中国科学: 生命科学 2021 年 第 51 卷 第 8 期: 1148 ~ 1155
SCIENTIA SINICA Vitae lifecn.scichina.com
《中国科学》杂志社 SCIENCE CHINA PRESS
评 述 中国医学科学院&北京协和医学院 北京协和医院(临床医学研究所)成立100周年专辑

中西医结合诊治糖尿病

屈岭, 田国庆*, 朴元林, 吴群励, 赵菲, 尹德海, 孙青, 张倩, 景光婵, 石玥, 史晓虎, 刘伟, 闫斌

中国医学科学院&北京协和医学院, 北京协和医院中医科, 北京 100730
* 联系人, E-mail: gq_tian@126.com

收稿日期: 2021-05-27; 接受日期: 2021-07-16; 网络版发表日期: 2021-08-19

摘要 糖尿病及其慢性并发症严重威胁着人类健康, 给全球带来巨大经济负担. 自20世纪70年代以来众多研究者采用中西医结合的方法对糖尿病及其并发症进行了研究, 取得了一定的成就, 为证实该领域中医药所发挥的作用提供了客观依据. 本文针对中西医结合诊治糖尿病及其并发症的研究进行了综述.

关键词 中西医结合, 糖尿病, 血瘀证, 糖尿病并发症

糖尿病是常见的慢性疾病, 严重威胁着人类健康, 给全球带来了巨大的经济负担. 据国际糖尿病联盟2019年发布的第九版全球糖尿病地图显示, 目前全球约4.63亿人患有糖尿病, 预计到2045年这一数字将会达到7亿, 全球每年的糖尿病相关医疗开支约为7600亿美元, 约有420万人死于糖尿病或其并发症, 约占全球全死因死亡的11.3%[1]. 中医认为糖尿病属于“消渴”“消瘅”等范畴, 早在《黄帝内经》中就有相关记载. 历经2000余年, 中医各代医家对“消渴病”的认识逐渐成熟和完善. 自20世纪70年代以来, 众多研究者采用中西医结合的方法对糖尿病及其并发症进行了研究, 取得了一定的成就. 本文针对中西医结合诊治糖尿病的研究进行了综述.

1 糖尿病血瘀证的中西医结合研究

消渴与血瘀相关的论述自古有之, 《灵枢·五变篇》中曾记载: “血气逆留, 髓皮充肌, 血脉不行, 转而为热, 热则消肌肤, 故为消瘅”, 提示瘀血可能是导致消瘅的病因. 《金匮要略》曰: “病者如热伏, 烦满, 口干燥而渴, 其脉反而无热, 此为阴伏, 是瘀血也”; 唐容川《血证论》曰: “瘀血在里则口渴, 所以然者, 血与气本不相离, 内有瘀血, 故气不得通, 不能载水津上升, 是以为渴, 名曰血渴, 瘀血去则不渴矣”等记载对瘀血所致烦渴的症状特点进行了描述.

在前人有关消渴与血瘀的论述基础上, 20世纪70年代北京协和医院祝谌予教授[2,3]结合自身临床观察, 发现许多糖尿病患者存在血瘀症状和体征, 1978年正式提出了糖尿病血瘀证的学术思想, 并报道了用活血化瘀法治疗糖尿病的临床病例, 通过对110例糖尿病患者的临床症状和体征进行辨证分型, 发现糖尿病临床虽可分为阴虚、气阴两虚、阴阳两虚、血瘀等不同证型, 但血瘀证可存在于临床各型之中[4], 引起了国内同行的高度重视. 其团队采用中西医结合方法开展糖

引用格式: 屈岭, 田国庆, 朴元林, 等. 中西医结合诊治糖尿病. 中国科学: 生命科学, 2021, 51: 1148–1155
Qu L, Tian G Q, Piao Y L, et al. Diagnosis and treatment of diabetes mellitus with integrated traditional Chinese and western medicine (in Chinese). Sci Sin Vitae, 2021, 51: 1148–1155, doi: 10.1360/SSV-2021-0168

尿病血瘀证的临床研究, 发现糖尿病血瘀证患者存在血液流变学异常, 包括全血黏度、血浆黏度增高, 红细胞变形能力下降, 体外形成血栓的湿重显著增加, 红细胞形态异常比例明显高于正常对照人群, 下肢痛及足痛患者小腿血流量减少, 足病患者减少更为显著. 血瘀证患者血浆血栓素B_2(TXB_2)水平升高、6-酮-前列环素$F_{1\alpha}$(6-Keto-$PGF_{1\alpha}$)水平降低, TXB_2/6-Keto-$PGF_{1\alpha}$升高, 红细胞超氧化物歧化酶(RBC-SOD)、血清丙二醛(MDA)、Na^+-K^+-ATP酶、Ca^{2+}-Mg^{2+}-ATP酶活性下降[5~11]. 进一步研究发现, 益气养阴活血方(由生黄芪、生地、苍术、元参、丹参、葛根、广木香、当归、益母草、赤芍、川芎组成), 能够减轻气阴两虚血瘀型糖尿病患者的临床血瘀征象, 调节血糖、血脂代谢, 改善全血黏度、血浆黏度、红细胞聚集、红细胞变形能力等血液流变学指标[8~12]. 以上研究为糖尿病血瘀证提供了客观依据及治疗方法, 并发现糖尿病患者在临床血瘀证出现之前就有血液流变学异常, 提出血瘀证可能贯穿于糖尿病的始终, 要尽早应用活血化瘀药物以“未病先防、既病防变”的治疗思路.

