

冬虫夏草的质量和功能研究进展*

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摘要 冬虫夏草 *Ophiocordyceps sinensis* 是名贵的药用与食用菌, 具有抗氧化、抗细菌、抗肿瘤及免疫调节等多种功能。冬虫夏草的正确鉴别、质量和功能评价有助于这一珍贵资源的研发。本文从如下方面综述冬虫夏草在质量和功能方面的研究进展: 1) 性状特征和真假鉴别; 2) 主要成分; 3) 药效功能; 4) 质量评价。

关键词 冬虫夏草, 性状特征, 真假鉴别, 主要成分, 质量评价

Progress in research on the quality and function of *Ophiocordyceps sinensis*

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Abstract *Ophiocordyceps sinensis* is a famous and valuable medicinal and edible mushroom with broad therapeutic antioxidant, antibacterial, anti-tumor, and immune stimulation, functions. Identification and evaluation of the quality and function of *O. sinensis* contributes to the research and development of this precious resource. This paper reviews progress in research on the quality and function of *O. sinensis* including its characteristics and identification, main components, pharmacological functions and quality evaluation.

Key words *Ophiocordyceps sinensis*, characteristic, identification, main components, evaluation of quality

冬虫夏草 *Ophiocordyceps sinensis* 属于子囊菌门 (Ascomycota), 粪壳菌纲 (Sordariomycetes), 肉座菌目 (Hypocreales), 线性虫草菌科 (Ophiocordycipitaceae), 线性虫草属 (*Ophiocordyceps*), 是冬虫夏草真菌寄生在蝙蝠科昆虫上形成的菌核和子座复合物 (Sung *et al.*, 2007; Yue *et al.*, 2013)。冬虫夏草是生长在青藏高原地区特有的物种, 全球仅分布在中国、不丹、印度、尼泊尔 4 国, 在我国主要分布在西藏、青海、四川、云南、甘肃等省 3 000~5 200 m 的高海拔地区 (Yue *et al.*, 2013)。

随着冬虫夏草的药效功能被证实, 国内外越来越关注冬虫夏草, 交易额呈增长的趋势 (Buenz *et al.*, 2005)。由于生境特殊、自然资源有限、价格昂贵, 冬虫夏草资源被过度采挖, 生态环境严重受损, 已濒临枯竭, 大部分地区的产量不到 25 年前的 10% (尹定华等, 2011)。然而, 人们对冬虫夏草的需求量日趋增多, 供不应求, 导致冬虫夏草的价格飙升。不法商贩为追求高额利润, 以假乱真、以次充好, 导致冬虫夏草市场出现混乱。本文论述冬虫夏草的性状特征和真假鉴别、主要成分、药效功能和质量评价等方面的研

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究概况,以期对冬虫夏草真假的鉴别和质量优劣的评价奠定基础。

1 冬虫夏草的性状特征和真假鉴别

1.1 冬虫夏草的性状特征

冬虫夏草的虫体部分似蚕,长 3~5 cm,直径 0.3~0.8 cm;表面深黄色至黄棕色,有环纹 20~30 个,近头部的环纹较细;头部红棕色,足 8 对,中部 4 对较明显,质脆,易折断,断面平坦,淡黄白色。子座部分细长圆柱形,长 4~7 cm,直径 0.2~0.4 cm;表面呈深棕色至棕褐色,有细纵皱纹,上部稍膨大,质柔韧,断面类白色。冬虫夏草气微腥,味微苦(康帅等,2013)。

1.2 冬虫夏草的混淆品与次品

1.2.1 偷换概念 冬虫夏草是线性虫草属的。其他品种的虫草如蛹虫草、凉山虫草、戴氏虫草等都不是真正的冬虫夏草,营养价值没有冬虫夏草高,有些虫草错误食用后对人体健康有害。

1.2.2 制造伪品 不法商贩用植物地蚕、石蚕、甘遂、甘露、僵蚕等冒充冬虫夏草的虫体,也有用淀粉、石膏、黄花菜等为原料人工模压、染色伪造冬虫夏草的虫体(徐如英,2010)。

1.2.3 黑心加重 不法商贩将冬虫夏草浸泡明矾水、饱和硫酸钾溶液或喷洒金属粉,或在冬虫夏草内部插入铁丝、铜丝,在子实体底部捏黑色泥粉、铁粉等以增加冬虫夏草的重量或让外观更漂亮(杨艳青和段军华,2012)。

1.2.4 以次充好 部分黑心商贩收购已经提取过有效成分的冬虫夏草次品,经过烘干、着色处理后将次品以高价卖出,愚弄消费者。劣质冬虫夏草气味极弱,虫体呈暗黄色,水洗或煎煮后褪色。

1.3 冬虫夏草的真假鉴别

1.3.1 形状鉴别 中国药典鉴别冬虫夏草真假主要通过观察样本的形状,包括虫体和子座的颜色、大小,足的数目,气味等。陈小秋等(2011)通过观察子座的有无、形状,虫体的颜色等特征区分冬虫夏草的真假。

1.3.2 显微鉴别 显微鉴别主要涉及对虫体进

行横切,观察虫体中央的结构,躯壳表皮有无着生绒毛、躯壳内有无菌丝等;对子座进行横切、纵切,观察子囊壳包埋位置,子囊壳及子囊孢子形态、大小等。

Au 等(2012)对香港市场上冬虫夏草和混淆品的虫体和子座进行横切面切割,制作成切片,观察子囊大小、着生的方式,复眼和体壁形状特征。康帅等(2013)对冬虫夏草及样本的虫体体壁和腹足进行切割,观察气门、气窝、趾的颜色、形状、大小,鉴别冬虫夏草的真假。

1.3.3 理化鉴别 目前,针对冬虫夏草的理化鉴别方法主要有:紫外吸收光谱法、红外光谱法、薄层色谱法、毛细管电泳法、蛋白电泳法、免疫分析鉴定法、高效液相色谱法和核磁指纹图谱等。高明等(2011)发现冬虫夏草乙醇提取液在 269.00 nm 和 206.20 nm 波长处有最大紫外吸收峰,张声俊(2011)用红外光谱技术对比真假冬虫夏草的油脂、蛋白质和多糖的波峰。顾峥嵘和张全龙(2003)采用薄层层析法,发现冬虫夏草乙醇提取液与标准品显示出相同颜色的斑点。古今等(2005)用高效毛细管电泳法发现冬虫夏草的 Tris-甘氨酸蛋白提取液的最高峰迁移时间与混淆品存在明显的差异。徐君(2006)在蛋白电泳法中,利用扫描图谱进行聚类分析虫草类别。李扬(2013)在免疫分析鉴定方法中,制备冬虫夏草的抗原,用金标试纸法检测冬虫夏草真假。Wang 等(2013)用高效液相色谱法(High performance liquid chromatography, HPLC)测定冬虫夏草,发现尿苷、鸟苷、腺苷是冬虫夏草中重要核苷类物质。武彦舒等(2008)用 HPLC 构建核苷指纹图谱,运用聚类分析鉴别冬虫夏草的真假;Guan 等(2011)构建多糖指纹图谱,发现冬虫夏草中含甘露糖、葡萄糖、半乳糖,不含半乳糖醛酸。陈罡等(2014)采用核磁共振技术构建核磁特征指纹图谱,鉴别冬虫夏草真假。

1.3.4 分子鉴别 冬虫夏草是真菌子座与蝙蝠蛾科幼虫的复合体,可以运用分子生物学技术从真菌和昆虫两方面对冬虫夏草进行真假鉴别。

目前,ITS 序列分析技术已成功应用于真菌分类学研究中,该技术快速、准确、简便(Rehner

and Buckley, 2005; Stensrud *et al.*, 2005; Feng *et al.*, 2009)。翁榕安和李树华(2008)运用 ITS 序列分析技术,发现冬虫夏草和蛹虫草两者的 ITS 相似度远小于 90%,可以推断为不同的种。多数学者认为,ITS 序列具种属特异性,用以鉴定冬虫夏草中的多种菌物具有优势(魏鑫丽等, 2006; Xiao *et al.*, 2009; 张永杰等, 2010; Zhang *et al.*, 2010; 朱佳石和吴建勇, 2015)。

在真核生物中,细胞色素 c 氧化酶 CO 基因具有昆虫种属特异性,在一定程度上用于检测种、属间的进化关系(Flomer *et al.*, 1994; Hebert *et al.*, 2003)。细胞色素 b Cytb 基因是线粒体中结构和功能被研究最为清楚的基因之一,进化速率适中,被用于研究种类遗传分化程度和系统进化(程舟等, 2007)。冬虫夏草真假的鉴别方法见表 1。

表 1 冬虫夏草的真假鉴别
Tabel 1 Identification of *Ophiocordyceps sinensis*

鉴别类型 Identifying type	鉴别参数或方法 Identification parameters or methods
形状鉴别	虫体和子座的颜色、大小,足的数目,气味等
显微鉴别	虫体切片:观察躯壳内绒毛和菌丝,体壁和腹足结构; 子座切片:观察子囊壳包埋位置,子囊壳及子囊孢子形态、大小等
理化鉴别	紫外吸收光谱法、红外光谱法、薄层色谱法、毛细管电泳法、 蛋白电泳法、免疫分析鉴定法、高效液相色谱法和核磁指纹图谱
分子鉴别	冬虫夏草菌 ITS 序列分析,虫体 CO 和 Cytb 序列分析

