

文章编号:1001-6880(2018)Suppl-0217-08

花青素的提取方法及药理活性研究进展

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摘要:花青素是一种广泛存在于植物组织细胞中的天然色素,因其来源丰富、药理活性优良而深受广泛关注。目前,花青素的提取方法众多,包括有机溶剂提取法、超临界二氧化碳萃取法、亚临界水提取法、超高压提取方法、辅助提取方法(酶辅助、超声波辅助、微波辅助)等。其药理活性主要表现在抗氧化活性、抗癌、抗炎症、预防心血管疾病、治疗眼科疾病等方面。本文通过查阅国内外文献,对花青素的提取方法及药理活性的研究进展进行了较为全面的阐述,这将为后续开展植物中花青素的高效提取及在食品、医药、保健品、化妆品等中方面的应用提供理论指导。

关键词:花青素;提取方法;药理活性;综述**中图分类号:**Q946.83 + 6; Q96**文献标识码:**A**DOI:**10.16333/j.1001-6880.2018.S.039

Progress on Extraction and Pharmacological Activity of Anthocyanin

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Abstract: Anthocyanin is a kind of natural pigment, which widely exists in various plant tissues cells. Anthocyanin has received intensive attention because of abundant sources and superior pharmacological activities. At present, there are many extraction methods of anthocyanin, including organic solvent extraction, supercritical carbon dioxide extraction, sub-critical water extraction, ultra-high pressure extraction, assisted extraction (e.g., enzyme-assisted, ultrasonic-assisted, microwave assisted), etc. Its pharmacological activities are mainly presented in antioxidant, anticancer, anti-inflammation, prevention of cardiovascular disease, the treatment of eye disease, etc. This paper mainly reviews on the extraction and pharmacological activities of anthocyanins through consulting domestic and foreign literatures, which will provide the theoretical guideline on the efficient extraction of anthocyanin in plants and applications in foods, medicine, health care products, cosmetics, and so on.

Key words:anthocyanin; pharmacological activity; extraction methods; review

花青素,又名花色素,是一种无毒的天然色素,对植物组织的显色起重要作用^[1-3]。花青素属于聚多酚类物质,由不同数量的儿茶素、表儿茶素聚合而成,依据聚合度数目不同,可将花青素分为单倍体、寡倍体、多聚体,其结构母体为2-苯基苯并呋喃(如图1)。自然界中植物花青素很少以游离形式存在,常与各种糖(如葡萄糖,鼠李糖,半乳糖,木棉糖等)通过糖苷键形成花色苷。花青素中单体的聚合方式、数量、空间位置、取代基团、键合方式都会影响其

结构,进而影响其性质^[4,5]。自20世纪50年代花青素第一次被法国科学家Jacque等^[6]从松树皮中提取后,各国科学家相继在植物的花^[7]、叶^[8]、莲^[9]、根^[10,11]、果实^[12]、种子^[13]、果皮^[14]等组织中发现大量花青素存在。通过对提取的花青素进行药理活性研究,发现它在消除体内自由基、抗氧化活性、抗癌、抗炎症、预防心血管疾病、治疗眼科疾病等都显示出良好的功效。此外,该物质在降低抗生素对人体危害方面也表现出一定的效果^[15,16]。

基于花青素良好的生理活性,以花青素作为功能性添加剂的产品如含花青素营养保健品^[17]、药品^[18]、饮料^[11]、染料^[19]、食品营养添加剂^[20]、化妆

品^[21,22]等已大量开发并得到应用。为了实现花青素的高产与高纯度提取以满足日益增长的需要,探索花青素的提取方法和药理活性意义深远。尤其地,考虑到花青素资源的丰富性、提取方法和药理活性的多样性,有必要对花青素的提取及药理活性进行较为全面的概述,为今后相关的研究提供参考和优化思路。

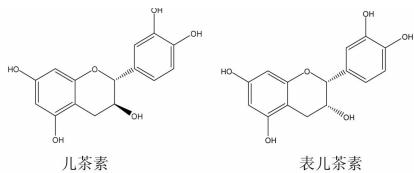


图 1 单倍体的化学结构

Fig. 1 Chemical structures of haploid

1 花青素的提取方法

传统的花青素提取方法主要是溶剂提取法,该工艺比较成熟,但存在提取过程复杂、提取物质的成分易变性等缺点^[23]。近年来出现的新兴提取方法有超临界二氧化碳萃取法、离子液体提取法、仪器辅助提取法(微波辅助提取法、超声波辅助提取法)、酶辅助提取法(果胶酶辅助提取、纤维素酶辅助提取)等。此外,亚临界水溶液提取法、超高压辅助提取法、高压脉冲电场辅助提取法还处于试验阶段,但其优势及独特性已经为花青素提取工艺提供了更多的思路^[24]。

