

黄精化学成分、药理作用研究进展及 质量标志物(Q-Marker)预测分析

汪成^{1,3}, 叶菊^{2*}, 何旭光^{1,3}, 唐媛媛^{1,3}

¹青海民族大学药学院, 西宁 810007; ²遵义医药高等专科学校, 遵义 563000;

³青海省青藏高原植物资源化学重点实验室, 西宁 810007

摘要: 中药黄精为百合科、黄精属植物黄精 *Polygonatum sibiricum* Red.、多花黄精 *Polygonatum cyrtonema* Hua 或滇黄精 *Polygonatum kingianum* Coll. et Hemsl. 的干燥根茎, 用药历史悠久, 性平、味甘, 归脾、肺、肾经, 具有养阴润肺、补脾益气、滋肾填精之功效, 用于治疗肺虚燥咳、脾胃虚弱、体倦乏力、口干食少、精血不足、内热消渴等。本文对黄精的化学成分及现代药理研究进行综述, 并基于其药理活性、药效物质、植物亲缘学、药材配伍、加工炮制和网络药理学等研究, 预测分析了其质量标志物(quality markers, Q-marker)。初步确定黄芩素、甘草素、 β -谷甾醇、薯蓣皂苷元、5, 4'-二羟基黄酮、3'-甲氧基大豆苷、新甘草苷和黄精多糖为黄精的质量标志物, 为黄精质量控制和临床用药提供参考依据。

关键词: 黄精; 质量控制; 化学成分; 药理作用; 网络药理学

中图分类号: R284; R285

文献标识码: A

文章编号: 1001-6880(2024)5-0881-20

DOI: 10.16333/j.1001-6880.2024.5.017

Research progress on chemical components and pharmacological effects of *Polygonati Rhizoma* and prediction analysis of quality marker

WANG Cheng^{1,3}, YE Ju^{2*}, HE Xu-guang^{1,3}, TANG Yuan-yuan^{1,3}

¹School of Pharmacy, Qinghai Minzu University, Xining 810007, China; ²Zunyi Medical And Pharmacy College, Zunyi 563000, China;

³Key Laboratory of Plant Resources of Qinghai-Tibet Plateau in Chemical Research, Xining 810007, China

Abstract: *Polygonati Rhizoma* is the rhizomes of *Polygonatum sibiricum* Red., *P. cyrtonema* Hua or *P. kingianum* Coll. et Hemsl. in the plants of the *Polygonatum* Mill. in the *Liliaceae* family, with a long history of medicinal use, flat nature, sweet taste, spleen, lung, and kidney meridian. It is used for the treatment of lung deficiency and dry cough, weakness of the spleen and stomach, tiredness and fatigue, dry mouth and little food, deficiency of essence and blood, internal heat and thirst. In this paper, we reviewed the chemical components and modern pharmaceuticals, studied rhizoma polygonal odor, predicted and analyzed its quality markers (Q-markers) based on pharmacological activities, pharmacodynamic substances, phytopharmacology, herb compounding, processing and concocting, and network pharmacology. Preliminarily, baicalein, glycyrrhizin, β -sitorsterol, diosgenin, 5, 4'-dihydroxyflavone, 3'-methoxy-solo side, neo glycyrrhizin, and polysaccharides of flavonoids were identified as quality markers, which will provide a reference basis for the quality control and the clinical use of the drug.

Key words: *Polygonati Rhizoma*; quality control; chemical components; pharmacological effect; network pharmacology

黄精又名仙人余粮、老虎姜、鸡头参等^[1], 2020版《中国药典》记载中药黄精为百合科植物滇黄精 *Polygonatum kingianum* Coll. et Hemsl.、黄精 *P. sibiricum* Red. 或多花黄精 *P. cyrtonema* Hua. 的干燥根茎, 主要分布于河北、甘肃、内蒙古、陕西和西南地区^[2]。《名医别录》记载:“黄精, 无毒, 主补中益气, 除风湿, 安五脏, 久服轻身, 延年不饥^[3]”。现代药理学研究证明, 黄精具有降血糖、降血脂、抗肿瘤、抗氧化、抗菌和免疫调节等药理活性。Peng^[4]、Qi^[5]等从黄精中分离得到了具有显著药理活性的多糖类、皂苷类、黄酮类和醌类等成分。众所周知, 中药广泛

收稿日期: 2023-11-24

接受日期: 2024-02-21

基金项目: 青海省基础研究计划(2021-ZJ-707); 黔北地区道地药材资源保护与利用研究团队(遵市科合 HZ(2023)454号)

* 通信作者 E-mail: yeju8145@163.com

的功效作用基于其丰富的代谢产物,筛选更适宜的质量评价物已成为中药质量研究的难点和热点^[6]。2016年刘昌孝院士^[7]提出中药质量标志物(quality markers, Q-marker)的概念,旨在对药材中具有安全性与有效性的标志性物质进行全程质量控制研究。目前,黄精质量评价仅依据多糖总量,具有一定的局限性和片面性,本文在综述其化学成分及药理活性的基础上,结合网络药理学、特征性化学成分和植物亲缘学分析出其质量标志物(Q-marker),为黄精质量控制研究提供参考依据。

1 化学成分

1.1 多糖类

多糖类成分在黄精中的占比最大(13.02% ~ 18.44%)^[8],药理作用最突出,是药典上规定的质量检测标志物,也是研究最系统、最全面的活性成分。但是,目前关于黄精多糖的提取、富集、活性研

究方面存在的一系列问题严重阻碍了其他方面的研究进展。一方面,多糖成分性质活泼,易被氧化或水解,贮存过程中多糖含量容易大幅下降。另一方面,虽然黄精多糖提取方法较多,但提取率均不高,且不同提取方法对其组成、糖苷键构型、分子量等产生了显著的影响,从而导致药理活性研究结果缺乏统一性。因此,应从提取工艺、贮存方法、化学组成、结构特征及生物活性等方面进行系统性研究。黄精多糖结构复杂多变,分子量巨大,相关研究多集中于单糖组成、糖苷键构型、一级结构、单糖链接方式等方面^[9]。每种多糖的单糖组成不同,包括:葡萄糖、阿拉伯糖、半乳糖、甘露糖、果糖、鼠李糖、木糖、葡萄糖醛酸、半乳糖醛酸、吡喃葡萄糖、吡喃鼠李糖和吡喃果糖,且物质量比也不同^[10],糖苷键构型有 α 型和 β 型,且糖残基型也不同。目前,从黄精中分离鉴定的多糖共14种(1~14),具体多糖成分见表1。

