血管内皮生长因子(VEGF)通过激活促血管生成信号网络发挥核心调控作用<sup>[6]</sup>。近年来,对VEGF相关信号通路的研究证实了该通路在干预PBC的血管生成方面具有有效性,其主要通过调控磷脂酰肌醇3-激酶/蛋白激酶B(PI3K/Akt)信号通路和丝裂原活化蛋白激酶(MAPK)信号通路,缺氧诱导因子1 $\alpha$ (HIF-1 $\alpha$ )/VEGF信号通路与 $\delta$ 样蛋白-4(DLL4)/缺口受体1(Notch1)等信号通路实现<sup>[7-8]</sup>。中医药具有多组分协同、整体调节及安全性高等独特优势,在筛选具有VEGF信号通路调控活性的中药活性成分方面展现出重要研究价值,并且VEGF相关信号通路近年来逐渐成为中医药防治乳腺癌研究的热点领域<sup>[9]</sup>。但目前该领域文献报道多样,尚未形成完整的系统性研究体系及总结。本文以中医药通过调控VEGF相关信号通路抗血管生成成为切入点,对干预PBC的相关研究进行归纳总结,探讨中医药用于早期防治PBC的应用价值,以期临床治疗策略的优化提供借鉴与参考。

### 1 VEGF相关信号通路介导血管生成的机制

VEGF作为目前已知最具特异性的促血管生成因子<sup>[10]</sup>,其作用机制涉及多维度信号级联与微环境重编程,通过调控内皮细胞增殖迁移、血管通透性及新生血管形成等过程,驱

动肿瘤发生发展与转移。VEGF家族包含VEGF-A/B/C/D/E及胎盘生长因子(PlGF)等成员,通过与酪氨酸激酶受体结合触发胞内信号转导<sup>[11]</sup>。其中VEGFR2作为核心功能受体,其与VEGF的特异性结合可激活下游信号通路,在病理性血管生成中起主导作用<sup>[12-13]</sup>。

其中调控血管内皮细胞增殖与迁移的核心机制是VEGF与VEGFR2结合后激活PI3K/Akt信号通路和MAPK<sup>[14]</sup>。机制解析表明,受体磷酸化触发磷脂酶C $\gamma$ (PLC $\gamma$ )活化,通过协同调控MAPK与PI3K信号通路,促进内皮细胞增殖及迁移<sup>[15]</sup>。此外,MAPK信号通路还可通过Ras/Raf/丝裂原活化蛋白激酶/细胞外信号调节激酶(Ras/Raf/MEK/ERK)信号通路级联反应驱动细胞周期进展和增殖<sup>[16]</sup>。同时,VEGF-A与VEGFR2结合后能活化PI3K,并促使Akt发生磷酸化,激活的VEGF-A/VEGFR2-PI3K/Akt信号轴可加速内皮细胞增殖、迁移,调控血管新生<sup>[17]</sup>。研究证实,双重阻断PI3K/Akt与MAPK信号通路可显著抑制VEGF介导的血管新生效应<sup>[18-19]</sup>。

缺氧是肿瘤微环境的核心特征,缺氧应激驱动的HIF-1 $\alpha$ /VEGF信号轴构成血管异常生成的关键调控枢纽。缺氧诱导的HIF-1 $\alpha$ 稳定性增加可特异性识别VEGF启动子区的缺氧反应元件(HRE),直接激活其转录活性<sup>[20]</sup>。VEGF可通过促进血管异常增生加剧肿瘤缺氧,形成正反馈环路,增强VEGF介导的血管生成<sup>[21]</sup>。HIF-1 $\alpha$ 在缺氧环境下可稳定表达,可介导机体对缺氧环境适应,这与实体瘤普遍存在的氧分压失衡特征高度相关<sup>[22]</sup>。分子靶向研究证实,干预HIF-1 $\alpha$ /VEGF信号级联可有效阻断乳腺癌血管生成,提示该通路可作为中医药多靶点干预的重要生物学基础<sup>[23]</sup>。

DLL4/Notch1信号通路也是参与血管生成的重要通路之一<sup>[24]</sup>。Notch1信号通路已被证明在调节肿瘤血管生成中起关键作用<sup>[25]</sup>。DLL4是Notch1的配体,通过控制内皮细胞活化、血管发育和成熟来调节血管生成,DLL4与Notch1的受体结合后将进一步促进VEGF等转录因子表达,促进血管新生<sup>[26]</sup>。也有研究发现,成纤维细胞生长因子2/成纤维细胞生长因子受体1(FGF2/FGFR1)信号通路的激活可协同增强VEGF效应,二者通过促进内皮细胞增殖及血管网络构建形成促血管生成微环境<sup>[27]</sup>。

VEGF还可通过激活Src激酶直接调控血管的通透性。

有研究发现, VEGFR-2的抗体(phospho-VEGF2, Tyr951)位点磷酸化后, 促进细胞间连接蛋白磷酸化, 导致内皮细胞间连接松解, 增加血管通透性<sup>[28-29]</sup>。血管通透性升高通过促进血浆蛋白外渗和释放纤维蛋白原和血小板衍生生长因子(PDGF)进一步支持血管的新生<sup>[30]</sup>。

VEGF介导的病理血管生成涉及多维信号级联与微环境重编程, 通过调控内皮细胞增殖迁移、血管通透性及新生血管网络构建, 驱动乳腺癌前病变恶性转化进程。乳腺癌前病变的发生与进展依赖于VEGF/VEGFR2信号枢纽的异常激活, 其通过PI3K/Akt、HIF-1 $\alpha$ 等信号通路形成促血管生成信号网络, 靶向干预VEGFR2磷酸化及其下游信号传导, 可有效阻断病理性血管生成链式反应, 这为中医药多组分协同调控提供了关键作用靶标。见图1。