1.1 溶剂提取法

溶剂提取法是在提取过程中,依据被提取成分在所选择溶剂中的溶解性质将所需成分从植物中提取出来的一种方法。在溶剂选择时,依据相似相溶原理,选用对被提取成分溶解度大,而对不需成分溶解度小的溶剂。在用溶剂提取植物中的有效成分时,溶剂首先经过扩散、渗透作用进入植物的细胞壁,然后溶解可溶性成分,这样经过一段时间以后,细胞内外会形成一定的浓度差,进而细胞里的浓溶液就会向外扩散^[25]。溶剂反复作用,直至细胞内外的溶液达到动态平衡。最后将所得饱和溶液过滤,即可得到初步的粗提取物。常用溶剂为甲醇、乙醇、丙酮、水等。20世纪50年代,Jacque等^[6]以沸水作为溶剂,首次从松树皮中提取出花青素。Knez等^[26]采用不同浓度的甲醇、乙醇、丙酮、乙酸乙酯进行了不同种类葡萄中花青素的提取研究。结果发现,对赤霞珠红葡萄而言,当温度为60 °C,用100 %

丙酮提取时产率最高,达1.2 mg/g,用70%乙酸乙酯提取率不到0.1 mg/g,而在同样条件下纯水没有提取出花青素。Silva等^[27]利用不同的溶剂提取蓝莓中的花青素,不同溶剂对应不同的花青素产率(如图2),水和丙酮提取率最低(46.7 ± 2.6 和 $32.8 \pm 2.9 \mu\text{g}/\text{mL}$,用甲醇提取率高达 $350 \mu\text{g}/\text{mL}$)。Ismail等^[23]采用十种传统有机溶剂提取钟花葡萄中的次生代谢产物,结果表明,使用0.1 mol/L HCl回流半小时,能够获得30%粗提取物。可见,有机溶剂提取法在植物花青素提取方面具有普遍的适用性,且提取效果明显优于单独用水浸提。然而,不容忽视的是大多数有机溶剂有一定的毒性,这可能导致提取的花青素中含有微量有毒有害物质,作为食品添加剂等时,可能存在安全隐患。

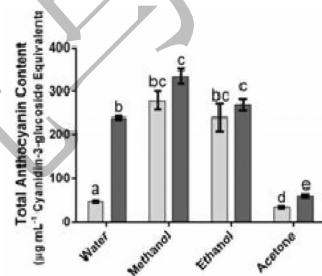


图 2 总花青素含量与不同提取溶剂(乙醇、甲醇、水,及是否酸化)关系图

Fig. 2 Total anthocyanin content of extracts produced using ethanol, methanol, acetone or water, with or without 0.01% HCl

1.2 超临界流体提取法

超临界流体技术提取法综合了常见的溶剂提取和蒸馏技术,利用特定流体在超临界状态下具有的特殊溶解性能对待提取组分进行分离提取的一种方法。物质处于超临界状态时,气化过程和液化过程同时进行,物质会兼具有液体的溶解性能和气体易于扩散的特征,从而有利于提取分离^[28]。研究发现CO₂不仅具有惰性、无毒、较低的超临界温度和压力,而且在提取花青素时效果理想^[29],因此已得到广泛使用。张浩等^[30]采用超临界CO₂萃取技术和索氏抽提法对葡萄籽残渣进行原花青素提取研究,结果发现两种方法所获得的原花青素基本相同,分别为61.80 g/kg(超临界法)和61.70 g/kg(索氏抽提法)。但从工艺角度来讲,超临界方法较索氏抽提法更加方便、清洁和环保,因为该方法通常在常温进行且无有机溶剂的参与。同样地,胡佳兴等^[31]也

证明超临界 CO₂ 法能够有效的提取葡萄籽中的花青素。进一步, Martínez 等^[32]采用超临界流体技术, 考察了不同溶剂(95% 乙醇、酸化水、蒸馏水)、不同温度(40~80 ℃)对蓝莓中花青素提取量的影响。研究表明, 当提取温度为 40 ℃、酸化水为溶剂时, 所得到的花青素产率最高, 为 9.7 mg/g。可见, 超临界流体技术作为一种新兴提取分离技术在花青素提取中效果显著, 可以预见该方法将在其它物质提取方面发挥重要作用^[33]。

1.3 亚临界水提取法

所谓亚临界水提取法, 就是利用亚临界水(100~347 ℃的水)的极性随温度改变而改变的特点, 通过改变温度和压强等条件来控制水的极性, 从而可以达到对提取物的选择性分离^[34]。亚临界水与环境水相比, 具有较低的极性、表面张力、离解能, 因而性能与有机溶剂很相似^[35], 因此, 它能够替代有机溶剂并达到类似的提取效果。Zhi 等^[37]采用亚临界水、纯水、60% 甲醇提取葡萄干皮中的花青素, 发现用亚临界水提取的花青素量相对较高(59.3 mg/g), 且耗时仅为 10 min, 效果明显优于传统有机溶剂提取法所得到的结果。Muangrat 等^[36]利用亚临界水提取法开展了干玉米不同部位(玉米皮、玉米粒、玉米棒、玉米穗)中花青素提取的研究, 取得了一定的效果。大量研究报道证明亚临界水提取法具有溶剂污染小、成本低、提取率高、速度快, 它不仅可以在工业提取花青素方面具有适用性, 而且也已经用于其他领域, 如从花椒皮中提取花椒精油^[38]; 从木瓜种子中提取油脂^[39]等。

