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毛蕊花糖苷药理活性和作用机制研究进展

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摘　要

毛蕊花糖苷(Verbascoside, VB)，作为苯乙醇苷类多酚化合物中的代表性成分，广泛存在于肉苁蓉等多种药用植物中，具备丰富的生物活性。现代药理研究表明，VB不仅在抗炎、抗氧化、神经保护、抗癌上效果显著，还能抗菌，调节免疫系统，保护肝脏、肾脏和肺，缓解疲劳，促进伤口愈合，对多种疾病具有潜在的治疗价值。本文综述了近年来关于VB的药理活性和作用机制的研究，旨在为VB的深入研究与应用提供参考。

关键词

毛蕊花糖苷，药理作用，研究进展

Advancements in the Pharmacological Activity and Mechanisms of Action of Verbascoside

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Abstract

Verbascoside (VB), a representative phenylethanoid glycoside polyphenolic compound, is abundantly found in various medicinal plants such as Cistanches Herba. Extensive biological activities have been documented. Modern pharmacological studies reveal that VB not only significantly benefits anti-inflammatory, antioxidant, neuroprotective, and anticancer activities, but also possesses antimicrobial properties, and protects the livers, kidneys and lungs. It alleviates fatigue and

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promotes wound healing, offering potential therapeutic value for multiple diseases. This paper reviews recent research on the pharmacological activities and mechanisms of action of VB, aiming to provide references for further research and application of VB.

Keywords

Verbascoside, Pharmacological Effects, Research Advancements

1. 引言

毛蕊花糖苷(Verbascoside, VB)，是著名药用植物肉苁蓉、地黄、女贞子、马鞭草等(见表 1)的主要活性成分[1]，其结构如图 1 所示。毛蕊花糖苷作为代表性的苯乙醇苷类多酚化合物，不仅在抗炎、抗氧化、神经保护、抗癌上效果显著，还能抗菌，调节免疫系统，保护肝脏、肾脏和肺，缓解疲劳，促进伤口愈合等，对多种疾病具有潜在的治疗价值[1] [2]。因此，本文将总结近年来有关 VB 药理活性和作用机制的研究进展。

Table 1. Partial natural sources of verbascoside and their contents
表 1. 毛蕊花糖苷的部分天然来源及其含量

来源	含量 mg/g	提取方式	参考文献
管花肉苁蓉 (*Cistanche tubulosa*)	16.10~85.90	50%甲醇提取	Yan, 2017 [3]
荒漠肉苁蓉 (*Cistanche deserticola*)	1.17~29.03	70%甲醇提取	Lu, 2013 [4]
地黄 (*Rehmannia glutinosa*)	0.63~4.78	甲醇提取	石海霞，2018 [5]
女贞子 (*Ligustri Lucidi Fructus*)	1.04~2.99	超声波辅助固相萃取(萃取剂：低共熔溶剂、吸附剂：ZnO)	Qian, 2024 [6]
车前草 (*Plantaginis lanceolatae folium*)	66.2 ± 5.0	60% 乙醇提取	Laanet, 2024 [7]
老鼠簕 (*Acanthus ebracteatus* Vahl)	1652.37 ± 129.11	水提取	Pongkitwitoon, 2024 [8]
马鞭草 (*Verbena oficinalis*)	3.51 ± 0.12	95%乙醇提取	Zhang, 2024 [9]
裸花紫珠 (*Callicarpa nudiflora* Hook.)	7.27	75%乙醇提取	Yang, 2024 [10]
桂花 (*Osmanthus fragrans*)	119.1	60%乙醇提取	Lee, 2020 [11]
白连翘 (*Abeliophyllum distichum*)茎	162.11	乙醇提取	Li, 2020 [12]