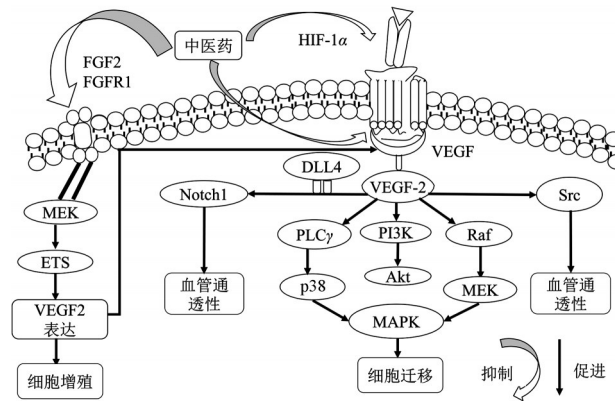


图1 中医药干预VEGF相关信号通路介导血管生成的病理机制  
Fig. 1 Pathological mechanism of traditional Chinese medicine intervention in VEGF-related signaling pathway-mediated angiogenesis

## 2 抗血管生成与PBC的关系

PBC涵盖乳腺不典型导管上皮增生、不典型小叶增生及乳腺导管乳头状瘤等。自Folkman提出肿瘤血管生成理论以来, VEGF在实体肿瘤血管新生中的核心作用已成为共识。PBC是正常组织向乳腺癌转变的关键阶段, 在此阶段, 新生血管为肿瘤细胞的生长与增殖提供营养条件, 大量实验表明VEGF在癌前病变血管新生过程中具有核心作用。在导管原位癌(DCIS)癌前病变中, VEGF的过表达已被证实是早期事件, 其转录水平升高与血管生成活性增强呈显著正相关<sup>[31]</sup>。近年来实验发现, 随着乳腺增生的程度不断增加, 组织内新生血管的活性也随之增强, 通过下调VEGF蛋白的表达可以有效干预乳腺非典型增生, 且VEGF-C、HIF-1 $\alpha$ 在乳腺癌组织的阳性表达率显著高于良性病变, 其促血管生成的效应是通过PI3K/Akt信号通路异常活化及缺氧微环境介导的HIF-1 $\alpha$ 依赖途径来实现<sup>[32-35]</sup>。靶向干预研究证实, 抑制VEGF/VEGFR信号轴可有效延缓癌前病变的进展。贝伐珠单抗作为首个抗VEGF的单克隆抗体, 通过竞争性抑制VEGF-A与受体结合, 显著抑制肿瘤新生血管的形成, 从而抑制肿瘤生长<sup>[36]</sup>。小分子酪氨酸激酶抑制剂(TKI)类药物(如阿帕替尼)则展现双重调控机制: 既抑制PI3K/Akt信号

通路介导的血管新生, 又阻断肿瘤细胞VEGF自分泌环路<sup>[37-38]</sup>。这些发现为中医药多靶点干预PBC血管生成提供了关键作用节点与机制参照。

## 3 中医药通过调控VEGF相关信号通路抗血管生成干预PBC

3.1 中医学对PBC的认识 在中医学领域, PBC归属于“乳癖”演变范畴, 龚居中在《外科活人定本》中提出乳癖“此症生于正乳之上, 乃厥阴、阳明经之所属……何谓之癖, 硬而不痛, 如顽核之类, 过久则成毒”, 首倡乳癖向“乳毒”传变的病机演变; 至清代余听鸿《外证医案汇编》深化病机认识, 谓“少阳行经之地, 气血皆薄, 加以情怀失畅, 气血痹郁, 故难治, 日久恐成岩证”, 系统构建了乳癖发生“岩变”的病机传变学说<sup>[39]</sup>。其病机演化呈现“初则肝郁气滞血瘀, 继则脾虚痰瘀互结, 终则肾损毒瘀凝岩”的三阶动态模型, 与现代医学“乳腺导管上皮增生→非典型增生→原位癌”的病理发展过程高度吻合。从“乳癖”到乳岩, 肝失疏泄、脾失运化、肾精亏损、冲任失调构成核心病机, 而气机郁滞、痰浊凝聚、瘀毒结聚则为标实之候。因而, 临床用药多以疏肝调枢以调气机, 健脾化痰以杜痰源, 活血通络以消癥结, 调摄冲任以固根本为治疗PBC及预防其进展的基本原则, 此治法暗合现代肿瘤学“阻断血管异常生成”的干预策略<sup>[40]</sup>。早在《黄帝内经》已有“未病先防, 既病防变”的思想。因而, 早期施治, 防治“岩变”是治疗PBC的核心。在PBC早期运用中医药, 可有效防止其演变, 越来越多的研究证实中医药可通过抗血管生成干预PBC的进展, 中医药在防治乳腺癌及PBC具有明显优势<sup>[41]</sup>。