1.4 超高压提取方法

超高压提取方法又名超高冷等静压提取法, 是通过在室温下对提取剂施加约 100~1000 MPa 的流体静压力, 并保持作用一段时间, 以使细胞内外压力平衡, 然后再释放压力, 导致细胞内外渗透压迅速变大, 细胞膜结构发生改变, 细胞内液被释放出, 从而达到有效组分提取分离的方法^[40]。杜月娇等^[41]利用超高压提取法提取山葡萄中的花青素, 提取率为(0.304 ± 0.007) g/100 g, 所用时间仅为 2 min, 而热浸提法提取花青素的得率为(0.240 ± 0.005 g/100 g), 耗时 30 min。可见, 超高压提取法不仅能缩短提取时间, 而且能提高花青素提取率。Ming 等^[42]研究了不同影响(压力、料液比、乙醇浓度)条件下, 超高压提取技术提取荔枝皮中的花青素, 发现当静压力为 295 MPa、作用时间为 13 min 时, 花青素

的得率达到 2.45%。然而, 周玮婧等^[43]利用乙醇为溶剂提取荔枝皮中的花青素时, 得率仅为 1.3%, 且耗时 120 min。这些结果充分说明超高压提取法的可行性、快速高效性及环境友好性^[42]。

1.5 辅助提取法

单一提取方法的采用, 虽然方法简单、操作方便, 但是其总体的提取效果较差。近年来, 为了提高花青素的提取效率, 不少学者提出两种提取方法结合(如微波辅助提取法、超声波辅助提取法、酶辅助提取法、超高压辅助提取法、高压脉冲电场辅助提取法)提取花青素, 成果更加显著。Duan 等^[44]利用微波辅助提取法提取了中国月桂树果实中的花青素, 提取率达到 3.03 mg/g, 耗时仅 15 min。Carvalho 等^[45]研究了不同因素影响下用微波辅助提取薰衣草花中的花青素, 并建立了数据理论模型, 为寻找最佳提取条件提供了参考。张辉青花等^[46]用果胶酶辅助提取洛神花中的花青素, 得率为 711.5 mg/100 g, 比未用酶辅助的参照实验得率提高了 119.8%。顾焰波等^[47]利用纤维素酶辅助提取了苹果皮中的原花青素, 发现最佳工艺条件为: 酶解浓度 1.0%, 酶解温度为 50 ℃, pH 值为 4.5, 提取时间 100 min, 所得苹果皮中原花青素的得率为 0.489%。Tomislav 等^[48]利用超声辅助低共熔溶剂提取了葡萄酒酒渣中的花青素, 耗时 30 min, 提取率为 6.40 mg/g, 而且污染小。Gao 等^[49]利用超声波辅助提取蓝莓酒果渣中的花青素, 并研究了提取温度和提取时间对提取效率的影响(如图 3), 得出最佳条件下提取率高达 4.11 mg/g。罗炜等^[50]利用脉冲电场辅助提取红莓果实中的花青素, 提取率较高, 方法具有实用性, 但是高压电场会使提取物分解而未被广泛使用。这些辅助提取方法具有较高的提取率, 耗时少, 条件温和, 属于环境友好型提取法, 符合绿色化学的观念, 也有利于保护花青素的稳定性。

此外, 用两种方法辅助提取也已有报道。陈茵茹等^[51]利用了超声微波双辅助提取了葡萄籽中的原花青素, 其效果明显优于单纯溶剂提取和用一种方法辅助提取的效果。顾焰波等^[47]利用助纤维素酶和果胶酶双辅助法提取莲房中的花青素, 结果双酶辅助比单一酶辅助提取率更高, 耗时短。李超^[52]等利用超声波辅助和亚临界水辅助提取脱脂葡萄中的花青素, 表明此方法不仅具有可行性, 且提取耗时短, 效率高。

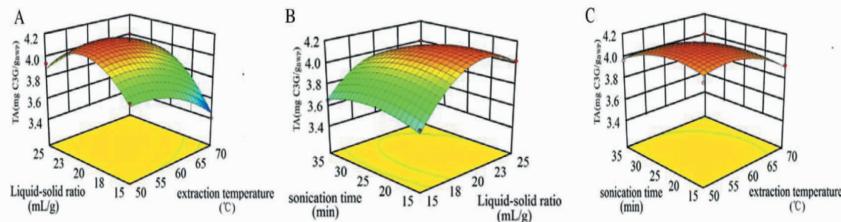


图 3 三个独立变量(温度、时间、料液比)对花青素提取率的影响

Fig. 3 Three independent variables (temperature, time, solid-liquid ratio) on the effect of extraction yields of total anthocyanins

2 药理活性与应用

花青素为黄酮类化合物,其分子结构中含有较多羟基官能团,这使得花青素具有特殊的药理活性。大量研究表明原花青素具有较强的抗氧化性和清除自由基的能力,并具有抗炎症、抗癌、抗心血管疾病、抗衰老、增强记忆、治疗眼科疾病等功效^[53]。此外,花青素可以通过抑制脂质过氧化反应来加快皮肤和血清中的抗氧化酶的合成速度和增加酶的活性^[54],因此成为低毒、高效、受欢迎的抗氧化剂。这些研究为花青素的应用提供了有力可靠的理论支撑。

