

• 专题报道 •

中药抗皮肤衰老作用与应用研究进展

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摘要: 随着人口老龄化的加剧和健康水平的不断提高, 如何预防和延缓皮肤衰老备受人们关注。皮肤衰老与年龄、紫外线辐射、生活方式等有关, 主要表现为皮肤松弛、皱纹、色斑等, 因此亟待寻求中药及相关化妆品解决皮肤衰老问题。中药具有抗氧化、增强人体免疫、促进机体新陈代谢、调节内分泌等作用, 现已成为抗皮肤衰老研究热点。通过综述皮肤衰老机制及中药抗皮肤衰老的研究进展, 以期为今后抗皮肤衰老中药的研究和开发提供参考依据。

关键词: 中药; 皮肤衰老; 抗衰老; 机制; 应用

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Application progress on anti-skin aging effect of traditional Chinese medicine

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Abstract: With the aging of population intensifies and the level of population health have improved, thus much attention has been directed to how to delaying or preventing skin aging. Skin aging is associated with age, ultraviolet and lifestyle, mainly characterized as skin sagging, wrinkles, pigmentation, so it is urgent to seek traditional Chinese medicine and related cosmetics to solve the problem of skin aging. Traditional Chinese medicine has the functions of anti-oxidation, enhancing human immunity, promoting body metabolism and regulating endocrine, therefore, it has become a research focus in anti-skin aging. This article reviews the skin aging mechanism and the research advances of traditional Chinese medicine anti-skin aging, in order to provide a reference for future research and development of anti-aging traditional Chinese medicine.

Key words: traditional Chinese medicine; skin aging; anti-aging; mechanism; application

皮肤衰老是内在因素和外在因素共同作用引起的

皮肤外观及各皮肤层结构和功能发生退行性变化的过程^[1]。皮肤衰老与年龄、紫外线辐射、生活方式等密切相关。当前我国人口老龄化问题愈发严重, 截至2020年, 65岁以上老年人口达到1.91亿, 占比13.5%^[2]。因此, 抗皮肤衰老研究备受关注。随着人们对抗皮肤衰老的需求逐步增长, 尤其是女性, 她们试图使用功效性化妆品及保健品来预防或逆转皮肤老化^[3], 而一些化学功效性化妆品、保健品存在接触性皮炎、痤疮等不良反应问题^[4], 人参、丹参、姜黄等中药因其天然温和、安全

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有效等特点在化妆品中应用广泛^[5],与化学功效性化妆品相比,中药化妆品具有独特的优势。由国家食品药品监督管理局在2021年4月30日公布的数据可知,中药占比30%左右。中药通过抗氧化和清除自由基、提高机体免疫、抗线粒体DNA损伤及调节内分泌等作用来延缓皮肤衰老,故探讨中药抗皮肤衰老已成为医学领域的研究热点,本文对近年来中药抗皮肤衰老机制及应用研究进展进行了归纳和总结,为今后抗皮肤衰老中药临床实验研究和开发提供参考与借鉴。

1 中药抗皮肤衰老机制

近半个多世纪以来,国内外研究人员提出了一系列衰老学说(图1),为研究皮肤衰老机制和开发抗皮肤衰老中药打下良好基础。现代医学认为皮肤衰老是多种因素作用引起的生理或病理变化,可分为内源性衰老和外源性衰老^[6]。内源性衰老是受遗传或内分泌因素影响;外源性衰老是受外界环境的影响,导致皮肤松弛粗糙、皱纹加深等^[1]。衰老机制包括自由基衰老学说、遗传衰老学说、神经内分泌功能减退学说、基质金属蛋白酶衰老学说、免疫衰老学说、线粒体损伤学说、光老化学说等^[7-11]。中医对衰老学说的认识是以脏腑为中心的,包括肾虚衰老学说、脾虚衰老学说、阴阳失调学说、气滞血瘀学说等^[12],且认为皮肤衰老主要与“脏腑虚损”、“气血津液不足”、“血淤阻滞”等有关^[13]。因此对具有活血化瘀、补肾益气、滋阴养血等功效的中药进行研究发现,补虚药、活血化瘀药等其他类中药在一定程度上通过发挥抗氧化与清除自由基、提高机体免疫、调节神经内分泌、防御紫外线辐射等作用机制来延缓皮肤衰老^[14]。

2 常用抗皮肤衰老中药的研究

近年来,大量中药抗皮肤衰老的研究表明多种中药及其提取物具有延缓皮肤衰老的作用。从现代药理学研究来说,中药具有抗氧化、增强免疫、调节皮肤代谢、促进胶原合成等作用;从中医学研究来说,中药具有补肾健脾、调节阴阳、调理气血等作用^[15]。实验研究发现以补虚药和活血化瘀药为主的中药在抗皮肤衰老方面应用广泛^[16-19],具有巨大的发展潜力。