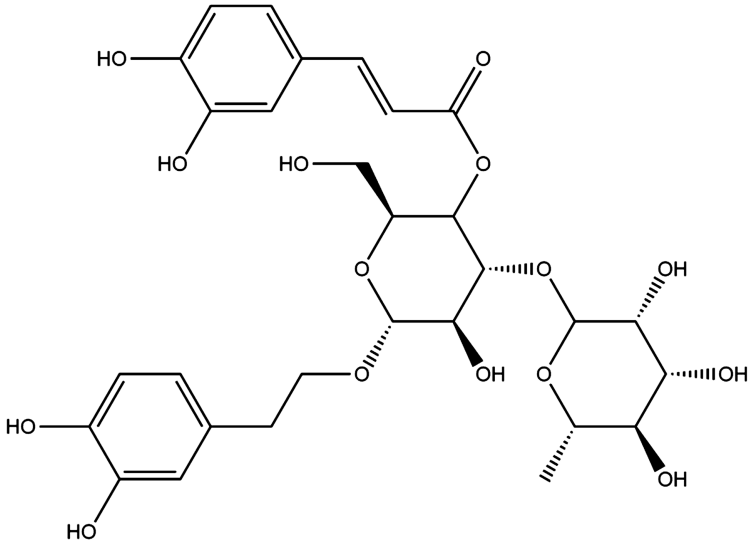

Figure 1. Chemical structure of verbascoside. The central glucose unit is linked at the C1 position to the α-hydroxyl of hydroxytyrosol via a glycosidic bond, connected to rhamnose at the C3 position, and bound to caffeic acid at the C4 position via an ester bond

图 1. 毛蕊花糖苷的化学结构式。中心葡萄糖单元 C1 位以糖苷键与羟基酪醇的 α-羟基相连，C3 位连接鼠李糖，C4 位以酯键与咖啡酸结合

2. 基础活性

氧化应激与炎症的相互作用是多种慢性疾病的关键致病因素[13]。氧化应激过程中产生的 ROS 将激活 TLR 等先天免疫受体，进而触发 NF-κB、AP-1 等多种转录因子的激活，促进炎症细胞因子的表达，从而引发慢性炎症。这种慢性炎症可进一步增强氧化应激，形成恶性循环，加速神经退行性疾病、癌症、糖尿病相关疾病的进展[14]。因此，VB 的显著抗炎及抗氧化效果对缓解上述疾病具有重要意义。如 VB 通过缓解氧化应激和抑制 NF-κB/MAPK 通路来减轻哮喘气道炎症[15]。

2.1. 抗炎

VB 的主要活性之一是抗炎，研究亦最为广泛。其通过有效抑制炎症的核心调节因子 NF-κB，减少如 TNF-α、IL-1、IL-6 等促炎性细胞因子及趋化因子的表达，从而在脑、肾脏、皮肤等多个部位显著抑制炎症[1] [2]。VB 也可通过抑制 PLA2 阻断炎症前体花生四烯酸的释放[16]；抑制促炎转录因子 AP-1、增强酪氨酸磷酸酶 SHP-1 的活性[17]从而阻断 iNOS 的表达[18]并选择性抑制 COX-2 以减少前列腺素 E2 的生成[19]，靶向 MAPK 通路有效减轻炎症因子的释放。

VB 可影响 Breg 细胞、肥大细胞等免疫细胞功能，调节细胞因子水平，从而在哮喘、过敏反应和炎症性皮肤疾病中发挥出保护作用[2] [20]。如 VB 可缓解小鼠特异性皮炎症状的抓挠行为和皮肤病变严重程度[21]。VB 可以激活树突状细胞的芳香烃受体，降低 IL-12 和 TNF-α 的产生并增加 IL-10 的水平，并且诱导 $Foxp3^+$调节性 T 细胞，改善过敏性哮喘小鼠的肺部炎症[20]。它可以通过调节 TLR4/PI3K 轴来促进人类和小鼠 Breg 细胞产生 IL-10，同时促进 $TLR4^+CXCR4^+$浆细胞产生 IL-10，降低 T 效应细胞数量，缓解小鼠的实验性干燥综合征[22]。VB 可下调 MDM2 抑制肥大细胞增殖[23]，抑制肥大细胞中的花生四烯酸和组胺释放和前列腺素 E2 产生[24]。在人类单核细胞 THP-1 模型中，VB 可以剂量依赖性地抑制 DNCB 诱导的细胞表面 CD86 和 CD54 上调、促炎性细胞因子 TNF-α 和 IL-6 的分泌以及 NF-κB 信号的激活[21]。