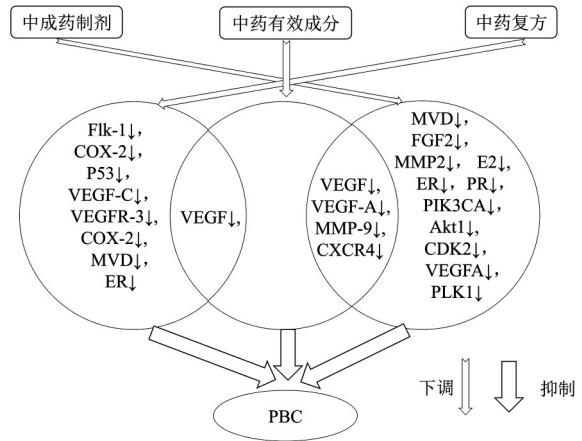
3.2 中成药干预 研究发现, 乳痛软坚片可抑制肝郁脾虚证PBC大鼠乳腺组织VEGF的表达, 降低微血管密度(MVD), 从而抑制血管新生, 进一步探索发现其机制可能与下调DLL4/Notch1/发状分裂增强子(Hes1)信号通路蛋白表达相关<sup>[42]</sup>。体外实验证实了柴芍乳癖颗粒能降低乳腺非典型增生大鼠MVD和VEGF蛋白表达, 疗效与他莫昔芬(TAM)相当, 且随浓度的增加, 作用效果更加明显, 表明对局部微血管生成的干预是柴芍乳癖颗粒阻断甚至逆转PBC的作用机制之一<sup>[32, 43]</sup>。西黄丸的不同剂型(丸剂、胶囊、浸提液)分别被证实临床、动物和细胞实验中均可有效降低VEGF、VEGFR2等蛋白表达, 抑制新生血管生成干预PBC<sup>[44-46]</sup>。乳岩内消霜外用涂抹患处, 消核颗粒内服干预, 均可显著下调VEGF、碱性成纤维细胞生长因子-2(FGF-2)在癌前病变大鼠乳腺组织中的表达, 病理学检测明显降低大鼠乳腺组织增生程度, 其机制可能是通过抑制血管生成因子表达, 阻断血管的生成<sup>[47-48]</sup>。邓卫芳等<sup>[49]</sup>研究发现消乳散结胶囊可以调节VEGF、基质细胞衍生因子受体4(CXCR4)的表达水平, 使其趋于正常状态, 尤其对VEGF的调整作用更为明显, 还可以调节雌激素(E<sub>2</sub>)分泌水平, 从而抑制乳腺非典型增生向乳腺癌进展。研究发现肝郁痰凝型PBC大鼠经皂翘消癖颗粒干预之后, 乳腺组织中非典型增生数量减少, 且以轻度非典型增生为主, 且皂翘消癖颗粒能够干预PI3K/Akt信号通路相关蛋白, 下调VEGF的表达, 干预PBC的进展<sup>[50]</sup>。加味蜂房丸能显著减小乳腺癌大鼠肿瘤直径, 调节经

7, 12-二甲基苯并蒽(DMBA)诱导的大鼠雌激素及孕酮水平,网络药理学研究发现其主要化合物成分能够降低 VEGFA、细胞周期蛋白依赖性激酶2(CDK2)、Polo样激酶1(PLK1)、基质金属蛋白酶-9(MMP-9)等乳腺癌相关蛋白表达,影响PI3K/Akt等信号通路,调控细胞周期及激素水平,预防PBC的发生及发展<sup>[51]</sup>。经典名方逍遥丸也有干预PBC的作用,研究发现,其能够显著降低大鼠乳腺癌前病变肉眼肿瘤的发生率,还可以调节E<sub>2</sub>和VEGF的水平使其由紊乱向常态转变<sup>[52]</sup>。消核颗粒与TAM作用类似,对降低PBC模型大鼠乳腺组织血管内皮细胞生长因子受体2(Flk-1)及FGF-2的表达有良好的作用,其下调FGF-2的表达可能是此方抑制血管生成,进而逆转PBC的主要途径<sup>[53]</sup>。二至丸剂量依赖性方式显著干预诱发性乳腺癌组织的生长恶化,其机制可能与下调VEGF和MMP-9的表达相关<sup>[54]</sup>。王聪等<sup>[55]</sup>的研究发现,丹鹿胶囊能显著降低PBC模型大鼠肿瘤的发生率,其与降低雌激素,干预PI3K、Akt蛋白的表达,从而提高体内抗氧化应激水平密切相关。

**3.3 中药复方干预** 温阳散结中药代表方阳和化岩汤在癌前病变的治疗中存在剂量-效应关系,高剂量阳和化岩汤显著降低实验组大鼠Flk-1和FGF-2的表达,抑制新生血管的形成,进而调节PBC中的病变程度<sup>[56]</sup>。此外,阳和化岩汤与疏肝健脾饮均可通过减低VEGF-C、VEGFR-3蛋白表达,干预淋巴管生成的上游信号通路,抑制癌前病变过程中淋巴管的生成进一步抑制PBC的进展<sup>[57-58]</sup>。通过对大鼠的体外实验研究发现,疏肝健脾解毒方对性腺轴有抑制作用,使ER的表达下降,从而抑制PI3K/Akt/哺乳动物雷帕霉素靶蛋白(mTOR)信号通路的表达<sup>[59]</sup>。同时,还能够下调乳腺组织MVD及VEGF水平,通过对新生血管的抑制在一定程度上降低乳腺组织非典型增生的倾向<sup>[60-62]</sup>。消痰解郁方运用于PBC动物模型时,会使PI3K和磷酸化(p)-Akt蛋白表达明显降低,证明其对PBC模型有明确治疗作用,其机制可能与消痰解郁方干预PI3K/Akt信号通路,干预血管生成及细胞增殖凋亡有密切联系<sup>[63-64]</sup>。

**3.4 中药有效成分干预** 梳理相关文献发现,部分中药有效成分在抗血管生成方面具有潜在优势,但多数集中于其对于乳腺癌的干预,中药有效成分通过调控VEGF相关信号通路干预PBC的研究较少。天然化合物丁香酚是一种有效的抗癌活性成分,实验研究证实其与TAM对于癌前病变和浸润性癌的发生率均有着显著降低,进一步分析发现,经过丁香酚干预之后PBC模型体内VEGF-A和MMP-9的表达明显减少<sup>[65]</sup>。杨丽霞等<sup>[66]</sup>通过加热回流的方法提取蓝萼香茶菜中二萜类物质,在体外试验中发现经蓝萼香茶菜提取物作用之后的PBC组织中VEGF、CXCR4蛋白及mRNA表达水平均明显降低,表明其可能通过抑制血管生成和趋化因子受体表达干预PBC的发生发展。莜术油能显著降低大鼠乳腺癌前病变组织中VEGF mRNA的表达,且随剂量的增加干预效果越好,其可能是抑制血管生成、阻断乳腺癌发生的有效机制<sup>[67-69]</sup>。通过抑制VEGF相关信号通路抗血管生成途径干预PBC的中医药总结见增强出版附加材料,中医药干预