2 冬虫夏草的主要成分

2.1 核苷类

核苷类物质是冬虫夏草中的重要生物活性成分,冬虫夏草含腺嘌呤、腺苷、鸟苷、尿嘧啶和胞嘧啶等核苷成分(Yu *et al.*, 2006; Zhao *et al.*, 2014)。核苷物质在中枢神经系统等多种生理活动中发挥着重要的作用(Li *et al.*, 2006),其中腺苷具有促进细胞分化、改善心脑血管血液循环、抑制蛋白质激酶和反转录酶活性等功能(Omar *et al.*, 2012; Niccoli *et al.*, 2013)。产地不同,冬虫夏草的核苷成分的组成与含量有所不同(夏文娟等, 2001; 肖远灿等, 2014);冬虫夏草的不同部位,其核苷成分也有差异(Ikeda *et al.*, 2008)。在核苷类物质中,腺苷、肌苷含量相对较高、稳定,可以作为冬虫夏草质量控制的指标。2010 年版的《中华人民共和国药典》把腺苷含量定为冬虫夏草的含量测定项目,规定冬虫夏草的腺苷含量不得少于 0.01%。

2.2 多糖类

多糖为冬虫夏草中含量高的药理活性物质,

冬虫夏草干品中多糖含量约为 3%~8%(Li *et al.*, 2001)。冬虫夏草在生长过程中,会产生大量的胞外多糖(Extracellular polysaccharides, EPS)和胞内多糖(Intracellular polysaccharides, IPS),由葡萄糖、甘露糖、半乳糖、木糖等单糖通过糖苷键形成直连、支链构成多糖(Cheung *et al.*, 2009)。冬虫夏草菌培养液分离出的 EPS 分子量大小为 5~200 ku,具有抗氧化、刺激多种细胞因子释放、延缓肾衰竭的作用(Yan *et al.*, 2009; Wang *et al.*, 2010, 2011)。冬虫夏草菌丝分离出的 IPS 分子量大小为 8.1~460 ku,具有抗氧化、降低胆固醇活性(Li *et al.*, 2003; Wang *et al.*, 2009; Kim, 2010)。真菌多糖是一种 β -型多糖,具有螺旋的三维立体结构,近似 DNA。多糖的抗肿瘤活性与多糖的分子量有关,分子量大于 1.6×10^6 时才具有抗肿瘤活性(Sasaki *et al.*, 1976)。多糖的活性除了与分子量有关外,还与多糖的溶解度、黏度、初级结构和高级结构有关。通过对多糖的酶解、色谱分析,多糖的组成和键的结构等指纹图谱构建出来,作为冬虫夏草质量控制的指标(Guan and Li, 2010)。

2.3 甾醇类

甾醇类化合物是真菌细胞膜的重要组成部分,同时还具有多种生物学活性(Volkman, 2003)。从冬虫夏草有机物提取液中可分离出胆甾醇、 β -谷甾醇、啤酒甾醇、麦角甾醇、麦角甾醇过氧化物(郇皆秀等, 2003)。麦角甾醇是冬虫夏草内主要甾醇,是维生素 D₂ 的重要前体,具有利抗癌、抑菌、抗纤维化、抑制抗药性等功能(Yan *et al.*, 2009; Hu *et al.*, 2014; Zhu *et al.*, 2014)。麦角甾醇可分为游离麦角甾醇和酯化麦角甾醇,野生冬虫夏草的虫体和子座中同时具有这两种成分,虫体酯化的麦角甾醇含量高于子座中的含量。麦角甾醇含量在冬虫夏草内相对稳定,可以作为冬虫夏草质量控制的指标(Yuan *et al.*, 2007)。

2.4 虫草酸

虫草酸又称 D-甘露醇,为奎宁酸的一种异构体(Sprecher and Sprinson, 1963),是冬虫夏草中的主要有效成分之一,具有降低脑血容量、利尿脱水、抗自由基、镇喘祛痰、促进消化等药理作用,对多种疾病有一定的疗效(陈洁丽等, 1997; Hanieh and Sakaguchi, 2009; Daviskas *et al.*, 2010; Diringier *et al.*, 2012; Min *et al.*, 2013)。冬虫夏草的虫草酸干重含量高于 3.4%,一般子座中的虫草酸含量约 29~85 mg/g。虫草酸含量随冬虫夏草子座发育成熟度增加而增加,同时与产地、寄主、生长期有关(蔡仲军, 2003)。虫草酸含量高低常被作为衡量冬虫夏草质量的重要指标。

2.5 氨基酸和蛋白质

冬虫夏草中含丰富的氨基酸和蛋白质,蛋白质的含量约 29.1%~33%。氨基酸有蛋氨酸、亮氨酸、谷氨酸、天冬氨酸、精氨酸、甘氨酸和酪氨酸等 18 种。水解后的氨基酸含量一般在 20%~25%,冬虫夏草菌丝中 3 种主要氨基酸分别是谷氨酸、天冬氨酸、赖氨酸,野生冬虫夏草中 3 种主要氨基酸分别是谷氨酸、天冬氨酸、精氨酸(Hsu *et al.*, 2002; Zhou *et al.*, 2009)。严冬和杨鑫堃(2014)通过比较发现西藏不同产地野生冬虫夏草的氨基酸种类和含量无显著性差

异,必需氨基酸相对均衡和合理。冬虫夏草丰富的氨基酸与家禽肉食互补,可提高营养价值,改善人体状况(钱爱萍等, 2010)。冬虫夏草的多肽具有抗氧化、抗癌细胞和治疗脑缺血再灌注损伤等功能(Jia *et al.*, 2005; Wang *et al.*, 2012)。

2.6 野生冬虫夏草和人工培养的冬虫夏草菌粉的活性成分含量比较

不少学者分析比较了野生冬虫夏草和人工培养的冬虫夏草菌粉的多种活性成分含量。数据库公布的部分冬虫夏草菌序列是不可靠的,可能原因是使用的研究材料不可靠或不明确,适于在低于 21℃ 下生长和生长缓慢是冬虫夏草菌的重要特征(Dong and Yao, 2011)。Li 等(2006)测定深层培养的冬虫夏草菌丝中核苷类(腺苷、鸟苷、尿嘧啶和肌苷)含量为 6.20 mg/g,振荡培养的冬虫夏草菌丝中核苷类含量为 1.60 mg/g,野生冬虫夏草子实体中核苷类含量为 1.80 mg/g。Hsu 等(2002)测定冬虫夏草发酵菌丝中甘露醇含量超过 7.99%,多糖主要由甘露糖、葡萄糖和半乳糖等以 1.00:3.82~16.61:1.28~1.60 摩尔比构成;冬虫夏草菌丝中甘露糖含量低于 5.83%,多糖主要由甘露糖、葡萄糖和半乳糖以 1.00:1.09~3.01:1.05~3.30 摩尔比构成。Li 等(2004)测定冬虫夏草菌丝中游离麦角甾醇含量为 2.71~3.23 mg/g,野生冬虫夏草中游离麦角甾醇含量为 0.97~1.43 mg/g。Wang 等(2009)测定冬虫夏草菌丝因受产地和培养方式等因素影响,冬虫夏草菌丝中虫草酸含量波动较大,为 3.17~82.07 mg/g,野生冬虫夏草中虫草酸含量为 89.77~91.80 mg/g。Hsu 等(2002)测定冬虫夏草发酵菌丝中氨基酸含量为 9.23%,其中谷氨酸含量为 1.12%,天冬氨酸含量为 1.05%,赖氨酸含量为 0.80%;野生冬虫夏草中氨基酸含量为 18.1%,其中谷氨酸含量为 2.64%~2.66%,天冬氨酸含量为 1.70%~1.84%,精氨酸含量为 1.53%~1.60%。

3 冬虫夏草的药理作用

3.1 抗氧化

冬虫夏草的水分提取液和乙醇提取液具有

高效的抗氧化活性,可抑制羟基自由基诱导形成的丙二醛,抑制脂质过氧化和低密度脂蛋白氧化,减少胆固醇酯在巨噬细胞内的积累(Yamaguchi *et al.*, 2000a, 2000b)。有学者采用黄嘌呤氧化实验、溶血诱导实验、脂质过氧化实验 3 种不同实验方法分析冬虫夏草水分提取液的抗氧化活性,结果证实冬虫夏草具有高效的抗氧化活性(Li *et al.*, 2001)。冬虫夏草菌丝中分离出的 1-(5-hydroxymethyl-2-furyl)- β -carbolin 对超氧离子具有较强的抑制活性,半数效应浓度(The half maximal inhibiting concentration IC_{50})为 $(0.45 \pm 0.15) \mu\text{mol/L}$ (Yang *et al.*, 2011);冬虫夏草发酵液中分离出的黑色素具有较强的 DPPH (1,1-diphenyl-2-picrylhydrazyl) 自由基清除活性和螯合亚铁离子的活性(Dong and Yao, 2012);冬虫夏草菌丝水提取液中含有高量的酚类和黄酮类化合物,与清除 DPPH 自由基和还原三价铁离子等活性密切相关(Rathor *et al.*, 2014)。赵聃聃等(2015)研究发现冬虫夏草菌丝多种有机溶剂提取液具有清除自由基的还原力,其抗氧化活性物质多集中在中极性部位。