2.1 清除自由基和抗氧化活性

花青素中的酚羟基基团作用于基体时,所释放的H⁺能与体系中的自由基结合,从而阻止了体内一些自由基反应的发生,因此体现出较强的清除自由基能力和抗氧化活性^[55]。羊芹等^[56]考察了花青素与维生素C(VC)对O₂⁻、·OH、H₂O₂和NO²⁻的消除作用,发现原花青素的抗氧化能力强于VC。Wei等^[57]通过体外实验证实了雀梅藤花青素对氢氧自由基、超氧自由基的清除能力。Eva等^[58]通过给实验动物(大鼠、鸡、鱼)饲喂不同剂量的紫麦花青素,然后测定其血液中的抗氧化指标,结果证明高含量的花青素有助于提高生物体的抗氧化能力改善肝脏功能。Luca等^[59]在不同基质中研究了蔷薇芽中的花青素淬灭过氧自由基的能力比α-生育酚做比较,发现芥子酸起主要抗氧化性作用。Hacer等^[60]研究了马蹄莲浆果中提取的花青素与其他非花青素酚类化合物的抗氧化能力,结果显示起抗氧化作用主要是花青素。然而,大量的抗氧化实验都是体外研究,并且动物模型实验居多,花青素在人体内的研究比较少,因此其在人体内的生理活性有待进一步考证。

2.2 抗炎症

炎症是机体对刺激做出的防御反应,很多疾病的发病与各种炎症有直接或间接的关系。大量文献

报道花青素在抗炎方面具有显著效果。Xu等^[61]发现蓝莓果实花青素提取物能够通过抑制单核-巨噬细胞炎症相关基因mRNA的表达而体现出抗炎药效。Huang等^[62]通过利用蓝莓花青素干预细胞培养基的体外实验,发现花青素能够抑制各种生物炎症表达因子,而具有较强的抗炎能力。Kim等^[63]以模型鼠为作用体,发现笃斯越桔花青素提取物能抑制模型鼠白细胞介素的增多,并减少了2,4-二硝基氯苯导致的特应性发炎、过敏、皮肤炎症而体现出抗炎能力。葛飞^[64]发现金荞麦花青素提取物通过降低溃疡性结肠炎小鼠结肠组织中的炎症因子浓度、结肠髓中过氧化酶的活性,抑制炎症相关基因mRNA的表达和蛋白质的合成而具有抗炎症能力。而这些研究成果可以用于开发各种与炎症有关的疾病保健品,防止慢性炎症。

2.3 心血管疾病方面的应用

心血管疾病已经成为威胁人类健康的主要疾病,如高血压心脏病、心肌梗死、心肌病、糖尿病心脏病等。研究发现,花青素在心血管疾病防御方面具有一定效果:1)通过消除心肌损伤后的自由基,缩小心肌梗死的范围;2)降血压;3)对心肌缺血再灌注造成损伤的肌细胞具有保护作用^[65]。伊丽孜拉·吐尔干^[66]和吴涛等^[67]将原花青素注射于糖尿病小鼠体内,通过测定小鼠盲肠中短链脂肪酸含量,发现盲肠中短链脂肪酸含量增加,这说明原花青素能够通过降低小鼠血糖而减小糖尿病型心脏病的风险。阚晓红^[68]等通过给心肌纤维化小鼠胃灌葡萄籽花青素,并测定心脏有关生理指标,发现葡萄籽花青素能通过抑制心肌纤维化保护心肌结构。Rimm等^[69]通过24年的跟踪研究发现,女性经常性地摄入富含花青素的水果后,患心血管疾病(如心肌梗死)的风险会降低。Jordan等^[70]综述了近年来花青素在人体和动物体内的抗心血管疾病的研究现状,结果显示花青素能够增加血管的舒张、降低内皮细胞功能

障碍,将在治疗心血管疾病方面具有广阔的应用前景。

2.4 抗癌药效

癌症对人类健康威胁很大,近几年其发病率越来越高,而这与人们的饮食习惯密切相关。目前的研究表明大量存在于水果和蔬菜中的花青素对癌症有一定疗效。王丽^[71]等通过给肿瘤模型鼠饲喂紫甘蓝花青素提取物,发现花青素具有促进黑色素瘤细胞系的凋亡、抑制肿瘤细胞增殖的能力。进一步,他们又用花青素提取物处理患有三阴性乳腺癌病人的乳腺癌细胞系,发现花青素能抑制乳腺癌细胞表达并能诱导乳腺癌相关细胞凋亡。Faria 等^[72]证实了蓝莓花青素对乳腺癌细胞增殖的抑制作用。于斌^[73]等用黑米花青素提取物干预移植人乳腺癌细胞株的瘤模型鼠细胞培养基,并通过测定相关生理指标,发现黑米花青素具有下调乳腺癌细胞促血管生成因子的表达、抑制移植瘤血管的生成、阻止肿瘤细胞的生长等作用。Gulati 等^[74]研究了紫茶花青素对人类肺癌细胞培养基的影响,发现花青素能够降低细胞的毒性、抑制癌细胞的分裂等能力。但是花青素并不能对癌细胞完全致命。