在此理论的影响下, 国内先后开展了应用清热活血、益气养阴活血、化痰活血等方法治疗糖尿病及其慢性并发症的中西医结合研究. 郭赛珊等人[9,10]通过随机对照临床试验观察到益气养阴活血方不仅能改善气阴两虚血瘀型2型糖尿病患者的临床症状, 而且可以降低空腹血糖及餐后2小时血糖, 优于安慰剂组(P<0.05), 后续研究发现该方还可部分延缓或逆转糖尿病前期患者转化为糖尿病[13]. 陈宽生等人[14]发现清热活血法可有效改善2型糖尿病患者症状; 应用益气养阴活血法治疗2型糖尿病, 能够显著减轻患者临床症状, 改善血糖、血脂以及全血黏度、红细胞聚集指数等反映血液流变学的指标[15]; 利用化痰活血法可明显降低肥胖型2型糖尿病患者空腹及餐后2小时血糖、糖化血红蛋白、胰岛素抵抗指数, 增高胰岛素敏感性, 降低全血黏度及纤维蛋白原[16]. 杨明会等人[17]选择气虚血瘀证的老年2型糖尿病患者60例, 随机分为两组, 单纯西药对照组30例, 进行常规基础治疗, 试验组30例, 在常规降糖西药治疗的基础上加用保元活血颗粒, 共治疗2个月, 发现试验组总有效率为90%; 对照组总有效率为50%; 两组总有效率比较差异有显著性(P<0.01).

2　糖尿病治疗的中西医结合研究

中医药治疗糖尿病历史悠久, 但是疗效方面多关注于多饮、多尿、多食、消瘦等症状改善情况. 通过中西医结合临床随机对照研究, 采用空腹及餐后血糖、糖化血红蛋白、胰岛素水平、血糖达标率等客观指标逐步为中药治疗糖尿病及糖尿病前期提供客观证据. 倪青等人[18]将糖尿病前期患者116例, 按2:1比例分为中药组、对照组, 两组患者均予适当控制饮食、健康教育、运动等一般治疗, 中药组在此基础上口服芪药消渴胶囊, 发现两组患者空腹血糖(fasting blood glucose, FBG)、餐后血糖(postprandial blood glucos, PBG)、糖化血红蛋白(HbAlc)治疗后均较治疗前下降(P<0.05, P<0.0l), 但两组间比较差异无统计学意义. 中药组2 h胰岛素较治疗前下降, 与对照组比较差异有统计学意义(P<0.05), 疗程结束及随访中药组复常率优于对照组(P<0.05). 张学红等人[19]将172例患者随机分为治疗组和对照组. 治疗组口服消糖平胶囊, 每次3粒, 每日3次, 二甲双胍每次0.25g, 每日2次; 对照组服用同等剂量的二甲双胍, 治疗后两组FBG, 2hPBG, HbAlc均降低(P<0.05或P<0.01), 且两组治疗后组间比较, 治疗组明显低于对照组(P<0.05).

近年来一些多中心随机对照试验(randomized controlled trial, RCT)为中药治疗糖尿病提供了高质量循证医学证据. 在5个中心对400名糖尿病患者进行为期12个月的治疗, 之后又再进行了12个月的随访, 与安慰剂组相比, 金芪降糖片组从糖尿病前期转变为糖尿病的风险低0.58倍(HR(95%CI): 0.58(0.384, 0.876), P=0.010). ITT分析显示, 金芪降糖片组完成治疗后的糖尿病发生率为16.5%, 而对照组为28.9%. 金芪降糖片组在接受12个月干预后血糖正常的患者百分比为41.8%, 而对照组为27.8%. 提示金芪降糖片可能是预防性治疗2型糖尿病的有效干预措施[20]. 另一篇为期12周80名受试者参与的RCT研究表明中药乌梅丸在降低空腹和餐后血糖水平及HbA1c方面无显著差异[21]. 一项多中心、随机双盲、平行对照临床研究发现96例稳定服用二甲双胍血糖仍不达标的2型糖尿病患者联合应用津力达颗粒使用2周后可使HbA1c降低0.92% (安慰剂组HbA1c降低0.53%), 并能改善胰岛素抵抗, 提高胰岛素敏感性及β细胞功能指数[22]. 480例初发2型糖尿病患者的多中心、随机双盲、安慰剂平行对照

临床研究发现糖敏灵丸干预12周后，HbA1c可降低1.03%，并能降低患者体重、身体质量指数(body mass index, BMI)及腰围[23]. 桑枝总生物碱片IIIa期临床试验是与西药(阿卡波糖)头对头比较的随机双盲研究，由北京协和医院梁晓春牵头，中国23家临床机构共同参与完成，共入组病例600例(桑枝总生物碱组360例，拜唐苹240例)，研究结果显示桑枝总生物碱可降低糖化血红蛋白0.93%，糖化血红蛋白达标为47.7%，与西药对照药相当，但胃肠不良反应减少近1/2[24].

