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基于网络药理学及分子对接技术探讨注射用血塞通(冻干)治疗脑梗死的作用机制

Mechanism of xuesaitong injection (lyophilized) in the treatment of cerebral infarction based on network pharmacology and molecular docking

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摘要:目的 用网络药理学及分子对接技术分析注射用析血塞通(冻干)治疗脑梗死的作用机制。**方法** 通过数据库筛选注射用血塞通(冻干)中5种重要活性成分(人参皂苷Rg1、人参皂苷Rb1、人参皂苷Re、三七皂苷R1、人参皂苷Rd)与急性脑梗死的交集靶点,构建靶点作用网络。用数字音频互联网设备(DAVID)数据库进行基因本体通路(GO)分析及京都基因与基因组百科全书(KEGG)通路富集分析,并进行分子对接验证。**结果** 三七总皂苷共筛选出非重复靶点61个,筛选出脑梗死非重复靶点5 737个,3个数据库的交集靶点共64个。药物作用靶点与疾病作用靶点取交集后获得交集靶点2个,分别为蛋白激酶Cβ(PRKCB)、肿瘤坏死因子(TNF),与疾病非重复靶点取交集后获得交集靶点51个;根据网络拓扑参数以及交集靶点结果,选取胱天蛋白酶3(CASP3)、TNF、核因子KappaB亚基1(NFKB1)、基质金属蛋白酶9(MMP9)、肿瘤蛋白p53(TP53)、PRKCB进行后续分子对接;GO功能富集分析显示,在生物过程方面,靶点基因主要参与基因表达的正向调控、细胞凋亡过程的负调控、miRNA转录的正向调控等条目,在细胞组分方面,靶点基因主要定位于细胞外空间、细胞外区域、血液为例、轴突和蛋白质复合物等区域,在分子功能方面,靶点蛋白主要具有相同蛋白结合、蛋白酶结合、热休克蛋白90(HSP90)蛋白结合等功能,富集结果在统计学上差异均具有统计学意义(均$P<0.05$);KEGG富集分析显示,注射用血塞通(冻干)治疗脑梗死的潜在作用靶点富集于晚期糖基化终产物-晚期糖基化终产物受体(AGE-RAGE)信号通路、脂质与动脉粥样硬化、流体剪切应力与动脉粥样硬化、癌症中的蛋白聚糖、丝裂原活化蛋白激酶(MAPK)信号通路、甲状腺激素信号通路、细胞凋亡通路等信号通路中,富集结果在统计学上差异均具有统计学意义(均$P<0.05$);分子对接显示,注射用血塞通(冻干)的主要活性成分与核心靶点蛋白的结合能力较好,其中人参皂苷Rg1与TNF的结合能最低,CASP3、PRKCB与多种活性成分均表现出较强的结合。**结论** 注射用血塞通(冻干)可能通过调控CASP3、TNF、NFKB1、MMP9、TP53、PRKCB等关键靶点,作用于细胞凋亡、炎症及动脉粥样硬化等通路,从而发挥治疗脑梗死的多靶点综合作用。

关键词:注射用血塞通(冻干);脑梗死;网络药理学;分子对接
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Abstract: Objective To analyze the role mechanism of xuesaitong injection (lyophilized) in the treatment of cerebral infarction by network pharmacology and molecular docking technology. **Methods** The intersection targets of five important active ingredients (Ginsenoside Rg1, Ginsenoside Rb1, Ginsenoside Re, Notoginsenoside R1, Ginsenoside