2.1 补虚药

《本草纲目》认为人的生老病死与脏腑、气血津液的强弱盛衰密切相关,人体脏腑、气血津液逐渐耗损直至亏虚,导致脏腑机能亦逐步衰退,在外表现出皮肤衰老等症^[20]。补虚药具有调节机体免疫、内分泌系统及中枢神经系统等功能^[21],且通过增强机体免疫能力,提高抗氧化酶活性,促进物质代谢等作用发挥抗皮肤衰老的作用。

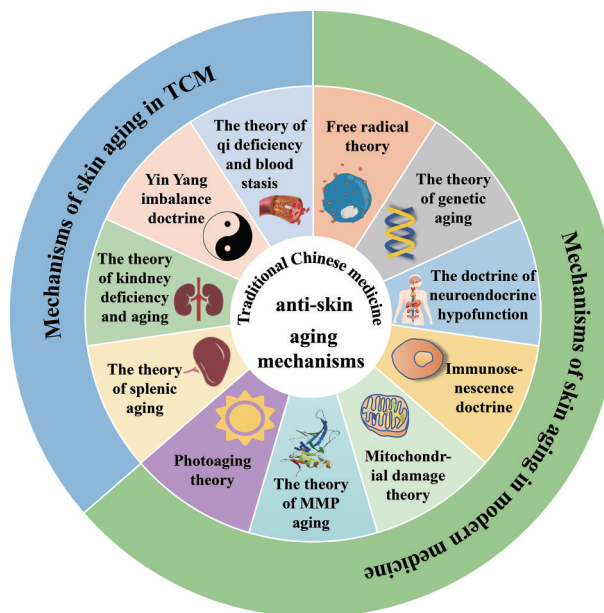


Figure 1 Schematic diagram of the classification of anti-skin aging mechanism in traditional Chinese medicine

2.1.1 人参 人参为五加科植物人参 *Panax ginseng* C.A. Mey. 的干燥根和根茎。始载于《神农本草经》,具有大补元气、复脉固脱、补脾益肺、生津养血等功效,能补肾壮阳。其化学成分主要为人参皂苷、多糖、氨基酸、挥发油等^[22]。现代药理研究表明,人参具有免疫调节、抗炎、抗氧化、延缓衰老等作用^[23]。Li等^[24]探讨人参皂苷对皮肤屏障损伤的保护机制,结果表明人参皂苷可改善紫外线B (ultraviolet B, UVB) 诱导的小鼠表皮屏障功能障碍,表现为表皮厚度增加,经表皮水分流失 (transepidermal water loss, TEWL) 增加,角质层含水量减少,研究结果提示人参皂苷可能通过作用于丝裂原活化蛋白激酶 (mitogen-activated protein kinase, MAPK) 信号通路来防止UVB照射下的皮肤屏障损伤。Lee等^[25]通过测定酪氨酸酶活性和细胞活力来检测人参皂苷 Rg3 (ginsenoside-Rg3, G-Rg3) 抑制黑色素生成的能力,研究表明 G-Rg3 以剂量依赖性方式显著抑制正常人表皮黑色素细胞和 B16F10 细胞黑素的合成,且通过激活细胞外调节蛋白激酶 (extracellular regulated protein kinases, ERK) 通路介导的小眼畸形相关转录因子 (microphthalmia-associated transcription factor, MITF) 和下游信号分子 (如酪氨酸酶和酪氨酸酶相关蛋白1) 来抑制黑色素生成,是一种有发展前景的安全皮肤美白剂。

2.1.2 红景天 红景天为景天科植物大花红景天 *Rhodiola crenulata* (Hook.f.et Thoms.) 的干燥根和根茎。始载于《四部医典》,具有益气活血、通脉平喘之功效,用于气虚血瘀。其主要活性成分为红景天苷 (salidro-

side, SAL), 具有抗氧化、抗炎、延缓皮肤衰老、调节免疫功能等药理作用^[26]。Yuan等^[27]研究探讨了SAL对人永生角质形成细胞(human immortalized keratinocytes, HaCaT)和豚鼠皮肤的光保护作用。研究表明经SAL预处理的HaCaT可增加核因子E2相关因子(nuclear factor erythroid 2-related factor 2, Nrf2)及其靶向基因NAD(P)H:醌氧化还原酶1(NAD(P)H:quinone oxidoreductase 1, NQO1)和血红素加氧酶1(heme oxygenase-1, HO-1)的基因和蛋白质表达,减少活性氧(reactive oxygen species, ROS)生成,并抑制UVB诱导的豚鼠皮肤中凋亡晒伤细胞和8-羟基-2-脱氧鸟苷(8-hydroxy-2-deoxyguanosine, 8-OHDG)阳性皮肤细胞的形成。此外,Peng等^[28]研究了SAL和丹皮酚联合应用对色素沉着的影响。结果表明,SAL和丹皮酚联合应用时其抑制酪氨酸酶活性效应明显提高,且减少皮肤色素沉着。