3 糖尿病慢性并发症的中西医结合研究

糖尿病周围神经病变(diabetic peripheral neuropathy, DPN)是糖尿病常见并发症之一，属于中医消渴病兼证范畴，但目前尚缺乏有效的改善手段. 梁晓春课题组[25]于20世纪90年代即提出DPN的核心病机是“肾虚血瘀、筋脉痹阻”，可采用补肾活血温经法治疗DPN的学术观点. 通过对192例2型糖尿病患者测定交感神经皮肤反应(sympathetic skin response, SSR)及传导速度分布(conduction velocity distribution, CVD)范围，在国内率先发现血瘀与阳虚等证候与CVD，SSR等电生理指标具有相关性，随病程延长血瘀证、阳虚证积分均显著增高. 临床实验证实，补肾活血温经中药可以改善DPN患者神经电生理指标，改善周围运动神经波幅、尺神经的运动神经传导速度，增加SSR波幅，改善麻木、怕凉、无力、疼痛等肢体症状，改善DPN患者红细胞山梨醇浓度、醛糖还原酶(AR)活性及Na^+-K^+-ATP酶活性；而且对于患者的肝肾功、血常规等无影响，服药期间无明确不良反应[26,27]. 实验研究发现，补肾活血温经中药能够改善糖尿病大鼠行为学异常，改善链脲佐菌素诱导的糖尿病大鼠(STZ-DM)的痛阈值，增快STZ-DM大鼠坐骨神经传导速度，进一步行光镜检查可见坐骨神经超微结构的改善. 同时改善糖尿病大鼠近端胃排空异常，减轻糖尿病大鼠胃自主神经病变. 本课题组对补肾温经活血法治疗DPN的机制也进行了进一步研究，从整体、细胞及分子水平上研究了补肾活血温经法对多元醇通路、糖基化终产物(AGEs)、神经营养因子、氧化应激、自噬及神经修复再生功能的影响，证实了“补肾活血温经法”可通过上述途径对DPN起到治疗作用[28~31]. 另有研究者对益气活血、通络止痛中药木丹颗粒治疗DPN的研究综述，发现该药亦对神经传导速度、神经形态学、代谢及氧化应激等方面具有影响[32]. 此外，有研究者发现复方芎芍胶囊对糖尿病大鼠体重或血糖水平无明显影响，但可显著改善机械性痛觉过敏、热痛觉过敏和神经传导速度，保持髓磷脂和轴突结构的完整性，这些作用可能与下调坐骨神经组织中凋亡相关蛋白的表达，降低AGEs和一氧化氮合成酶(NOS)水平，并增强血清中的抗氧化酶SOD活性有关[33].

2型糖尿病患者轻度认知功能障碍(高达60%)和痴呆(50%~100%)发生率显著升高[34]. 然而目前糖尿病相关认知功能障碍发病机制尚未完全阐明. 近年来研究提示氧化应激、神经炎症反应、下丘脑-垂体-肾上腺皮质轴功能亢进、Aβ沉积和tau蛋白过度磷酸化、内质网应激、自噬、血脑屏障通透性增加、神经元凋亡等多种病理过程参与其中，临床缺乏有效的治疗药物. 糖尿病相关认知障碍属于中医消渴病兼证范畴. 古人散在描述消渴呆病多从“肾虚、肝郁、痰”等方面论治. 现代研究者主要围绕毒、瘀、脾阴虚、心等方面展开系列研究[35~37]. 临床研究证实脑复聪能有效改善辨证分型证属脾肾亏虚、痰浊血瘀的轻度认知功能障碍患者的认知功能[38]. 实验研究表明补肾活血方、脑复聪方可以改善缺血再灌注脑损伤小鼠学习记忆功能，减轻海马神经细胞凋亡[39~43]；抑制体外培养的海马神经元及神经胶质细胞经炎症反应、内质网应激、海马神经元凋亡等途径对糖尿病相关认知功能障碍起到治疗作用[44~46]. 石杉碱A是一种从中草药青苔石杉石楠中提取的生物碱，是一种特异性可逆的乙酰胆碱酯酶抑制剂，其能改善高脂诱导肥胖小鼠的物体识别能力和空间记忆，上调皮质中的胰岛素和磷酸化的Akt水平，降低了皮质β-分泌酶(BACE1)的表达[47]. 黄芪多糖可降低STZ诱导的糖尿病大鼠的空腹血浆葡萄糖水平和体重，改善认知能力，减少海马CA1区的死细胞数量，上调了CREB，NMDA和CaMK Ⅱ的磷酸化水平[48].

糖尿病肾病(diabetic kidney disease, DKD)在中医学中属于消渴肾病范畴. 梁晓春课题组通过基础研究证实中药复方菟箭合剂可以显著降低单肾切除DKD模型鼠尿蛋白排泄量，减轻肾小球肥大和肾小球细胞外基质增多的病理变化，抑制肾小球系膜细胞表型转化，抑制肾脏TGF-β1的表达[49]，抑制肾皮质蛋白激酶C途径的激活[50]. 体外实验证实菟箭合剂含药血清可

