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椰子油用于治疗肺部疾病研究进展*

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摘要:目的 为肺部疾病的防治提供新的方向。方法 检索中国知网、万方、维普、PubMed 数据库中椰子油治疗肺部疾病的相关文献, 分析椰子油的活性成分及治疗肺部疾病的作用机制, 总结其临床应用。结果 椰子油的活性成分脂肪酸不仅对细菌性肺炎及病毒性肺炎有明显作用, 也是一种天然抗癌剂, 能抑制 A549 非小细胞的生长。结论 椰子油在治疗肺部疾病中表现出了多种药理学活性, 包括抗炎、抗菌、调节免疫、抗病毒、抗肿瘤等。但目前尚无足够证据证明椰子油的摄入量与心血管疾病明确相关, 有待进一步研究。

关键词:椰子油; 月桂酸; 月桂酸甘油酯; 肺部疾病

Research Progress of the Application of Coconut Oil in the Treatment of Lung Diseases

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Abstract: Objective To provide a new direction for the prevention and treatment of lung diseases. **Methods** Relevant studies on

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coconut oil in the treatment of lung diseases in databases such as CNKI, WanFang, VIP, and PubMed were searched, the active ingredients of coconut oil and its mechanism in the treatment of lung diseases were analyzed, and its clinical application was summarized. **Results** The active ingredient fatty acid of coconut oil not only have obvious effects in bacterial pneumonia and viral pneumonia, but also is a natural anticancer agent that can inhibit the growth of A549 non-small cell lung cancer. **Conclusion** Coconut oil shows a variety of pharmacological activities in lung diseases, including anti-inflammatory, anti-bacterial, immunomodulatory, anti-viral and anti-tumor effects. However, there is currently insufficient evidence to prove a clear correlation between the intake of coconut oil and cardiovascular disease, and further research is needed.

Key words: coconut oil; lauric acid; monolaurin; lung diseases

椰子 *Cocos nucifera* L. 是我国重要的热带农作物, 属常绿乔木, 适宜在低海拔地区生长, 其果实具有很高的经济价值和营养价值。初榨椰子油(VCO)是从成熟的椰子中提取的食用油, 无色, 不溶于水, 通过热萃取和冷萃取过程获得^[1]。VCO含有丰富的饱和脂肪酸, 如月桂酸、肉豆蔻酸、棕榈酸(PA)、辛酸、癸酸、硬脂酸、己酸、棕榈油酸(痕量), 还含有丰富的不饱和脂肪酸, 如油酸、亚油酸、亚麻酸^[2]。VCO在许多领域开辟了新的应用前景, 除用于烹饪外, 还因其降胆固醇、抗癌、抗肝硬性、抗糖尿病、抗氧化、抗炎、抗病毒、调节免疫、抗菌、皮肤保湿等特性而备受关注^[3], 且在治疗肺部疾病中也有广泛应用。为此, 本研究中检索了中国知网、万方、维普、PubMed数据库中VCO治疗肺部疾病的相关文献, 分析了VCO的活性成分及其治疗肺部疾病的作用机制, 并总结其临床应用。现报道如下。

1 VCO的主要活性成分脂肪酸及其作用机制

1.1 月桂酸

月桂酸是VCO的主要脂肪酸, 能与甘油酯结合形成月桂酸甘油酯, 具有抗菌、抗炎特性。环氧合酶-2(COX-2)是一种关键酶, 可催化花生四烯酸转化为前列腺素的限速步骤, 在炎症反应过程中起关键作用^[4]。目前, 选择性COX-2抑制剂已被认为是治疗炎症的有效方法。JACK等^[5]研究发现, 月桂酸甘油酯与COX-2蛋白有很强的相互作用, 可能是通过与靶蛋白活性位点中氨基酸残基的氢键和疏水键相互作用而破坏其功能, 从而发挥抗炎作用。

月桂酸甘油酯对包膜病毒和大多数革兰阳性菌(如链球菌、葡萄球菌)的抗菌活性较强^[6]。月桂酸甘油酯还能通过增强免疫功能而增强其抗菌、抗炎作用。有研究显示, 月桂酸甘油酯通过增加促炎细胞因子, 激活和吸引白细胞到感染部位, 引发快速、强烈的炎症反应, 产生有限的活性氧(ROS), 从而减少组织损伤^[7]。WITCHER等^[8]的研究也发现, 月桂酸甘油酯可通过增加T淋巴细胞改善免疫功能。

1.2 肉豆蔻酸

肉豆蔻酸是存在于VCO中的饱和脂肪酸, 其能酰

化蛋白质, 如肉豆蔻酰化^[9]。肉豆蔻酰化是肉豆蔻酸通过肉豆蔻酰辅酶A与蛋白质N端甘氨酸的不可逆共价键合。肉豆蔻酰化过程依赖于关键酶N-肉豆蔻酰转移酶(NMT), NMT是许多真核生物和病毒生长与发育不可或缺或酶的酶, 通常以同工酶的形式存在于体内^[10]。有研究表明, 肉豆蔻酰化是抑制病毒复制的潜在治疗靶点^[11]。