VEGF相关信号通路介导血管生成防治PBC的作用机制见图2。



注:ER.雌激素受体;PR.孕酮受体

图2 中医药干预VEGF相关信号通路介导血管生成防治PBC的作用机制

Fig. 2 Mechanism of traditional Chinese medicine intervention in VEGF-related signaling pathway-mediated angiogenesis in prevention and treatment of PBC

#### 4 结语与展望

近年来,乳腺癌的发病率越来越高,严重威胁人类生命健康,阻止PBC向乳腺癌的进一步转化至关重要,其中抑制血管生成是改善癌前病变的关键。干预VEGF相关信号通路是干预新生血管形成的核心,但临床运用靶向干预VEGF信号途径的血管生成抑制剂具有较大的不良反应。中医药来源广泛,作用靶点丰富,临床应用中医药防治癌前病变具有很大的潜力和优势,近年来日益受到广大学者的研究和关注。越来越多研究发现中医药制剂,复方,及中药有效成分通过抑制VEGF相关通路抑制血管生成,对PBC的进展具有良好干预作用,主要包括干预与VEGF密切相关的PI3K/Akt信号通路、MAPK信号通路、HIF-1 $\alpha$ /VEGF信号通路、Src激酶和DLL4/Notch1途径来抑制血管内皮细胞的增殖与迁移,调控血管的通透性和细胞增殖的微环境。然而,中医药在这一领域的发展也面临重要挑战。现有文章集中在探究VEGF通路及其上下游信号通路之间的关系,而缺乏对各通路之间相互作用机制的深入研究与探讨。此外,目前此方面的研究大多停留于中成制剂及复方层次,且专注于动物及细胞实验,临床试验开展较少,临床数据匮乏,如何精准分析中药成分与血管生成抑制的相关性,揭示复杂成分及复方之间的内在联系和作用机制仍需深入研究。同时,加快完善临床循证依据,是促进中医药防治PBC的临床应用及推广的有效途径。大规模、多中心、高质量的临床研究,不仅有助于促进中药新药研发与临床应用的转化,提升中医药在此领域的应用效果,还可推动中药配伍及新型剂型的创新发展。临床开发更加有效、安全的抗癌前病变血管生成新药的进展令人期待。

【利益冲突】 本文不存在任何利益冲突。

[参考文献]