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Rd) in xuesaitong injection (lyophilized) and acute cerebral infarction were screened by database, and the target action network was constructed. Gene ontology (GO) pathway analysis and Kyoto encyclopedia of genes and genomes (KEGG) pathway enrichment analysis were performed by using digital - audio - video internet devince (DAVID) database, and molecular docking verification was performed. **Results** A total of 61 non - redundant targets were screened for Panax notoginseng saponins, and 5 737 non - redundant targets were identified for cerebral infarction. The intersection of three databases yielded 64 common targets. After intersecting the drug targets with the disease targets, two overlapping targets were obtained: protein kinase C beta (PRKCB) and tumor necrosis factor (TNF). Intersection with the non - redundant disease targets yielded 51 overlapping targets. Based on network topology parameters and the intersection target results, caspase - 3 (CASP3), TNF, nuclear factor kappa B subunit 1 (NFKB1), matrix metalloproteinase - 9 (MMP9), tumor protein p53 (TP53), and PRKCB were selected for subsequent molecular docking. The results of GO functional enrichment analysis showed that in terms of biological processes, the target genes were mainly involved in the positive regulation of gene expression, the negative regulation of apoptosis process, and the positive regulation of miRNA transcription. In terms of cell components, the target genes were mainly located in extracellular space, extracellular region, blood, axon and protein complex. In terms of molecular function, the target proteins mainly had the same protein binding, protease binding, Heat shock protein 90 (HSP90) protein binding and other functions, and the enrichment results were statistically significant (all $P < 0.05$). The results of KEGG enrichment analysis revealed that the potential targets of xuesaitong injection (lyophilized) in the treatment of cerebral infarction were enriched in advanced glycation end products - receptor for advanced glycation end products (AGE - RAGE) signaling pathway, lipid and atherosclerosis, fluid shear stress and atherosclerosis, proteoglycans in cancer, MAPK signaling pathway, thyroid hormone signaling pathway, apoptosis pathway and other signaling pathways, and the enrichment results were statistically significant ($P < 0.05$). The results of molecular docking displayed that the main active ingredients of xuesaitong injection (lyophilized) had good binding ability with the core target protein, among which Ginsenoside Rg1 had the lowest binding energy with TNF, and CASP3, PRKCB showed strong binding with various active ingredients. **Conclusion** Xuesaitong injection (lyophilized) may play a multi - target comprehensive role in the treatment of cerebral infarction by regulating CASP3, TNF, NFKB1, MMP9, TP53, PRKCB and other key targets, acting on pathways such as apoptosis, inflammation and atherosclerosis.

Key words: xuesaitong injection (lyophilized); cerebral infarction; network pharmacology; molecular docking

脑梗死发病机制复杂,涉及炎症反应、氧化应激、细胞凋亡及神经保护机制失衡等多种病理过程[1]。目前,临床上主要采用溶栓、机械取栓等治疗手段,但疗效有限,且存在一定的药物不良反应和再灌注损伤风险。网络药理学通过构建"药物 - 成分 - 靶点 - 疾病"网络来探讨药物干预疾病的整体调控规律,为研究中药多成分、多靶点、多通路的作用机制提供了新的思路[2]。分子对接技术可进一步从分子水平验证活性成分与关键靶点的结合能力,为阐明药物作用机制提供参考[3]。近年来,采用上述方法寻求安全有效的药物干预方案治疗脑梗死的研究越来越多。注射用血塞通(冻干)的主要活性成分为三七总皂苷,具有活血化瘀、改善微循环、抗炎及抗氧化等药理作用[4]。临床研究表明,注射用血塞通(冻干)可改善脑梗死患者的神经功能缺损,但其具体的分子机制尚未阐明[5]。因此,本研究基于网络药理学与分子对接技术,系统分析注射用血塞通(冻干)治疗脑梗死的潜在作用靶点与信号通路,为其临床应用与新药研发提供理论依据。

资料与方法

1 注射用血塞通(冻干)、脑梗死靶点筛选

根据注射用析血塞通(冻干)的药物说明书,其主要成分为三七总皂苷。根据 2025 年药典[6],三七总皂苷中三七皂苷 R1、人参皂苷 Rg1、人参皂苷 Re、人参皂苷 Rb1、人参皂苷 Rd 总量不得低于 77%(供注射用),故本文选取以上 5 种活性成分作为研究对象。