1.3 PA

PA是一种饱和脂肪酸, 常见于棕榈油中, 也多见于CVO中。现代药理学研究表明, PA具有抗炎、抗氧化和增强免疫力的作用。PA是一种很有前途的抗肿瘤药物, 通过诱导肿瘤细胞凋亡, 抑制肿瘤细胞增殖、转移和侵袭, 增强对化学治疗(简称化疗)的敏感性, 改善免疫功能, 并干扰癌细胞周期, 导致细胞周期主要停滞在G₁期, 从而抑制肿瘤细胞生长^[12]。

2 VCO在治疗肺部疾病中的应用

2.1 肺炎

2.1.1 概述

肺炎分为社区获得性肺炎和医院获得性肺炎, 是目前导致肺部疾病患者住院或死亡的主要原因^[13]。肺炎链球菌、金黄色葡萄球菌、流感嗜血杆菌、肺炎克雷伯菌、铜绿假单胞菌、非典型病原体(嗜肺军团菌、肺炎支原体和衣原体)是导致肺炎的主要病原体^[14]。目前, VCO主要用于治疗细菌性肺炎和病毒性肺炎。

2.1.2 细菌性肺炎

VCO具有明显的抗炎、抗菌作用, 能缓解肺部炎症的进展。月桂酸甘油酯对大多数革兰阳性菌(如链球菌、葡萄球菌等)具有抗菌活性^[6], 主要通过与其质膜的相互作用, 非特异性地作用于细菌表面的信号转导系统^[15]。月桂酸甘油酯抑制革兰阳性菌外毒素的产生主要通过双组分系统阻止信号转导, 干扰转录, 从而发挥抗菌作用^[16]。月桂酸甘油酯通过脂寡糖(而非脂多糖)对革兰阴性菌起杀菌作用^[17]。多数医院的获得性肺炎病例由革兰阴性病原体引起, 以肺炎克雷伯菌为代表。由于革兰阴性菌存在完整的脂多糖, 故月桂酸甘油酯对革兰阴性菌的抑制作用有限。但有研究发现, 月桂酸甘油酯能联合其他抗菌药物在体外和体内增加对革兰

阴性菌株的抗菌活性,在肺部细菌感染模型中,多黏菌素B联合月桂酸甘油酯可通过加速细菌清除和降低死亡率挽救肺炎克雷伯菌感染的小鼠^[18]。铜绿假单胞菌是一种普遍存在的微生物,通常会导致医院获得性感染,包括肺部、血液系统、尿路等感染。有研究表明,月桂酸甘油酯纳米胶囊能有效杀灭铜绿假单胞菌^[18]。

2.1.3 病毒性肺炎

新型冠状病毒(COVID-19)是一种攻击呼吸道的病毒,与严重急性呼吸综合征(SARS)病毒密切相关^[19],两者均属冠状病毒,主要引起的人类疾病为呼吸系统感染,其相同的特性为病毒粒子外均有包膜覆盖。

月桂酸及月桂酸甘油酯基于3种机制发挥抗COVID-19作用,即病毒膜的解体、抑制病毒成熟和防止病毒蛋白与宿主细胞膜的结合^[20]。月桂酸比其他脂肪酸具有更强的抗病毒特性,月桂酸甘油酯在复制周期的成熟阶段结束时抑制病毒^[21]。脂质和磷脂是构成微生物或病毒的外部。SUBROTO等^[22]研究认为,月桂酸甘油酯的抗病毒机制为溶解脂质和磷脂,导致外膜解体。病毒外膜的损伤会导致病毒破裂并死亡。PROJAN等^[15]研究认为,月桂酸甘油酯的抗病毒机制为通过干扰生物体的信号传导,影响病毒RNA的组装,从而抑制病毒的成熟或繁殖。月桂酸甘油酯还能干扰病毒与哺乳动物细胞的融合,对包膜RNA和DNA病毒(如冠状病毒)具有杀灭作用^[23-25]。月桂酸具有与严重急性呼吸综合征冠状病毒2型(SARS-CoV-2)相似的结构脂质,对SARS-CoV-2病毒感染具有潜在的防御作用^[26]。

肉豆蔻酸是存在于VCO中的饱和脂肪酸,同样具有抗病毒作用。肥胖是导致SARS-CoV-2病毒载量较高、严重COVID-19肺炎的风险因素。肺表面活性物质是脂质和蛋白质的复杂混合物,90%为脂质,主要为磷脂酰胆碱(PC),10%为蛋白质。二肉豆蔻酰磷脂酰胆碱(DMPC)与PA肉豆蔻酰磷脂酰胆碱(PMPC)是其中的脂质。DU等^[27]的研究表明,提高肥胖小鼠肺表面活性物质中的DMPC和PMPC水平,能减轻野生型和D614G突变型SARS-CoV-2感染,故增加肺表面活性剂中的DMPC和PMPC可能是预防和治疗COVID-19感染疾病的创新策略。但目前的研究仍有局限性,由于侵入性太强,尚未研究人类肥胖症中的磷脂谱,无法从肥胖患者获得用于脂质组学分析的肺表面活性剂,未来将以肥胖灵长类动物作为研究对象进行研究,可能会获得有用的信息。