- [ 1 ] SUNG H, FERLAY J, SIEGEL R L, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries[J]. *CA-Cancer J Clin*, 2021, 71(3):209-249.
- [ 2 ] TAO X, LI T, GANDOMKAR Z, et al. Incidence, mortality, survival, and disease burden of breast cancer in China compared to other developed countries[J]. *Asia Pac J Clin Oncol*, 2023, 19(6):645-654.
- [ 3 ] 莫森,王泽洲,郑莹,等. 2022年全球及中国乳腺癌流行病学特征分析[J]. *海军军医大学学报*, 2025, 46(4):497-503.
- MO M, WANG Z Z, ZHENG Y, et al. Breast cancer in the world and China in 2022: An analysis on epidemic status[J]. *Acad J Nav Med Univ*, 2025, 46(4):497-503.
- [ 4 ] 张昊天,邱叶贝,苏燃,等. 乳岩内消霜通过调控 Nrf2/SLC7A11/GPX4 信号通路促进乳腺癌前病变细胞铁死亡的机制[J]. *中国实验方剂学杂志*, 2025, 31(7):98-107.
- ZHANG H T, QIU Y B, SU R, et al. Mechanism of Ruyan Neixiao cream in promoting ferroptosis in breast precancerous lesion cells by regulating Nrf2/SLC7A11/GPX4 signaling pathway[J]. *Chin J Exp Tradit Med Form*, 2025, 31(7):98-107.
- [ 5 ] FOLKMAN J. Tumor angiogenesis: Therapeutic implications[J]. *N Engl J Med*, 1971, 285(21):1182-1186.
- [ 6 ] NILAJA B, AKSHITA S, VIKRANT P, et al. Angiogenesis induction in breast cancer: A paracrine paradigm[J]. *Cell Biochem Funct*, 2021, 39(7):860-873.
- [ 7 ] EROLES P, BOSCH A, PEREZ-FIDALGO J A, et al. Molecular biology in breast cancer: Intrinsic subtypes and signaling pathways[J]. *Cancer Treat Rev*, 2012, 38(6):698-707.
- [ 8 ] ENGEL J, WIEDER V, BAUER M, et al. Prognostic and predictive impact of NOTCH1 in early breast cancer[J]. *Breast Cancer Res Treat*, 2025, 209(1):27-38.
- [ 9 ] 陈梦帆,姚昶. 中医药抗血管生成治疗乳腺癌研究进展[J]. *河北北方学院学报:自然科学版*, 2025, 41(6):61-65.
- CHEN M F, YAO C. Research progress of anti-angiogenic treatment of breast cancer with traditional Chinese medicine[J]. *J Hebei North University: Nat Sci Edi*, 2025, 41(6):61-65.
- [ 10 ] RAMADAN S W, ZAHER M D, ALTAIE M A, et al. Potential therapeutic strategies for lung and breast cancers through understanding the anti-angiogenesis resistance mechanisms[J]. *Int J Mol Sci*, 2020, 21(2):565-565.
- [ 11 ] APTE S R, CHEN S D, FERRARA N. VEGF in signaling and disease: Beyond discovery and development[J]. *Cell*, 2019, 176(6):1248-1264.
- [ 12 ] GOEL H L, MERCURIO A M. VEGF targets the tumour cell[J]. *Nat Rev Cancer*, 2013, 13(12):871-882.
- [ 13 ] GU Y, TANG T, QIU M, et al. Clotiquinol inhibits angiogenesis by promoting VEGFR2 degradation and synergizes with Akt inhibition to suppress triple-negative breast cancer vascularization[J]. *Angiogenesis*, 2025, 28(2):13.
- [ 14 ] 王璐,赵琳,张丽芬,等. VEGF通过激活 ERK/MAPK 通路促进三阴性乳腺癌肿瘤干细胞的形成[J]. *南方医科大学学报*, 2021, 41(10):1484-1491.
- WANG L, ZHAO L, ZHANG L F, et al. Vascular endothelial growth factor promotes cancer stemness of triple-negative breast cancer via MAPK/ERK pathway[J]. *J South Med Univ*, 2021, 41(10):1484-1491.
- [ 15 ] PARK S A, JEONG M S, HA K T, et al. Structure and function of vascular endothelial growth factor and its receptor system[J]. *BMB Rep*, 2018, 51(2):73.
- [ 16 ] 李赟,阮英,孙燕玲,等. 川陈皮素调节 RAS/RAF/MEK/ERK 信号通路对直肠癌细胞增殖、迁移和侵袭的影响[J]. *药物评价研究*, 2024, 47(11):2567-2573.
- LI Y, RUAN Y, SUN Y L, et al. Effects of nobiletin on proliferation, migration, and invasion of rectal cancer cells by regulating RAS/RAF/MEK/ERK signaling pathway[J]. *Drug Eval Res*, 2024, 47(11):2567-2573.
- [ 17 ] 马孝秋,左韬,马贤德,等. 基于 VEGFA/VEGFR2-PI3K/Akt 信号轴探讨化癥明目方含药血清抑制高糖及 VEGF 诱导人视网膜微血管内皮细胞血管新生的分子机制[J]. *中药新药与临床药理*, 2025, 36(2):197-205.
- MA X Q, ZUO T, MA X D, et al. Exploring the molecular mechanism of Huayu Mingmu recipe-containing serum on the inhibition of high glucose and VEGF-induced angiogenesis in human retinal microvascular endothelial cells based on VEGFA/VEGFR2-PI3K/Akt signal axis[J]. *Tradit Chin Drug Res Clin Pharmacol*, 2025, 36(2):197-205.
- [ 18 ] TUFAIL M, HU J J, LIANG J, et al. Predictive, preventive, and personalized medicine in breast cancer: Targeting the PI3K pathway[J]. *J Transl Med*, 2024, 22(1):15.
- [ 19 ] 高爱琴. 紫草素通过 MAPK 和 Akt/mTOR 信号通路抑制肿瘤血管生成和肿瘤生长[D]. 昆明:昆明理工大学, 2020.
- GAO A Q. Shikonin inhibits tumor angiogenesis and tumor growth by targeting MAPK and Akt/mTOR signaling pathway[D]. Kunming: Kunming University of Science and Technology, 2020.
- [ 20 ] BAI M, XU P, CHENG R, et al. ROS-ATM-CHEK2 axis stabilizes HIF-1 $\alpha$  and promotes tumor angiogenesis in hypoxic microenvironment[J]. *Oncogene*, 2025, 44(21):1609-1619.
- [ 21 ] 侯晓萌,孙洪亮,张中国,等. 氧化还原调控的表观遗传修饰在乳腺癌中的作用[J]. *生物化学与生物物理进展*, 2018, 45(12):1224-1231.
- GOU X M, SUN H L, ZHANG Z G, et al. Epigenetic modification of redox regulation in breast cancer[J]. *Prog Biochem Biophys*, 2018, 45:1224-1231.
- [ 22 ] 杨永志,陈炜. 果糖-1,6-二磷酸酶 1 和缺氧诱导因子 1 $\alpha$  在乳腺癌组织中的表达及其临床意义[J]. *中国卫生检验杂志*, 2021, 31(5):606-609.
- YANG Y Z, CHEN W. Expression of fructose-1, 6-