2.5 抗衰老,增强记忆

近年来,国内外学者开展了花青素在抗衰老、延长记忆方面的研究,发现花青素具有较好的抗衰老、增强记忆力等功效。Wei 等^[75]分别给实验大鼠饲喂和注射不同剂量的黑沙果花青素,通过测定有关生理指标,发现花青素能够减少相关炎症因子表达,减轻 DNA 损伤,从而阻止由于年龄增大造成的能力下降。韩雪等^[76]用蔷薇花青素处理果蝇培养基,并分别记录比较与非处理组的寿命,发现经过蔷薇花青素处理的果蝇寿命明显高于未处理组。武雪玲等^[77]发现黑果枸杞的花青素提取物对 AD 痴呆型大鼠的记忆损伤有改善作用。可见,花青素具有预防痴呆症的潜在作用,并能够抗衰老,增强记忆。

2.6 对眼科疾病的疗效

花青素在眼科领域的应用研究,特别是在白内障、葡萄膜炎、角膜病和视网膜病等方面具有较好的前景,旨在通过进一步发掘其广泛的药理学功效,进而不久的将来能为眼科临床提供一种有效的药物。Durukan 等^[78]通过给患有白内障的大鼠服用从葡萄籽中提取的花青素,发现葡萄籽花青素具有延缓白内障进展的作用。Naomi 等^[79]给患有糖尿病性白内障大鼠服用可可豆中的花青素提取物发现可

可豆花青素提取物对大鼠的白内障具有一定的治愈药效。Robert 等^[80]发现给用准激光手术致伤眼睛的兔子注射花青素,眼角膜基质损伤程度会减轻。

3 结语

花青素来源丰富、药理活性优良,具有广阔的应用前景。目前有关花青素的提取方法和药理活性的研究已经取得了较大进步。然而,花青素研究中仍然存在提取率及纯度偏低、基于花青素的生理活性机制研究不够成熟等问题,这阻碍了花青素的进一步开发利用。因此,建议在从分子角度探索花青素结构特性,从而选择绿色高效的提取方法。另一方面,药理活性研究体外实验居多,建议在生物体内进行药理活性研究,以提供更加可靠的理论依据。国内外对优异性能的天然产物需求量很大,花青素的开发研究势在必行。

参考文献

- 1 Smeriglio A, et al. Chemistry, pharmacology and health benefits of anthocyanins [J]. *Phytother Res*, 2016, 30:1265-1286.
- 2 Chen HC(陈会丛), et al. Experimental studies on the toxic effect of grape seed proanthocyanidin extract [J]. *Sci Technol Food Ind*(食品工业科技), 2014, 35(2):41-43.
- 3 Ji DM(季冬梅), Yang XL(杨雪莲). Research progress of anthocyanin in plants [J]. *J Green Sci Technol*(绿色科技), 2017, 7:150-151.
- 4 Li M(李敏). Study on component analysis stability and oxidation resistance of Different anthocyanins [D]. Nanjing: Nanjing University of Finance and Economics(南京财经大学), 2013.
- 5 Zhang HW(张慧文), et al. Progress in procyanidins research [J]. *Food Sci*(食品科学), 2015, 5:296-304.
- 6 Masquelier J. Plant extract with a proanthocyanidins content as therapeutic agent having radical scavenger effect and use thereof [P]. US 4698360, 1987.
- 7 Oh SM, et al. Simultaneous analysis of anthocyanins and flavonols in various flower colors of rhododendron schlippenbachii (royal azalea) [J]. 2017, 3:104-113.
- 8 Ishikura N. Anthocyanins and flavones in leaves and seeds of perilla plant [J]. *Agr Biol Chem*, 2006, 5:1855-1860.
- 9 Chen S, et al. Simultaneous analysis of anthocyanin and non-anthocyanin flavonoid in various tissues of different lotus (*Nelumbo*) cultivars by HPLC-DAD-ESI-MSn [J]. *PloS One*, 2013, 84:e62291.
- 10 Hua Z, et al. Bioaccessibility, bioavailability and anti-inflam-