3.2 抗菌

冬虫夏草的抗菌物质具有广谱性,对原核生物中的革兰氏阴性菌(如大肠埃希菌)和阳性菌(如金黄色葡萄球菌)、芽孢杆菌(如枯草芽孢杆菌、苏云金芽孢杆菌)和非芽孢杆菌(如鼻疽杆菌)、放线菌(如链霉菌)均有拮抗性,但对酵母和丝状真菌没有抗菌活性(程显好和白毓谦, 1995; 武忠伟等, 2008)。董开忠等(2014)用头孢曲松钠溶液诱导小鼠菌群失调,冬虫夏草菌丝可能通过调节血清血管活性肠肽和 P 物质含量来调整菌群失调小鼠肠道内有益菌的比例。

3.3 抗肿瘤

冬虫夏草提取物在体外具有明显地抑制、杀伤肿瘤细胞的活性,其中核苷类(衍生物)、甾醇类和多糖类与抗肿瘤活性有关。Wu 等(2007)发现冬虫夏草菌丝的乙酸乙酯提取液对小鼠黑色素瘤细胞具有抑制作用;Matsuda 等(2009)

证实以甲醇和乙酸乙酯从冬虫夏草菌丝体分离出的多种甾醇类化合物具有抗早幼白血病 HL-60 癌细胞的活性。Aghaei 等(2012)和 Otsuki 等(2012)发现腺苷能上调抑癌基因 p53 的表达,阻滞细胞周期的进展,诱导癌细胞发生凋亡。Mei 等(2014)从冬虫夏草分离了一种能抑制肉瘤细胞增殖的杂多糖,在一定浓度下能诱导肉瘤细胞的凋亡。罗小平等(2012)以肿瘤移植成功的大白兔为模型,证实了野生冬虫夏草水溶液抑制兔肝内部肿瘤细胞的生长,减少肿瘤细胞转移的发生率。冬虫夏草抗肿瘤细胞机制可能涉及到:直接的细胞毒性,诱导肿瘤细胞发生凋亡,激活或增强免疫功能(Zhang and Wu, 2007; Zhao *et al.*, 2011; Chen *et al.*, 2012)。

3.4 降血糖和降血脂

冬虫夏草主要通过刺激胰岛素分泌、抑制肝葡萄糖输出、促进肝脏葡萄糖代谢酶活力和降低葡萄糖转运蛋白含量等来达到降低血糖的作用,而且只有血糖值高于正常时才有效(赵可蕊等, 2006)。研究者用链脲佐菌素和肾上腺素诱导小鼠产生糖尿病,通过注射、口服冬虫夏草提取液等方式增加肝葡萄糖激酶、己糖激酶、葡萄糖磷酸脱氢酶等活性,降低血糖的浓度,但正常小鼠的胰岛素含量没有受到影响(Kiho *et al.*, 1993, 1999)。

在给小鼠喂高脂食物时,通过口服冬虫夏草提取液能增加血清的脂肪氧化,增加高密度脂蛋白的胆固醇水平、减少极低密度脂蛋白和低密度蛋白的胆固醇水平,从而达到降低血浆中胆固醇水平(Koh *et al.*, 2003; Yamaguchi *et al.*, 2000b)。

3.5 保护肝和肾

动物测试和临床实验证实冬虫夏草具有保肝作用,麦角甾醇和多糖是保护肝脏的活性物质。在 CCl_4 诱导的急性肝损伤小鼠中,冬虫夏草菌丝提取液能减轻肝细胞坏死程度,对化学性肝损伤有辅助保护功能(杨槐俊等, 2013)。同时,冬虫夏草提取液能减轻肝脏炎症,减少胶原沉积,还能防止肝纤维化(Peng *et al.*, 2014)。

在二甲基亚硝胺诱导的大鼠肝纤维化模型中,冬虫夏草制剂(百令肝胶囊)能促进损伤细胞再生,降低肝纤维化面积,从而起到减缓肝纤维化进程和恢复肝脏功能的作用(钱莺等,2013)。

中药理论认为冬虫夏草具有补肾的功能,研究发现冬虫夏草补肾功能来自于增加体内的17-羟基-皮质类固醇和17-酮-类固醇(Zhu *et al.*, 1998)。患有糖尿病大鼠的肾脏是慢性缺氧的,缺氧诱导因子(Hypoxia inducible factor-1 α , HIF-1 α)和血管表皮生长因子(Vascular endothelial growth factor, VEGF)表达量是高于正常大鼠的。研究发现冬虫夏草通过降低HIF-1 α 和VEGF表达量来治疗慢性缺氧损伤(袁明霞等,2013)。在糖尿病肾病或肾缺血-再灌注大鼠模型中,冬虫夏草和冬虫夏草制剂(金水宝)降低蛋白尿含量,减轻肾小管损伤,对肾具有保护作用(黄可等,2014;张莉等,2014)。施海涛等(2013)研究发现金水宝能降低糖尿病肾病患者转化生长因子表达量,延缓肾小球硬化。在肾移植患者中,Ding等(2011)结合使用环孢菌素A和冬虫夏草制剂(百令胶囊)能减少急性排斥反应、病症并发症。

在临床中,冬虫夏草和其他一些药物结合起来使用治疗肝病和肾病,其治疗效果显著地高于使用单一药物(Ahmed *et al.*, 2012)。

3.6 对呼吸系统的作用

冬虫夏草能增强肾上腺素,扩张支气管炎,松弛支气管平滑肌,后延哮喘发作时间,减轻老年肺气肿、肺心病、慢性哮喘症状,延缓复发时间,起到止咳平喘作用。魏涛等(2002)选用二月龄小鼠作为研究对象,结果发现冬虫夏草菌丝体能降低浓氨水致咳小鼠的咳嗽次数,延长咳嗽潜伏期。在Sprague Dawley大鼠急性支气管哮喘模型中,金水宝抑制炎症细胞及炎症因子在肺内聚集,缓解哮喘症状(郭之强和颜春松,2011)。钱皓瑜(2004)在临床试验中,证实冬虫夏草能显著改善慢性阻塞性肺疾病(Chronic obstructive pulmonary disease, COPD)患者肺通气功能,提高血氧分压,降低血浆内皮素。孙雯等(2010)

研究发现冬虫夏草菌粉提取液能减少哮喘儿童哮喘过程中炎症蛋白的过度表达,减轻炎症反应。冬虫夏草对肺功能的保护作用可能是通过降低气道炎症反应,减少支气管肺泡灌洗液中的基质金属蛋白酶-9的表达而实现的(管彩虹等,2013)。

3.7 对心血管系统的作用

冬虫夏草对心血管系统的作用主要表现在:降低血压、减慢心率,增强心肌耐缺氧能力,抗心律失常,抑制血小板聚集,调节血脂平衡等。

当用冬虫夏草煎剂给高血压大鼠灌胃,能明显降低大鼠血压,并且逆转肾性高血压时所发生的心肌肥大(吴秀香等,2001)。当以Brown Norway大鼠作为研究模型时,冬虫夏草提取液能降低大鼠血管平滑肌的增殖能力,降低动脉硬化化的形成,有助于器官的移植(Zhang *et al.*, 2012)。金水宝可以降低炎症反应,有效改善肺心病患者的血管内皮功能和左室舒张功能(张晓斌等,2012);百令胶囊能明显改善维持性血液透析(Maintenance hemodialysis, MHD)患者的体内氧化应激水平,减少心脑血管事件的发生率(王英,2013)。也有学者发现,从冬虫夏草菌丝分离的一种水溶性多糖能抑制细胞内部信号和血小板激活,对于治疗心血管疾病具有潜在的应用价值(Lu *et al.*, 2014)。

3.8 调节免疫

冬虫夏草对多种疾病的防治发挥着重要的药理作用,对免疫功能起着双向调节作用。Li等(2009)发现野生冬虫夏草水分提取液通过树突细胞调节辅助T细胞Th1/Th2比例来调节免疫反应。冬虫夏草菌丝体分离出来的胞外多糖对小鼠体内的癌细胞具有抑制作用,同时提高腹腔巨噬细胞的吞噬能力,提高淋巴细胞的繁殖能力,显著地提高免疫能力(Zhang *et al.*, 2008; Yue *et al.*, 2013)。Wu等(2014)从冬虫夏草中提取多糖-cordysinan,它对巨噬细胞没有副作用,可刺激巨噬细胞分泌细胞因子和趋化因子,促进免疫细胞参与免疫应答。通过向培养基添加冬虫夏草菌

丝提取液,能增加多种细胞因子的表达、分泌,消除外毒素 B 的抑制作用 (Kuo *et al.*, 2007)。冬虫夏草内多种活性物质在细胞免疫和细胞因子等方面协同参与提高免疫功能 (Zhou *et al.*, 2008)。

4 冬虫夏草质量优劣的评价

冬虫夏草作为中国传统的名贵中草药,具有多种药效活性。多年来,科学工作者证实冬虫夏草具有抗氧化、抗菌、抗癌细胞和调节免疫等功效。国内的冬虫夏草品种繁多,有青海草、川草、藏草和滇草等之称,其质量优劣的评价一直存在着争议。部分人士以单株虫草质量重、虫草饱满和虫草干者为优,这种评价方式易受主客观因素影响,难以让人信服。

