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【文献综述】

表没食子儿茶素没食子酸酯(EGCG)抗氧化作用在眼科研究中的应用△

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Research advance of the mechanism of epigallocatechingallate against oxidative damage in ophthalmology

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【Abstract】 Epigallocatechingallate (EGCG) is an effective component of tea polyphenols from green tea extract, which possesses very strong antioxidant activity. In the past few years, EGCG has been widely studied for its antioxidant activity. Studies have shown that EGCG can inhibit cell apoptosis through anti-oxidation pathways, thereby protecting cells from oxidative damage. Some scholars have focused on EGCG research on the prevention and control of eye diseases. In the present paper, we reviewed the application of EGCG in ophthalmology.

【Key words】 epigallocatechingallate; anti-oxidation; ophthalmology

【摘要】 表没食子儿茶素没食子酸酯(epigallocatechingallate,EGCG)为绿茶提取物茶多酚的有效成分,具有非常强的抗氧化活性,近年来EGCG得到广泛的研究。研究表明,EGCG可以通过抗氧化作用抑制细胞凋亡,从而保护细胞,减少氧化损伤。近年来一些学者专注于EGCG对眼科疾病防治的研究。本文就EGCG抗氧化作用在眼科的应用进行综述。

【关键词】 表没食子儿茶素没食子酸酯;抗氧化作用;眼科
【中图分类号】 R776.1

表没食子儿茶素没食子酸酯(epigallocatechingallate,EGCG)为绿茶提取物茶多酚的有效成分,它是绿茶的主要活性和水溶性成分,是儿茶素中含量最高的组分。EGCG β环上有多个酚羟基,可以提供质子,能够有效清除脂类自由基,切断脂类氧化的链式反应,防止脂质的过氧化。此外,EGCG具有非常强的抗氧化活性,可抑制有关氧化酶的活性,并与其他抗氧化剂有协同作用,从而保护和修复抗氧化系统。研究表明,EGCG能够保护细胞和DNA免受损害,具有显著的抗氧化、清除体内自由基、抗突变、抗病毒、调节机体免疫功能、诱导肿瘤细胞凋亡及光保护等一系列生物学活性。近年来,一些学者专注于EGCG对眼科疾病防治的研究。本文就EGCG抗氧化作用在眼科的应用进行综述。

1 EGCG保护机制的研究

1.1 EGCG的生物学特性 茶多酚(tea polyphenols,TP)是茶叶中多酚类物质的总称,包括黄烷醇类、花色苷类、黄酮类、黄酮醇类和酚酸类等,其中以黄烷醇类物质(儿茶素)最为重要,占TP总量的65%~80%,主要含有4种单体:EGCG、表儿茶素没食子酸酯(epieabechingallate,ECG)、表儿茶素(epicatechin,EC)及表没食子儿茶素(epigallocateehin,EGC)。其中,EGCG含量最高,占儿茶素的80%左右,也是茶多酚中生物活性最强的成分[1]。研究表明,EGCG能够保护细胞和DNA免受损害,具有显著的抗氧化、清除体内自由基、抗突变、抗病毒、调节机体免疫功能、诱导肿瘤细胞凋亡及光保护等一系列生物学活性[2-3]。由于EGCG在绿茶中的含量较高,同时具有非常强的抗氧化活性,近年来,EGCG得到广泛的研究,并且成为一种受人们欢迎的药品。研究

表明,EGCG 可以预防慢性疾病,如神经变性疾病、肥胖、癌症、2 型糖尿病、动脉粥样硬化及心脏疾病等[4-8]。同时,EGCG 能够保护心脏、肾脏、神经系统、角膜、视网膜及晶状体等,减轻氧化对它们的损伤[9-14]。

1.2 EGCG 抗氧化和抗凋亡作用 研究表明,EGCG 具有抗氧化和抗凋亡的作用[15]。EGCG 分子中含有 8 个酚性羟基结构,具有淬灭单线态氧、清除自由基的能力,其抗氧化活性是超氧化物歧化酶(superoxide dismutase,SOD)的 6 倍,是维生素 E 的 20 倍[16]。它还可能通过清除活性氧(reactive oxygen species,ROS)[17],抑制细胞内生物大分子的过氧化,进而改变细胞内氧化还原状态,从而抑制细胞凋亡。EGCG 发挥抗氧化作用的机制主要包括:(1)清除自由基;(2)增加抗氧化酶的活性;(3)络合诱导氧化的金属离子;(4) 促进体内抗氧化物再生。Park 等[18]研究发现,EGCG 可以通过清除 ROS,调节 Bcl-2 家族基因及 caspases 的表达、抑制 NO 诱导的牙釉质细胞的凋亡;Zhou 等[19]研究发现,EGCG 可以通过清除 ROS 及减少线粒体损伤来抑制血管紧张素Ⅱ诱导的人脐静脉血管内皮细胞的凋亡;Saito 等[20]认为 EGCG 可以通过抑制氧化应激引起的 DNA 损伤及通过上调血红素氧合酶-1 和 Bcl-2 的表达来抑制细胞凋亡。Adikesavan 等[21]研究发现,EGCG 可以减少氧化应激对心肌的损伤,同时可以通过抑制线粒体介导的细胞凋亡保护心脏。

1.3 EGCG 对紫外线诱导损伤的保护作用 紫外线辐射性氧化损伤的病理机制可概括为:紫外线照射产生的 ROS 如单线氧、超氧阴离子和羟自由基等,可破坏 DNA 结构,激活蛋白激酶。ROS 首先损伤细胞,诱发细胞 DNA 发生改变、蛋白质和脂质损伤、改变细胞膜通透性,影响酶的活性,最终导致细胞凋亡。