2.1.3 黄芪 黄芪为豆科植物蒙古黄芪 *Astragalus membranaceus* (Fisch.) Bge. Var. *mongholicus* (Bge.) Hsiao 或膜荚黄芪 *Astragalus membranaceus* (Fisch.) Bge. 的干燥根。始载于《神农本草经》,黄芪“益元气而补三焦”^[29],具有补气升阳、益卫固表、生津养血等功效。其主要活性成分为黄酮和多糖。黄芪具有多种药理活性,如免疫调节作用、抗炎、抗疲劳、延缓衰老、促进人体新陈代谢等^[30]。作为一种新型的皮肤抗污染剂,黄芪可通过调节HaCaT细胞的凋亡和增殖,减轻大气污染对皮肤的屏障破坏^[31]。Wen等^[32]探讨黄芪甲苷对UVB辐射下光老化细胞的抗光老化作用。结果表明,黄芪甲苷通过增强自噬作用来抑制UVB诱导的氧化应激和光老化。

2.1.4 甘草 甘草为豆科植物甘草 *Glycyrrhiza uralensis* Fisch.、胀果甘草 *Glycyrrhiza inflata* Bat. 或光果甘草 *Glycyrrhiza glabra* L. 的干燥根和根茎。始载于《神农本草经》,具有补气益气、调和诸药等功效,补脾胃不足而益中气。其主要成分有甘草酸(glycyrrhizic acid, GA)和甘草苷。药理研究表明甘草具有抗炎、抗氧化、皮肤美白、免疫调节等作用^[33-35]。Li等^[36]研究了甘草苷对UVB照射大鼠皮肤损伤的保护作用。研究发现将甘草苷应用于大鼠暴露皮肤可减少UVB照射引起的ROS、促炎细胞因子和MMP的增加,并增加去乙酰化酶(sirtuin3, SIRT3)和胶原 $\alpha 1$ 的水平。说明甘草苷对UVB损伤的保护机制可能通过SIRT3/ROS/核因子- κ B(nuclear factor kappa-B, NF- κ B)途径发挥作用。Afnan等^[37]研究了GA对UVB诱导的氧化损伤的保护作用。结果表明GA通过氧化应激引发的信号级联(包括MAPK/NF- κ B激活)以及细胞凋亡来保护皮

肤免受UVB介导的光损伤。

2.1.5 白芍 白芍为毛茛科植物芍药 *Paeonia lactiflora* Pall. 的干燥根。始载于《神农本草经》,具有养血调经、敛阴止汗、柔肝止痛、平抑肝阳之功效,用于血虚萎黄、肝阳上亢。芍药苷(paeoniflorin, PF)是白芍的主要活性成分,是一种具有调节免疫、抗炎和抗氧化等药理作用的药物^[38]。Kong等^[39]研究评估了PF在体外对紫外线诱导皮肤损伤的保护作用。结果表明PF治疗可显著降低UVB辐射诱导的角质形成细胞凋亡,减少ROS产生,并抑制人表皮角质形成细胞中p38和p35的激活,减轻UVB诱导的皮肤损伤。Lu等^[40]研究PF对紫外线A(ultraviolet A, UVA)辐射人真皮成纤维细胞(human diploid fibroblasts, HDF)的光保护作用,研究发现PF预处理可显著提高MTS[3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethylphenyl)-2-(4-sulfophenyl)-2 hydrogen tetrazolium, inner salt]细胞增殖活性,减少细胞凋亡及ROS和丙二醛(malondialdehyde, MDA)的生成,提高超氧化物歧化酶(superoxide dismutase, SOD)活性,增加Nrf2及其靶基因HO-1和NQO1的表达,结果表明,PF通过Nrf2/HO-1/NQO1信号通路,抑制UVA诱导的光损伤。此外,Jung等^[41]还研究发现芍药苷具有美白和延缓皮肤衰老双重作用,是美白和抗衰老化妆品的天然原料。