目前,我国中药质量评价基本上属于“唯成分论”的评价模式。这种评价模式是参照国外天然药物的质量控制方法,借鉴化学药品质量控制的模式建立的。Guo 等 (2006) 结合使用 HPLC 和质谱检测 (Mass spectrometric, MS) 技术,测定发现四川野生冬虫夏草中核苷类含量最多。陈婷等 (2013) 用 HPLC 同时测定西藏那曲、青海玉树、四川康定、云南迪庆和甘肃甘南野生冬虫夏草样品中腺苷和麦角甾醇含量,发现青海玉树、西藏那曲样品中腺苷和麦角甾醇含量较高。将各地区野生冬虫夏草中氨基酸含量进行比对分析,发现青海和西藏冬虫夏草中的氨基酸含量低于四川和云南冬虫夏草 (于斌等, 2012)。

对于冬虫夏草这种中草药,只检测其中几种活性成分不能反映其所体现的整体疗效,难以有效、全面地监控和评价。随着研究工作的深入,这种质量评价模式逐渐显现弊端,遇到更多的挑战 (Xiao *et al.*, 2013)。2010 年版《中国药典》明确提出中药的质量标准逐步由单一指标成分定性定量测定,向活性有效成分及生物测定的综合检测过渡。因此,科学家研究并建立中药生物效价检测的方法,控制其质量。

冬虫夏草中含有腺苷、肌苷、麦角甾醇、虫草酸和多糖 5 种活性成分,含量较高且稳定,具

有有多种药用功效。对于冬虫夏草而言,可将形态、活性成分和药理活性结合从多角度对其质量作出评价。Li 等 (2001) 研究发现人工培养的冬虫夏草菌丝和野生冬虫夏草具有相似的抗氧化能力。张巧霞等 (2005) 发现人工培养的冬虫夏草菌丝和野生冬虫夏草有机溶剂提取物能抑制小鼠黑色素瘤细胞 B16,人工培养菌丝的抑制效果优于野生冬虫夏草。孙超等 (2015) 结合形态、分子鉴别方法,对采自青海、四川、西藏和云南的野生冬虫夏草样品进行了质量参数测定,结果所采集的样品均为冬虫夏草;4 种样品的虫草酸和多糖含量均高于腺苷、肌苷和麦角甾醇含量;以上 5 种活性成分含量,云南和青海冬虫夏草均高于西藏和四川冬虫夏草;在清除 DPPH 自由基活性方面,云南和西藏冬虫夏草则高于青海和四川冬虫夏草;而在抑制 MT-1 活性上不同产地的冬虫夏草差异不显著。

5 展望

目前,冬虫夏草被列为国家二级保护物种,资源的枯竭和需求的旺盛导致了其价格的飞涨。市场上出现的某些假冒冬虫夏草产品严重影响了消费者的利益。本文在综述了关于冬虫夏草最新研究成果的基础上认为,规范冬虫夏草生产与销售市场的管理制度,加强冬虫夏草的规模化繁殖技术研究,鼓励在原产地建立冬虫夏草产业基地,是解决当前冬虫夏草供需矛盾的必由之路。

参考文献 (References)

- Ahmed AF, El-Maraghy NN, Abdel Ghaney RH, Eishazly SM, 2012. Therapeutic effect of captopril, pentoxifylline, and *Cordyceps sinensis* in pre-hepatic portal hypertensive rats. *The Saudi Journal of Gastroenterology*, 18(3): 182–187.
- Aghaei M, Karami-Tehrani F, Panjehpour M, Panjehpour M, Fallahian F, 2012. Adenosine induces cell-cycle arrest and apoptosis in androgen-dependent and-independent prostate cancer cell lines, LNCap-FGC-10, DU-145, and PC3. *Prostate*, 72(4): 361–375.
- Au D, Wang L, Yang D, Mork DK, Chan AS, Xu H, 2012. Application of microscopy in authentication of valuable Chinese medicine I--*Cordyceps sinensis*, its counterfeits, and related products. *Microscopy Research and Technique*, 75(1): 54–64.

- Buenz EJ, Bauer BA, Osmundson TW, Osmundson TW, Motley TJ, 2005. The traditional Chinese medicine *Cordyceps sinensis* and its effects on apoptotic homeostasis. *Journal of Ethnopharmacology*, 96(1/2): 19–29.
- Cai ZJ, Yi DH, Huang TF, Chen SJ, Li QS, 2003. Comparison of the mannitol content in *Cordyceps* from different growing areas. *China Pharmacy*, 14(8): 505–506. [蔡仲军, 尹定华, 黄天福, 陈仕江, 李泉生, 2003. 不同产地冬虫夏草甘露醇含量比较. 中国药房, 14(8): 505–506.]
- Chen G, Huang L, Li WJ, Zhan ZP, Xin LB, Ai Z, Qian ZM, Liu GZ, 2014. The establishment of NMR characteristic fingerprint of *Cordyceps sinensis* and its identification study. *Modernization of Traditional Chinese Medicine and Materia Medica-World Science and Technology*, 16(11): 2371–2379. [陈罡, 黄亮, 李文佳, 詹泽苹, 辛立波, 艾中, 钱正明, 刘国柱, 2014. 冬虫夏草核磁特征指纹图谱建立及鉴别研究. 世界科学技术-中医药现代化, 16(11): 2371–2379.]
- Chen JL, Jiang DH, Zhang WH, Liang LP, 1997. Effect of mannitol for the treatment of experimental rat models with focal cerebral ischemia. *Chinese Journal of Experimental Neurology*, 30(3): 161–164. [陈洁丽, 江德华, 张卫华, 梁立平, 1997. 甘露醇在脑缺血动物实验中的治疗作用. 中华神经科杂志, 30(3): 161–164.]
- Chen T, Liu Q, Mo ZK, Xu MC, Chen RT, 2013. Determination of adenosine, cordycepin, and ergosterol in *Cordyceps sinensis* by HPLC. *Chinese Journal of Experimental Traditional Medical Formulae*, 19(6): 161–163. [陈婷, 刘群, 莫灼康, 徐敏嫦, 陈润添, 2013. HPLC 同时测定冬虫夏草中腺苷、虫草素和麦角甾醇. 中国实验方剂学杂志, 19(6): 161–163.]
- Chen W, Yuan F, Wang K, Song D, Zhang W, 2012. Modulatory effects of the acid polysaccharide fraction from one of anamorph of *Cordyceps sinensis* on Ana-1 cells. *Journal of Ethnopharmacology*, 142(3): 739–745.
- Chen XQ, Liu BL, Zhao ZZ, Lin WJ, Luo GW, Chen HB, 2011. Studies on macroscopic and microscopic identification of *Cordyceps sinensis* and its counterfeits. *China Journal of Chinese Material Medica*, 36(9): 1141–1144. [陈小秋, 刘宝玲, 赵中振, 林文健, 罗国伟, 陈虎彪, 2011. 冬虫夏草与其混淆品的性状及显微鉴别研究. 中国中药杂志, 36(9): 1141–1144.]
- Chen Z, Geng Y, Liang HH, Yang XL, Li S, Zhu YG, Guo GP, Zhou TS, Chen JK, 2007. Investigation of the phylogenetic relationship of the host of *Cordyceps sinensis*, *Hepialus* with mitochondrial Cytb gene sequences. *Progress in Natural Science*, 17(8): 1045–1052. [程舟, 耿杨, 梁洪卉, 杨晓伶, 李珊, 朱云国, 郭光普, 周铜水, 陈家宽, 2007. 用线粒体 Cytb 基因序列探讨冬虫夏草寄主蝠蛾的系统进化关系. 自然科学进展, 17(8): 1045–1052.]
- Cheng XH, Bai YQ, 1995. Preliminary study on antibacterial substances of *Cordyceps sinensis* mycelium and fermentation broth. *Edible Fungal of China*, 14(3): 37–38. [程显好, 白毓谦, 1995. 冬虫夏草菌丝体及发酵液中抗菌活性物质的初步研究. 中国食用菌, 14(3): 37–38.]
- Cheung JK, Li J, Cheung AW, Zhu Y, Bi CW, Duan R, Choi RC, Lau BW, Tsim KW, 2009. Cordysinocan, a polysaccharide isolated from cultured *Cordyceps*, activates immune responses in cultured T-lymphocytes and macrophages: signaling cascade and induction of cytokines. *Journal of Ethnopharmacology*, 124(1): 61–68.
- Daviskas E, Anderson SD, Eberl S, Young IH, 2010. Beneficial effect of inhaled mannitol and cough in asthmatics with mucociliary dysfunction. *Respiratory Medicine*, 104(11): 1645–1653.
- Ding C, Tian PX, Xue W, Ding X, Yan H, Pan X, Feng X, Xiang H, Hou J, Tian J, 2011. Efficacy of *Cordyceps sinensis* in long term treatment of renal transplant patients. *Frontiers in Bioscience*, 3: 301–307.
- Diringer MN, Scalfani MT, Zazulia AR, Videen TO, Dhar R, Powers WJ, 2012. Effect of mannitol on cerebral blood volume in patients with head injury. *Neurosurgery*, 70(5): 1215–1218.
- Dong CH, Yao YJ, 2011. On the reliability of fungal materials used in studies on *Ophiocordyceps sinensis*. *Journal of Industrial Microbiology & Biotechnology*, 38(8): 1027–1035.
- Dong CH, Yao YJ, 2012. Isolation, characterization of melanin derived from *Ophiocordyceps sinensis*, an entomogenous fungus endemic to the Tibetan Plateau. *Journal of Bioscience and Bioengineering*, 113(4): 474–479.
- Dong KZ, Fu SW, Sheng L, Mi YJ, Su L, 2014. Effect of *Cordyceps sinensis* mycelium on serum vasoactive intestinal peptide and substance P in mice with intestinal dysbacteriosis. *Medical Journal of Chinese People's Liberation Army*, 39(11): 873–876. [董开忠, 傅思武, 胜利, 米友军, 苏露, 2014. 冬虫夏草菌丝体对肠道菌群失调小鼠血清 VIP 及 SP 的影响. 解放军医学杂志, 39(11): 873–876.]
- Feng K, Wang S, Hu DJ, Yang FQ, Wang HX, Li SP, 2009. Random amplified polymorphic DNA (RAPD) analysis and the nucleosides assessment of fungal strains isolated from natural *Cordyceps sinensis*. *Journal of Pharmaceutical and Biomedical Analysis*, 50(3): 522–526.
- Flomer O, Black M, Hoeh W, Lutz R, Vrijenhoek R, 1994. DNA primers for amplification of mitochondrial cytochrome c oxidase subunit from diverse metazoan invertebrates. *Molecular Marine Biology and Biotechnology*, 3(5): 294–299.
- Gao M, Wang JS, Zeng JL, Mai MX, Ma YD, 2011. Identification of *Cordyceps sinensis* and several common adulterants. *Journal of Chinese Medicinal Materials*, 34(2): 213–216. [高明, 王俊升, 曾金玲, 麦敏芯, 马永德, 2011. 冬虫夏草与几种常见伪品的