- bisphosphatase 1 and hypoxia-inducible factor 1 $\alpha$  in breast cancer and its clinical significance [J]. *Chin J Health Lab Technol*, 2021, 31(5): 606-609.
- [23] ZHANG P C, LIU X, LI M M, et al. AT-533, a novel Hsp90 inhibitor, inhibits breast cancer growth and HIF-1 $\alpha$ /VEGF/VEGFR-2-mediated angiogenesis *in vitro* and *in vivo* [J]. *Biochem Pharmacol*, 2020, 172: 113771.
- [24] FENG M, SANTHANAM R K, XING H, et al. Inhibition of  $\gamma$ -secretase/Notch pathway as a potential therapy for reversing cancer drug resistance [J]. *Biochem Pharmacol*, 2024, 220: 115991.
- [25] GAO Y, WANG J, ZHAO M, et al. Atractylenolide III attenuates angiogenesis in gastric precancerous lesions through the downregulation of delta-like ligand 4 [J]. *Front Pharmacol*, 2022, 13: 797805.
- [26] SHI Q, XUE C, ZENG Y, et al. Notch signaling pathway in cancer: From mechanistic insights to targeted therapies [J]. *Signal Transduct Target Ther*, 2024, 9(1): 128.
- [27] 张晓蕾, 许国莹, 王士珍, 等. miR-186-5p对冠心病大鼠血管内皮细胞损伤及FGF2/FGFR1信号通路的影响[J]. *天津医药*, 2021, 49(11): 1169-1174.
- ZHANG X L, XU G Y, WANG S Z, et al. Effects of miR-186-5p on vascular endothelial cell injury and FGF2/FGFR1 signaling pathway in rat model of coronary heart disease [J]. *Tianjin Med J*, 2021, 49(11): 1169-1174.
- [28] 林建昌, 陈晓东, 江琼. 磷酸化Tyr951信号蛋白在糖尿病大鼠创面组织内皮细胞迁移中的作用[J]. *海峡药学*, 2019, 31(8): 28-30.
- LIN J C, CHEN X D, JIANG Q. Role of phosphorylated Tyr951 signal protein in endothelial cell migration in diabetic rats [J]. *Strait Pharm J*, 2019, 31(8): 28-30.
- [29] MATSUMOTO T, BOHMAN S, DIXELIUS J, et al. VEGF receptor-2 Y951 signaling and a role for the adapter molecule TSAd in tumor angiogenesis [J]. *EMBO J*, 2005, 24(13): 2342-2353.
- [30] 魏庆双, 梁吉, 祁美慧, 等. 针灸促进血管新生作用机制研究进展[J]. *中国中医急症*, 2021, 30(2): 369-372.
- WEI Q S, LIANG J, QI M H, et al. Research progress on the mechanism of acupuncture and moxibustion promoting angiogenesis [J]. *J Emerg Syndromes Tradit Chin Med*, 2021, 30(2): 369-372.
- [31] ZHONG J, SU M, JIANG Y, et al. VEGFR2 targeted microbubble-based ultrasound molecular imaging improving the diagnostic sensitivity of microinvasive cervical cancer [J]. *J Nanobiotechnology*, 2023, 21(1): 220.
- [32] 龙俊瑶, 刘慧. 柴芍乳癖颗粒对乳腺非典型增生大鼠MVD及VEGF蛋白表达的影响[J]. *中医药导报*, 2024, 30(10): 32-35, 47.
- LONG J Y, LIU H. Effect of Chaishao Rupi granules on the expression of MVD and VEGF protein in rats with mammary atypical hyperplasia [J]. *Guid J Tradit Chin Med and Pharmacy*, 2024, 30(10): 32-35, 47.
- [33] 刘焱, 宋璐, 林敏. 乳腺癌组织内VEGF-C、HIF-1 $\alpha$ 表达与血管生成的相关性研究[J]. *中外医学研究*, 2024, 22(28): 73-77.
- LIU Y, SONG L, LIN M. Correlation between the expression of VEGF-C, HIF-1 $\alpha$  and angiogenesis in breast cancer tissues [J]. *Chin Fore Med Res*, 2024, 22(28): 73-77.
- [34] 邓佳琳, 贡翊斐, 王小平, 等. 散结消癭方通过调控HIF-1 $\alpha$ /VEGF信号通路对甲状腺滤泡状癌荷瘤裸鼠血管生成的影响[J]. *中成药*, 2024, 46(11): 3795-3799.
- DENG J L, GONG Y F, WANG X P, et al. Effect of Sanjie Xiaofang on angiogenesis in tumor-bearing nude mice with thyroid follicular carcinoma by regulating HIF-1 $\alpha$ /VEGF signaling pathway [J]. *Chin Tradit Pat Med*, 2024, 46(11): 3795-3799.
- [35] SONG X, XIAO J, WU J, et al. Decellularized amniotic membrane promotes the anti-inflammatory response of macrophages via PI3K/Akt/HIF-1 $\alpha$  pathway [J]. *Chin Chem Lett*, 2025, 36(1): 109844.
- [36] 姚远方, 高飞, 张雪松, 等. 载药微球加载贝伐珠单抗介入栓塞治疗兔VX2肝癌的抗血管生成效果[J]. *介入放射学杂志*, 2021, 30(3): 254-257.
- YAO Y F, GAO F, ZHANG X S, et al. The anti-angiogenesis effect of interventional embolization using drug-loaded microspheres with bevacizumab in treating rabbit VX2 hepatocellular carcinoma [J]. *J Intervent Radio*, 2021, 30(3): 254-257.
- [37] ZHONG N, ZHUANG W, HUANG Q, et al. Apatinib inhibits the growth of small cell lung cancer via a mechanism mediated by VEGF, PI3K/Akt and Ki-67/CD31 [J]. *J Cell Mol Med*, 2021, 25(21): 10039-10048.
- [38] PENG S, ZHANG Y, PENG H, et al. Intracellular autocrine VEGF signaling promotes EBDC cell proliferation, which can be inhibited by Apatinib [J]. *Cancer Lett*, 2016, 373(2): 193-202.
- [39] 曾奕斐, 赵迪, 王君月, 等. 中医药调控相关信号通路防治乳腺癌及癌前病变研究进展[J]. *中国实验方剂学杂志*, 2026, 32(5): 290-301.
- ZENG Y F, ZHAO D, WANG J Y, et al. Progress of Chinese medicine in regulating related signalling pathways to prevent and control breast cancer and precancerous lesions [J]. *Chin J Exp Tradit Med Form*, 2026, 32(5): 290-301.
- [40] 程晓蕾. 中药干预大鼠乳腺癌前病变研究的Meta分析及EMT标记物在乳腺良恶性组织中的表达[D]. 济南: 山东中医药大学, 2020.
- CHENG X L. Meta-analysis on the intervention of traditional Chinese medicine in the breast cancer precancerous lesions and the expression of EMT markers in benign and malignant breast tissues [D]. Jinan: Shandong University of Traditional Chinese Medicine, 2020.
- [41] 孟博博, 芮苒, 尹诺男, 等. 中医药治疗乳腺癌前病变的Meta分析[J]. *中医学报*, 2020, 35(2): 433-440.
- MENG B B, RUI R, YIN N N, et al. Meta-analysis of TCM in