表1 黄精多糖类成分

Table 1 Polysaccharide from Polygonati Rhizoma

编号 No.	多糖化合物 Polysaccharide compound	单糖组成 Monosaccharide composition	单糖摩尔比 Molar ratio of monosaccharides	糖苷键构型 Glycoside bond configuration	参考文献 Ref.
1	PSP1	Man: Glc: Gal	14.96:2.13:82.91	β	11
2	PSP2	Rha: Glc: Gal: Xyl	20.54:2.06:74.37:3.03	β	11
3	PSP3	Gal: Rha: Ma: nGlc: Xyl	1.38:57.69:2.02:37.17:1.74	β	11
4	PSP4	Gal: Rha: Man: Xyl	2.00:72.63:20.74:4.63	β	11
5	PSP-1a	Gal: Ara: Rha: Xyl: Glc	0.18:1.5:97.25:0.77:0.3	β	12
6	PCP1	Ara: Gal: Glc: Man: GluA: GalA	2.1:24:20.7:33.5:0.5:19.3	主要 β 型,少量 α 型	13
7	PCP2	Ara: Gal: Glc: Man: Xyl: GluA: GalA	18.5:59.8:2.3:0.4:5.3:4.7	主要 β 型,少量 α 型	13
8	PCP3	Ara: Gal: Glc: Man: Xyl: GluA: GalA	22.2:58.7:3.9:4.9:0.5:8.5:1.5	主要 β 型,少量 α 型	13
9	PCP4	Ara: Gal: Glc: Man: Xyl: GluA: GalA	21:61.3:2.7:6.7:0.4:7.9:0.1	主要 β 型,少量 α 型	13
10	PSPC	Rha: Ara: Man: Glc: Gal: GalA	2.66:6.32:36.1:15.09:29.63:10.2	β	14
11	PSPW	Rha: Ara: Man: Gal: GalA	1.85:5.5:78.77:13.84	-	15
12	PKPs-1	Glc: Man: GalA: Gal: GluA: Ara	7.22:1:0.16:0.11:0.05:0.02	β	13
13	PSP	Fru: Glc	8.7:1	β	16
14	P-2,3,4	Glc: Gal: Ara: Xyl: Rha: GluA: Fru: Glc	-	β	12

注:Man:甘露糖;Glc:葡萄糖;Gal:半乳糖;Rha:鼠李糖;Xyl:木糖;Ara:阿拉伯糖;GluA:葡萄糖醛酸;GalA:半乳糖醛酸;Fru:果糖;“-”:文献无数据。

Note:Man; mannose; Glc; glucose; Gal; galactose; Rha; rhamnose; Xyl; xylose; Ara; arabinose; GluA; Glucuronic acid; GalA; Galacturonic acid; Fru; Fructose;“-”:No data available in the literature.

1.2 皂苷类

皂苷类是黄精的第二大活性成分(1.82% ~ 6.49%)^[8],包括三萜皂苷类、甾体皂苷类及其他皂苷类。

1.2.1 甾体皂苷类

虽然从多花黄精中分离得到的甾体皂苷成分不多,但其生物合成途径已逐步明晰,该途径主要包括萜类化合物骨架合成以及倍半萜和三萜的生物合

成,共涉及 12 种关键酶,其中环阿屯醇合酶(CAS)和甾醇-22-去饱和酶(CYP710 A)的基因数目仅有 1 个,这为进一步研究关键酶的功能及调控机制奠定了基础。截至目前,从黄精中分离出的甾体皂苷类化合物共 88 个,其中螺甾烷醇型和异螺甾烷醇型共

65 个(15~79),呋甾烷醇型共 23 个(80~102)。药典收录的 3 个品种均含有螺甾烷醇型和异螺甾烷醇型,其中滇黄精和黄精中鉴定的呋甾烷醇型甾体皂苷分别有 9 和 14 个(见表 2 和图 1)。