- 鉴别. 中药材, 34(2): 213–216.]
- Gu J, Liu P, Feng JY, 2005. Identification of *Cordyceps* and counterfeits by high performance capillary electrophoresis method. *Pharmaceutical Care and Research*, 5(3): 230–233. [古今, 刘萍, 冯建涌, 2005. 用高效毛细管电泳法鉴别冬虫夏草及其伪品. 药学服务与研究, 5(3): 230–233.]
- Gu ZR, Zhang QL, 2003. Identification of *Cordyceps sinensis* and its adulterants. *Jiangsu Pharmaceutical and Clinical Research*, 11(4): 30–31. [顾峥嵘, 张全龙, 2003. 冬虫夏草与其伪品的鉴别. 江苏药学与临床研究, 11(4): 30–31.]
- Guan CH, Liu J, Lou YF, 2013. Effect of *Cordyceps sinensis* on pulmonary function and metalloproteinase-9 of bronchoalveolar lavage fluid matrix in rats with COPD. *Modern Practical Medicine*, 25(7): 775–777. [管彩虹, 刘进, 楼雅芳, 2013. 冬虫夏草对 COPD 大鼠肺功能及肺泡灌洗液基质金属蛋白酶-9 的影响. 现代实用医学, 25(7): 775–777.]
- Guan J, Li SP, 2010. Discrimination of polysaccharides from traditional Chinese medicines using saccharide mapping-enzymatic digestion followed by chromatographic analysis. *Journal of Pharmaceutical and Biomedical Analysis*, 51(3): 590–598.
- Guan J, Zhao J, Feng J, Hu DJ, Li SP, 2011. Comparison and characterization of polysaccharides from natural and cultured *Cordyceps* using saccharide mapping. *Analytical and Bioanalytical Chemistry*, 399(10): 3465–3474.
- Guo FQ, Li A, Huang LF, Liang YZ, Chen BM, 2006. Identification and determination of nucleosides in *Cordyceps sinensis* and its substitutes by high performance liquid chromatography with mass spectrometric detection. *Journal of Pharmaceutical and Biomedical Analysis*, 40(3): 620–630.
- Guo ZQ, Yan CS, 2011. Effect of *Cordyceps sinensis* and dexamethasone on AQP1 expression of the lung tissue in acute bronchial asthma SD rats. *Shandong Medical Journal*, 51(21): 23–25. [郭之强, 颜春松. 冬虫夏草及地塞米松对 SD 大鼠急性支气管哮喘肺组织 AQP1 表达的影响. 山东医药, 51(21): 23–25.]
- Hanieh H, Sakaguchi E, 2009. Effect of D-mannitol on feed digestion and cecotrophic system in rabbits. *Animal Science Journal*, 82(2): 157–162.
- Hebert PD, Cywinska A, Ball SL, Dewaard JR, 2003. Biological identification through DNA barcodes. *Proceeding of the Royal Society Biological Sciences*, 270(1512): 313–321.
- Hsu TH, Shiao LH, Hsieh C, Chang DM, 2002. A comparison of the chemical composition and bioactive ingredients of the Chinese medicinal mushroom Dong Chong Xia Cao, its counterfeit and mimic, and fermented mycelium of *Cordyceps sinensis*. *Food Chemistry*, 78(4): 463–469.
- Hu X, Jiang D, Li F, Wu Z, Huang Y, Song S, Wang Z, 2014. Ergosterol reverses multidrug resistance in SGC7901/Adr cells. *Pharmazie*, 69(5): 396–400.
- Huang K, Xie JH, An N, Huang LT, Wang YJ, Pan QJ, Pan QJ, Liu HF, Liu WJ, 2014. The research of *Cordyceps* decrease the tubular damage through anti-oxidation and anti-aging in diabetic rats. *Medical Innovation of China*, 11(22): 15–17. [黄可, 谢淑华, 安宁, 黄柳涛, 王燕劲, 潘庆军, 刘华锋, 刘伟敬, 2014. 冬虫夏草通过抗氧化及抗衰老减轻糖尿病肾病大鼠肾小管损伤的研究. 中国医学创新, 11(22): 15–17.]
- Ikedo R, Nishimura M, Sun Y, Wada M, Nakashima K, 2008. Simple HPLC-UV determination of nucleosides and its application to the authentication of *Cordyceps* and its allies. *Biomedical Chromatography*, 22(6): 630–636.
- Jia JM, Ma XC, Wu CF, Wu LJ, Hu GS, 2005. Cordycedipeptide A, a new cyclodipeptide from the culture liquid of *Cordyceps sinensis* (Berk.) Sacc. *Chemical & Pharmaceutical Bulletin*, 53(5): 582–583.
- Kang S, Zhang J, Lin RC, 2013. Macroscopic and microscopic characteristics of Chinese caterpillar fungus. *Acta Pharmaceutica Sinica*, 48(3): 428–434. [康帅, 张继, 林瑞超. 冬虫夏草的性状和显微鉴定研究. 药学报, 48(3): 428–434.]
- Kiho T, Hui J, Yamane A, Ukai S, 1993. Polysaccharides in fungi. XXXII. hypoglycemic activity and chemical properties of a polysaccharide from the cultural mycelium of *Cordyceps sinensis*. *Biological & Pharmaceutical Bulletin*, 16(12): 1291–1293.
- Kiho T, Ookubo K, Usui S, Ukai S, Hirano K, 1999. Structural features and hypoglycemic activity of a polysaccharide (CS-F10) from the cultured mycelium of *Cordyceps sinensis*. *Biological & Pharmaceutical Bulletin*, 22(9): 966–970.
- Kim SD, 2010. Isolation, structure and cholesterol esterase inhibitory activity of a polysaccharide, PS-A, from *Cordyceps sinensis*. *Journal of The Korean Society for Applied Biological Chemistry*, 53: 784–789.
- Koh JH, Kim JM, Chang UJ, Suh HJ, 2003. Hypocholesterolemic effect of hot water extract from mycelia of *Cordyceps sinensis*. *Biological & Pharmaceutical Bulletin*, 26(1): 84–87.
- Kuo CF, Chen CC, Lin CF, Jan MS, Huang RY, Luo YH, Chuang WJ, Sheu CC, Lin YS, 2007. Abrogation of streptococcal pyrogenic exotoxin B-mediated suppression of phagocytosis in U937 cells by *Cordyceps sinensis* mycelium via production of cytokines. *Food and Chemistry Toxicology*, 45(2): 278–285.
- Li C, Li Z, Fan M, Cheng W, Long Y, Ding T, Ming L, 2006. The composition of *Hirsutella sinensis*, anamorph of *Cordyceps sinensis*. *Journal of Food Composition and Analysis*, 19: 800–805.
- Li CY, Chiang CS, Tsai ML, Tsai ML, Hseu RS, Shu WY, Chuang CY, Sun YC, Chang YS, Lin JG, Chen CS, Huang CL, Hsu IC, 2009. Two-sided effect of *Cordyceps sinensis* on dendritic cells