- treating breast cancer precancerous lesions [J]. *Acta Chin Med*, 2020, 35(2): 433-440.
- [42] 杨华, 龙俊瑶, 龚婕, 等. 乳痛软坚片通过调控 DLL4/Notch1/Hes1 通路对乳腺癌前病变肝郁血瘀证大鼠血管新生的影响[J]. *中成药*, 2025, 47(3): 774-781.  
YANG H, LONG J Y, GONG J, et al. Effects of Rutong Ruanjian tablets on angiogenesis in a rat model of preneoplastic breast cancer of Liver-Qi stagnation and blood stasis pattern via DLL4/Notch1/Hes1 pathway[J]. *Chin Tradit Pat Med*, 2025, 47(3): 774-781.
- [43] 龙俊瑶. 柴芍乳癖颗粒对大鼠乳腺癌前病变组织中 MVD 及 VEGF 蛋白表达的影响[D]. 长沙: 湖南中医药大学, 2021.  
LONG J Y. Experimental investigation on the effect of Chaishao RuPi pellet on the expressions of MVD and VEGF proteins in breast precancerous lesion of rats[D]. Changsha: Hunan University of Chinese Medicine, 2021.
- [44] 张咏佳, 黄潘雯, 张永太, 等. 西黄丸干预大鼠乳腺癌前病变的效果及机制研究[J]. *中国中药杂志*, 2023, 48(13): 3546-3555.  
ZHANG Y J, HUANG P W, ZHANG Y T, et al. Effect and mechanism of Xihuang pill on rats with precancerous lesions of breast[J]. *China J Chin Mater Med*, 2023, 48(13): 3546-3555.
- [45] 关艳, 关兴. 西黄胶囊治疗乳腺癌前病变临床观察[J]. *中国中医药现代远程教育*, 2023, 21(8): 63-65.  
GUAN Y, GUAN X. Clinical observation on Xihuang capsule in the treatment of precancerous lesions of breast cancer[J]. *Chin Med Mod Dis Educ China*, 2023, 21(8): 63-65.
- [46] 李德辉, 范焕芳, 孙春霞, 等. 西黄丸浸提液对人乳腺癌前病变细胞 mTOR 与 VEGF 表达的影响[J]. *湖南中医杂志*, 2017, 33(6): 145-148.  
LI D H, FAN H F, SUN C X, et al. Effects of liquid extract of Xihuang pill on mTOR and VEGF expression in precancerous cells of human breast cancer[J]. *Hunan J Tradit Chin Med*, 2017, 33(6): 145-148.
- [47] LIN S, JIANG X, ZHANG G, et al. The Chinese herbal formula Ruyan Neixiao cream inhibits angiogenesis of precancerous breast lesions via regulation of Ras/Raf/MEK/ERK signaling pathway [J]. *Integr Cancer Ther*, 2022, doi: 10.1177/15347354211069397.
- [48] 梁世杰, 张桂娟, 马民, 等. 乳岩内消霜外用对大鼠乳腺癌前病变组织 VEGF、FGF2 表达的影响[J]. *暨南大学学报: 自然科学与医学版*, 2015, 36(6): 484-489.  
LIANG S J, ZHANG G J, MA M, et al. Effect of topical Ruyan Neixiao cream for VEGF and FGF2 expression in rat breast with mammary precancerous lesions[J]. *J Jinan Univ Nat Sci Med Ed*, 2015, 36(6): 484-489.
- [49] 邓卫芳, 裴晓华. 消乳散结胶囊对乳腺癌前病变大鼠乳腺组织 CXCR4 及 VEGF 表达的影响[J]. *河南中医*, 2020, 40(9): 1360-1364.  
DENG W F, PEI X H. The influence of capsule for dispersing breast mass on the expression of CXCR4 and VEGF in breast tissue of rats with precancerous lesion of breast cancer [J]. *Henan Tradit Chin Med*, 2020, 40(9): 1360-1364.
- [50] 董夏. 皂翘消癖颗粒对 SD 大鼠肝郁痰凝型乳腺癌前病变的效应及机制研究[D]. 西安: 陕西中医药大学, 2020.  
DONG X. Study on the mechanism of Zaoqiao Xiaopi granule on the precancerous lesion of breast cancer SD rats with liver stagnation and phlegm coagulation [D]. Xi'an: Shanxi University of Chinese Medicine, 2020.
- [51] 李泽红. 中药加味蜂房丸对乳腺癌预防及治疗作用的机制研究[D]. 呼和浩特: 内蒙古医科大学, 2020.  
LI Z H. Mechanism of Chinese medicine Jiawei Fengfang pill on prevention and treatment of breast cancer [D]. Hohhot: Inner Mongolia Medical University, 2020.
- [52] 邓卫芳, 贾颖, 裴晓华. 逍遥丸对乳腺癌前病变大鼠乳腺组织 CXCR4 及 VEGF 表达的影响[J]. *中华中医药杂志*, 2019, 34(4): 1386-1390.  
DENG W F, JIA Y, PEI X H. Effects of Xiaoyao pills on the expression of CXCR4 and VEGF in breast tissue of rats with breast carcinoma precancerous lesion [J]. *China J Tradit Chin Med Pharm*, 2019, 34(4): 1386-1390.
- [53] 汤磊磊. 消核颗粒对大鼠乳腺癌前病变 FLK-1、FGF-2 表达的影响[D]. 合肥: 安徽中医药大学, 2017.  
TANG L L. Effect of Xiaohe granule on the expression of FLK-1 and FGF-2 in precancerous breast lesion of rats [D]. Hefei: Anhui University of Chinese Medicine, 2017.
- [54] 尚广彬, 曾莉萍, 赵益, 等. 二至丸对诱发性乳腺癌组织中 VEGF 和 MMP-9 表达的影响[J]. *中国实验方剂学杂志*, 2013, 19(13): 270-273.  
SHANG G B, ZENG L P, ZHAO Y, et al. Effect of Erzhi pill on expressions of VEGF and MMP-9 in induced rat breast cancer [J]. *Chin J Exp Tradit Med Form*, 2013, 19(13): 270-273.
- [55] 王聪, 许岩磊, 姚昶. 丹鹿胶囊调控 PI3K-Akt 通路改善乳腺癌前病变的慢性氧化应激机制[J]. *中华中医药杂志*, 2024, 39(11): 6049-6053.  
WANG C, XU Y L, YAO C. Mechanism of chronic oxidative stress on Danlu capsules regulating PI3K-Akt pathway to improve breast cancer precancerous lesions [J]. *China J Tradit Chin Med Pharm*, 2024, 39(11): 6049-6053.
- [56] 王云龙, 陈芬, 王芳. 阳和化岩汤干预乳腺癌前病变的效果及机制研究[J]. *中华中医药学刊*, 2021, 39(3): 44-47.  
WANG Y L, CHEN F, WANG F. Effect and mechanism of Yanghe Huayan decoction on breast precancerous lesions [J]. *Chin Arch Tradit Chin Med*, 2021, 39(3): 44-47.
- [57] 吴雪雪. 阳和化岩汤干预乳腺癌前病变 VEGF-C、VEGFR-3 的临床及实验研究[D]. 济南: 山东中医药大学, 2014.  
WU X X. The clinical and experimental research of VEGF-C and VEGFR-3 through Yanghe Huayan decoction's effect on breast precancerous lesion [D]. Jinan: Shandong University of Traditional Chinese Medicine, 2014.