2.2. 抗氧化应激

氧化应激指体内氧化和抗氧化机制失衡，该状态促使大量氧化中间体的形成，进而引起分子损伤和氧化还原信号的中断。这种失衡可在不同程度上导致多种疾病，如神经退行性疾病、癌症的发生与进展[25]。研究表明，VB 能有效地直接清除氧、氮、铁等自由基[26]，效果与抗坏血酸相当。更关键的是，VB 通过激活抗氧化通路 Nrf2/ARE 及其 HO-1、SOD 和 GSH-Px 等下游抗氧化酶的活性和水平，从而抑制如 H_2O_2 诱导的 PC12 细胞[27]、6-OHDA 诱导的斑马鱼多巴胺神经元[28]、UVB 照射后的 HaCaT 细胞[29]等产生的 ROS 和脂质过氧化，缓解氧化应激。VB 结构上的咖啡酸和羟基酪醇，尤其后者的酚羟基，是发挥体内外抗氧化功效的主要活性部位[30] [31]。

3. 适应症

3.1. 神经保护

VB 已展现出显著的神经保护活性。该化合物通过降低氧化应激、靶向 NF-κB 和 NLRP3 炎症小体等抑制神经炎症、抑制凋亡和上调自噬等，对阿尔兹海默症、帕金森、认知障碍、抑郁等有一定治疗潜力[2] [32]。

VB 可缓解氧化应激引发的神经元损伤与凋亡[33]。VB 通过增强 Nrf2-线粒体自噬途径来抑制铁死亡，从而改善线粒体功能、减少氧化应激，保持体内外帕金森模型中多巴胺神经元健康[34]。Li 等[28]发现毛蕊花糖苷可穿过血脑屏障并通过激活 Nrf2/ARE 信号通路来缓解氧化应激，预防 6-OHDA 诱导的斑马鱼多巴胺神经元损伤。

持续性神经炎症将导致神经元的损伤与丢失[35]。NLRP3 炎症小体的组装触发 caspase-1 激活，进而促进 IL-1β 与 IL-18 的释放，引发进一步炎症。VB 对 NLRP3 的抑制作用，已成为继 NF-κB 之后，神经保护研究的新焦点[36]。VB 通过抑制 NLRP3，降低了 ASC 活性、caspase-1、IL-1β 和 IL-18 减轻体外和体内帕金森模型中 SAL 诱导的细胞焦亡依赖性神经毒性[37]，并抑制脑出血后的神经炎症和神经元凋亡[38]。VB 通过抑制 HMGB1/TLR4/NLRP3 信号传导，减少小胶质细胞炎症活动和细胞焦亡，降低大鼠大脑中动脉闭塞模型脑梗塞面积并保持血脑屏障完整性，展现对缺血性中风的治疗潜力[39]。此外，VB 通过阻断 NF-κB-p65 信号传导，抑制 APP/PS1 小鼠脑组织中小胶质细胞和星形胶质细胞活化，减轻神经炎症，从而对阿尔茨海默病发挥神经保护作用[40]。

通过调节肠道微生物群结构和代谢产物，VB 在神经退行性疾病和精神障碍的治疗中具有显著潜力。口服 VB 可以显著降低氧化应激，减轻肠道炎症，恢复肠粘膜屏障，并重建肠道微生物群的结构。这种调节作用进一步上调了肠道微生物群代谢物如短链脂肪酸和氨基酸的水平，从而有效缓解了 d-半乳糖诱导的认知障碍[41]。VB 通过肠道菌群－脑轴抑制神经炎症并改善肠道通透性，在慢性应激诱发的抑郁模型中，调节肠道微生物组成并减少神经炎症反应，改善了抑郁样行为和突触损伤[42]。在糖尿病小鼠模型中，VB 能够通过调节肠道微生物群(增加有益菌的种类和数量)、改善血清代谢物水平(如 γ-氨基丁酸、L-谷氨酸、L-赖氨酸和牛磺酸)以及增强认知表现，显著抑制胰岛素抵抗，降低血糖和血脂，并改善糖尿病相关的认知缺陷[43]。