细胞内 ROS 的平衡依赖于细胞内正常新陈代谢和抗氧化系统清除能力之间的动态平衡。机体内的抗氧化系统包括:非酶系统[如谷胱甘肽(glutathione,GSH)、胆红素、维生素 E 和维生素 C]和酶促反应系统[如 SOD、过氧化氢酶、谷胱甘肽过氧化物酶(GSH-Px)以及谷胱甘肽还原酶(GSH-Pb)]。机体内抗氧化系统与氧化物之间的失衡,将对机体造成损伤。

EGCG 对紫外线诱导的细胞损伤具有保护作用。EGCG 可通过调节 micro-RNA 的表达来抵抗紫外线 B 对人皮肤成纤维细胞的损伤[22]。EGCG 还可以通过清除活性氧、减少黑色素生成,减轻紫外线对 HaCaT 细胞的损伤[23]。Chaudhury 等[24]研究证实 EGCG 可以通过抗氧化应激作用保护人 γB-晶状体蛋白免受紫外线的损伤。

2 EGCG 抗氧化与光保护作用在眼科的应用

由于 EGCG 的抗氧化作用和光保护作用,近年来一些学者专注于 EGCG 对眼科疾病防治的研究。

2.1 EGCG 对视网膜色素上皮细胞的保护作用 Cao 等[25]发现 EGCG 可以通过抑制氧化应激及调节 JNK1/c-Jun 通路来保护紫外线 B 诱导的 ARPE19 细胞的凋亡。EGCG 通过升高 survivin 基因的表达,减轻线粒体功能紊乱和减少 DNA 碎片,从而保护紫外线 B 对视网膜色素上皮细胞的损伤[26]。EGCG 可以调节视网膜色素上皮细胞的自我吞噬作用来减少紫外线 B 对视网膜的损伤[27]。有研究表明,EGCG 可以减轻 H_2O_2 诱导的鼠视网膜色素上皮的损伤[28],这表明,EGCG 在预防与 H_2O_2 诱导氧化损伤相关的视网膜疾病方面有潜在作用。

2.2 EGCG 对神经节细胞的保护作用 EGCG 具有明显的神经保护作用,其作用机制与 EGCG 的抗氧化作用有关[29-30]。目前关于 EGCG 对视神经的保护作用主要集中在其对视网膜神经节细胞(retinal ganglion cells,RGC)的保护作用。有研究表明,一定浓度的 EGCG 对 H_2O_2、紫外线照射诱导的 RGC-5 的氧化损伤有保护作用[31-32]。姜利斌等[33]研究发现,EGCG 对大鼠视神经钳伤后 RGC 具有一定的保护作用,并推测 EGCG 可能是通过抗氧化、清除自由基等作用而保护视神经。

2.3 EGCG 对晶状体上皮细胞的保护作用 有学者发现 EGCG 可抑制地塞米松损伤所诱导的兔晶状体上皮细胞凋亡,并推测 EGCG 可以通过清除自由基使体内抗氧化体系再生,抑制过氧化反应,从而抑制细胞凋亡[34]。同时,一些研究发现 EGCG 对紫外线 B 造成的晶状体上皮细胞的损伤有保护作用[28],EGCG 可以减少紫外线 B 诱导的人晶状体上皮细胞内 ROS 的产生及 NADPH 氧化酶的活性[35-36],对 DNA 的损伤有拮抗作用[37],为 EGCG 用于白内障的防治提供新的思路。司南等[38]应用紫外线 B 照射新西兰大白兔后给予不同浓度的 EGCG 滴眼液,发现 EGCG 滴眼液可以进入兔眼房水发挥抗氧化作用,其中以浓度为 200 $\mu mol \cdot L^{-1}$ 的 EGCG 滴眼液的抗氧化作用效果最佳。EGCG 可以通过抑制 caspase-3、caspase-9 的表达[39]或抑制线粒体通路介导的细胞凋亡保护晶状体上皮细胞免受过氧化氢的损伤[40]。EGCG 可能通过提高细胞内 SOD、GSH-Px 含量,降低 MDA 含量,发挥其较强的抗氧化作用[14];进而通过调节 Bcl-2/Bax、p53、c-fos 和 c-myc 的表达[41],抑制高糖所诱导的晶状体上皮细胞的凋亡。

2.4 EGCG 对角膜的保护作用 角膜碱烧伤后白细胞激活、炎症细胞浸润和释放大量氧自由基是导致角膜损伤的主要途径,炎症反应与氧化反应又相互影响,且炎症也与新生血管有密切关系;EGCG 可有效促进碱烧伤后鼠角膜上皮修复,抑制新生血管形成和炎症细胞浸润[42-43]。联合抗真菌和抗氧化治疗可减少真菌性角膜炎的氧化应激。有研究表明,

联合应用伏立康唑和EGCG,与单用伏立康唑相比,前者可明显减轻真菌性角膜炎所引起的炎症反应[44]。EGCG可有效抑制人角膜缘上皮细胞内ROS的产生,从而保护角膜缘上皮细胞免受氧化损伤[45],为EGCG在干眼的防治提供了依据。此外,EGCG可增加抗氧化系统酶的活性及抑制脂质过氧化反应和蛋白质氧化来保护紫外线B对角膜的损伤[46]。

3 结论

EGCG具有多种生物活性,其抗氧化作用一直是人们研究的重点。近年来一些学者专注于EGCG对眼科疾病防治的研究。一定浓度的EGCG对视网膜上皮细胞、视网膜神经节细胞、晶状体上皮细胞及角膜细胞等均有保护作用,为EGCG在眼科的应用提供了依据。

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