- in different physiological stages. *Journal of Leukocyte Biology*, 85(6): 987–995.
- Li JX, Li J, Xu LZ, Yang SL, Zou ZM, 2003. Studies on the chemical constituents of *Cordyceps sinensis* in Tibet. *Chinese Pharmaceutical Journal*, 38(7): 499–501. [郚皆秀, 李进, 徐丽珍, 杨世林, 邹忠梅, 2003. 西藏冬虫夏草化学成分研究. 中国药学杂志, 38(7): 499–501.]
- Li Y, 2013. Research on immune identification technology of *Cordyceps sinensis*. Master dissertation. Shengyang: Liaoning University: 2013. [李扬, 2013. 冬虫夏草免疫鉴定技术研究. 硕士学位论文. 沈阳: 辽宁大学.]
- Li SP, Li P, Dong TTX, Tsim KW, 2001. Anti-oxidant activity of different types of natural *Cordyceps sinensis* and cultured *Cordyceps mycelia*. *Phytomedicine*, 8(3): 207–212.
- Li SP, Li P, Lai CM, Gong YX, Kan KK, Dong TT, Tsim KW, Wang YT, 2004. Simultaneous determination of ergosterol, nucleosides and their bases from natural and cultured *Cordyceps* by pressurised liquid extraction and high-performance liquid chromatography. *Journal of Chromatography A*, 1036: 239–243.
- Li SP, Yang FQ, Tsim WK, 2006. Quality control of *Cordyceps sinensis*, a valued traditional Chinese medicine. *Journal of Pharmaceutical and Biomedical Analysis*, 41(5): 1571–1584.
- Li SP, Zhao KJ, Ji ZN, Song ZH, Dong TT, Lo CK, Cheung JK, Zhu SQ, Tsim KW, 2003. A polysaccharide isolated from *Cordyceps sinensis*, a traditional Chinese medicine, protects PC12 cells against hydrogen peroxide-induced injury. *Life Sciences*, 73(19): 2503–2513.
- Lu WJ, Chang NC, Jayakumar T, Liao JC, Lin MJ, Wang SH, Chou DS, Thomas PA, Sheu JR, 2014. Ex vivo and in vivo studies of CME-1, a novel polysaccharide purified from the mycelia of *Cordyceps sinensis* that inhibits human platelet activation by activating adenylate cyclase/cyclic AMP. *Thrombosis Research*, 134(6): 1301–1310.
- Luo XP, Liu X, Cao WT, Deng H, 2012. Study on the effect of transcatheter super-selective tumor-feeding intraarterial infusion of rabbit implanted VX2 hepatic tumor by *Cordyceps sinensis*. *Chongqing Medicine*, 41(31): 3246–3249. [罗小平, 刘曦, 曹闻挺, 邓昊, 2012. 冬虫夏草经肿瘤滋养动脉插管注入对兔 VX2 肝癌模型的疗效研究. 重庆医学, 41(31): 3246–3249.]
- Matsuda H, Akaki J, Nakamura S, Okazaki Y, Kojima H, Tamesada M, Yoshikawa M, 2009. Apoptosis-inducing effects of sterols from the dried powder of culture mycelium of *Cordyceps sinensis*. *Chemical & Pharmaceutical Bulletin*, 57(4): 411–414.
- Mei YX, Yang W, Zhu PX, Peng N, Zhu H, Liang YX, 2014. Isolation, characterization, and antitumor activity of a novel heteroglycan from cultured mycelia of *Cordyceps sinensis*. *Planta Medica*, 80(13): 1107–1112.
- Min X, Li X, Hiura S, Kawasaki K, Xiao J, Sakaguchi E, 2013. Effect of D-mannitol on nitrogen retention, fiber digestibility and digesta transit time in adult rabbits. *Animal Science Journal*, 84(7): 551–555.
- National Pharmacopoeia Committee, 2010. Chinese Pharmacopoeia. Beijing: China Medical Science Press. 682. [国家药典委员会, 2010. 中国药典. 北京: 中国医药科技出版社. 682.]
- Niccoli G, Rigattieri S, De Vita MR, Valgimigli M, Corvo P, Fabbiochi F, Romagnoli E, De Caterina AR, La Torre G, Lo Schiavo P, Tarantino F, Ferrari R, Tomai F, Olivares P, Cosentino N, D'Amario D, Leone AM, Porto I, Burzotta F, Trani C, Crea F, 2013. Open-label, randomized, placebo-controlled evaluation of intracoronary adenosine or nitroprusside after thrombus aspiration during primary percutaneous coronary intervention for the prevention of microvascular obstruction in acute myocardial infarction: the reopen-AMI study (intracoronary nitroprusside versus adenosine in acute myocardial infarction). *Jacc-Cardiovascular Interventions*, 6(6): 580–589.
- Omar MA, Verma S, Clanachan AS, 2012. Adenosine-mediated inhibition of 5'-AMP-activated protein kinase and p38 mitogen-activated protein kinase during reperfusion enhances recovery of left ventricular mechanical function. *Journal of Molecular and Cellular Cardiology*, 52(6): 1308–1318.
- Otsuki T, Kanno T, Fujita Y, Tabata C, Fukuoka K, Nakano T, Gotoh A, Nishizaki T, 2012. A3 adenosine receptor-mediated p53-dependent apoptosis in Lu-65 human lung cancer cells. *Cellular Physiology and Biochemistry*, 30(1): 210–220.
- Peng Y, Tao Y, Wang Q, Shen L, Yang T, Liu Z, Liu C, 2014. Ergosterol is the active compound of cultured mycelium *Cordyceps sinensis* on antiliver fibrosis. *Evidence-based Complementary and Alternative Medicine*, 2014: 537234.
- Qian AP, Yan SA, Lin XX, Chen WW, 2010. The content of amino acid in the poultry meat and its nutritive evaluation. *Chinese Agricultural Science Bulletin*, 26(13): 94–97. [钱爱萍, 颜孙安, 林香信, 陈卫伟, 2010. 家禽肉中氨基酸组成及营养评价. 中国农学通报, 26(13): 94–97.]
- Qian HY, 2004. Survey of artificial *Cordyceps sinensis* for chronic obstructive pulmonary disease. *Journal of Medical Forum*, 25(11): 20–24. [钱皓瑜, 2004. 人工冬虫夏草治疗慢性阻塞性肺疾病的观察. 医药论坛杂志, 25(11): 20–24.]
- Qian Y, Fu XC, Hu R, Shen LM, Bai HB, 2013. Effects of corbrin shugan capsule on dimethylnitrosamine-induced hepatic fibrosis in rats. *Journal of Zhejiang University (Medical Sciences)*, 42(5): 561–566. [钱莺, 傅旭春, 扈荣, 沈丽美, 白海波, 2013. 百令疏肝胶囊对二甲基亚硝胺诱导的大鼠肝纤维化作用. 浙江大学学报 (医学版), 42(5): 561–566.]
- Rathor R, Mishra KP, Pal M, Amitabh S, Vats P, Kirar V, Negi PS,