2.1.6 当归 当归为伞形科植物当归 *Angelica sinensis* (Oliv.) Diels 的干燥根。始载于《神农本草经》,具有补血活血、调经止痛之功效,补阴中之阳。其主要活性成分有挥发油、阿魏酸和当归多糖等^[42]。现代药理研究表明,当归具有抗炎、免疫调节等作用^[43]。Chen等^[44]研究当归挥发油对UVB辐射皮肤光老化的预防作用。结果表明当归挥发油显著抑制UVB诱导的肿瘤坏死因子- α (tumor necrosis factor- α , TNF- α)和白细胞介素-1 β (IL-1 β)的过量产生,且减少表皮上皮炎症的增殖。Sun等^[45]利用UVB照射HDF细胞后使用当归醇提物进行治疗。结果表明当归醇提物降低了MMP的产生,并通过减少胶原蛋白的降解来抵御皮肤光老化。

2.1.7 何首乌 何首乌为蓼科植物何首乌 *Polygonum multiflorum* Thunb. 的干燥块根。始载于《开宝本草》,何首乌具有补肝肾、益精血、乌须发、强筋骨等功效,《开宝本草》称之“久服长筋骨,益精髓,延年不老”^[46]。其主要活性成分为大黄酚和大黄素,具有抗衰老、抗炎、抗氧化和免疫调节等药理作用^[47]。Liu等^[48]研究表明,何首乌具有延缓皮肤衰老的作用,可调节衰老皮肤有丝分裂吞噬作用,减少线粒体损伤,提高抗氧化能力。

2.2 活血化瘀药

皮肤衰老-血瘀相关理论始载于《黄帝内经》^[49]。其中《灵枢·天年》曰:“六十岁……血气懈怠。七十岁,

脾气虚, 皮肤枯”。《素问·病机气宜保命集》中提到年衰之人“精耗血衰……血气凝泣”。这些均表明随着年龄的增长, 机体代谢减慢, 血瘀是致使皮肤衰老的重要原因^[18]。活血化瘀药通过改善微循环, 增强机体免疫功能, 抗脂质过氧化等作用机制发挥抗皮肤衰老的作用^[16]。

2.2.1 姜黄 姜黄为姜科植物姜黄 *Curcuma longa* L. 的干燥根茎。始载于《新修本草》, 具有活血行气、通经止痛的功效, 用于气滞血瘀。姜黄素是其主要活性成分, 临床研究表明姜黄素具有强大的抗氧化、抗炎和抗菌作用, 可治疗皮肤创伤、晒伤、早衰等^[50]。Sumiyoshi 等^[51]研究了姜黄是否可以预防 UVB 照射的皮肤损伤, 实验结果表明姜黄通过抑制慢性辐射引起的 MMP-2 表达增加来预防 UVB 诱导的皮肤光老化, 减少皱纹和黑色素的形成。

2.2.2 银杏叶 银杏叶为银杏科植物银杏 *Ginkgo biloba* L. 的干燥叶。始载于《滇南本草》, 具有活血化瘀、通络止痛等功效。其主要活性成分为黄酮^[52]。药理研究表明, 银杏叶具有抗氧化、抗病毒、抗炎和免疫调节等药理活性^[53]。Kim 等^[54]对银杏叶提取物的抗氧化衰老作用进行了探讨, 通过实验研究发现银杏叶提取物可降低 HaCaT 细胞中的过氧化氢 (H_2O_2) 诱导的细胞毒性和降解真皮胶原的关键酶 MMP-1 的水平, 表明其可能通过刺激抗氧化反应保护角质形成细胞免受氧化应激损伤, 降低 MMP-1 的表达, 减少皱纹的生成。

2.2.3 丹参 丹参为唇形科植物丹参 *Salvia miltiorrhiza* Bge. 的干燥根和根茎。始载于《神农本草经》, 丹参具有活血祛瘀、通经止痛、清心除烦、凉血消痈之功效。其主要活性成分为丹参酮^[55]。现代药理研究表明, 丹参具有抗氧化、抗炎、抗纤维化、改善微循环等药理作用^[56]。Suntar 等^[57]研究了丹参提取物的抑制酪氨酸酶活性和抗氧化活性, 研究表明丹参具有增强伤口愈合的能力, 促进胶原纤维形成, 并抑制酪氨酸酶活性, 减少黑色素产生。

2.3 其他类

除上述中药外, 现代药理研究发现解表药、泻下药等中药也具有较好的抗皮肤衰老作用。实验研究^[58,59]表明解表药葛根抗皮肤衰老与清除自由基, 提高机体抗氧化酶活性有关; 泻下药芦荟通过发挥抗氧化剂作用来延缓皮肤衰老。