注射用血塞通(冻干)靶点收集 使用中药分子机制生物信息学分析工具(a bioinformatics annotation database for molecular mechanism of traditional chinese medicine, BATMAN - TCM)数据库(http://bionet.ncpsb.org.cn/batman - tcm/#/home)、中药系统药理学数据库与分析平台(traditional chinese

medicine systems pharmacology database and analysis platform, TCMSP)数据库(https://www.tcmsp-e.com/load_intro.php?id=43)、SwissTargetPrediction 数据库(https://www.swisstargetprediction.ch/)检索和预测三七总皂苷的 5 种主要活性成分的作用靶点。BATMAN-TCM 数据库检索步骤:选择“Search”栏,在“Formula (Pinyin name)”中分别填写活性成分名称,“Score cutoff”选择 0.90,其余设置选择默认,提交结果并获取筛选后的靶点。SwissTargetPrediction 数据库检索步骤:在 pubchem 数据库(https://pubchem.ncbi.nlm.nih.gov/)中检索活性成分的简化分子线性输入系统(simplified molecular input line entry system,SMILES)结构式,在 SwissTargetPrediction 数据库中输入 SMILES 获取预测结果。

脑梗死靶点收集 分别在 Genecards(https://www.genecards.org/)、在线人类孟德尔遗传(online mendelian inheritance in man, OMIM)(https://www.omim.org/)、Drugbank(https://go.drugbank.com/)数据库中,检索“cerebral infarction”的靶点。

靶点筛选 收集到的各数据库的靶点上传至韦恩图绘制网(https://bioinfogp.cnb.csic.es/tools/venny/index.html),绘制交集韦恩图,获取交集靶点(包括 3 者相交和两两相交),所得即为药物/疾病作用靶点。将药物作用靶点与疾病作用靶点、疾病非重复靶点分别取交集,获取交集靶点。

2 靶点作用网络构建

用 R 4.3.1 软件绘制活性成分-交集靶点作用网络图。将交集靶点上传至相互作用基因/蛋白质检索工具(search tool for the retrieval of interacting genes/proteins,String)数据库(https://cn.string-db.org/)构建蛋白质相互作用网络,筛选最小交互置信度为 0.9 的非孤立节点,分析网络拓扑参数,筛选分子对接靶点。

3 基因富集分析

将交集靶点上传至用于注释、可视化和综合发现的数据库(the database for annotation, visualization and integrated discovery, DAVID)数据库(https://david-bioinformatics.nih.gov/)进行基因本体通路(gene ontology,GO)分析及京都基因与基因组百科全书(Kyoto encyclopedia of genes and genomes,KEGG)通路富集分析。采用 R 4.3.1 软件对分析结果进行可视化。

4 分子对接

在 PubChem 数据库中检索 5 种活性成分的 SMILES 结构式,采用 Avogadro 软件对 5 种活性成分进行 3D 分子建模。在结构生物信息学研究合作组织蛋白质数据库(research collaboratory for structural bioinformatics protein data bank, RCSB PDB)数据库(https://www.rcsb.org/)检索筛选出的分析对接靶点,并下载 3D 结构的 PDB 文件。将活性成分和分子对接靶点的 3D 分子结构文件上传至在线分子对接网站 CB-Dock2(http://183.56.231.194:8001/cb-dock2/index.php)进行分子对接,选择对接结合能最低(< -7.0 kcal·mol^{-1})的结果,在 Pymol 软件上进行可视化和结果分析。

结 果

1 注射用血塞通(冻干)、脑梗死靶点筛选结果

注射用血塞通(冻干)靶点:BATMAN-TCM 数据库检索出 183 个作用靶点,TCMSP 数据库中检索出三七皂苷 R1 的 1 个作用靶点,SwissTargetPrediction 预测人参皂苷 Rg1 的 100 个作用靶点。因TCMSP、SwissTargetPrediction 数据库无法获取大部分活性化合物