- Misra K, 2014. Scientific validation of the Chinese caterpillar medicinal mushroom, *Ophiocordyceps sinensis* (Ascomycetes) from India: immunomodulatory and antioxidant activity. *International Journal of Medicinal Mushrooms*, 16(6): 541–553.
- Rehner SA, Buckley E, 2005. A beauveria phylogeny inferred from nuclear ITS and EF1- α sequences: evidence for cryptic diversification and links to *Cordyceps* teleomorphs. *Mycologia*, 97(1): 84–98.
- Sasaki T, Takasuka N, Chihara G, Maeda YY, 1976. Antitumor activity of degraded products of lentinan: its correlation with molecular weight. *Annual Review of Genomics and Human Genetics*, 67(2): 191–195.
- Shi HT, Wang XF, Dong CL, Zhang Y, Guo CL, Pan SJ, Yu HT, 2013. Effects of Dongchong Xiacao on patients with DN and human mesangial cells (HMCs) cultured in vitro. *Acta Chinese Medicine and Pharmacology*, 41(3): 154–156. [施海涛, 王雪峰, 董春玲, 张玉, 国春玲, 潘淑杰, 于海涛, 2013. 冬虫夏草提取物对糖尿病肾病及肾小球系膜细胞 TGF- β 1 基因的影响. 中医要学报, 41(3): 154–156.]
- Sprecher M, Sprinson DB, 1963. A reinvestigation of the structure of cordycepic acid. *Journal of Organic Chemistry*, 28(9): 2490–2491.
- Stensrud O, Hywel-Jones NL, Schumacher T, 2005. Towards a phylogenetic classification of *Cordyceps*: ITS nrDNA sequence data confirm divergent lineages and paraphyly. *Mycological Research*, 109(1): 41–56.
- Sun C, Qiu XH, Cao L, Han RC, 2015. The determination of quality parameters of *Ophiocordyceps sinensis* from different origins. *Journal of Environmental Entomology*, 37(5): 1049–1054. [孙超, 丘雪红, 曹莉, 韩日畴, 2015. 不同产地冬虫夏草的质量参数测定. 环境昆虫学报, 37(5): 1049–1054.]
- Sun W, Yu J, Shi YM, Zhang H, Wang Y, Wu BB, 2010. Effect of *Cordyceps* extract on cytokines and transcription factors in peripheral blood mononuclear cells of asthmatic children during remission stage. *Journal of Chinese Integrative Medicine*, 8(4): 341–346. [孙雯, 俞建, 时毓民, 张皓, 王莹, 吴冰冰, 2010. 冬虫夏草菌粉提取液对哮喘缓解期儿童外周血单核细胞中相关细胞因子及转录因子表达的影响. 中西医结合学报, 8(4): 341–346.]
- Sung GH, Hywel-Jones NL, Sung JM, Luangsa-Ard JJ, Shrestha B, Spatafora JW, 2007. Phylogenetic classification of *Cordyceps* and clavicipitaceous fungi. *Study in Mycology*, 57: 5–59.
- Volkman JK, 2003. Sterols in microorganisms. *Applied Microbiology and Biotechnology*, 60(5): 495–506.
- Wang J, Liu YM, Cao W, Yao KW, Liu ZQ, Guo JY, 2012. Anti-inflammation and antioxidant effect of cordymin, a peptide purified from the medicinal mushroom *Cordyceps sinensis*, in middle cerebral artery occlusion-induced focal cerebral ischemia in rats. *Metabolic Brain Disease*, 27(2): 159–165.
- Wang S, Yang FQ, Feng K, Li DQ, Zhao J, Li SP, 2009. Simultaneous determination of nucleosides, myriocin, and carbohydrates in *Cordyceps* by HPLC coupled with diode array detection and evaporative light scattering detection. *Journal of Separation Science*, 32 (23/24): 4069–4076.
- Wang Y, 2013. The effect of *Cordyceps sinensis* on oxidative stress in maintenance hemodialysis patients. *Chinese Journal of Geriatric Care*, 11(1): 31–32. [王英, 2013. 冬虫夏草对维持性血液透析患者氧化应激的影响. 中国老年保健医学, 11(1): 31–32.]
- Wang Y, Yin H, Lv X, Wang Y, Gao H, Wang M, 2010. Protection of chronic renal failure by a polysaccharide from *Cordyceps sinensis*. *Fitoterapia*, 81(5): 397–402.
- Wang Z, Li N, Wang M, Wang Y, Du L, Ji X, Yu A, Zhang H, Qiu F, 2013. Simultaneous determination of nucleosides and their bases in *Cordyceps sinensis* and its substitutes by matrix solid-phase dispersion extraction and HPLC. *Journal of Separation Science*, 36(14): 2348–2357.
- Wang ZM, Peng X, Daniel Lee KL, Tang JC, Cheung CK, Wu JY, 2011. Structural characterization and immunomodulatory property of an acidic polysaccharide from mycelia culture of *Cordyceps sinensis* fungus CS-HK1. *Food Chemistry*, 125: 637–643.
- Wei RA, Li SH, 2008. Identification of *Cordyceps* and its adulterants *Cordyceps militaris* using ITS sequencing. *Journal of Hunan Normal University*, 5(3): 42–45. [翁榕安, 李树华, 2008. 冬虫夏草与其混伪品北虫草的 ITS 测序鉴别. 湖南师范大学学报, 5(4): 42–45.]
- Wei T, Wei WL, Gong XJ, Jin ZL, 2002. Investigation of the effects of *Cordyceps sinensis* mycelium on expectoration, cough, antibacterial and anti-inflammatory. *Food Science*, 23(3): 126–130. [魏涛, 魏威凛, 贡晓娟, 金宗濂, 2002. 冬虫夏草菌丝体镇咳、祛痰及抗菌消炎作用的研究. 食品科学, 23(3): 126–130.]
- Wei XL, Yin XC, Guo YL, Shen LY, Wei JC, 2006. Analyses of molecular systematics on *Cordyceps sinensis* and its related taxa. *Mycosystema*, 25(2): 192–202. [魏鑫丽, 印象初, 郭英兰, 沈南英, 魏江春, 2006. 冬虫夏草及其相关类群的分子系统分析. 菌物学报, 25(2): 192–202.]
- Wu DT, Meng LZ, Wang LY, Lv GP, Cheong KL, Hu DJ, Guan J, Zhao J, Li SP, 2014. Chain conformation and immunomodulatory activity of a hyperbranched polysaccharide from *Cordyceps sinensis*. *Carbohydrate Polymers*, 110: 405–414.
- Wu JY, Zhang QX, Leung PH, 2007. Inhibitory effects of ethyl acetate extract of *Cordyceps sinensis* mycelium on various cancer cells in culture and B16 melanoma in C57BL/6 mice. *Phytomedicine*, 14(1): 43–49.

- Wu XX, Ma KL, Li SY, An DW, Xia GL, 2001. Effect of *Cordyceps sinensis* on blood pressure in renal hypertensive rats. *Journal of Jinzhou Medical College*, 22(2): 10–11. [吴秀香, 马克玲, 李淑云, 安鼎伟, 夏桂兰, 2001. 冬虫夏草降压作用实验研究. 锦州医学院学报, 22(2): 10–11.]
- Wu YS, Zhou DL, Yan D, Ren YS, Fang YL, Xiao XH, Du XX, Wang J, 2008. HPLC fingerprint analysis of *Cordyceps* and mycelium of cultured *Cordy*. *China Journal of Chinese Materia Medica*, 33(19): 2212–2214. [武彦舒, 周丹蕾, 鄢丹, 任永申, 方艺霖, 肖小河, 杜晓羲, 王建, 2008. 天然虫草与虫草菌丝体的 HPLC 指纹图谱研究. 中国中药杂志, 33(19): 2212–2214.]
- Wu ZW, Wang YB, Zhao XF, Dou YP, 2008. Antibacterial activity of fermentation broth by *Cordyceps sinensis* and *Cordyceps militaris*. *Journal of Microbiology*, 28(4): 47–50. [武忠伟, 王运兵, 赵现方, 龚艳萍, 2008. 冬虫夏草和蛹虫草发酵液抗菌活性研究. 微生物学杂志, 28(4): 47–50.]
- Xia WJ, Zeng XY, Yuan HL, Yin DH, Yang DJ, Qin SY, Xiao XH, 2001. Quantitative determination of adenosine in *Cordyceps sinensis* from different habitats. *China Journal of Chinese Materia Medica*, 26(8): 540–542. [夏文娟, 曾晓英, 袁海龙, 尹定华, 杨大坚, 秦松云, 肖小河, 2001. 不同产地冬虫夏草腺苷含量的测定. 中国中药杂志, 26(8): 540–542.]
- Xiao JH, Qi Y, Xiong Q, 2013. Nucleosides, a valued chemical maker for quality control in traditional Chinese medicine *Cordyceps*. *Recent Patents on Biotechnology*, 7(2): 153–166.
- Xiao W, Yang JP, Zhu P, Cheng KD, He HX, Zhu HX, Wang Q, 2009. Non-support of species complex hypothesis of *Cordyceps sinensis* by targeted rDNA-ITS sequence analysis. *Mycosystema*, 28(6): 724–730.
- Xiao YC, Hu FZ, Dong Q, Chi XF, Ji K, 2014. Comparative study of fifteen kinds of nucleosides in *Cordyceps sinensis* from different origin of Yushu prefecture, Qinghai province. *Chinese Pharmaceutical Journal*, 49(22): 1983–1988. [肖远灿, 胡风祖, 董琦, 迟晓峰, 冀括, 2014. 青海玉树不同产地冬虫夏草中 15 种核苷类成分比较研究. 国药杂志, 49(22): 1983–1988.]
- Xu J, 2006. Key quality control techniques and evaluation system for research of the cultured *Cordyceps sinensis*. Master dissertation. Shandong: Shandong University of Traditional Chinese Medicine. [徐君, 2006. 人工培养北虫草质量控制关键技术与质量评价体系研究. 硕士学位论文. 山东: 山东中医药大学.]
- Xu RY, 2010. Identification of *Cordyceps sinensis*. *China Pharmaceuticals*, 19(24): 69–70. [徐如英, 2010. 冬虫夏草的真伪鉴别. 中国药业, 19(24): 69–70.]
- Yamaguchi Y, Kagota S, Nakamura K, Shinozuka K, Kunitomo M, 2000a. Antioxidant activity of the extract from fruiting bodies of cultured *Cordyceps sinensis*. *Phytotherapy Research*, 14(8): 647–649.
- Yamaguchi Y, Kagota S, Nakamura K, Shinozuka K, Kunitomo M, 2000b. Inhibitory effects of water extracts from fruiting bodies of cultured *Cordyceps sinensis* on raised serum lipid peroxide levels and aortic cholesterol deposition in atherosclerotic mice. *Phytotherapy Research*, 14(8): 650–652.
- Yan D, Bao HY, Bau T, Li Y, Kim YH, 2009. Antitumor components from *Naematoloma fasciculare*. *Journal of Microbiology and Biotechnology*, 19(10): 1135–1138.
- Yan D, Yang XY, 2014. Analysis of amino acid composition and evaluation of nutritional quality in *Cordyceps sinensis* from different regions of Tibet. *Chinese Agricultural Science Bulletin*, 30(3): 281–284. [严冬, 杨鑫垚, 2014. 西藏不同产地冬虫夏草中氨基酸成分分析及其营养价值评价. 中国农学通报, 30(3): 281–284.]
- Yan JK, Li L, Wang ZM, Leung PH, Wang WQ, Wu JY, 2009. Acidic degradation and enhanced antioxidant activities of exopolysaccharides from *Cordyceps sinensis* mycelial culture. *Food Chemistry*, 117: 641–646.
- Yang HJ, Guo SP, Xue L, 2014. Auxiliary protective effects of the mycelial extracts from *Ophiocordyceps sinensis* on chemical-induced liver injuries in mice. *Mycosystema*, 33(2): 394–400. [杨槐俊, 郭素萍, 薛莉, 2014. 冬虫夏草菌丝提取物对化学性肝损伤的辅助保护作用. 菌物学报, 33(2): 394–400.]
- Yang ML, Kuo PC, Hwang TL, Wu TS, 2011. Anti-inflammatory principles from *Cordyceps sinensis*. *Journal of Natural Products*, 74(9): 1996–2000.
- Yang YQ, Duan JH, 2012. Discrimination of *Cordyceps sinensis* from the counterfeit. *World Journal of Integrated Traditional and Western Medicine*, 7(1): 31–33. [杨艳青, 段军华, 2012. 冬虫夏草与其伪品的鉴别. 世界中西医结合杂志, 7(1): 31–33.]
- Yi DH, Chen SJ, Mai KS, 2011. Thinking of *Cordyceps* resources protection, regeneration and sustainable utilization. *China Journal of Chinese Materia Medica*, 36(6): 814–816. [尹定华, 陈仕江, 马开森, 冬虫夏草资源保护、再生及持续利用的思考. 中国中药杂志, 36(6): 814–816.]
- Yu B, Feng FY, Liang LK, Zhu LQ, Zhao WL, 2012. Analysis on habit and amino acid content of *Cordyceps sinensis*. *Arid Zone Research*, 29(5): 791–796. [于斌, 冯凤英, 梁留科, 朱连奇, 赵文亮, 2012. 冬虫夏草的生境及氨基酸含量分析. 干旱区研究, 29(5): 791–796.]
- Yu L, Zhao J, Li SP, Fan H, Hong M, Wang YT, Zhu Q, 2006. Quality evaluation of *Cordyceps* through simultaneous determination of eleven nucleosides and bases by RP-HPLC. *Journal of Separation Science*, 27(7): 953–958.
- Yuan JP, Wang JH, Liu X, Kuang HC, Zhao SY, 2007. Simultaneous determination of free ergosterol and ergosterol esters in *Cordyceps sinensis* by HPLC. *Food Chemistry*, 105: 1755–1759.