VB 可以上调自噬和下调细胞凋亡，增加清除神经元中的 Aβ 等毒性蛋白聚集体和受损细胞器的能力，减少神经元丢失，从而保护神经。VB 可以诱发果蝇的神经元细胞系和脂肪体中的自噬，降低了鱼藤酮诱导的细胞凋亡和活性氧生成，增加神经元中的线粒体膜电位，并通过自噬－溶酶体途径促进了 α-突触核蛋白过表达细胞模型中蛋白聚集体的清除[44]。VB 通过促进自噬(MAP1LC3A 上调)、抗凋亡(caspase-3、Bax 下调和 Bcl-2 上调)、抗炎(iNOS、TNF-α 和 IL-1β 下调)和抗氧化(Nrf2、Keap-1 上调)调节自噬和

凋亡途径促进脊髓损伤后的运动恢复[45]。VB 与熊果酸的联合应用能通过 AKT/mTOR 信号通路协同预防神经毒性。Qu 等[46]指出，该组合可能为阿尔茨海默病提供潜在的治疗策略，通过增强细胞活力、抗凋亡、恢复线粒体膜电位、降低 caspase-3 活化、减少 AKT 和 mTOR 磷酸化，以及增加 ATG5 和 Beclin-1 的表达，从而发挥保护作用。WANG 等[47]的研究表明，VB 通过减轻内质网应激，在减少 Aβ 蛋白刺激的 U251 细胞和 APP/PS1 小鼠凋亡方面具有显著效果，展现了对阿尔茨海默病的神经保护作用。

VB 可以缓解 Aβ 等毒性蛋白聚集体对神经元细胞的影响。如通过抑制 GSK3β 的活性，VB 有效修复因 Aβ40 和 Aβ42 异常聚集和 tau 过度磷酸化引起的改善阿尔茨海默病的病理现象和认知障碍[48]。

此外，VB 具有神经营养作用。VB 可促进 P12 细胞神经突增长和细胞增殖[49]，通过促进海马中神经生长因子和原霉素受体激酶 A 的表达来增强衰老小鼠的记忆力[50]。

3.2. 抗癌

VB 通过抑制细胞增殖促进凋亡，抗侵袭和转移等实现对黑色素瘤、胶质母细胞瘤、肝癌、食管鳞状细胞癌、胰腺癌、结直肠癌等癌症的抑制，减少肿瘤大小并减少耐药性[51]。

抑制增殖，促进凋亡：VB 有选择性细胞毒性[52]，可以加剧癌细胞的氧化应激触发凋亡[25]，并保护正常细胞免受氧化损伤，从而减少副作用[53]。VB 是参与增殖、抗肿瘤药物耐药性和细胞凋亡的蛋白激酶 C 及其亚型、ATP、磷酸受体的抑制剂[53] [54]。通过调节 HIPK2-p53 信号，VB 可促进人类结直肠癌中的细胞凋亡[55]。VB 也可下调 CCN1 并抑制 AKT/NF-κB 通路，促进 M1 巨噬细胞极化，抑制卵巢癌细胞增殖和迁移，并促进细胞凋亡，在体内实验中抑制卵巢癌生长[56]。

抗侵袭和转移：在肝癌研究中，VB 与五味子木脂素联合治疗可以通过 ERK1/2 信号通路抑制 EMT，并降低 CCL20 的表达，进而抑制肝癌细胞的增殖和迁移，同时增强细胞凋亡[57]。此外，VB 还通过 HMGB1/RAGE 和 TGF-β 途径抑制前列腺癌细胞的 EMT，从而减少细胞的增殖和侵袭性[58]。在胰腺癌中，VB 通过下调 V0/V1 表达抑制癌相关成纤维细胞的增殖和迁移[59]。同时，VB 还通过抑制由 METTL3 调控的 miR-31-5p/HIPK2 轴，抑制口腔鳞状细胞癌细胞的增殖、迁移和侵袭[60]，此外，VB 通过上调蛋白酪氨酸磷酸酶 SHP-1 的活性并抑制 STAT3 的磷酸化，抑制胶质母细胞瘤的增殖、迁移和侵袭，同时促进细胞凋亡[61]。