- matory effects of anthocyanins from purple root vegetables using mono-and co-culture cell models [J]. *Mol Nutr Food Res*, 2017, 10 : 1600928.
- 11 Matsufuji H, et al. Stability to light, heat, and hydrogen peroxide at different pH values and DPPH radical scavenging activity of acylated anthocyanins from red radish extract [J]. *J Agr Food Chem*, 2007, 9:3692-3701.
- 12 Yingqi LU, et al. Research progress in anthocyanin of colored potatoes [J]. *Chin Potato J*, 2017, 31:165-176.
- 13 Mojica L, et al. Black bean coat anthocyanin-rich extracts and pure anthocyanins modulated molecular markers of diabetes [J]. *The Faseb J*, 2017, 31:4205-4206.
- 14 Yang ZJ(杨志娟), et al. Extraction, purification and qualitative analysis of proanthocyanidins from pitaya peel [J]. *Food Sci(食品科学)*, 2015, 36:75-79.
- 15 Li C(李聪), et al. The research progress of extraction, separation and pharmacological effects of procyanidins [J]. *Int J Tradit Chin Med(国际中医中药杂志)*, 2017, 39:285-288.
- 16 Li W, et al. Research progress in anthocyanins from lycium ruthenicum [J]. *Biot Resour*, 2017, 39:162-167.
- 17 Wu YM(吴映梅). Nutrition and health function of grape seed and its development and utilization [J]. *J Anhui Agr Sci(安徽农业科学)*, 2017, 45:105-106.
- 18 Zhang ZH(杨志宏), et al. Natural pharmaceutical compositions, methods for their preparation and their use in pharmaceuticals [P]. CN104983900A, 2015.
- 19 Haddar W, et al. Application of anthocyanins as natural dye extracted from Brassica oleracea L. var. capitata frubra: dyeing studies of wool and silk fibres [J]. *Nat Prod Res*, 2017, 29:1342080.
- 20 Khoo HE, et al. Anthocyanidins and anthocyanins: colored pigments as food, pharmaceutical ingredients, and the potential health benefits [J]. *Food Nutr Res*, 2017, 61:1361779.
- 21 Kostick RH, et al. Color cosmetics-coloring/staining the skin from fruit and plant color pigments [P]. US 20060280762A1, 2006.
- 22 Niziołukaszewska Z, et al. Hydrophilic dogwood extracts as materials for reducing the skin irritation potential of body wash cosmetics [J]. *Molecules*, 2017, 22:320.
- 23 Abdul, et al. A comparative study of conventional and supercritical fluid extraction methods for the recovery of secondary metabolites from Syzygium campanulatum Korth [J]. *Biomed Biotechnol(生物医学与生物技术)*, 2016, 17:683-691.
- 24 Zheng S, et al. Comparison of different extraction methods and antioxidant activity of anthocyanins from eggplant peel [J]. *J Chin Inst Food Sci Tech*, 2017, 17(1):92-99.
- 25 Chen XJ(陈小婕), Yin WY(阴文娅). Study on the extraction methods of anthocyanins in plants [J]. *Sci Technol Food Ind(食品工业科技)*, 2013, 34:395-399.
- 26 Vatai T, et al. Extraction of phenolic compounds from elderberry and different grape marc varieties using organic solvents and/or supercritical carbon dioxide [J]. *J Food Eng*, 2009, 90:246-254.
- 27 Silva S, et al. Production of a food grade blueberry extract rich in anthocyanins; selection of solvents, extraction conditions and purification method [J]. *J Food Meast Charact*, 2017, 11:1248-1253.
- 28 Eliasson L, et al. Effect of drying technique and particle size of bilberry press cake on the extraction efficiency of anthocyanins by pressurized carbon dioxide extraction [J]. *LWT-Food Sci Technol*, 2017, 85:510-516.
- 29 Porto CD, et al. Supercritical fluid extraction of polyphenols from grape seed (*Vitis vinifera*) : study on process variables and kinetics [J]. *J Supercrit Fluid*, 2017, 130:239-245.
- 30 Zhao H(张浩), et al. Influence of two extraction methods on the quality of New Zealand grape seed oil and proanthocyanidins in residue [J]. *Food Sci Technol(食品科技)*, 2017, 42:221-226.
- 31 Hu JX(胡佳兴), et al. Optimum technology for supercritical CO₂ extraction of OPC from grapestone [J]. *Chin J Hosp Pharm(中国医院药学杂志)*, 2008, 28:968-970.
- 32 Del Pilar Garcia-Mendoza M, et al. Extraction of phenolic compounds and anthocyanins from ju? ara (*Euterpe edulis* Mart.) residues using pressurized liquids and supercritical fluids [J]. *J Supercrit Fluid*, 2017, 119:9-16.
- 33 Klinchongkon K, et al. Extraction of oligosaccharides from passion fruit peel by subcritical water treatment [J]. *J Food Process Eng*, 2017, 40:e12269.
- 34 Monrad JK, et al. Subcritical solvent extraction of anthocyanins from dried red grape pomace [J]. *J Agr Food Chem*, 2010, 58:2862-2868.
- 35 Cacace JE, Mazza G. Pressurized low polarity water extraction of biologically active compounds from plant products [J]. *Fun Food Ingredient Nutrac Pro Technol*, 2006:135-155.
- 36 Muangrat R, et al. Subcritical solvent extraction of total anthocyanins from dried purple waxy corn; Influence of process conditions [J]. *J Food Process Pres*, 2017;e13252.
- 37 Yu ZY, Howard LR. Subcritical water and sulfured water extraction of anthocyanins and other phenolics from dried red grape skin [J]. *J Food Sci*, 2005, 70:270-276.
- 38 Zhong LJ(钟炼军), et al. Study on extraction of high contentality of *zanthoxylum bungeanum* maxim by subcritical fluid [J]. *Modern Food Sci Technol(现代食品科技)*, 2017, 10:1-5.