表 2 甾体皂苷类成分

Table 2 Steroidal saponins components

编号 No.	化合物 Compound	来源 Source	参考文献 Ref.
15	(25S)-Spirostan-5-en-12-one-3-O-D-glucopyranosyl-(1→2)-O-[β-D-xylopyranosyl(1→3)]-O-β-D-glucopyranosyl(1→4)-β-D-galactopyranoside	PC	24
16	(25S)-Spirostan-5-en-12-one-3-O-β-D-glucopyranosyl-(1→2)-O-[β-D-glucopyranosyl-(1→3)]-O-β-D-glucopyranosyl-(1→4)-β-D-galactopyranoside	PC	24
17	静特诺皂苷元 Gentrogenin	PC,PK	24-27
18	(25S)-滇黄精苷 G (25S)-Kingianoside G	PK	28-30
19	(25S)-康定玉竹苷 D ₁ (25S)-Pratioside D ₁	PK,PS	28,29,31
20	(25S)-滇黄精苷 A (25S)-Kingianoside A	PK	27-30
21	滇黄精苷 H Kingianoside H	PK	32
22	滇黄精苷 I Kingianoside I	PK	32
23	滇黄精苷 B Kingianoside B	PK	27,33
24	Cyrtanemoside A	PC	34
25	新波托皂苷元 Neobotogenin	PC	34
26	(3β,25R)-Spirost-5-en-12-one-3-[(O-β-D-glucopyranosyl-(12)-O-[β-D-glucopyranosyl-(1→3)]-O-β-D-xylopyranosyl-(1→4)-β-D-galactopyranosyl)-oxy]	PC	34
27	滇黄精苷 J Kingianoside J	PK	29
28	(25R)-Spirost-5-en-3β,17α-diol-3-O-β-D-glucopyranosyl(1→4)-β-D-fucopyranosyl	PS	31,35
29	(25R)-Spirost-5-en-3β,17α-diol-3-O-β-D-glucopyranosyl(1→2)-β-D-glucopyranosyl(1→4)-β-D-fucopyranosyl	PS	31,35
30	(25R)-Spirost-5-en-3β,12β-diol-3-O-β-D-glucopyranosyl(1→4)-β-D-fucopyranosyl	PS	35
31	重楼皂苷 VII Polyphyllin VII	PK	25
32	(25R)-Spirost-5-en-3β,17α-diol-3-O-β-D-glucopyranosyl-(1→3)-[α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside	PK	25
33	西伯利亚蓼苷 B Sibiricoside B	PS	36
34	新巴拉次薯蓣苷元 A 3-O-β-石蒜四糖苷 Neoprazerigenin A 3-O-β-lycotetraoside	PS	36
35	新巴拉次薯蓣皂苷元 Neoprazerigenin A	PS	36
36	(23S,25R)-Spirost-5-ene-3β,14α,23-triol	PS	36
37	(3β,23S,25R)-3,23-Diacetate, spirost-5-ene-314,23-triol	PS	36
38	重楼皂苷 VI Polyphyllin VI	PK	29
39	(25R)-螺甾-5-烯-3β,17α-二醇-3-O-β-D-吡喃葡萄糖基(1→4)-β-D-吡喃半乳糖苷	PS	31
40	(25R)-螺甾-5-烯-3β,17α-二醇-3-O-β-D-吡喃葡萄糖基(1→2)-β-D-吡喃葡萄糖基(1→4)-β-D-吡喃半乳糖苷	PS	31
41	3-O-β-D-Glucopyranosyl(1→3)-β-D-glucopyranosyl(1→4)-[α-L-rhamnopyranosyl(1→2)]-β-D-glucopyranoside-diosgenin	PS	37
42	(25R)-Spirost-5-ene-3β-ol-3-O-α-L-rhamnopyranosyl(1→4)-β-D-glucopyranoside	PS	37

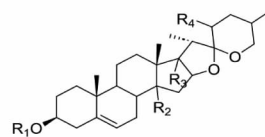
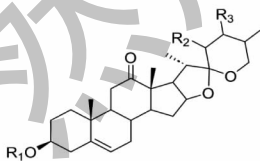
续表 2(Continued Tab. 2)

编号 No.	化合物 Compound	来源 Source	参考文献 Ref.
43	(25 <i>R</i>)-Spirost-5-ene-3 β -ol-3- <i>O</i> - α - <i>L</i> -rhamnopyranosyl(1 \rightarrow 2)-[α - <i>L</i> -rhamnopyranosyl(1 \rightarrow 4)] β - <i>D</i> -glucopyranosid	PS	37
44	约莫皂苷元 Yamogenin	PS, PK	36, 38
45	新西伯利亚蓼苷 D Neosibiricoside D	PS	38, 39
46	麦冬皂苷 C' Ophiopogonin C'	PK	25
47	薯蓣皂苷元 Diosgenin	PC, PS	26, 40, 41
48	新西伯利亚蓼苷 C Neosibiricoside C	PS	39
49	(25 <i>S</i>)-蜘蛛抱蛋苷 (25 <i>S</i>)-Aspidistrin	PS	36
50	Funkioside C	PK	27
51	薯蓣皂苷 Dioscin	PS, PK, PC	29, 40, 41
52	纤细薯蓣皂苷 Gracillin	PK	29
53	重楼皂苷 I Polyphyllin I	PK	29
54	重楼皂苷 B Polyphyllin B	PK	29
55	延龄草苷 Trillin	PS	41
56	(25 <i>S</i>)-螺甾-5-烯-3 β -醇-3- <i>O</i> - β - <i>D</i> -吡喃葡萄糖基(1 \rightarrow 4)- β - <i>D</i> -吡喃岩藻糖苷	PS	31
57	(25 <i>S</i>)-螺甾-5-烯-3 β -醇-3- <i>O</i> - β - <i>D</i> -吡喃葡萄糖基(1 \rightarrow 4)- β - <i>D</i> -吡喃半乳糖苷	PS	31
58	新西伯利亚蓼苷 B Neosibiricoside B	PS	38, 39
59	Huangjinoside C	PS	38, 42
60	新西伯利亚蓼苷 A Neosibiricoside A	PS	39
61	(25 <i>R</i>)-螺甾-5-烯-3 β , 12 β -二醇-3- <i>O</i> - β - <i>D</i> -吡喃葡萄糖基(1 \rightarrow 4)- β - <i>D</i> -吡喃岩藻糖苷	PS	31
62	(25 <i>R</i>)-螺甾-5-烯-3 β , 12 β -二醇-3- <i>O</i> - β - <i>D</i> -吡喃葡萄糖基(1 \rightarrow 4)- β - <i>D</i> -吡喃半乳糖苷	PS	31
63	黄精皂苷元 Huangjingenin	PS	42
64	Huangjinoside D	PS	42
65	Huangjinoside E	PS	42
66	Huangjinoside F	PS	42
67	Huangjinoside G	PS	42
68	Huangjinoside H	PS	42
69	Huangjinoside I	PS	42
70	Huangjinoside J	PS	42
71	Huangjinoside K	PS	42
72	Huangjinoside L	PS	42
73	Huangjinoside M	PS	42
74	Huangjinoside N	PS	42
75	Huangjinoside O	PS	42
76	Huangjinoside A	PS	42, 43
77	Huangjinoside B	PS	38, 42
78	重楼皂苷 H Polyphyllin H	PS	25
79	滇黄精苷 K Kingianoside K	PS	29
80	西伯利亚蓼苷 A Sibiricoside A	PS	36, 38
81	(25 <i>R</i> , 22 ξ)-羟基-弯蕊开口箭苷 C (25 <i>R</i> , 22 ξ)-hydroxylwattinoside C	PK	30, 32

续表 2(Continued Tab. 2)