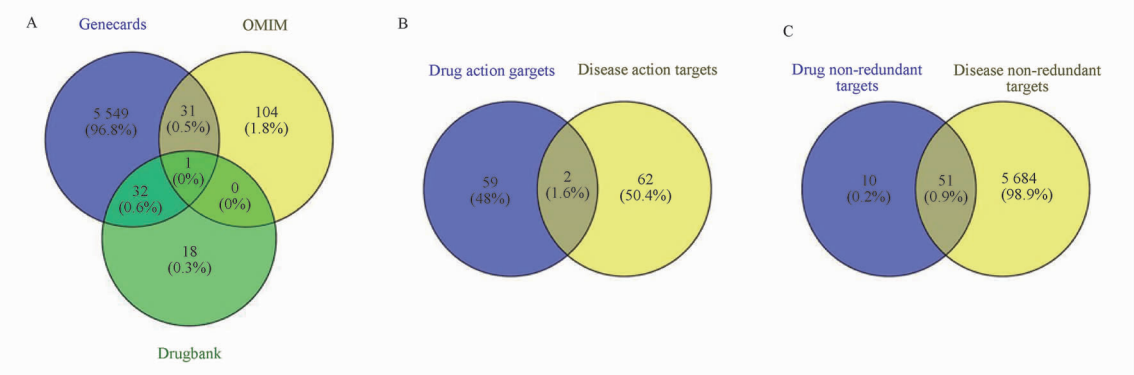

图 1 脑梗死靶点、药物作用靶点与疾病作用靶点的韦恩图

Figure 1 Venn diagram of cerebral infarction targets, drug action targets and disease action targets

A: Venn diagram of disease targets from three databases. B: Venn diagram of drug action targets and disease action targets. C: Venn diagram of the intersection between drug action targets and disease non-redundant targets.

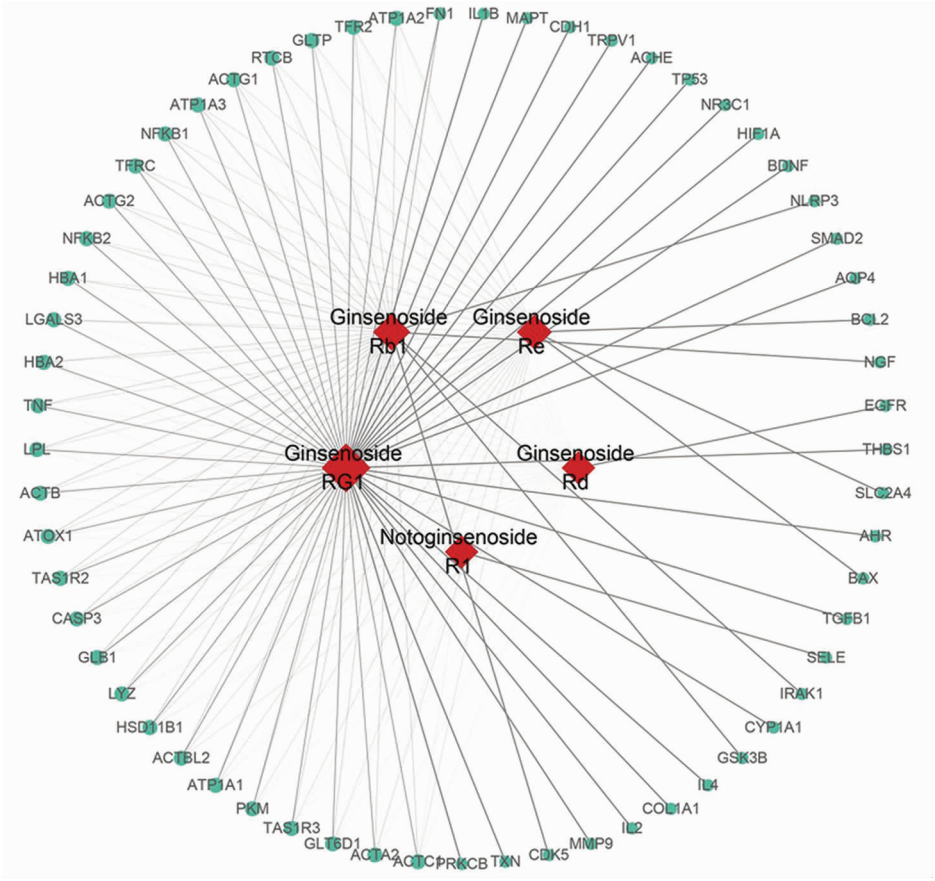

图 2 注射用血塞通(冻干)的活性成分 – 交集靶点网络图

Figure 2 Active component ingredients of xuesaitong injection lyophilized – intersection target network diagram