2.3.1 葛根 葛根为豆科植物野葛 *Pueraria lobata* (Willd.) Ohwi 或甘葛藤 *Pueraria thomsonii* Benth. 的干燥根。始载于《神农本草经》, 具有解肌退热, 生津, 透疹, 升阳止泻的功效。葛根素是其主要活性成分之一, 药理研究表明葛根具有抗氧化、抗炎、免疫调节、美白等生物活性^[60]。Kamiya 等^[61]研究发现葛根素可阻止正常

人真皮成纤维细胞 (normal human dermal fibroblast, NHDF) 衰老表型的发展, 缓解皮肤成纤维细胞中与衰老相关的功能缺陷。Heo 等^[58]研究评估了葛根乙醇提取物 (pueraria lobata ethanol extract, PLE) 对 UVB 诱导的 HDF 细胞氧化应激的细胞保护活性, 研究发现经 PLE 处理的 HDF 细胞降低 ROS 水平, 增加胶原蛋白生成, 结果表明 PLE 可促进 HDF 细胞的胶原蛋白生成并维持透明质酸 (hyaluronic acid, HA) 水平, 从而抑制光老化。

2.3.2 芦荟 芦荟为百合科植物库拉索芦荟 *Aloe barbadensis* Miller、好望角芦荟 *Aloe ferox* Miller 或其他同属近缘植物叶的汁液浓缩干燥物。始载于《海药本草》, 具有泻下通便、清肝泻火、杀虫疗疔的功效。其主要由表皮层和芦荟凝胶组成, 芦荟凝胶的成分为多糖、芦荟苷和氨基酸等。据报道, 芦荟具有杀菌、抗炎、抗衰老、免疫调节和伤口愈合等药理作用^[62]。Bendjedid 等^[59]通过测定羟基自由基的消除能力实验发现, 芦荟叶提取物表现出强抗氧化活性, 并在体外测定显示光保护活性。Misawa 等^[63]研究了芦荟凝胶提取物 (*Aloe vera* gel extract, AVGE) 对 UVB 诱导的小鼠皮肤光老化的保护作用, 研究发现 AVGE 可降低促炎细胞因子 (IL-1 β 和 TNF- α) 和 MMP-2、3、12 和 13 的过度升高, 改善 UVB 引起的皮肤干燥和皱纹形成, 结果表明 AVGE 通过抗炎和调节 MMP 来防止皮肤光老化。

2.3.3 绿茶 茶为山茶科山茶属植物茶 *Camellia sinensis* O Ktunze [*Thea sinensis* L.]。始载于《神农本草经》。绿茶是未经发酵的茶, 保留了许多天然物质, 具有茶多酚、儿茶素、氨基酸、生物碱等多种活性成分^[64]。目前已发现绿茶具有抗炎、抗氧化衰老、抗菌和皮肤美白等药理作用^[65]。Chaikul 等^[66]研究绿茶在 B16F10 黑色素瘤细胞和 HDF 细胞中的抗皮肤老化活性。研究表明绿茶具有抗皮肤衰老活性, 通过抑制酪氨酸酶和酪氨酸酶相关蛋白-2 活性, 有效减少黑色素的产生。Wang 等^[67]研究了表没食子儿茶素没食子酸 (epigallocatechin gallate, EGCG) 对空气污染 HDF 细胞皮肤老化的作用。结果表明, EGCG 通过调节空气污染 HDF 细胞的 NF- κ B、激活蛋白-1 (activator protein-1, AP-1) 和 MAPK 信号通路来降低 MMP 的产生, 清除 ROS, 保护胶原合成, 有效抑制空气污染诱导的皮肤衰老。

2.3.4 珍珠粉 珍珠为珍珠贝科 (Pteriidae) 动物马氏珍珠贝 *Pteria martensii* (Dunker)、蚌科 (Unionidae) 动物三角帆蚌 *Hyriopsis cumingii* (Lea) 或褶皱冠蚌 *Cristaria plicata* (Leach) 等双壳类动物受刺激形成的珍珠。始载于《开宝本草》, 具有安神定惊、明目消翳、解毒生肌、润肤祛斑的功效。其主要化学成分为碳酸钙。现代药理研究表明, 珍珠粉具有抗氧化、抗炎、美白、延缓皮肤

衰老等作用^[68]。Zhang等^[69]实验研究发现珍珠粉提取物可提高小鼠的过氧化氢酶(catalase, CAT)、谷胱甘肽过氧化物酶(glutathione peroxidase, GSH-Px)和SOD活性,降低MDA水平,并抑制促炎细胞因子(1L-1 β 、1L-6、PEG2、TNF- α 和COX-2)的产生,对紫外线诱导的小鼠具有光老化保护作用。Liu等^[70]研究表明珍珠粉具有美白作用,抑制酪氨酸酶活性,减少体内黑色素生成,是一种公认的美白佳品。