编号 No.	化合物 Compound	来源 Source	参考文献 Ref.
82	(25 <i>S</i>)-滇黄精苷 F (25 <i>S</i>)-Kingianoside F	PK	30,32
83	(25 <i>R</i>)-26-(β -Glucopyranosyl)-22-methylfurost-5-ene-3 β ,14 α ,26-triol 3- <i>O</i> - β -lycotetraoside	PS	36
84	(3 β ,25 <i>R</i>)-26-(β - <i>D</i> -Glucopyranosyloxy)-22-hydroxyfurost-5-en-3-yl-4- <i>O</i> - β - <i>D</i> -glucopyranosyl- β - <i>D</i> -galactopyranoside	PK	27
85	(3 β ,25 <i>R</i>)-26-(β - <i>D</i> -Glucopyranosyloxy)-22-methoxyfurost-5-en-3-yl-4- <i>O</i> - β - <i>D</i> -glucopyranosyl	PK	27
86	原薯蓣皂苷 Protodioscin	PS	41
87	甲基原薯蓣皂苷 Methyl protodioscin	PS	41
88	原纤细薯蓣皂苷 Protogracillin	PS	41
89	甲基原纤细薯蓣皂苷 Methyl protogracillin	PS	41
90	Polygonoide A	PS	41
91	26- <i>O</i> - β - <i>D</i> -吡喃葡萄糖-3 β ,26-二醇-(25 <i>R</i>)- Δ 5,22(23)-二烯-呋甾-3- <i>O</i> - β - <i>D</i> -吡喃葡萄糖苷	PS	41
92	26- <i>O</i> - β - <i>D</i> -吡喃葡萄糖-3 β ,26-二醇-(25 <i>R</i>)- Δ 5,20(22)-二烯-呋甾-3- <i>O</i> - β - <i>D</i> -吡喃葡萄糖苷	PS	41
93	Huangjioside P	PS	42
94	(25 <i>S</i>)-滇黄精苷 C (25 <i>S</i>)-Kingianoside C	PK	27,29,30,32
95	(25 <i>S</i>)-滇黄精苷 D (25 <i>S</i>)-Kingianoside D	PK	27,30,32,33
96	(25 <i>S</i>)-滇黄精苷 E (25 <i>S</i>)-Kingianoside E	PK	30,32
97	(3 β ,25 <i>R</i>)-Furost-5-en-12-one,3-[(4- <i>O</i> - β - <i>D</i> -glucopyranosyl- β - <i>D</i> -galactopyranosyl) oxy]-26-(β - <i>D</i> -glucopyranosyloxy)-22-methoxy	PK	27
98	(3 β ,25 <i>R</i>)-Furost-5-en-12-one,3-[(6-deoxy-4- <i>O</i> - β - <i>D</i> -glucopyranosyl- β - <i>D</i> -galactopyranosyl) oxy]-26-(β - <i>D</i> -glucopyranosyloxy)-22-methoxy	PK	27
99	滇黄精苷 Z Kingianoside Z	PS	44
100	Polygonoide B	PS	36
101	Huangjioside Q	PS	42
102	Huangjioside R	PS	42

注:PS:黄精;PC:多花黄精;PK:滇黄精

Note:PS:*P. sibiricum*. ;PC:*P. cyrtonea*. ;PK:*P. kingianum*.

- 15 R₁=Glc 1→2 (Xyl 1→3)Glc 1→4 Gal R₂=H R₃=H
 16 R₁=Glc 1→2 (Glc 1→3)Glc 1→4 Gal R₂=H R₃=H
 17 R₁=H R₂=H R₃=H
 18 R₁=Glc 1→2 Glc 1→4 Gal R₂=OH R₃=H
 19 R₁=Glc 1→2 Glc 1→4 Gal R₂=H R₃=H
 20 R₁=Glc 1→4 Gal R₂=H R₃=H
 21 R₁=Glc 1→4 Gal R₂=H R₃=OH
 22 R₁=Glc 1→2 Glc 1→4 Gal R₂=H R₃=OH
 23 R₁=Glc 1→4 Fuc R₂=H R₃=H
 24 R₁=Glc 1→2 (Glc 1→3)Glc 1→4 Gal R₂=H R₃=H
 25 R₁=H R₂=H R₃=H
 26 R₁=Glc 1→2 (Glc 1→3)Xyl 1→4 Gal R₂=H R₃=H
 27 R₁=Glc 1→4 Gal R₂=OH R₃=H

- 28 R₁=Glc 1→4 Fuc R₂=H R₃=OH R₄=H
 29 R₁=Glc 1→2 Glc 1→4 Fuc R₂=H R₃=OH R₄=H
 30 R₁=Glc 1→4 Fuc R₂=H R₃=OH R₄=H
 31 R₁=Rha 1→4 Rha 1→4(Rha 1→2)Glc R₂=H R₃=OH R₄=H
 32 R₁=Rha 1→2(Glc 1→3)Glc R₂=H R₃=OH R₄=H
 33 R₁=Glc 1→2(Xyl 1→3)Glc 1→4 Gal R₂=OH R₃=H R₄=OH
 34 R₁=Glc 1→2(Xyl 1→3)Glc 1→4 Gal R₂=OH R₃=H R₄=H
 35 R₁=H R₂=OH R₃=H R₄=H
 36 R₁=H R₂=OH R₃=H R₄=OH
 37 R₁=Acetyl R₂=OH R₃=H R₄=Carbethoxy
 38 R₁=Rha 1→2 Glc R₂=OH R₃=H R₄=H
 39 R₁=Glc 1→4 Gal R₂=H R₃=OH R₄=H
 40 R₁=Glc 1→2 Glc 1→4 Gal R₂=H R₃=OH R₄=H

续图 1(Continued Fig.1)