以抑制高糖环境培养的肾小球系膜细胞Akt(Thr308)的激活，提高Akt抑制物PTEN的活性[51]. 由于临床上DKD特征性表现为持续蛋白尿, 而在治疗DKD大量蛋白尿时黄芪是最为常用的中药，且有大量的研究证实黄芪及其提取物可具有抑制DKD时肾脏的氧化应激、Akt激活和NF-κB激活的作用, 对DKD有很好的治疗效果[52]. 尹德海课题组[53,54]研究证实黄芪菟箭合剂不仅能显著降低尿白蛋白排出率，还观察到能改善糖尿病大鼠的肾脏的病理改变，保护足细胞结构完整、减少足细胞足突分离，具有肾小球足细胞保护作用, 机制可能与该药抑制PI3K/AKT通路及其相关的炎症反应有关. 体外细胞培养实验也证实, 黄芪菟箭合剂含药血清可抑制高糖培养下的系膜细胞增殖活性增加, 降低细胞内COLIV，FN以及炎症因子的表达；可能与含药血清激活PTEN、抑制PI3K/AKT通路有关[55]. 黄葵胶囊已被中国国家食品药品监督管理局批准用于治疗肾脏疾病. 多项随机对照试验的报道该药能使糖尿病肾病患者的蛋白尿显著降低，其机制可能是通过减少TGF-α, TGF-β1表达和干预p38MAPK信号通路来改善肾脏的肾脏炎症损伤以及抑制ROS-ERK1/2-NLRP3炎性小体[56]. 杜仲可上调核因子红系2相关因子2的表达，下调AGE受体的表达，即通过抑制AGEs的形成和RAGE的表达以及通过Glo1和Nrf2途径降低氧化应激, 可改善糖尿病小鼠的肾脏损害[57]. 雷公藤及其提取物可减少尿蛋白并保护肾脏功能，它的药理机制涉及抗发炎、抗氧化、抗肾小球硬化和抗纤维化，这是通过平衡Th1/Th2细胞，调节巨噬细胞浸润，调节p38 MAPK, NF-κB, TGF-β, Wnt/β-catenin, Akt, Notch1, 上调自噬和下调β-arrestin-1以及通过GSK3β依赖性机制增强肾小球足细胞中环孢素A的细胞骨架稳定活性等途径来实现[58~60].

4　总结与展望

1976年，北京协和医院在全国率先成立了中西医结合治疗糖尿病专科门诊，特请中华医学会糖尿病学分会创办人、第一届主任委员池芝盛教授和名老中医祝谌予教授共同出诊，开启了中西医结合诊治糖尿病的新模式. 采用中西医结合的思想和方法研究中医药诊治糖尿病及其慢性并发症自20世纪70年代以来持续至今, 研究设计日趋成熟完善, 研究成果逐步为世界所接受, 为挖掘中医药宝库提供了崭新的途径.

然而，当前仍有多数实验研究仅限于应用现代医学的指标验证中医药的作用靶点，在机制探索方面尚缺乏创新性. 目前降糖中药(或有效成分、或单体)的筛选模型常常局限于现有西药已知的治疗途径，反而一些常用西药降糖药物的发现却源自某些草药和植物. 例如, 二甲双胍的发现与山羊豆(*Galega officinalis*)这种传统草药有关[61]，钠-葡萄糖共转运蛋白-2抑制剂被法国化学家Petersen　C偶然在苹果树的树皮中发现[62]. 中医药的宝库值得深入挖掘，今后对于已被临床研究证实的确实有效的中药方药(或单有效成分、或单体)的机理研究过程中应通过中西医结合的思想和方法，大胆尝试探索糖尿病新的治疗靶点和新的机制途径.

此外，糖尿病及其并发症方面临床研究虽然已开展众多多中心RCT研究，但研究多以实验室指标等替代结局为主要疗效评价标准，研究周期相对较短，尤其是糖尿病慢性并发症方面，经得起循证医学检验的研究结果尚不充分. 因此，今后中西医结合糖尿病及其慢性并发症的临床研究尚需开展以生存率、心脑血管事件、生活质量等患者-重要结局为终点事件的高质量研究.

参考文献

1　Diabetes Atlas E E C. IDF Diabetes Atlas Nineth Edition 2019. 8 ed. 2019

2　Zhu S Y. A case report on the treatment of diabetes with the method of promoting blood circulation and removing blood stasis (in Chinese). J New Med, 1978, 5: 8–9 [祝谌予. 用活血化瘀法为主治疗糖尿病病例报告. 新医药学杂志, 1978, 5: 8–9]

3　Zhu S Y. Treatment of diabetes with Jiangtanghuoxue decoction (in Chinese). Beijing Trad Chin Med, 1989, 4: 3–4 [祝谌予. 降糖活血方治疗糖尿病. 北京中医, 1989, 4: 3–4]

4　Zhu S Y, Guo S S, Liang X C. Discussion on diabetes TCM syndrome differentiation indicators and treatment prescriptions (in Chinese). Shanghai J Trad Chin Med, 1982, 6: 5–6 [祝谌予, 郭赛珊, 梁晓春. 对糖尿病中医辨证指标及施治方药的探讨. 上海中医药杂志, 1982, 6: 5–6]