改善对抗肿瘤药物的耐药性：VB 通过抑制 PI3K/AKT 通路，显著增强了癌细胞对 5-氟尿嘧啶的敏感性，促进 G1 细胞周期停滞，减少细胞增殖并诱导结直肠癌细胞凋亡[62]。VB 与酪氨酸激酶抑制剂(如伊马替尼和达沙替尼)联合使用时，有效降低 Abl 磷酸化并改变下游 p38-MAPK/JNK 通路，增强慢性粒细胞白血病细胞凋亡和氧化应激的诱导[63]。

3.3. 抗菌

VB 或含 VB 的植物提取物已被证明能抑制金黄色葡萄球菌、耐药性隐球菌等，并可改善多重耐药[64]。中高剂量的 VB 处理能够显着减少肉类样品中的细菌数量，延缓腐败速度，延长保质期[65]。此外，每日用乳铁素/VB 外用乳剂可有效减少特应性皮炎犬的细菌过度生长和临床症状[66]。

通过竞争性抑制 SrtA，VB 减少耐甲氧西林金黄色葡萄球菌粘附到宿主组织并形成生物膜的能力，其最低抑菌浓度为 512 μg/mL [67]。此外，VB 可以通过竞争性结合金黄色葡萄球菌的 Stp1 催化活性位点，或通过结合“瓣区”诱导 Stp1 活性位点的构象变化，从而强力抑制其活性，降低金黄色葡萄球菌中毒力蛋白的表达[68]。

VB 对耐药性菌株有更好抑菌效果，并改善其耐药性。通过改变细菌细胞膜通透性、破坏细菌膜的完整性，诱导细菌细胞形态变化，从而根除生物膜等，VB 增强了万古霉素对金黄色葡萄球菌和铜绿假单胞菌的抑菌活性[65]，以及增强庆大霉素对金黄色葡萄球菌和大肠杆菌的效果，改善多重耐药[69]。

3.4. 内器官保护

3.4.1. 保肾

VB 能够缓解糖尿病肾病、慢性肾小球肾炎、急性肾炎及阻塞性肾病的病程，其机制主要涉及保护足细胞免受凋亡、抑制炎症因子、抗氧化作用以及抗肾纤维化。

糖尿病肾病是糖尿病主要并发症之一，改善肾功能、降低尿蛋白、减轻病理改变是治疗糖尿病肾病的重要策略。db/db 糖尿病小鼠和 HK-2 细胞模型表明，VB 可以降低血糖[70]、保护足细胞免于凋亡[71]，降低尿白蛋白，延缓肾纤维化，改善肾脏病理病变，延缓糖尿病肾病病程[72] [73]。VB 通过靶向特定的生化和信号通路有效缓解糖尿病肾病的肾脏纤维化和异常代谢。VB 可调节 AKT/GSK-3β 信号通路抑制足细胞凋亡[71]，调控 PI3K/AKT/NF-κB 信号通路减轻细胞焦亡[70]，降低炎症因子 MCP-1、IL-1β、TNF-α、IL-6 的表达[72]，抑制 TGF-β/Smad [72]和抗氧化和调节自噬溶酶体途径缓解肾脏纤维化[73]。Wang 等[72]采用代谢组学分析 db/db 小鼠血清，发现 VB 可能通过调节脂质代谢、乙醛酸和二羧酸代谢以及花生四烯酸代谢紊乱的代谢途径保护对糖尿病肾病有治疗作用。Gao 等[74]进一步用非靶向和靶向代谢组学分析研究 db/db 小鼠尿液、血清和肾脏样本中的代谢特征，发现 VB 通过调节氨基酸代谢，使色氨酸、谷氨酰胺等代谢物的水平正常化。结合网络药理学发现 VB 作用途径与糖、脂类、氨基酸代谢有关，主要影响内分泌和免疫系统。

肾脏组织炎症反应的反复进展和持续存在是慢性肾炎发生和发展的主要机制。VB 在 PHN 大鼠模型中展现出良好的治疗效果，包括减少尿蛋白和血清肌酐浓度，抑制炎症细胞标志物的表达，并调节血小板聚集和免疫细胞功能，从而抑制肾脏中的 TGF-β 和纤连蛋白表达，减轻纤维化病变。同时，代谢组学和网络药理学揭示了 VB 对炎症和免疫有广泛调节的作用[75]。