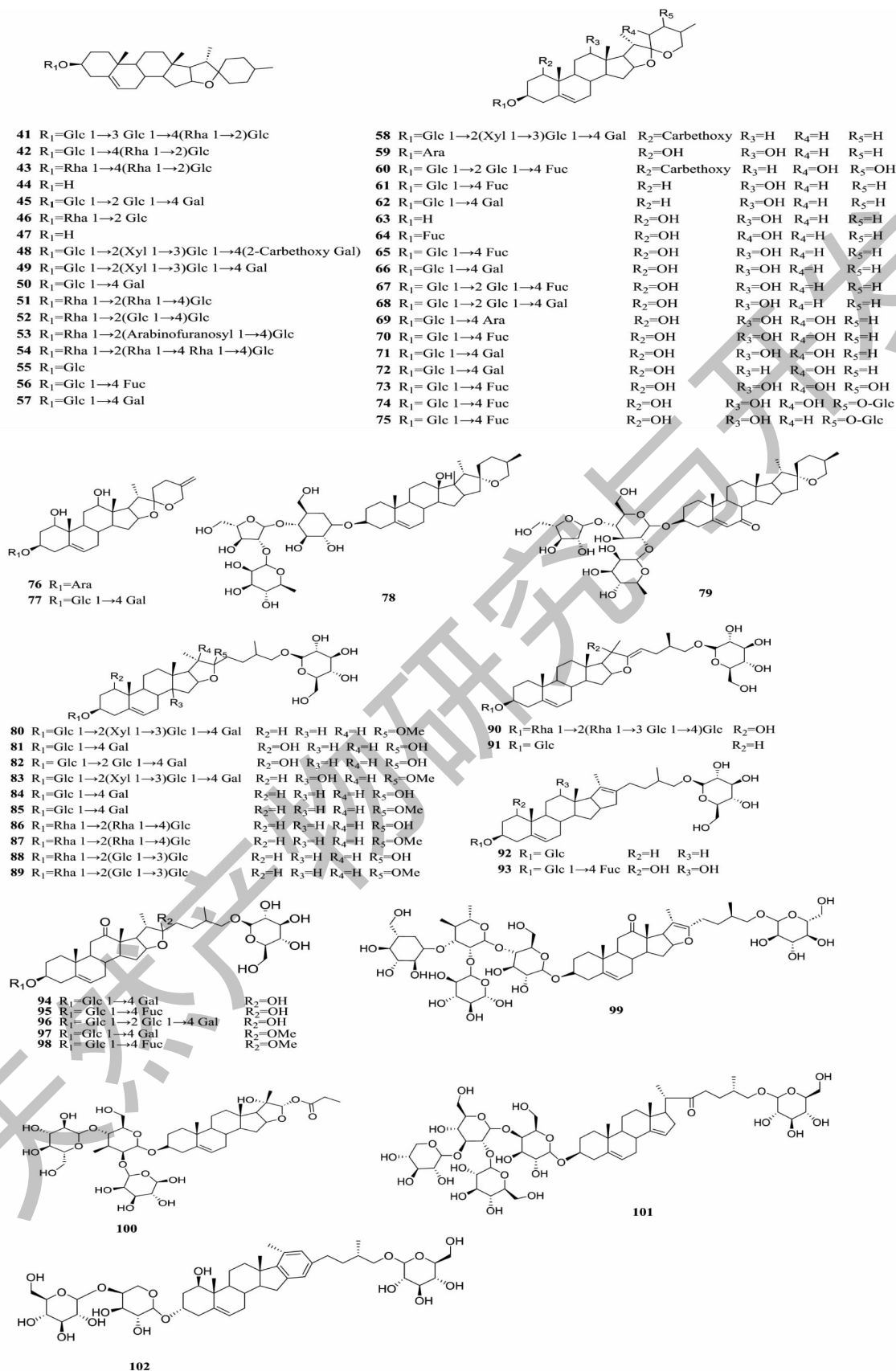


图1 甾体皂苷类结构

Fig. 1 Structures of steroidal saponins

1.2.2 三萜皂苷类

当前,从黄精中共分离得到 12 个三萜皂苷类成分(103 ~ 114),其中 3 个来自滇黄精 *P. kingia-*

num., 9 个来自黄精 *P. sibiricum.*, 按化学结构可分为齐墩果烷型、乌苏酸型和达玛烷型 3 种(见表 3 和图 2)。

表 3 三萜皂苷类成分

Table 3 Triterpenoid saponins components

编号 No.	化合物 Compound	来源 Source	参考文献 Ref.
103	3β-羟基-(3→1)葡萄糖-(4→1)葡萄糖-齐墩果烷 3β-Hydroxy-(3→1) glucose-(4→1) glucose-oleanane	PS	17
104	3β,30β-二羟基-(3→1)葡萄糖-(2→1)葡萄糖-齐墩果烷 3β,30β-Dihydroxy-(3→1) glucose-(2→1) glucose-oleanane	PS	17
105	3β-羟基-(3→1)葡萄糖-(2→1)葡萄糖-齐墩果酸 3β-Hydroxy-(3→1) glucose-(2→1) glucose-oleanolic acid	PS	17
106	3β-羟基-(3→1)葡萄糖-(4→1)葡萄糖-(28→1)阿拉伯糖-(2→1)阿拉伯糖-齐墩果酸 3β-Hydroxy-(3→1) glucose-(4→1) glucose-(28→1) arabinose-(2→1) arabinose-oleanolic acid	PS	17
107	积雪草苷 Asiaticoside	PS	17, 18
108	羟基积雪草苷 Madecassoside	PS	17, 18
109	Polygonoide C	PS	19
110	Polygonoide D	PS	19
111	Polygonoide E	PS	19
112	人参皂苷 Rb ₁ Ginsenoside Rb ₁	PK	20
113	人参皂苷 RC Ginsenoside RC	PK	21
114	伪人参皂苷 F ₁₁ Pseudoginsenoside F ₁₁	PK	22, 23