中药活性成分及提取物抗皮肤衰老作用机制见表1^[24,27,32,36,40,44,48,51,54,57,59,61,66,69]。

3 常见抗皮肤衰老中药复方的研究

随着抗皮肤衰老中药研究的不断发展,中药复方也备受重视。中药多以复方的形式应用,与单味中药相比,中药复方具有提高疗效,减少毒副作用等优势。因而中药复方在延缓皮肤衰老上具有广阔的前景。

3.1 小柴胡汤

小柴胡汤出自《伤寒杂病论》,由柴胡、黄芩、人参、半夏、甘草、生姜、大枣组成。王春宇等^[71]建立HDF细胞H₂O₂损伤模型,使用不同浓度(20、50、100 $\mu\text{g}\cdot\text{mL}^{-1}$)小柴胡汤水煎液干预H₂O₂损伤的HDF细胞,结果表明小柴胡汤水煎液干预的细胞活力、SOD活性显著提高,MDA含量和ROS荧光强度显著降低,提示其对

H₂O₂诱导的HDF细胞氧化应激损伤具有明显的保护作用,其机制可能与通过降低NF- κ B通路表达来延缓皮肤衰老。

3.2 四君子汤

四君子汤出自《和剂局方》,是益气补中、健脾益胃的经典名方,主要由人参、白术、茯苓、甘草组成。陈红等^[72]将D-半乳糖所致亚急性衰老大鼠以低、高剂量的四君子汤进行灌胃6周后,测定大鼠肝脏SOD、GSH-Px和MDA含量。结果表明衰老大鼠体内SOD、GSH-Px水平明显提高,显著降低MDA含量,提示四君子汤能增强其抗氧化能力,发挥延缓皮肤衰老作用。

3.3 玉屏风散

玉屏风散出自《究原方》,由防风、黄芪、白术组成,为补益剂,具有益气固表止汗之功效。马卓飞等^[73]建立细胞光老化模型,使用不同浓度的玉屏风散含药血清进行干预,观察细胞衰老情况。结果表明玉屏风散干预后的细胞DNA总体甲基化水平升高,线粒体的破坏减轻,细胞形态也有显著的改善,提示玉屏风散对HDF细胞光老化的保护作用机制可能与调控细胞DNA总体甲基化水平有关。

3.4 地芝丸

地芝丸出自《御药院方》,由生地黄、天冬、枳壳、菊

Table 1 Anti-skin aging mechanism of active ingredient of traditional Chinese medicine and its extracts

Traditional Chinese medicine	Active ingredient	Mechanism of action	Ref.
<i>Ginseng</i>	Saponin, polysaccharide	Scavenging free radicals and improving skin antioxidant enzyme activity; enhance collagen content and reduce skin wrinkles; inhibit melanin production.	[24]
<i>Rhodiola</i>	Salidroside	Eliminate free radicals and improve the activity of endogenous antioxidant enzymes; inhibit lipid peroxidation; protection against ultraviolet radiation.	[27]
<i>Astragalus</i>	Polysaccharide, flavone	Remove oxygen free radicals and improve antioxidant effect; improve the immune function of the body; repair skin barrier effect.	[32]
Liquorice	Glycyrrhizic acid, liquiritin	Inhibit oxidative damage and prevent skin photoaging; regulating immune function.	[36]
<i>Paeoniae Radix Alba</i>	Paeoniflorin	Remove excessive free radicals and improve antioxidant effect; protection against ultraviolet radiation.	[40]
<i>Angelica sinensis</i>	Volatile oil, ferulic acid, polysaccharide	Directly remove free radicals and enhance skin superoxide dismutase; promote skin metabolism, regulate skin immune function, and improve skin microcirculation.	[44]
<i>Polygonum multiflorum</i>	Emodin, chrysophanol	Improve antioxidant capacity and promote collagen synthesis; anti mitochondrial DNA damage; effectively resist UV damage.	[48]
<i>Carcuma longa</i>	Curcumin	Scavenging free radicals, anti-aging; inhibit inflammatory reaction; reduce melanin production.	[51]
<i>Ginkgo leaf</i>	Flavone	Improve antioxidant capacity, inhibit MMP, and reduce wrinkle formation.	[54]
<i>Salvia miltiorrhiza</i>	Tanshinone	With antioxidant activity, it can enhance skin metabolism and promote collagen synthesis.	[57]
<i>Pueraria lobata</i>	Puerarin, isoflavone	Remove free radicals and enhance skin cell metabolism; whitening and anti-inflammatory, inhibiting photoaging.	[61]
<i>Aloe</i>	Polysaccharide, barbaloin	Scavenging free radicals; improve the activity of antioxidant enzymes; enhance the immune function of the body.	[59]
<i>Camellia sinensis</i>	Tea polyphenol, catechin	Remove excessive free radicals and promote collagen synthesis; inhibit melanin production.	[66]
Pearl powder	Pearl powder extract	Resist skin photoaging and inhibit the production of inflammatory factors; reduce melanin production; Promote skin collagen synthesis.	[69]