ACHE: Acetylcholinesterase; ACTA2: Actin, alpha 2, smooth muscle, aorta; ACTB: Actin beta; ACTBL2: Actin, beta – like 2; ACTC1: Actin, alpha, cardiac muscle 1; ACTG1: Actin gamma 1; ACTG2: Actin gamma 2, smooth muscle; AHR: Aryl hydrocarbon receptor; AQP4: Aquaporin 4; ATOX1: Antioxidant 1 copper chaperone; ATP1A1: ATPase Na +/K + transporting subunit alpha 1; ATP1A2: ATPase Na +/K + transporting subunit alpha 2; ATP1A3: ATPase Na +/K + transporting subunit alpha 3; BAX: BCL2 associated X, apoptosis regulator; BCL2: BCL2 apoptosis regulator; BDNF: Brain derived neurotrophic factor; CASP3: Caspase 3; CDH1: Cadherin 1; CDK5: Cyclin dependent kinase 5; COL1A1: Collagen type I alpha 1 chain; CYP1A1: Cytochrome P450 family 1 subfamily A member 1; EGFR: Epidermal growth factor receptor; FN1: Fibronectin 1; GLB1: Galactosidase beta 1; GLT6D1: Glycosyltransferase 6 domain containing 1; GLTP: Glycolipid transfer protein; GSK3B: Glycogen synthase kinase 3 beta; HBA1: Hemoglobin subunit alpha 1; HBA2: Hemoglobin subunit alpha 2; HIF1A: Hypoxia inducible factor 1 subunit alpha; HSD11B1: Hydroxysteroid 11 – beta dehydrogenase 1; IL1B: Interleukin 1 beta; IL2: Interleukin 2; IL4: Interleukin 4; IRAK1: Interleukin 1 receptor associated kinase 1; LGALS3: Galectin 3; LPL: Lipoprotein lipase; LYZ: Lysozyme; MAPT: Microtubule associated protein tau; MMP9: Matrix metallopeptidase 9; NFKB1: Nuclear factor kappa B subunit 1; NFKB2: Nuclear factor kappa B subunit 2; NGF: Nerve growth factor; NLRP3: NLR family pyrin domain containing 3; NR3C1: Nuclear receptor subfamily 3 group C member 1; PKM: Pyruvate kinase M1/M2; PRKCB: Protein kinase C beta; RTCB: RNA 2′,3′– cyclic phosphate and 5′ – OH ligase; SELE: Selectin E; SLC2A4: Solute carrier family 2 member 4; SMAD2: SMAD family member 2; TAS1R2: Taste 1 receptor member 2; TAS1R3: Taste 1 receptor member 3; TFR2: Transferrin receptor 2; TFRC: Transferrin receptor; TGFB1: Transforming growth factor beta 1; THBS1: Thrombospondin 1; TNF: Tumor necrosis factor; TP53: Tumor protein p53; TRPV1: Transient receptor potential cation channel subfamily V member 1; TXN: Thioredoxin.

的作用靶点,最终仅纳入 BATMAN – TCM 数据库检索结果,三七总皂苷共筛选出非重复靶点61 个。脑梗死靶点:Genecards、OMIM、Drugbank 分别检索出 5 613、136、51 个疾病靶点,非重复靶点 5 737 个,3 个数据库的交集靶点共 64 个。药物作用靶点与疾病作用靶点取交集后获得交集靶点 2 个,分别为蛋白激酶 Cβ(protein kinase C beta,PRKCB)、肿瘤坏死因子(tumor necrosis factor,TNF),与疾病非重复靶点取交集后获得交集靶点 51 个,见图 1。

2 靶点作用网络

分析 51 个交集靶点相互作用网络图的网络拓扑结构显示,网络包含 67 个节点,183 边,平均Degree为 5.46,三七总皂苷中的 5 个活性成分均为枢纽节点,人参皂苷 Rg1、人参皂苷 Rb1、人参皂苷 Re、三七皂苷 R1、人参皂苷 Rd 的 Degree 分别为 52、36、33、31、31。在基因靶点中,CASP3、TNF、NFKB1、ATP1A2 等 15 个靶