人类呼吸道合胞病毒(RSV)是婴儿、老年人、免疫功能低下者及心脏病患者严重下呼吸道感染的主要原

因^[28]。若儿童期感染RSV,可能在以后的生活中易引发持续性或复发性喘息和哮喘^[29]。目前,用于防治RSV感染的药物有限,故需研发新的药物,以治疗由RSV引起的呼吸道感染。有研究表明,饱和的中链脂肪酸及其相应的甘油单酯和脂肪醇可迅速灭活RSV病毒^[30],月桂酸甘油酯、葵酸对RSV和副流感病毒具有显著的抑制活性,葵酸甘油酯对甲型流感病毒也表现出了明显的抗病毒作用^[31]。

2.2 哮喘

哮喘为常见的气道慢性炎症性疾病,这种炎症会导致喘息、呼吸困难、胸闷、咳嗽反复发作,尤其是夜间或清晨^[32]。目前,虽有多种药物用于缓解哮喘,但因其长期使用的副作用,使越来越多的研究聚焦于天然产物(如VCO)。嗜酸性粒细胞是哮喘中最突出的炎性细胞,可能是哮喘发病机制中发生上皮损伤的介质。有研究发现,VCO中的月桂酸能有效消除嗜酸性粒细胞等炎性细胞,从而缓解支气管哮喘的症状,但不能预防其发作^[33]。VCO可作为过敏性肺部疾病的辅助治疗,其可通过氧化应激,与一氧化氮通路的相互作用,逆转支气管周围炎性浸润、上皮增生、平滑肌增厚和过度收缩^[34]。VCO可能是治疗哮喘的潜在补充和替代药物。但目前认为,VCO会增加总胆固醇及低密度脂蛋白胆固醇的含量^[35],故如何降低VCO对总胆固醇及低密度脂蛋白胆固醇的影响,是未来的研究方向。

2.3 结核病

结核病为人类最古老、最致命的疾病,主要发病于低收入和中等收入国家,造成了重大的健康、社会和经济负担^[36]。有研究表明,VCO中的月桂酸甘油酯具有较强的抗结核杆菌作用,能通过形成ROS并对细胞膜造成损害,抑制生物膜的形成,杀死结核杆菌,抑制结核杆菌的繁殖和复制,降低结核分枝杆菌菌落数量^[37]。痰液转阴率为判定结核病治疗效果的指标,VCO中的月桂酸能通过抑制病菌的繁殖和复制而提高痰液的转阴率,故能作为治疗结核病的附加补充剂。

2.4 肺癌

肺癌的发病率和死亡率均很高^[38]。目前虽有抑制癌细胞生长的化疗药物和靶向药物,但因对正常细胞的严重毒性作用而限制了其临床应用^[39],且化疗药物会产生耐药性,导致其毒性增强而降低了治疗效果^[40]。这引起了越来越多研究者的关注,进而探究治疗肺癌的药物。

天然抗癌剂可能为癌症患者提供了新的治疗选择,如长春花中的长春新碱^[41]、喜树^[42]、褐色钟花树^[43],VCO也是近年来被发现的天然抗癌剂。VCO的活

性成分有抗氧化和抗肿瘤作用,如PA能通过改变细胞的形态变化(包括凋亡小体的形成、细胞质空泡化和细胞核浓缩),从而抑制肺癌细胞的生长能力,尤其是诱导A549非小细胞的凋亡^[44]。但VCO激活细胞凋亡途径的作用机制仍未知,需进一步探究。

甲氨蝶呤是一种化疗药物,但因其毒性,临床应用有限。有研究发现,将甲氨蝶呤掺入椰子油纳米乳剂中,可提高其对A549非小细胞肺癌细胞的细胞毒效能,并可消除其在肺和大脑中诱导的氧化应激^[45]。椰子油中含有各种脂肪酸,除较熟悉的月桂酸外,还含有PA、肉豆蔻酸。以月桂酸、肉豆蔻酸、PA的混合物为原料制备负载超顺磁性氧化铁纳米颗粒和紫杉醇微粒,对恶性来源的人肺上皮细胞有很高的体外疗效,且能抑制A549非小细胞肺癌细胞的生长^[46]。

3 结语

VCO是一种富含饱和脂肪酸的天然物质,如月桂酸、PA等,已被证明食用安全。VCO用于治疗肺部疾病已有一些研究,其活性成分具有较广泛的抗菌作用,可作为一种广谱抗菌剂,同时还能抑制嗜酸性粒细胞等炎性细胞,发挥抗炎作用。此外,在抗病毒及抗肿瘤方面也有显著作用,能杀死各种类型的病毒,尤其是包膜病毒;还能作为一种天然抗癌剂。但饱和脂肪酸一直备受争议,如升高血脂、增加心血管疾病风险等,目前尚无足够证据证明VCO的摄入量和心血管疾病明确相关,且有研究发现VCO能增加高密度脂蛋白胆固醇含量,对总胆固醇和低密度脂蛋白胆固醇的不利影响似乎较小,VCO对心血管方面的作用还需进一步研究。

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