花组成,具有滋养肺肾二阴的作用。刘晶等^[74]将D-半乳糖致衰老小鼠以不同剂量(6.825、13.65、27.3 g·kg⁻¹)的地芝丸煎液进行灌胃,连续6周。结果显示衰老小鼠的皮肤组织形态明显改善,SOD、水通道蛋白3(aquaporin-3, AQP-3)含量增高,MDA含量降低,角蛋白19(keratin19, K19)表达增加,提示地芝丸可能通过促进AQP3、K19的表达对衰老小鼠起到延缓皮肤衰老的作用。

3.5 金水六君煎

金水六君煎出自《景岳全书》,由当归、熟地黄、陈皮、半夏、茯苓、炙甘草组成。彭圆等^[75]对D-半乳糖所致亚急性衰老小鼠每日按浓度0.70 g·mL⁻¹灌胃等体积的金水六君煎,连续6周。结果表明小鼠皮肤组织中的SOD和羟脯氨酸(hydroxyproline, HYP)明显增高,皮肤增厚,真皮胶原纤维增加,排列紧密,提示金水六君煎具有提高自由基抵御能力,降低氧化应激损伤。

3.6 人参固本丸

人参固本丸由天冬、麦冬、熟地黄、生地黄、人参组成,具有滋阴益气,固本延年之功效。方哲等^[76]将D-半乳糖致衰老小鼠每日以4.5 g·kg⁻¹剂量灌胃人参固本丸水煎液,连续42天。结果表明人参固本丸可增强小鼠体内组织SOD、CAT活力,降低MDA含量,提高抗氧化酶活性,减少脂质过氧化物生成。

3.7 延寿液

延寿液出自《太平圣惠方》枸杞子散,由黄芪、枸杞子组成。刘甜甜等^[77]对臭氧衰老造模的大鼠分别灌胃不同浓度(45、90、180 mg·mL⁻¹)的延寿液,连续45天后,检测大鼠皮肤组织的各生化指标。结果表明显著提高SOD活力,MDA含量降低,转化生长因子- β (transforming growth factor- β , TGF- β)含量升高,MMP-1的表达降低,提示延寿液通过抑制MMP-1表达,调控TGF- β 修复衰老皮肤,维持胶原纤维结构正常。

3.8 四物汤

四物汤最早见于《仙授理伤续断秘方》,由白芍、当归、熟地黄、川芎组成,功用补血活血。西旺等^[78]将20月龄衰老小鼠每日灌胃1次四物汤(给药剂量4.68 g·kg⁻¹),连续30天。结果表明四物汤明显改善衰老小鼠体内代谢紊乱,促进细胞修复,减轻氧化损伤,从而延缓皮肤衰老。

4 抗皮肤衰老中药的应用研究

随着对抗皮肤衰老中药的机制研究和临床实验的开展,抗皮肤衰老中药及其复方的开发日益备受关注。人们也开始开发具有抗衰老活性成分的化妆品来延缓皮肤衰老,中药化妆品具有广阔的发展前景。

4.1 单味中药抗皮肤衰老的临床应用

目前已发现多种中药具有抗皮肤衰老的作用,且

已有研究人员对这些中药进行了延缓皮肤衰老化妆品的初步实验研究和开发。

朱丽平等^[79]对人参抗衰老面膜进行临床功效测试,评价了面膜抗衰老的功效。临床功效测试显示,使用人参抗衰老面膜,能显著提高皮肤角质层的含水量和皮肤弹性,降低TEWL,减少面部皱纹。表明人参抗衰老面膜具有淡化细纹,减少皱纹的功效。张浩等^[80,81]对库拉索芦荟大分子凝胶的保湿和修复功效进行了测定,结果表明库拉索芦荟大分子凝胶在低浓度下能够增加角质形成细胞的AQP和紧密连接蛋白1(zonulaoccludens-1, ZO-1)的表达,并有效促进炎症细胞反向迁移及促进斑马鱼尾再生,说明万绿牌芦荟大分子原液具有保湿和修复作用。陈努菊^[82]研发出了一款红景天保湿抗衰乳,具有调节皮肤新陈代谢,抗老防衰,长久保湿滋润的效果。金佳颖^[83]开发珍珠贝系列化妆品,制备了珍珠保湿乳液、珍珠美白霜及珍珠防晒霜,实验结果显示,美白霜能抑制酪氨酸酶活性,并减少黑色素瘤B16细胞的相对黑色素含量;防晒霜的日光防晒系数(sun protection factors, SPF)均在25以上,能抑制紫外线辐射,抵御光老化。