在急性肾炎中，VB 通过抑制 NF-κB 信号通路(TLR4, MyD88, Iκ-Bα, NF-Kb, p65)有效缓解 LSP 诱导的肾功能障碍和炎症[76]，并通过其抗氧化、抗炎、抗凋亡作用减少横纹肌溶解症引起的急性肾损伤[77]。

在阻塞性肾病中，VB 可通过抑制 HMGN1/TLR4/TREM-1 信号通路减少炎症和纤维化，降低血肌酐、血尿素氮及尿蛋白水平，改善了单侧输尿管梗阻大鼠的肾功能。这包括降低炎症和肾脏损伤相关蛋白如 F4/80、Mcp-1、KIM-1 的表达，以及纤维化相关蛋白 α-SMA 和 β-catenin 的表达[78]。

3.4.2. 保肝

VB 对肝脏缺血再灌注损伤、非酒精性脂肪性肝炎、酒精性肝炎、肝脏氧化性损伤的保护性作用主要与抗炎和抗氧化相关。

在肝脏缺血再灌注损伤模型中，VB 通过抑制 HMGB1-TLR3/4-IRF1 信号传导，逆转肝窦状内皮细胞衰老，并恢复受损的窦状网络从而显著改善肝缺血再灌注伤害。这种机制的关键在于 ACT 破坏了 HMGB1 与 LSEC 上的受体 TLR 和 TLR4 的结合，从而阻止了炎症细胞因子和趋化因子的转录[79]。在非酒精性脂肪性肝炎中，以 VB 为主成分的 *Lippia citriodora* 提取物，降低了 TNF-α 和 ROS 的产生，以及减弱了人类肝细胞和肝星状细胞共培养模型中游离脂肪酸过量引起的胶原沉积[80]。酒精性肝炎研究中，VB 调节 NF-kB 的激活减少 HEPG2 和 Wistar 大鼠模型中炎症因子的产生，抑制 caspase-3 的活性，减少了酒精诱导的肝细胞凋亡，显著降低血清 ALT、AST 和 TG 水平，恢复白蛋白和 GSH 水平，从而减轻肝损伤[81]。此外，VB 通过增加抗氧化酶 GSH、SOD、CAT 活性抑制 ROS 的产生，抑制 caspase-3 的活化并防止细胞凋亡保护肝细胞免受 t-BHP 诱导的氧化损伤[82]。

3.4.3. 保肺

VB 能够缓解肺纤维化、急性肺损伤和病毒导致的肺损伤，其机制主要与激活 Smad/TGF-β1 通路，抑制 NF-κB 激活、抗氧化作用。

肺纤维化：VB通过抑制氧化应激和下调Smad/非Smad通路，减少TGF-β1诱导的Smad2/3、ERK/p38、MAPK磷酸化及胶原蛋白I表达，有效减缓肺纤维化的进程[83]。

急性肺损伤中，VB通过降低粘附分子和促炎细胞因子的表达，并抑制NF-κB活化，显著减轻眼镜蛇毒因子诱导的小鼠急性肺损伤模型中病理学损伤[84]。此外，在LPS诱导的急性肺损伤中，VB也通过抑制NF-κB激活，减弱了炎症细胞浸润和肺上皮细胞中的炎症细胞因子TNF-α、IL-1β和IL-6的产生，改善肺功能[85]。

VB对呼吸道合胞病毒(RSV)诱导的肺损伤有保护作用，有效减轻RSV感染引起的肺病理损伤及病毒复制，并降低促炎因子水平。通过下调HMGB1、p-Iκbα/Iκbα、p-p65/p65、RIP1、RIP3、MLKL、PGAM5和DRP1，VB抑制了RSV诱导的坏死性凋亡和线粒体功能障碍。代谢组学分析表明，VB治疗后代谢物的变化与氨基酸和能量代谢密切相关[86]。