注:PS:黄精;PC:多花黄精;PK:滇黄精

Note:PS:*P. sibiricum.*;PC:*P. cyrtonema.*;PK:*P. kingianum.*

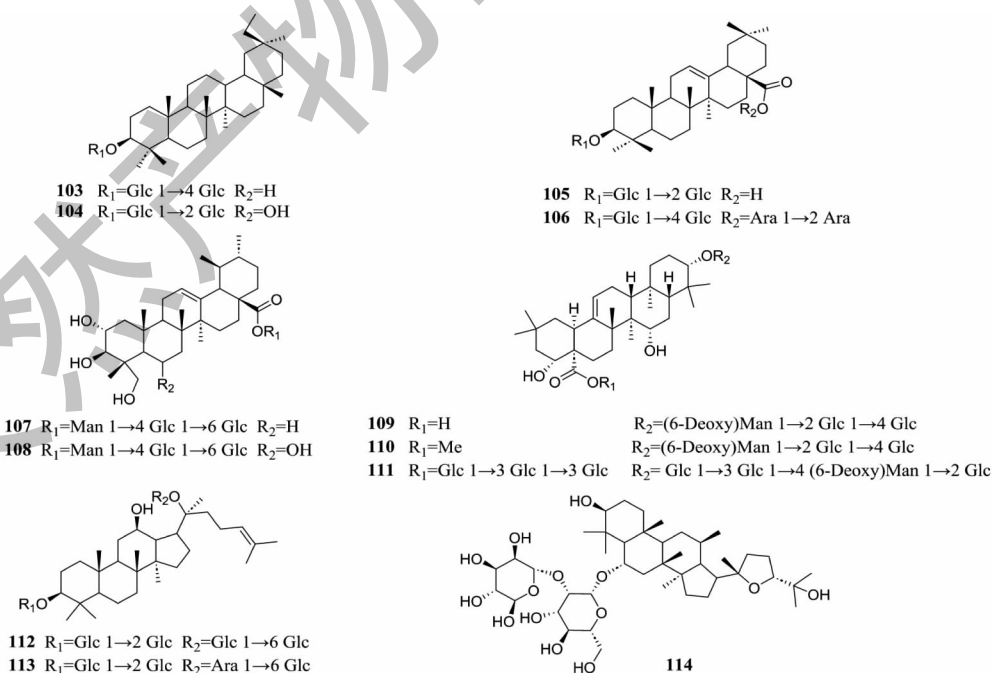


图 2 三萜皂苷类结构

Fig. 2 Structures of triterpenoid saponins

1.2.3 其他皂苷化合物

黄精中除了含有甾体皂苷和三萜皂苷外,还含有 C_{21} 甾类化合物(115 ~ 117),其母核是 21 个碳原

子组成的甾体衍生物以及植物甾醇类化合物(118 ~ 121),其化学结构是 17-位的侧链含有 9-10 个碳原子的脂肪烃(见表 4 和图 3)。

表 4 C_{21} 甾类与植物甾醇类成分

Table 4 C_{21} steroid and phytosterol components

编号 No.	化合物 Compound	来源 Source	甾体类型 Steroid type	参考文献 Ref.
115	3 β -[(<i>O</i> - β -D-Glucopyranosyl) oxy] -pregna-5,16-dien-20-one	PS	C_{21} 甾类 C ₂₁ Steroids	41
116	3 β -[(<i>O</i> - α -L-Rhamnopyranosyl-(1 \rightarrow 2)- β -D-glucopyranosyl) oxy] -pregna-5,16-dien-20-one	PS	C_{21} 甾类 C ₂₁ Steroids	41
117	Pregn-5-en-3 β -ol-20-one-3- <i>O</i> -bis- β -D-glucopyranosyl-(1 \rightarrow 2,1 \rightarrow 6)- β -D-glucopyranoside	PS	C_{21} 甾类 C ₂₁ Steroids	45
118	胡萝卜苷 Daucosterol	PC,PK,PS	植物甾醇类 Phytosterols	46-48
119	β -谷甾醇 β -Sitosterol	PC,PS	植物甾醇类 Phytosterols	41,47,49
120	棕榈酸-3 β -谷甾醇酯	PK	植物甾醇类 Phytosterols	48
121	豆甾-5-烯-3 β ,7 α (β)-二醇	PS	植物甾醇类 Phytosterols	50

注:PS:黄精;PC:多花黄精;PK:滇黄精

Note:PS;*P. sibiricum.*;PC;*P. cyrtoneuma.*;PK;*P. kingianum.*

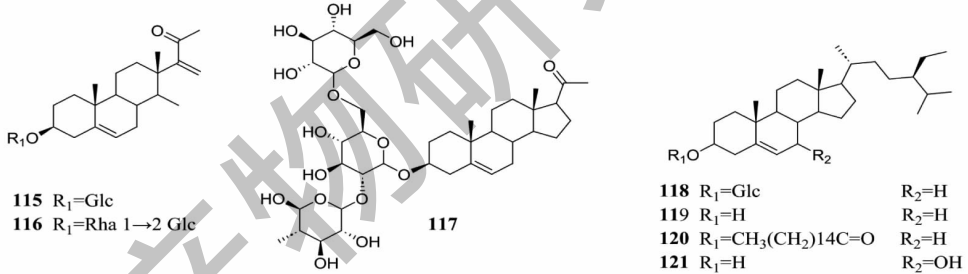


图 3 C_{21} 甾类与植物甾醇类结构

Fig. 3 Structures of C_{21} steroids and phytosterols

1.3 黄酮类

黄精的第三大成分为黄酮类(0.21% ~ 0.71%)^[8],相关其提取工艺方面的研究较多,但富集分离方面的研究较少,目前仅分离鉴定出 37 个

(122 ~ 158),主要类型有高异黄酮、查尔酮和二氢黄酮等,其中高异黄酮类是黄精的特征性成分(见表 5 和图 4)。

表 5 黄酮类成分

Table 5 Flavonoid compounds

编号 No.	化合物 Compound	来源 Source	参考文献 Ref.
122	5,7-Dihydroxy-3-(2'-hydroxy-4'-methoxybenzyl)-chroman-4-one	PC,PS	51-53
123	5,7-Dihydroxy-6-methyl-3-(2',4'-dihydroxybenzyl)-chroman-4-one	PC	51,52
124	5,7-Dihydroxy-6-methyl-3-(4'-hydroxybenzyl)-chroman-4-one	PC,PS	51,52
125	(3S)-3,7-Dihydroxy-8-methoxy-3-(3',4'-methylenedioxybenzyl)-chroman-4-one	PC	51

续表 5 (Continued Tab. 5)