- Yuan M, Tang R, Zhou Q, Liu KH, Xiao Z, 2013. Effect of *Cordyceps sinensis* on expressions of HIF-1 α and VEGF in the kidney of rats with diabetic nephropathy. *Journal of Central South University (Medical Science)*, 38(5): 448–457. [表明霞, 唐荣, 周巧玲, 刘抗寒, 肖舟, 2013. 冬虫夏草对糖尿病大鼠组织 HIF-1 α 及 VEGF 表达的影响. 中南大学学报 (医学版), 38(5): 448–457.]
- Yue K, Ye M, Zhou ZJ, Sun W, Lin X, 2013. The genus *Cordyceps*: a chemical and pharmacological review. *Journal of Pharmacy and Pharmacology*, 65(4): 474–493.
- Zhang L, Yan Y, Hu XH, He Y, 2014. Protective effect of *Cordyceps sinensis* on diabetic nephropathy in a rat model. *Jiangxi Medical Journal*, 49(11): 1188–1192. [张莉, 鄢艳, 胡秀华, 何艳, 2014. 冬虫夏草对大鼠糖尿病肾病的保护作用机制研究. 江西医药, 49(11): 1182–1192.]
- Zhang QX, Liao BK, Wu JY, Hu ZD, 2005. Comparison of antitumor effect of extracts in cultivated *Cordyceps sinensis* fungus HK-1 and natural *Cordyceps sinensis*. *Chinese Traditional and Herbal Drugs*, 36(9): 1346–1349. [赵巧霞, 梁保康, 吴建勇, 胡宗定, 2005. 人工虫草菌 HK-1 与天然虫草提取物的抗肿瘤活性比较. 中草药, 36(9): 1346–1349.]
- Zhang QX, Wu JY, 2007. *Cordyceps sinensis* mycelium extract induces human premyelocytic leukemia cell apoptosis through mitochondrion pathway. *Experimental Biology and Medicine*, 232(1): 52–57.
- Zhang SJ, 2011. Three-step FTIR identification and study of *Cordyceps*. *Journal of Mountain Agriculture and Biology*, 30(3): 230–234. [张声俊, 红外光谱法对冬虫夏草的三级鉴定和研究. 山地农业生物学报, 30(3): 230–234.]
- Zhang W, Li J, Qiu S, Chen J, Zheng Y, 2008. Effects of the exopolysaccharide fraction (EPSF) from a cultivated *Cordyceps sinensis* on immunocytes of H22 tumor bearing mice. *Fitoterapia*, 79(3): 168–173.
- Zhang XB, Yang QH, Xiao Y, Cao M, Chen SX, Gao BA, 2012. Effects of *Cordyceps sinensis* on endothelial function, inflammatory mediators and left ventricular diastolic function in patients with pulmonary heart disease. *Lishizhen Medicine and Materia Medica Research*, 23(8): 1890–1891. [张晓斌, 杨京会, 肖玉, 曹敏, 陈世雄, 高宝安, 2012. 冬虫夏草对肺心病患者血管内皮功能、炎症细胞因子和左室舒张功能的影响. 时珍国医国药, 23(8): 1890–1891.]
- Zhang Y, Yang M, Gong S, Yang Y, Chen B, Cai Y, Zheng S, Yang Y, Xia P, 2012. *Cordyceps sinensis* extracts attenuate aortic transplant arteriosclerosis in rats. *Journal of Surgical Research*, 175(1): 123–130.
- Zhang YJ, Sun BD, Zhang S, Wang M, Liu XZ, Gong WF, 2010. Mycobiotal investigation of natural *Ophiocordyceps sinensis* based on culture-dependent investigation. *Mycosystema*, 29(4): 518–527. [张永杰, 孙炳达, 张姝, 旺姆, 刘杏忠, 巩文峰, 2010. 分离自冬虫夏草可培养真菌的多样性研究. 菌物学报, 29(4): 518–527.]
- Zhang YJ, Zhang SZ, Liu XZ, Wen HA, Wang M, 2010. A simple method of genomic DNA extraction suitable for analysis of bulk fungal strains. *Letters in Applied Microbiology*, 51(1): 114–118.
- Zhao DD, Huang LD, Suo FY, Wu CK, Lu S, Ye X, 2015. Study on antioxidant activities of cultured *Ophiocordyceps sinensis*. *Edible Fungi of China*, 34(1): 65–69. [赵聃聃, 黄罗冬, 索菲娅, 吴长奎, 卢帅, 叶星, 2015. 冬虫夏草菌培养物抗氧化活性研究. 中国食用菌, 34(1): 65–69.]
- Zhao J, Xie J, Wang LY, Li SP, 2014. Advanced development in chemical analysis of *Cordyceps*. *Journal of Pharmaceutical and Biomedical Analysis*, 87: 271–289.
- Zhao KR, Wang WT, Zhao ZY, 2006. Pharmacological actions of *Cordyceps sinensis*. *World Phytomedicine*, 21(3): 105–108. [赵克蕊, 王维亭, 赵专友, 2006. 冬虫夏草的药理作用. 国外医药, 21(3): 105–108.]
- Zhao YY, Shen X, Chao X, Ho CC, Cheng XL, Zhang Y, Lin RC, Du KJ, Luo WJ, Chen JY, Sun WJ, 2011. Ergosta-4, 6, 8(14), 22-tetraen-3-one induces G2/M cell cycle arrest and apoptosis in human hepatocellular carcinoma HepG2 cells. *Biochimica et Biophysica Acta General Subjects*, 1810(4): 384–390.
- Zhou X, Luo L, Dressel W, Shadier G, Krumbiegel D, Schmidtke P, Zepp F, Meyer CU, 2008. Cordycepin is an immunoregulatory active ingredient of *Cordyceps sinensis*. *American Journal of Chinese Medicine*, 36(5): 967–980.
- Zhou XW, Gong ZH, Su Y, Lin J, Tang KX, 2009. *Cordyceps* fungi: natural products pharmacological function and development products. *Journal of Pharmacy and Pharmacology*, 61: 279–291.
- Zhu JS, Halpern GM, Jones K, 1998. The scientific rediscovery of a precious ancient Chinese herbal regimen: *Cordyceps sinensis*-Part II. *Journal of Alternative and Complementary Medicine*, 4(4): 429–457.
- Zhu JS, Wu JY, 2015. Genetic heterogeneity of natural *Cordyceps sinensis* with co-existence of multiple fungi. *Chinese Journal of Cell Biology*, 37(2): 284–298. [朱佳石, 吴建勇, 2015. 天然冬虫夏草多菌共生生物体分子异质性的检验与讨论. 中国细胞生物学学报, 37(2): 284–298.]
- Zhu R, Zheng R, Deng YY, Chen Y, Zhang S, 2014. Ergosterol peroxide from *Cordyceps cicadae* ameliorates TGF- β 1-induced activation of kidney fibroblasts. *Phytomedicine*, 21(3): 372–378.