4.2 中药复方抗皮肤衰老的临床应用

抗皮肤衰老中药复方制剂多为温和安全的补益药,如养颜驻颜口服液,葆青口服液,养颜青蛾丸,七白散等。王明军等^[84]考察养颜驻颜口服液对皮肤衰老的改善作用。研究表明,养颜驻颜口服液能提高裸鼠皮肤中HA、HYP、弹性蛋白、总胶原蛋白及血清HA含量($P < 0.05$ 或 $P < 0.01$),减轻皮肤失水老化、改善皮肤衰老状态。葆青口服液由当归芍药散添加胶原蛋白等辅料而来,当归芍药散具有养血调肝,健脾渗湿的功效。王蒙蒙等^[85]探讨葆青口服液抗皮肤衰老的作用机制,结果表明葆青口服液具有清除自由基、抗氧化及调节免疫作用,还具备良好的雌激素作用,调控下丘脑-垂体-卵巢轴,延缓皮肤衰老。养颜青蛾丸由青蛾丸加减方制成,青蛾丸记载于《太平惠民和剂局方》,具有补肾强腰的功效。Tian等^[86]研究养颜青蛾丸对H₂O₂诱导NHDF过早衰老中衰老表型、 β -连环蛋白及p16^{INK4a}表达的影响,结果表明,养颜青蛾丸可抑制H₂O₂诱导的皮肤细胞衰老,调节氧化应激损伤,上调 β -连环蛋白的表达,并抑制p16^{INK4a}的表达水平。且在临床应用中,养颜青蛾丸能够减轻色素沉着,减少皮肤皱纹,促进面部年轻化^[87]。Liu等^[70]对七白霜的抗黑色素生成作用进行了探讨,七白霜由白莲、白芨、白芷、白术、芍药、茯苓和珍珠粉组成,可下调UVB诱导的B16F10细胞中的上游转录因子ZEB2、 β -连环蛋白和CREB2来消除酪氨酸酶活性和MITF介导的酪氨酸酶表达。结果表

明,其通过抑制促黑素相关转录因子的关键作用来减少UVB诱导的黑色素生成。

5 总结与展望

随着经济水平的提高和人口老龄化的加剧,国内外研究人员就现代医学和中医学方面提出了一系列皮肤衰老机制,在中药抗皮肤衰老研究中取得了一定进展。多种中药含有的皂苷、多糖、黄酮等活性成分通过清除自由基、调节免疫、减少线粒体DNA损伤、提高物质新陈代谢、改善皮肤微循环等作用来延缓皮肤衰老,在临床研究和开发抗皮肤衰老中药和化妆品具有广阔的发展前景。然而目前中药在抗皮肤衰老研究中仍存在许多问题和挑战。第一,由于皮肤衰老是一个多因素共同作用的现象,加之皮肤衰老机制的复杂性,尚未有一种衰老理论可以完全解释皮肤衰老发生的全过程,需要更多的研究去进一步证实。第二,绝大多数中药抗皮肤衰老临床研究与现代医学皮肤衰老机制相关,未能联系中医皮肤衰老机制,导致中药抗皮肤衰老研究缺乏整体性和系统性。第三,现今由于中药复方的配伍关系、组方规律及作用机制的不确定性,针对中药复方的研究相对较少,多强调某一中药的某一活性成分的抗皮肤衰老作用。而中医以整体观念和辨证论治为主要特点,在临床也多以复方配伍应用。对于抗皮肤衰老的中药复方还需进一步研究,同时还可以对中药复方进行拆方研究,通过加减方及调整剂量,明确中药复方中的主要活性物质及配伍规律,提高中药复方的药效水平,为中药创新研究奠定基础。

因此,在今后应以中医基础理论为指导,运用现代医学科学技术,多方面、多层次研究中药抗皮肤衰老机制,进一步证实皮肤衰老的本质,创新抗皮肤衰老研究思路,充分挖掘和发挥中药及其复方在延缓皮肤衰老方面的优势和潜力,推动研发安全、有效的抗衰老中药及化妆品。

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