- [58] 李斐斐,刘晓菲,张洋,等.疏肝健脾饮对乳腺癌前病变裸鼠淋巴管生成的影响研究[J].现代中西医结合杂志,2019,28(21):2292-2296.  
LI F F, LIU X F, ZHANG Y, et al. Effect of Shugan Jianpi decoction on lymphangiogenesis in nude mice with precancerous lesions of breast cancer[J]. Mod J Integr Tradit Chin West Med, 2019, 28(21): 2292-2296.
- [59] 李琳霏,杨晓,王容容,等.疏肝健脾解毒方对乳腺癌前病变肝郁证大鼠模型乳腺组织血管生成的影响[J].湖南中医药大学学报,2019,39(10):1195-1199.  
LI L P, YANG X, WANG R R, et al. Effects of Shugan Jianpi Jiedu Formula on angiogenesis of breast tissue in breast cancer rat model with precancerous lesion of Liver Qi stagnation syndrome[J]. J Hunan Univ Chin Med, 2019, 39(10): 1195-1199.
- [60] 李琳霏,时健,何丹,等.疏肝健脾解毒方对乳腺癌前病变防治作用机制研究[J].中国现代应用药学,2024,41(5):619-625.  
LI L P, SHI J, HE D, et al. Preventive and therapeutic mechanism of Shugan Jianpi Jiedu decoction on precancerous lesions of breast cancer[J]. Chin J Mod Appl Pharm, 2024, 41(5): 619-625.
- [61] 李琳霏,时健,谭小宁,等.疏肝健脾解毒方抑制性腺轴和PI3K/AKT/mTOR信号通路影响乳腺癌前病变[J].中西医结合杂志,2024,44(8):959-965.  
LI L P, SHI J, TAN X N, et al. Shugan Jianpi Jiedu formula inhibits gonadal axis and PI3K/Akt/mTOR signaling pathways to affect breast precancerous lesions [J]. Chin J Integr Tradit Chin West Med, 2024, 44(8): 959-965.
- [62] 李琳霏.基于ER及PI3K/Akt/mTOR通路探讨疏肝健脾解毒方防治乳腺癌前病变的分子机制[D].长沙:湖南中医药大学,2022.  
LI L P. Exploration on the molecular mechanism of Shugan Jianpi Jiedu Decoction in the prevention and treatment of breast precancerous lesions based on ER and PI3K/Akt/mTOR pathway[D]. Changsha: Hunan University of Chinese Medicine, 2022.
- [63] ZHAO J, PANG T, JIAO J, et al. Xiaotan Jieyu prescription alleviates breast precancerous lesions through PI3K/Akt signaling pathway[J]. Evid Based Complement Alternat Med, 2020, doi:10.1155/2020/4129461.
- [64] 赵婧,魏品康,修丽娟,等.消痰解郁方对乳腺癌前病变MCF-10AT细胞PI3K/Akt通路的影响及机制[J].第二军医大学学报,2017,38(4):520-523.  
ZHAO J, WEI P K, XIU L J, et al. Effect of Xiaotan Jieyu decoction on PI3K/Akt pathway of MCF-10AT cells and its mechanism[J]. Acad J Second Mil Med Univ, 2017, 38(4): 520-523.
- [65] LIU Y, ZHANG G, MA Y, et al. Eugenol inhibits NEAT1 as a ceRNA in pre-cancerous breast lesions[J]. Heliyon, 2025, 11(1): e41353.
- [66] 杨丽霞,邓卫芳,陈鸿,等.蓝萼香茶菜二萜类物质对乳腺癌前病变肝郁肾虚证模型大鼠的干预作用[J].中国实验方剂学杂志,2018,24(2):140-145.  
YANG L X, DENG W F, CHEN H, et al. Effect of diterpenoids on breast cancer precancerous lesions, liver depression and kidney deficiency pattern model rats[J]. Chin J Exp Tradit Med Form, 2018, 24(2): 140-145.
- [67] 宋爱莉,许振国.莪术油对大鼠乳腺癌前病变组织中VEGF mRNA表达的影响[J].中华中医药学刊,2012,30(4):679-681.  
SONG A L, XU Z G. Zedoary turmeric oil effect on rats with precancerous lesions of breast carcinoma in VEGF mRNA expression [J]. Chin Arch Tradit Chin Med, 2012, 30(4): 679-681.
- [68] 许振国,宋爱莉,殷玉琨,等.莪术油对大鼠乳腺癌前病变组织VEGF mRNA表达的影响[J].中华肿瘤防治杂志,2012,19(8):570-574.  
XU Z G, SONG A L, YIN Y K, et al. Effect of zedoary turmeric oil for VEGF mRNA expression in precancerous lesion of rats mammary [J]. Chin J Cancer Prev Treat, 2012, 19(8): 570-574.
- [69] 许振国.莪术油对大鼠乳腺癌前病变组织血管生成及相关调控因子表达的研究[D].济南:山东中医药大学,2012.  
XU Z G. Study about zedoary turmeric oil on angiogenesis and expression of related regulatory factors in breast precancerous of rats [D]. Jinan: Shandong University of Traditional Chinese Medicine, 2012.

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