- 39 Wang L, et al. Subcritical fluid extraction of chinese quince seed: optimization and product characterization [J]. *Molecules*, 2017, 22:528.
- 40 Xi J. Ultrahigh pressure extraction of bioactive compounds from plants a review [J]. *Crit Rev Food Sci Nutriton*, 2017, 57:1097-1106.
- 41 Du YJ(杜月娇), et al. Optimization of ultra-high pressure extraction of anthocyanins from *vitis amurensis* rupr. and analysis of its anthocyanin composition [J]. *Food Sci(食品科学)*, 2017, 38:258-263.
- 42 Zhang R, et al. Optimized ultra-high-pressure-assisted extraction of procyanidins from lychee pericarp improves the antioxidant activity of extracts [J]. *Biosci Biotechnol Biochem*, 2017, 81:1576-1585.
- 43 Zhou WJ(周玮婧). Extraction, purification and antioxidation of procyanidins from litchi Chinese pericarp [D]. Wuhan: Huazhong Agricultural University(华中农业大学). 2010.
- 44 Duan WK, et al. Microwave-assisted extraction of anthocyanin from Chinese bayberry and its effects on anthocyanin stability [J]. *Food Sci Technol*, 2015, 35:524-530.
- 45 Farzaneh V, Carvalho IS. Modelling of microwave assisted extraction(MAE) of anthocyanins(TMA) [J]. *J Appl Res Med Aromat Plant*, 2017, 6:92-100.
- 46 Zhang HQH(张辉青花), et al. Extraction process optimization of anthocynins in Roselle (*Hibiscus sabdariffa* Linn) based on enzyme hydrolysis [J]. *Appl Chem Ind(应用化工)*, 2017, 46:607-610.
- 47 Gu YB(顾焰波), et al. Study on extraction technology of procyanidins from apple pericarp assisted by cellulase enzyme [J]. *China Food Additive(中国食品添加剂)*, 2014, 6: 102-106.
- 48 Bosiljkov T, et al. Natural deep eutectic solvents and ultrasound-assisted extraction: green approaches for extraction of wine lees anthocyanins [J]. *Food Bioprod Process*, 2017, 102:195-203.
- 49 He B, et al. Optimization of ultrasound-assisted extraction of phenolic compounds and anthocyanins from blueberry (*Vaccinium ashei*) wine pomace [J]. *Food Chem*, 2016, 204:70-76.
- 50 Luo W(罗炜), et al. Effect of PEF on extraction of anthocyanin [J]. *High V Eng(高电压技术)*, 2009, 6:1430-1433.
- 51 Chen YR(陈茵茹), et al. Extraction of oligoprocyanidins from grape seed with ultrasonic treatment followed by microwave treatment [J]. *China Brewing(中国酿造)*, 2012, 8:23-28.
- 52 Li C(李超), et al. Ultrasound-assisted subcritical water extraction of proanthocyanidins from defatted grape seed and its antioxidantactivity [J]. *China Journal Chinese Materia Med(中国中药杂志)*, 2010, 8:967-972.
- 53 Tsuda T. Dietary anthocyanin-rich plants: biochemical basis and recent progress in health benefits studies [J]. *Mol Nutr Food Res*, 2012, 56:159-170.
- 54 Wang JN(王佳宁), et al. Research progress on the extraction method and pharmacological action of proanthocyanidin [J]. *Shanghai J Trad Chin Med(上海中医药杂志)*, 2015, 10:94-97.
- 55 Fracassetti D, et al. Ellagic acid derivatives, ellagitannins, proanthocyanidins and other phenolics, vitamin C and antioxidant capacity of two powder products from camu-camu fruit (*Myrciaria dubia*) [J]. *Food Chem*, 2013, 139:578-588.
- 56 Yang Q(羊芹), et al. Study on antioxidantive activity of procyanidins from the leaves of willow [J]. *J Southwest U(西南大学学报)*, 2009, 6:106-110.
- 57 Lei K, et al. In Vitro Antioxidant activity of the anthocyanins in sageretia theezans brongn fruit [J]. *Inter J Food prop*, 2016, 19:210-221.
- 58 Mrkvicová E, et al. The influence of feeding purple wheat with higher content of anthocyanins on antioxidant status and selected enzyme activity of animals [J]. *Acta Veterinaria Brno*, 2017, 85:371-376.
- 59 Matera R, et al. Acylated anthocyanins from sprouts of *raphanus sativus* cv. sango: isolation, structure elucidation and antioxidant activity [J]. *Food Chem*, 2015, 166:397-406.
- 60 Coklar H, Akbulut M. Anthocyanins and phenolic compounds of *mahonia aquifolium* berries and their contributions to antioxidant activity [J]. *J Funct Food*, 2017, 35:166-174.
- 61 Xu W, et al. Inhibitory effect of gardenblue blueberry (*vaccinium ashei* Reade) anthocyanin extracts on lipopolysaccharide-stimulated inflammatory response in RAW 264. 7 cells [J]. *J Zhejiang U Sci B*, 2016, 17:425-436.
- 62 Huang WY, et al. Anti-inflammatory effect of the blueberry anthocyanins malvidin-3-glucoside and malvidin-3-galactoside in endothelial cells [J]. *Molecules*, 2014, 19: 12827-12841.
- 63 Kim MJ, Choung SY. Mixture of polyphenols and anthocyanins from *vaccinium uliginosum* L. Alleviates DNCB-induced atopic dermatitis in NC/Nga Mice [J]. *Evid Based Complement Altern Med*, 2012, 5:265-266.
- 64 Ge F(葛飞). Anti-inflammatory effect of ethanol extracts of *fagopyrum cymosum*(Trev) on ulcerative colitis models [D]. Nanjing: Nanjing University Of Chinese Medicine(南京中医药大学), 2016.
- 65 Yang XY(杨学颖), et al. Advances in the study of the mechanism of procyanidins in the treatment of cardiovascular