5 Zhu S Y, Guo S S, Liang X C, et al. Hemorheology of diabetic patients and observation of changes before and after treatment with integrated traditional Chinese and western medicine (in Chinese). J Integrated Trad Chin Western Med, 1983, 3: 143–145 [祝谌予, 郭赛珊, 梁晓春, 等. 糖尿病患者的血液流变性及中西医结合治疗前后变化的观察. 中西医结合杂志, 1983, 3: 143–145]
6 Guo S S, Liang X C, Zhu S Y. Observation of red blood cell filterability in diabetic patients (in Chinese). Shanxi Med J, 1988, 5: 336 [郭赛珊, 梁晓春, 祝谌予. 糖尿病患者红细胞可滤过性观察. 山西医药杂志, 1988, 5: 336]
7 Guo S S, Liang X C, Yin F H, et al. Measurement of calf blood flow in diabetic patients and observation of the effect of activating blood circulation and removing blood stasis treatment on it (in Chinese). J Integrated Trad Chin Western Med, 1990, 11: 644, 664–666 [郭赛珊, 梁晓春, 殷凤华, 等. 糖尿病患者小腿血流量测定及活血化瘀法治疗对其影响的观察. 中西医结合杂志, 1990, 11: 644, 664–666]
8 Liang X C, Guo S S, Wang X D, et al. The relationship between plasma TXB2, 6-Keto-PGF1α levels, whole blood viscosity and blood stasis syndrome and microangiopathy in diabetic patients (in Chinese). J Integrated Trad Chin Western Med, 1992, 5: 297–298 [梁晓春, 郭赛珊, 王香定, 等. 糖尿病患者血浆TXB2、6-Keto-PGF1α水平、全血黏度与血瘀证及微血管病的关系. 中国中西医结合杂志, 1992, 5: 297–298]
9 Guo S S, Liang X C, Zhu S Y, et al. Effect of Yiqi Yangyin Huoxue recipe on *in vitro* thrombosis test in patients with diabetic blood stasis syndrome (in Chinese). Res Med, 1989, 3: 37–38 [郭赛珊, 梁晓春, 祝谌予, 等. 益气养阴活血方对糖尿病血瘀证病人体外血栓形成试验的影响. 中医药研究, 1989, 3: 37–38]
10 Guo S S, Liang X C, Hong G, et al. Treatment of tongue quality and whole blood viscosity changes in diabetic patients with Yiqi Yangyin Huoxue decoction (in Chinese). Chin J Trad Chin Med, 1989, 2: 33–34 [郭赛珊, 梁晓春, 洪光, 等. 益气养阴活血方治疗糖尿病人的舌质及全血黏度的变化. 中医杂志, 1989, 2: 33–34]
11 Guo S S, Liang X C, Wang X D, et al. Clinical observation on 60 cases of diabetes with deficiency of Qi and Yin treated by Jiangtang Chinese pills (in Chinese). J Integrated Trad Chin Western Med, 1993, 5: 294–295 [郭赛珊, 梁晓春, 王香定, 等. 降糖中药片治疗气阴两虚型糖尿病60例临床观察. 中国中西医结合杂志, 1993, 5: 294–295]
12 Liang X C, Guo S S, Yang J X, et al. Effects of Chinese medicine for lowering blood sugar on RBC-SOD, MDA, Ins, AchE in diabetic patients with deficiency of both Qi and Yin (in Chinese). Chin J Trad Chin Med, 1994, 7: 388, 414–415 [梁晓春, 郭赛珊, 杨静霞, 等. 降糖中药片对气阴两虚型糖尿病患者RBC-SOD、MDA、Ins、AchE的影响. 中医杂志, 1994, 7: 388, 414–415]
13 Li H P, Liang X C, Tian G Q, et al. Study on the effect of traditional Chinese medicine Yiqi Shengjin Huoxue Capsule on the outcome of prediabetes patients (in Chinese). Beijing Trad Chin Med, 2013, 32: 49–51 [李化萍, 梁晓春, 田国庆, 等. 中药益气生津活血胶囊对糖尿病前期患者转归影响的研究. 北京中医药, 2013, 32: 49–51]
14 Chen K S. Observation on the effect of clearing heat and promoting blood circulation on type 2 diabetes (in Chinese). Guidelines Chin Med, 2013, 11: 592–593 [陈宽生. 清热活血法治疗2型糖尿病的疗效观察. 中国医药指南, 2013, 11: 592–593]
15 Zhang Z L, Li H L, Dong Y M, et al. Observation on the effect of Huoxue Jiangtang decoction on the metabolism and hemorheology of type 2 diabetes (in Chinese). Chin J Basic Med Trad Chin Med, 2004, 7: 70–71 [张志玲, 李惠林, 董彦敏, 等. 活血降糖饮对2型糖尿病代谢及血液流变学的疗效观察. 中国中医基础医学杂志, 2004, 7: 70–71]
16 Feng J H, Xu Y S. Clinical study on the treatment of 30 cases of type 2 diabetes with the method of removing phlegm and promoting blood circulation (in Chinese). Chin J Trad Chin Med, 2004, 3: 191–194 [冯建华, 徐云生. 化痰活血法治疗2型糖尿病30例临床研究. 中医杂志, 2004, 3: 191–194]
17 Yang M H, Lu J Z, Dou Y Q, et al. Clinical observation on treatment of 30 cases of senile type 2 diabetes with Qi deficiency and blood stasis syndrome with Baoyuan Huoxue granules (in Chinese). J Trad Chin Med, 2005, 46: 751–752 [杨明会, 路军章, 窦永起, 等. 保元活血颗粒治疗老年2型糖尿病气虚血瘀证30例临床观察. 中医杂志, 2005, 46: 751–752]
18 Ni Q, Zhang X K, Cui N. Clinical observation of Qi Yao Xiaoke capsule intervention in 76 cases of type 2 diabetes patients (in Chinese). J Integrated Trad Chin Western Med, 2012, 32: 1628–1631 [倪青, 张效科, 崔娜. 芪药消渴胶囊干预2型糖尿病前期患者76例的临床观察. 中国中西医结合杂志, 2012, 32: 1628–1631]
19 Zhang X H, Chang F Y, Zhang B R, et al. Clinical observation of Xiaotangping capsule in the treatment of 109 patients with type 2 diabetes and insulin resistance (in Chinese). Chin J Trad Chin Med, 2007, 48: 812–813 [张学红, 常风云, 张炳冉, 等. 消糖平胶囊治疗2型糖尿病胰岛素抵抗患者109例临床观察. 中医杂志, 2007, 48: 812–813]
20 Wang H, Guo L, Shang H, et al. JinqiJiangtang tablets for pre-diabetes: a randomized, double-blind and placebo-controlled clinical trial. Sci Rep, 2017, 7: 11190
21 Tu X, Xie C G, Wang F, et al. *Fructus Mume* formula in the treatment of type 2 diabetes mellitus: a randomized controlled pilot trial. Evidence-