点的 Degree 为 5。活性成分－交集靶点网络,见图 2。

分析交集靶点的蛋白质相互作用网络图显示,共 41 个节点,124 条相互作用边,平均节点 Degree 为 6.15,网络直径为 8,平均路径长度为 2.89。根据网络拓扑参数综合结果,选取胱天蛋白酶 3(caspase 3,CASP3)、TNF、核因子 KappaB 亚基 1(nuclear factor kappa B subunit 1,NFKB1)、基质金属蛋白酶 9(matrix metallopeptidase 9,MMP9)、肿瘤蛋白 p53(tumor protein P53,TP53)以及药物作用靶点与疾病作用靶点交集的 PRKCB 进行后续分子对接,见表 1 和图 3。

表 1 注射用血塞通(冻干)的活性成分－交集靶点网络图的网络拓扑参数结果

Table 1 Network topology parameter results of the Active component ingredients of xuesaitong injection lyophilized – intersection target network diagram

Target	Degree	Betweenness	Closeness	Eigenvector
TP53	20	149.05	0.02	0.65
TNF	16	105.11	0.02	1.00
CASP3	14	133.71	0.02	0.50
MMP9	16	36.38	0.01	0.91
TGFB1	14	38.28	0.01	0.87
NFKB1	12	77.28	0.02	0.65
FN1	12	63.94	0.01	0.64
EGFR	10	39.41	0.01	0.54

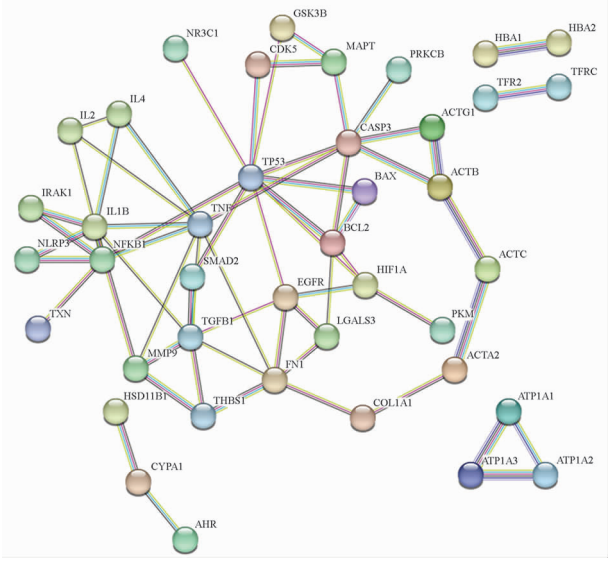

图 3 注射用血塞通(冻干)－脑梗死的交集靶点的蛋白质相互作用网络图

Figure 3 Protein – protein interaction network diagram of the intersection target of xuesetong injection lyophilized – cerebral infarction

3 基因富集分析结果

GO 功能富集分析显示,在生物过程方面,靶点基因主要参与基因表达的正向调控、细胞凋亡过程的负调控、miRNA 转录的正向调控等条目。在细胞组分方面,靶点基因主要定位于细胞外空间、细胞外区域、血液微粒、轴突和蛋白质复合物等区域。在分子功能方面,靶点蛋白主要具有相同蛋白结合、蛋白酶结合、热休克蛋白 90(heat shock protein 90,HSP90)蛋白结合等功能,富集结果在统计学上差异均具有统计学意义($P<0.05$)。

KEGG 富集分析显示,注射用血塞通(冻干)治疗脑梗死的潜在作用靶点富集于晚期糖基化终产物－晚期糖基化终产物受体(advanced glycation end products – receptor for advanced glycation end products,AGE – RAGE)、脂质与动脉粥样硬化、流体剪切应力与动脉粥样硬化、癌症中的蛋白聚糖、丝裂原活化蛋白激酶(mitogen – activated protein kinase,MAPK)信号通路、甲状腺激素信号通路、细胞凋亡通路等信号通路中,富集结果在统计学上差异均具有统计学意义(均$P<0.05$)。