3.5. 抗疲劳

VB可从线粒体自噬、氧化应激、能量代谢等多个方面缓解疲劳。

VB可以通过抑制PHD2，激活HIF-1α/BNIP3信号通路，并进一步促进PINK1/Parkin介导的线粒体自噬，改善肌肉质量和线粒体功能，以缓解癌症相关疲劳[87]。Sciandra等[88]的研究表明，VB能通过增强小鼠成肌细胞和肌管的最大耗氧率及线粒体备用呼吸能力，改善线粒体功能障碍。其作用机制包括激活Nrf2/HO-1通路，增加HO-1的转录水平，并在成肌细胞中上调PGC-1α，以对抗氧化应激，从而缓解肌肉疲劳。VB还通过抑制5-HT的合成和TPH2蛋白的表达，并增加运动大鼠尾壳核中5-HT1B的表达，显著减轻运动引起的疲劳，其效果与咖啡因相当[89]。此外，VB能通过增强能量代谢和减少氧化应激，减轻肝脏和骨骼肌水肿及炎症浸润，表现出在缺氧条件下抗疲劳的潜力[90]。

3.6. 促进伤口愈合

伤口愈合需要伤口部位角质形成细胞和真皮成纤维细胞的迁移和增殖，随后发生ECM的重塑。过度炎症会促进组织损伤并延迟愈合[91]。VB可抑制UVB照射后的MMP-9分泌[92]，在划痕实验中增强成纤维细胞和角质形成细胞的迁移，抑制LPS诱导的促炎细胞因子的产生并上调抗氧化酶活性[92]，在皮肤伤口修复过程中促进ECM的重塑[93] [94]。

高血糖水平会诱发氧化应激和炎症，影响牙龈伤口愈合[95]。VB可通过抑制PKC/HMGB1/RAGE/NFκB信号通路，增加抗氧化酶SOD的活性，降低氧化应激指标8-OHdG以及细胞凋亡，上调了PGC1-α和NRF1的表达并促进了线粒体的生物合成减少氧化应激，下调促炎细胞因子(如IL-6和IL-1β)减轻炎症，改善糖尿病患者口腔伤口愈合障碍[96]。

3.7. 其他

缓解神经性痛觉：VB无法提高假手术动物的痛阈值，但能通抑制小胶质细胞活化、抗凋亡和抗氧化活性，有效减轻大鼠慢性压迫性损伤后的神经性疼痛[97]。鞘内注射VB可通过激活大鼠慢性压迫性损伤模型中的μ阿片受体来减轻脊髓神经性疼痛，如减轻机械和冷痛觉过敏，并改善运动表现。同结构化合物咖啡酸或羟基酪醇单独都不能介导该活性[98]。

调节脂肪代谢：VB通过抑制CDK6和mTORC1，减轻TFEB的磷酸化并增加其核转位，诱导PGC-1α转录辅激活因子，从而驱动UCP1依赖的褐变程序，促进白色脂肪组织向米色脂肪细胞产热转化。该过程独立于自噬，通过增强线粒体呼吸强度、上调脂肪酶(如ATGL和HSL)的表达和活性增强脂肪细胞的脂肪分解。且VB诱导的米色细胞仍然具有恢复为白色脂肪细胞的能力[99]。

4. 总结与展望

VB 展现了丰富的药理作用，主要与其抗炎、抗氧化应激、促进自噬、抑制/促进凋亡活性相关。此外，VB 能通过作用于多个靶点来影响同一疾病的进程，是极具开发价值的天然活性成分。最新的研究进展，如 VB 可通过 Nrf2-线粒体自噬途径来抑制多巴胺神经元铁死亡，对 NLRP3 炎症小体的抑制，以及对脂肪代谢的调节作用等，进一步揭示了 VB 的药理作用机制。

近期对 VB 的药理机制探讨中，多项研究运用生物信息学技术，例如代谢组学、网络药理学及分子对接，筛选出了 VB 的潜在靶点和信号通路，包括 PHD2 [70]和 PKC 及其同工型[53]抑制剂。这些技术预期将进一步帮助深化理解并拓展 VB 的作用机制和适应症。

尽管 VB 的生物利用度低至 0.12%，口服后仍对神经损伤类疾病、结肠炎等展示出显著疗效[2]。这一现象可能归因于其活性代谢产物，如羟基酪醇、咖啡酸和 3,4-二羟基苯乙酸的作用，或 VB 对肠道菌群的调节功能。更详细的机制仍需进一步探索。

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