编号 No.	化合物 Compound	来源 Source	参考文献 Ref.
126	7-Hydroxy-3-(2'-hydroxy-3',4'-dimethoxybenzyl)-chroman-4-one	PK	48,54
127	2',7-Dihydroxy-3',4'-dimethoxyisoflavanoside	PK	48
128	5,7-Dihydroxy-6,8-dimethyl-3-(4'-hydroxybenzyl)-chroman-4-one	PS、PC	41-43
129	7-Hydroxy-3-(3'-methoxy-4'-hydroxybenzyl)-chroman-4-one	PS、PK	44
130	5,7-Dihydroxy-6,8-dimethyl-3-(2'-hydroxy-4'-methoxybenzyl)-chroman-4-one	PC、PS	44,53
131	5,7-Dihydroxy-8-methyl-3-(2',4'-dihydroxybenzyl)-chroman-4-one	PS	44
132	5-Hydroxy-7-methoxy-3-(2'-hydroxy-4'-methoxybenzyl)-chroman-4-one	PS	53
133	5,7-Dihydroxy-8-methyl-3-(2'-hydroxy-4'-methoxybenzyl)-chroman-4-one	PS、PC	53
134	5,7-Dihydroxy-3-(4'-hydroxybenzyl)-chroman-4-one	PS、PC	52,53
135	5,7-Dihydroxy-8-methyl-3-(4'-hydroxybenzyl)-chroman-4-one	PC、PS	53
136	Odoratumone A	PS	38
137	5,7-Dihydroxy-6-methyl-8-methoxy-3-(4'-hydroxybenzyl)-chroman-4-one	PS、PC	38
138	Odoratumone B	PS	38
139	Disporopsin	PK、PC	52
140	Polygonatone H	PK	25
141	5,7-Dihydroxy-6,8-dimethyl-3-(2'-methoxy-4'-hydroxybenzyl)-chroman-4-one	PC	52
142	5,7-Dihydroxy-6-methyl-3-(4'-methoxybenzyl)-chroman-4-one	PC	52
143	甲基麦冬黄烷酮 B Methylophiopogonanone B	PC	52
144	5,7-Dihydroxy-3-(4'-methoxybenzyl)-chroman-4-one	PC	52
145	5-Hydroxy-7-methoxy-6,8-dimethyl-3-(2'-hydroxy-4'-methoxybenzyl)-chroman-4-one	PC	52
146	5,7-Dihydroxy-6,8-dimethyl-3-(2',4'-dihydroxybenzyl)-chroman-4-one	PS	50
147	5,7-Dihydroxy-3-(4'-hydroxybenzylidene)-chroman-4-one	PC	52
148	芹菜素 Apigenin	PC	51
149	山柰酚 Kaempferol	PC	51
150	杨梅素 Myricetin	PS	45
151	(6aR,11aR)-10-羟基-3,9-二甲氧基紫檀烷 (6aR,11aR)-10-Hydroxy-3,9-dimethoxypterane	PK	55
152	甘草素 Liquiritigenin	PK	55
153	异甘草素 Isoliquiritigenin	PK	55
154	Polygonatone D	PC	52
155	芹菜素-7-O-β-D-葡萄糖苷 Apigenin-7-O-β-D-glucoside	PS	45
156	芹菜素-8-C-半乳糖苷 Apigenin-8-C-galactoside	PS	38
157	新甘草苷 Lquiritin	PK	48
158	新异甘草苷 Neoisoliquiritigenin	PK	48

注:PS:黄精;PC:多花黄精;PK:滇黄精

Note:PS:*P. sibiricum.*;PC:*P. cyrtonema.*;PK:*P. kingianum.*

1.4 生物碱类

同一植物中所含的生物碱,一般来源同一个前体。因此,凡含有生物碱的植物,往往含有多种结构相似的同类生物碱成分。近年来,国内外研究者从

黄精中分离出生物碱类化合物 16 个(159 ~ 174),其中,从滇黄精中分离得到了黄精碱 B 和新吡啶里西酮滇黄精酮,其余 14 个从多花黄精和黄精中分离得到(见表 6 和图 5)。