Based Comple Alternat Med, 2013, 2013: 1–8
22 Lian F, Tian J, Chen X, et al. The efficacy and safety of Chinese herbal medicine Jinlida as add-on medication in type 2 diabetes patients ineffectively managed by metformin monotherapy: a double-blind, randomized, placebo-controlled, multicenter trial. PLoS ONE, 2015, 10: e0130550
23 Tong X L, Wu S T, Lian F M, et al. The safety and effectiveness of TM81, a Chinese herbal medicine, in the treatment of type 2 diabetes: a randomized double-blind placebo-controlled trial. Diabetes Obes Metab, 2013, 15: 448–454
24 Qu L, Liang X, Tian G, et al. Efficacy and safety of mulberry twig alkaloids tablet for the treatment of type 2 diabetes: a multicenter, randomized, double-blind, double-dummy, and parallel controlled clinical trial. Dia Care, 2021, 44: 1324–1333
25 Wu Q L, Liang X C, Jiang N, et al. Sympathetic nerve skin reaction in patients with type 2 diabetes and research on TCM syndromes (in Chinese). J Integrated Trad Chin Western Med Emergency Med, 2008, 1: 24–27 [吴群励, 梁晓春, 姜楠, 等. 2型糖尿病患者交感神经皮肤反应检测及中医证候研究. 中国中西医结合急救杂志, 2008, 1: 24–27]
26 Sun L Q, Liang X Q, Jiang N, et al. The relationship between TCM syndrome characteristics and nerve conduction velocity in 172 patients with diabetic peripheral neuropathy (in Chinese). Chin Rehabilit Theory Practice, 2008, 2: 166–168 [孙连庆, 梁晓春, 姜楠, 等. 172例糖尿病周围神经病变患者中医证候特点与神经传导速度的关系. 中国康复理论与实践, 2008, 2: 166–168]
27 Liang X C, Cui L Y, Guo S S, et al. Clinical observation of Jinmaitong in the treatment of diabetic peripheral neuropathy (in Chinese). J Integrated Trad Chin Western Med, 1999, 9: 517–519 [梁晓春, 崔丽英, 郭赛珊, 等. 筋脉通治疗糖尿病周围神经病变的临床观察. 中国中西医结合杂志, 1999, 9: 517–519]
28 Xie J, Song W, Liang X, et al. Jinmaitong ameliorates diabetic peripheral neuropathy in streptozotocin-induced diabetic rats by modulating gut microbiota and neuregulin 1. Aging, 2020, 12: 17436–17458
29 Sun Q, Wang C, Yan B, et al. Jinmaitong ameliorates diabetic peripheral neuropathy through suppressing TXNIP/NLRP3 inflammasome activation in the streptozotocin-induced diabetic rat model. Diabetes Metab Syndr Obes, 2019, 12: 2145–2155
30 Song W, Jiang W, Wang C, et al. Jinmaitong, a traditional Chinese compound prescription, ameliorates the streptozocin-induced diabetic peripheral neuropathy rats by increasing sciatic nerve IGF-1 and IGF-1R expression. Front Pharmacol, 2019, 10: 255
31 Wu Y N, Liang X C, Yang D, et al. Effects of Chinese medicinal compound jinmaitong on the expression of nitrotyrosine and nerve growth factor in the dorsal root ganglia of diabetic rats. Acta Acad Med Sin, 2016, 38: 507–513
32 Qi Y, Leng J H. Research progress in the mechanism of Mudan granule on painful diabetic peripheral neuropathy (in Chinese). J Difficult Diseases, 2020, 19: 473–476 [齐月, 冷锦红. 木丹颗粒对痛性糖尿病周围神经病变的作用机制研究进展. 疑难病杂志, 2020, 19: 473–476]
33 Yu M X, Lei B, Song X, et al. Compound XiongShao Capsule ameliorates streptozotocin-induced diabetic peripheral neuropathy in rats via inhibiting apoptosis, oxidative-nitrosative stress and advanced glycation end products. J Ethnopharmacol, 2021, 268: 113560
34 Rawlings A M, Sharrett A R, Albert M S, et al. The association of late-life diabetes status and hyperglycemia with incident mild cognitive impairment and dementia: the ARIC study. Dia Care, 2019, 42: 1248–1254
35 Su D L, Song F Y, He Y X. Jiangtang Jiedu capsules in treating 60 cases of type 2 diabetes (in Chinese). J Trad Chin Med, 1996, 1: 23–25 [粟德林, 宋福印, 何玉信. 降糖解毒胶囊治疗2型糖尿病60例. 中医药学报, 1996, 1: 23–25]
36 Song F Y, Wang Y Y, Huang Q Y. Discussion on brain damage caused by poison and diabetic encephalopathy (in Chinese). J Beijing Univ Trad Chin Med, 2000, 23: 7–9 [宋福印, 王永炎, 黄启福. 试论毒损脑络与糖尿病性脑病. 北京中医药大学学报, 2000, 23: 7–9]
37 Yue R S, Zhang F R, Gong G M. A new perspective on the understanding of diabetic cognitive dysfunction in TCM-“pancreas (spleen)-brain-kidney axis” establishment of the pathogenesis theory of diabetic disease (in Chinese). Sichuan Trad Chin Med, 2009, 27: 28–29 [岳仁宋, 张发荣, 龚光明. 糖尿病性认知功能障碍中医认识新视角-“胰(脾)-脑-肾轴”消渴病呆病病机学说的建立. 四川中医, 2009, 27: 28–29]
38 Cui Y Z, Li F R, Zhang M R. Clinical observation on 16 cases of patients with mild cognitive dysfunction of kidney deficiency and blood stasis treated by Naofucong Decoction (in Chinese). J Trad Chin Med, 2016, 56: 1577–1579 [崔雅忠, 李伏容, 张孟仁. 脑复聪方治疗肾虚血瘀型轻度认知功能障碍患者16例临床观察. 中医杂志, 2016, 56: 1577–1579]
39 Tian G Q, Lu H Q, Guo S S, et al. Effect of Bushen Huoxue Recipe on learning and memory function and central neurotransmitter in diabetic mice (in Chinese). Chin J Trad Chin Med, 2009, 50: 460–462 [田国庆, 卢贺起, 郭赛珊, 等. 补肾活血方对糖尿病小鼠学习记忆功能及中枢神经递质的影响. 中医杂志, 2009, 50: 460–462]
40 Tian G Q, Guo S S, Lu H Q, et al. Effects of Bushen Huoxue Recipe on learning and memory function and hippocampal neuronal apoptosis in mice with ischemia-reperfusion brain injury (in Chinese). J Integrated Trad Chin Western Med, 2003, 23: 123–127 [田国庆, 郭赛珊, 卢贺起, 等.