4 注射用血塞通(冻干)治疗脑梗死的分子对接验证

分子对接显示,注射用血塞通(冻干)的主要活性成分与核心靶点蛋白的结合能力较好,其中人参皂苷 Rg1 与 TNF 的结合能最低,CASP3、PRKCB 与多种活性成分均表现出较强的结合,见表 2。选取结合能低于 -9.0 kcal · mol^{-1} 的对象进行可视化,人参皂苷 Rb1 与 TNF 在 GLU23、GLY66、GLN67、LEU30、ASN39、PRO8 形成氢键,人参皂苷 Rg1 与 TNF 在 GLU23、GLY66、GLY40、GLN67、LEU30、ASN39、TYR141 形成氢键,与 CASP3 在 PHF、ASP3、MET61、GLY60 形成氢键,三七皂苷 R1 与 PRKCB 在 ARG239、ASN287 形成氢键,与 MMP9 在 ARG143 形成氢键,人参皂苷 Re 与 PRKCB 在 TRP605、LYS607、ILE603、ASP604、ASN287 形成氢键,见图 4。

表 2 注射用血塞通(冻干)的活性成分与靶点蛋白的结合能(kcal · mol^{-1})

Table 2 Binding energies between active components of xuesetong injection lyophilized and target proteins (kcal · mol^{-1})

Target	Ginsenoside RG1	Ginsenoside Rb1	Notoginsenoside R1	Ginsenoside Re	Ginsenoside Rd
CASP3	−9.1	−7.6	−7.8	−7.9	−8.5
TNF	−9.6	−8.9	−8.9	/	−8.7
NFKB1	−7.0	−7.3	−7.0	−7.3	−7.4
MMP9	−9.0	/	−10.5	/	−8.6
TP53	−7.6	−7.6	−7.8	−7.9	/
PRKCB	−8.9	−8.8	−9.8	−12.8	−9.5

/ :The binding energy was higher than −7.0 kcal · mol^{-1}.

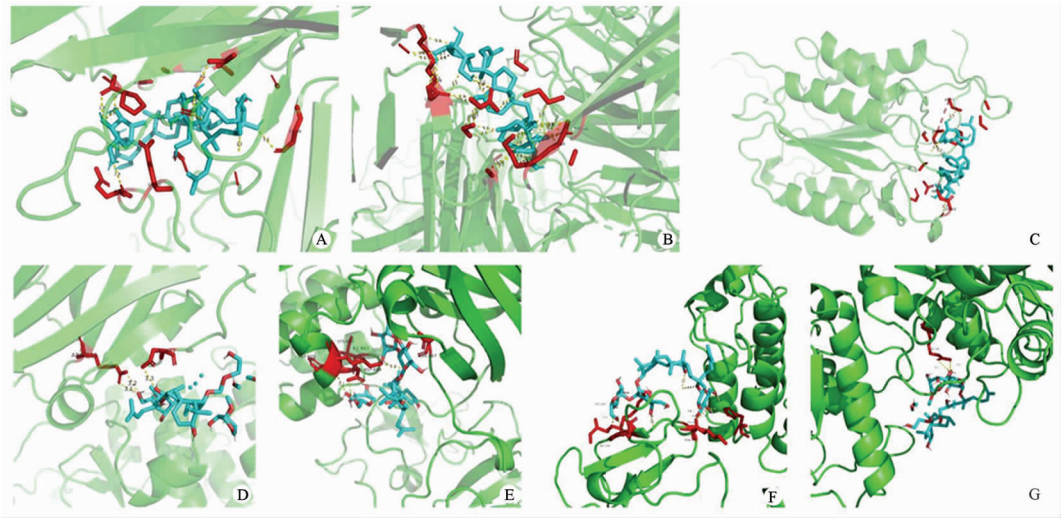

图 4 注射用血塞通(冻干)的活性成分与靶点蛋白的分子对接图

Figure 4 Molecular docking diagram of active components of xuesetong injection lyophilized and target proteins

A:Molecular docking diagram of ginsenoside Rb1 with target TNF; B and C:The molecular docking diagrams of ginsenoside Rg1 with targets TNF and CASP3, respectively; D, E, and F:The molecular docking diagrams of notoginsenoside R1, ginsenoside Re, and ginsenoside Rd with target PRKCB, respectively; G:The molecular docking diagram of notoginsenoside R1 with target MMP9.