- diseases [J]. *Clin J Med Officers* (临床军医杂志), 2013, 41:1197-1200.
- 66 Elzira Tergan(伊丽孜拉·吐尔干). Purification and hypoglycemic effect in vitro to procyanindin from grape seed extracts [D]. Wulumuqi: Xinjiang university (新疆大学), 2014.
- 67 Wu T(吴涛), et al. Hypoglycemic effect of grape seed proanthocyanidins in diabetic mice [J]. *Modern Food Sci Technol* (现代食品科技), 2016, 8:42-47.
- 68 Kan XH(阚晓红). The protective effects and molecular mechanism of grape seed procyanidin extracts on hypertensive myocardial [D]. Qingdao: Shandong university (山东大学), 2016.
- 69 Cassidy A, et al. Habitual intake of anthocyanins and flavonoids and risk of cardiovascular disease in men [J]. *Am J Clin Nutr*, 2016, 104:587-594.
- 70 Reis JF, et al. Action mechanism and cardiovascular effect of anthocyanins: a systematic review of animal and human studies [J]. *J Transl Med*, 2016, 14:315.
- 71 Wang L(王丽). Mechanisms of red cabbage anthocyanin inhibits triple-negative breast cancer and melanoma [D]. Beijing: China Agricultural University (中国农业大学), 2016.
- 72 Faria A, et al. Blueberry anthocyanins and pyruvic acid adducts: anticancer properties in breast cancer cell lines [J]. *Phytother Res*, 2010, 24:1862-1869.
- 73 Yu B(于斌). Effect and mechanisms of black rice anthocyanins inhibiting angiogenesis of human breast cancer over-express HER-Z/neu [D]. Chongqing: Third Military Medical University(第三军医大学), 2010.
- 74 Joshi R, et al. Anthocyanins enriched purple tea exhibits antioxidant, immunostimulatory and anticancer activities [J]. *J Food Sci Technol*, 2017, 54(7):1-11.
- 75 Wei J, et al. Anthocyanins from black chokeberry(aroniamelanocarpa elliot) delayed aging-related degenerative changes of brain [J]. *J Agr Food Chem*, 2017, 65:5973-5984.
- 76 Han X(韩雪), et al. Stability and anti-aging effect of oligomeric proanthocyanidin from *Rhodiola rosea* L. [J]. *Sci Tech Food Ind* (食品工业科技), 2017, 5:120-123.
- 77 Wu XL(武雪玲), et al. Memory enhancing and antioxidant activities of *Lycium ruthenicum murray* anthocyanin extracts in an A β 42-induced rat model of dementia [J]. *Modern Food Sci Technol* (现代食品科技), 2017, 3:29-34.
- 78 Durukan AH, et al. Ingestion of IH636 grape seed proanthocyanidin extract to prevent selenite-induced oxidative stress in experimental cataract [J]. *J Cataract Refr Surg*, 2006, 2:1041-1045.
- 79 Osakabe N, et al. Ingestion of proanthocyanidins derived from cacao inhibits diabetes-induced cataract formation in rats [J]. *Exp Bio Med*, 2004, 229:33-39.
- 80 Robert AM, et al. Effect of procyanidolic oligomers on corneal collagen of rabbits treated by excimer laser photoablation [J]. *Biomed pharmacother*, 2006, 60:113-120.

(上接第 236 页)

- 92 Chen SL(陈士林). Ecological suitability regionalization for traditional Chinese medicinal(中国药材产地生态适宜性区划) [M]. *Science Press*, 2011, 71-73.
- 93 Zhang Q(张琼). The intrinsic factors affecting the yield of *Gastrodia* [J]. *Ginseng research* (人参研究), 2010, 22(4): 42.
- 94 Guan P(关萍), et al. Comparison of gastrodin content in wild and cultivated [J]. *Chin J Chin Mater Med* (中国中药杂志), 2005, 30:1698-1699.
- 95 Liu XQ(刘小琴), et al. Comparison gastodin in different varieties and tissues of *Gastrodia elata* [J]. *Lishizhen Med Mater Med Res* (时珍国医国药), 2009, 20:908-909.

- 96 Wang QY(王秋颖), et al. A preliminary study on the breeding of *Gastrodia elata* variety [J]. *Chin J Chin Mater Med* (中国中药杂志), 2001, 26:744-746.
- 97 Li L(李梁), et al. Analysis and evaluation of ecological environment of *Gastrodia* in China [J]. *Modern Chin Med* (中国现代中药), 2004, 6(6):14-16.
- 98 Zhou Y(周元). Study on biological characteristic of *Gastrodia elata* Bl [D]. Yangling: Northwest A&F University(西北农林科技大学), 2005.