补肾活血方对缺血再灌注脑损伤小鼠学习记忆功能及海马神经细胞凋亡的影响. 中国中西医结合杂志, 2003, 23: 123–127]

41 Guo S S, Zhang M R, Zuo P P, et al. Effects of Bushen Huoxue Recipe on intelligence and cholinergic system of cerebral cortex in mice with cerebral ischemia (in Chinese). J Integrated Trad Chin Western Med (Special Ed Basic Theory Res), 2001, 21: 42–44 [郭赛珊, 张孟仁, 左萍萍, 等. 补肾活血方对脑缺血小鼠智能及大脑皮层胆碱能系统的影响. 中国中西医结合杂志(基础理论研究特辑), 2001, 21: 42–44]

42 Zhang M R, Guo S S, Xu H Y, et al. The effect of Naofucong on SOD and GSH-PX in the brain of mice with cerebral ischemia (in Chinese). Chin J Preventive Med, 2004, 5: 324–326 [张孟仁, 郭赛珊, 徐慧媛, 等. 脑复聪对脑缺血小鼠脑内SOD和GSH-PX的影响. 中国预防医学杂志, 2004, 5: 324–326]

43 Zhang M, Jing G C, Zhang M R. The effect of Naofucong on cognitive function, hippocampal NF-κB and astrocytes in STZ-DM rats (in Chinese). Chin J Trad Chin Med, 2014, 32: 1991–1994 [张梅, 景光婵, 张孟仁. 脑复聪对STZ-DM大鼠认知功能及海马NF-κB、星型胶质细胞的影响. 中华中医药学刊, 2014, 32: 1991–1994]

44 Tian G, Lu H, Guo S, et al. Effects of Bushen Huoxue formula on the learning and memory function and the cerebral neurotransmitters in diabetic mice. J Trad Chin Med, 2010, 30: 201–205

45 Jing G C, Zhang M R, Ji C, et al. Effect of Chinese herbal compound Naofucong on the inflammatory process induced by high glucose in BV-2 cells. Chin J Integr Med, 2016, 22: 832–839

46 Jing G C, Liu D, Liu Y Q, et al. Nao-Fu-Cong ameliorates diabetic cognitive dysfunction by inhibition of JNK/CHOP/Bcl2-mediated apoptosis *in vivo* and *in vitro*. Chin J Nat Meds, 2020, 18: 704–713

47 Wang H Y, Wu M, Diao J L, et al. Huperzine A ameliorates obesity-related cognitive performance impairments involving neuronal insulin signaling pathway in mice. Acta Pharmacol Sin, 2020, 41: 145–153

48 Zhang G, Fang H, Li Y, et al. Neuroprotective effect of astragalus polysacharin on streptozotocin (STZ)-induced diabetic rats. Med Sci Monit, 2019, 25: 135–141