讨　论

本研究筛选出药物非重复靶点 61 个、脑梗死靶点 5 737 个,2 者交集为 51 个潜在治疗靶点,表明注射用血塞通(冻干)在脑梗死治疗中可能通过多靶点协同作用产生整体调控效应,符合中药"多成分、多靶点、多通路"的药理特点。活性成分 - 靶点网络分析显示,5 种活性成分均为网络中的关键枢纽成分,其中人参皂苷 Rg1 的 Degree 值最高,可能是发挥脑保护作用的主要活性成分。蛋白质相互作用网络特点为高聚类、短路径,这提示对核心节点进行干预可能会产生较大的影响。已有研究表明,人参皂苷 Rg1 可通过抗氧化、抗炎和抑制神经元凋亡等途径改善脑缺血再灌注损伤[7-8];人参皂苷 Rb1 则可通过抑制炎症介质释放、促进血管再生及改善能量代谢、铁死亡等机制发挥神经保护作用[9-10]。TP53、CASP3 与细胞凋亡密切相关,TNF 和 NFKB1 则参与炎症信号传导及免疫应答调节[11-12],PRKCB 也被证实与高脂饮食介导的血管功能障碍相关[13]。由此推测,注射用血塞通(冻干)可能通过调节炎症反应与细胞凋亡平衡,从而减轻脑缺血造成的神经损伤。

GO 功能富集结果证实血塞通可能通过调节神经细胞凋亡和基因表达,改善血管功能及神经突触传导,通过调控蛋白复合体稳定性及信号转导过程发挥神经保护作用。在 KEGG 结果中,AGE - RAGE 信号通路在糖代谢紊乱及炎症反应中起重要作用,过度激活可导致血管内皮损伤及动脉粥样硬化形成[14];MAPK 通路是调节细胞存活、炎症及凋亡的核心通路之一[15];流体剪切应力、动脉粥样硬化通路与血流动力学改变及内皮功能密切相关[16-17],这提示血塞通可能通过抗炎、抗凋亡及改善血管内皮功能等机制改善脑梗死病理状态。既往文献也报道,三七皂苷 R1 在脑缺血再灌注模型大鼠中可显著抑制炎症相关信号通路,减轻神经炎症和血脑屏障破坏,通过调控炎症级联响应改善脑卒中结局[18]。人参皂苷 Rg1 在神经系统疾病中可通过抑制 MAPK 信号家族、减少炎症介质和氧化应激,从而阻断促炎信号[19]。人参皂苷 Rb1 通过减少中性粒细胞外陷阱诱导的内皮激活发挥抗动脉粥样硬化作用[20]。但目前,研究皂苷类与 AGE - RAGE 信号通路关系的研究较少。由此推测,血塞通可能通过多成分、多靶点协同调控炎症反应、血管功能及细胞存活相关信号通路,来改善脑梗死病理状态。

分子对接显示,人参皂苷 Re 与 PRKCB 结合能最低,在 5 个位点形成氢键,增强结合稳定性,提示其与 PRKCB 之间可能存在较强的相互作用。CASP3、PRKCB 与多种皂苷成分均表现出较强结合,说明其在调控神经细胞凋亡中可能是重要的作用节点,从分子水平验证了网络药理学预测的合理性。此外,本研究中分子对接的结合能强度与网络拓扑的枢纽地位并

不完全一致,人参皂苷 Re 通过与 PRKCB 强结合,对其进行精准调控,而人参皂苷 Rg1、人参皂苷 Rb1 虽然与单个靶点的结合强度并非最强,2 者却均能与较多的关键靶点进行有效结合,通过多靶点协同发挥调控作用。但皂苷类化合物多为大分子,其与靶蛋白的真实结合与分子对接的预测结果相比可能存在差异,因此后续还需进一步研究。

综上所述,注射用血塞通(冻干)治疗脑梗死可能通过调控炎症反应、细胞凋亡及血管功能等多条信号通路实现多靶点综合干预,活性成分与 CASP3、TNF、NFKB1、MMP9、TP53、PRKCB 等核心靶点的相互作用可能是其发挥神经保护作用的关键分子基础,未来应开展体内外实验以验证上述预测性结论。

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