49 Yin D H, Liang X C, Zheng F L, et al. Phenotype transformation of glomerular mesangial cells in diabetic rats and the effect of Tujian mixture (in Chinese). J Integrated Trad Chin Western Med, 2003, 23: 772–776 [尹德海, 梁晓春, 郑法雷, 等. 糖尿病大鼠肾小球系膜细胞表型转化及菟箭合剂的作用. 中国中西医结合杂志, 2003, 23: 772–776]

50 Piao Y L, Liang X C, Yang N, et al. Study on the effect of Tujian mixture on protein kinase C activity in kidney tissue of diabetic rats (in Chinese). Chin J Chin Mater Med, 2004, 29: 7685–7689 [朴元林, 梁晓春, 杨楠, 等. 菟箭合剂对糖尿病大鼠肾组织蛋白激酶C活性作用的研究. 中国中药杂志, 2004, 29: 7685–7689]

51 Yin D H, Liang X C, Zhang H, et al. The effect of Tujian mixture containing serum on the phosphorylation of Akt and PTEN in glomerular mesangial cells cultured under high glucose conditions (in Chinese). Chin J Inf Trad Chin Med, 2010, 17: 31–32 [尹德海, 梁晓春, 张宏, 等. 菟箭合剂含药血清对高糖条件培养的肾小球系膜细胞磷酸化Akt和PTEN的作用. 中国中医药信息杂志, 2010, 17: 31–32]

52 Sun L I, Li W, Li W, et al. Astragaloside IV prevents damage to human mesangial cells through the inhibition of the NADPH oxidase/ROS/Akt/NF-κB pathway under high glucose conditions. Int J Mol Med, 2014, 34: 167–176

53 Yang C, Yin D H, Pu Y L, et al. Effect of Huangqi Tujian Mixture on PI3K-Akt-mTOR signaling pathway in the kidney of diabetic rats (in Chinese). J Integrated Trad Chin Western Med Nephropathy, 2016, 17: 862–866 [杨辰, 尹德海, 朴元林, 等. 黄芪菟箭合剂对糖尿病大鼠肾脏PI3K-Akt-mTOR信号通路的影响. 中国中西医结合肾病杂志, 2016, 17: 862–866]

54 Shi X H, Piao Y L, Yin D H, et al. Study on the protective mechanism of Huangqi Tujian mixture on kidney podocytes in diabetic rats (in Chinese). J Med Res, 2019, 48: 62–65 [史晓虎, 朴元林, 尹德海, 等. 黄芪菟箭合剂对糖尿病大鼠肾脏足细胞保护作用机制的研究. 医学研究杂志, 2019, 48: 62–65]

55 Guo C, Shen J C, Pu Y L, et al. The effect of Huangqi Tujian mixture on the proliferation of glomerular mesangial cells in rats with high glucose and its mechanism (in Chinese). Beijing Trad Chin Med, 2020, 39: 910–915 [郭传, 沈佳晨, 朴元林, 等. 黄芪菟箭合剂对高糖状态大鼠肾小球系膜细胞增殖的影响及其机制探讨. 北京中医药, 2020, 39: 910–915]

56 Li N, Tang H, Wu L, et al. Chemical constituents, clinical efficacy and molecular mechanisms of the ethanol extract of *Abelmoschus manihot* flowers in treatment of kidney diseases. Phytother Res, 2021, 35: 198–206

57 Do M H, Hur J, Choi J, et al. Eucommia ulmoides ameliorates glucotoxicity by suppressing advanced glycation end-products in diabetic mice kidney. Nutrients, 2018, 10: 265

58 Huang W J, Liu W J, Xiao Y H, et al. Tripterygium and its extracts for diabetic nephropathy: efficacy and pharmacological mechanisms. Biomed Pharmacother, 2020, 121: 109599

59 Zhang H F, Jin J, Liang S K, et al. Tripterygium glycoside protects diabetic kidney disease mouse serum-induced podocyte injury by upregulating autophagy and downregulating β-arrestin-1. Histol Histopathol. 2019, 34: 943–952
60 Liang X H, Chen B H, Wang P, et al. Triptolide potentiates the cytoskeleton-stabilizing activity of cyclosporine A in glomerular podocytes via a GSK3β dependent mechanism. Am J Transl Res, 2020, 12: 800–812
61 Bailey C J. Metformin: historical overview. Diabetologia, 2017, 60: 1566–1576
62 Payne J N, Badwaik V D, Waghwani H K, et al. Development of dihydrochalcone-functionalized gold nanoparticles for augmented antineoplastic activity. Int J Nanomed, 2018, 13: 1917–1926

Diagnosis and treatment of diabetes mellitus with integrated traditional Chinese and western medicine

QU Ling, TIAN GuoQing, PIAO YuanLin, WU QunLi, ZHAO Fei, YIN DeHai, SUN Qin, ZHANG Qian, JING GuangChan, SHI Yue, SHI XiaoHu, LIU Wei & YAN Bin

Department of Traditional Chinese Medicine, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100730, China

Diabetes and its chronic complications pose a serious threat to human health and impose a huge economic burden on the world. Under the guidance of the Communist Party of China after the founding of China, many scholars have studied diabetes and its complications by integrated traditional Chinese and western medicine since the 1970s, and made certain achievements, providing an objective basis for confirming the role played by traditional Chinese medicine in this field. This article reviews the research on the diagnosis and treatment of diabetes mellitus and its complications by integrated traditional Chinese and western medicine.

integrated traditional Chinese and western medicine, diabetes, blood stasis, diabetic complications

doi: 10.1360/SSV-2021-0168