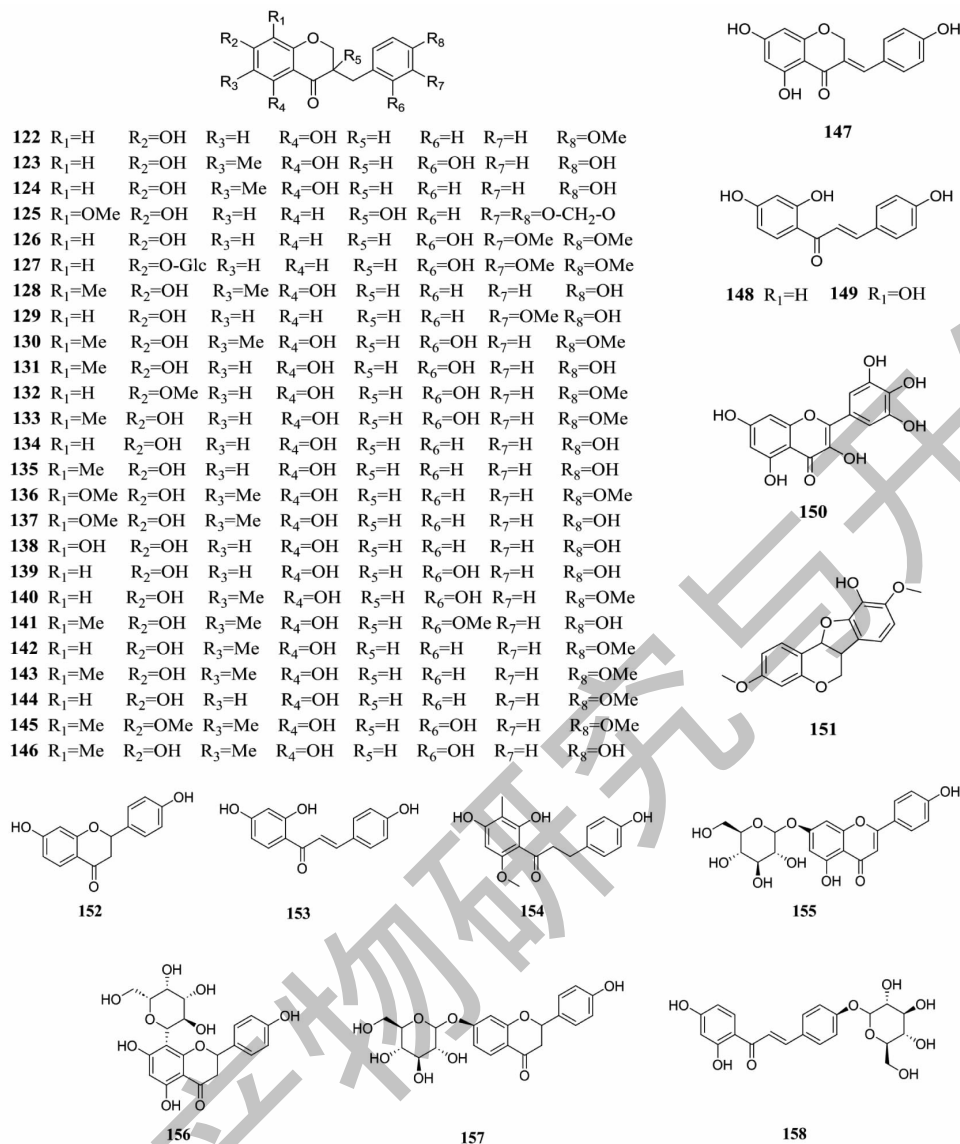


图4 黄酮类结构

Fig. 4 Structures of Flavonoid compounds

表6 生物碱类成分

Table 6 Alkaloid components

编号 No.	化合物 Compound	来源 Source	参考文献 Ref.
159	黄精碱 A Polygonatine A	PC、PS	56
160	黄精碱 B Polygonatine B	PC、PK	56
161	新吡啶里西酮滇黄精酮 Kingaone	PK	54
162	1H-吡啶-3-甲醛 Indole-3-carboxaldehyde	PC	24
163	5-羟基-2-羟甲基吡啶 5-Hydroxy-2-pyridinemethanol	PS	49
164	5-羟基吡啶-2-甲酸甲酯 5-Hydroxypyridine-2-carboxylate	PS	50
165	2,3,4,6-Tetrahydro-1H- β -carboline-3-carboxylic acid	PS	50

续表 6 (Continued Tab. 6)

编号 No.	化合物 Compound	来源 Source	参考文献 Ref.
166	川芎嗪 Perlolyrine	PS	50
167	4-(9H- β -Carbolin-1-yl) 4-oxo-but-2-enoic acid methyl ester	PS	50
168	5-(9H- β -Carbolin-1-yl) -pentane-1,2,5-triol	PS	50
169	酒渣碱 Flazine	PS	50
170	<i>N</i> -反式-对香豆酰基章鱼胺 <i>N-trans-p-Coumaroyloctopamine</i>	PC	51
171	<i>N</i> -反式-阿魏酰真蛸胺 <i>N-trans-Feruloyloctopamine</i>	PC	26
172	3-(4-Hydroxy)- <i>N</i> -[2-(4-hydroxyphenyl)-2-methoxyethyl]-2-propenamamide	PS	57
173	3-(4-Hydroxy-3-methoxyphenyl)- <i>N</i> -[2-(4-hydroxyphenyl)-2-methoxy-ethyl]-2-propenamamide	PS	57
174	<i>N</i> -反式-对香豆酰基酪胺 <i>N-trans-p-Coumaroyltyramine</i>	PS	57

注:PS:黄精;PC:多花黄精;PK:滇黄精

Note:PS:*P. sibiricum.*; PC:*P. cyrtonea.*; PK:*P. kingianum.*

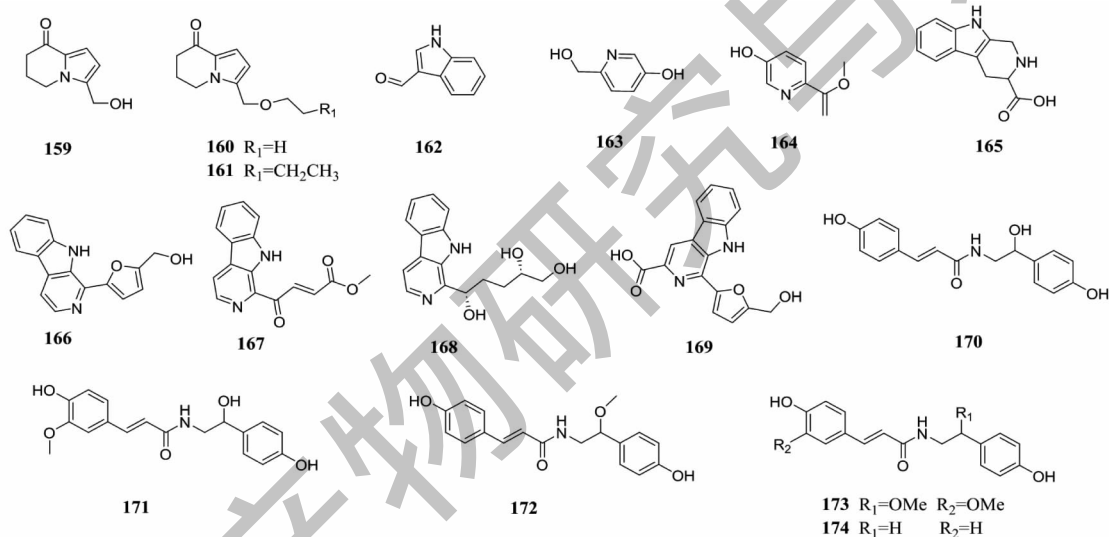


图 5 生物碱类结构

Fig. 5 Structures of alkaloid compounds

1.5 苯丙素类

已有研究证明,木脂素类同系物母核化学结构中,酚羟基的存在会增强其抗脂质过氧化和清除自由基的生物活性,且黄精所含木脂素类成分含量显著高于同科其他属药用植物,这为黄精具有更强的

生物活性和直接内服的吸收方式奠定了科学依据。根据文献报道和 TCMSP 数据库检索,从黄精和多花黄精中分离鉴定的苯丙素类主要是木脂素类及少量的简单苯丙素类,共 13 个化合物(175 ~ 187)(见表 7 和图 6)。

表 7 苯丙素类成分

Table 7 Phenylpropyl compounds

编号 No.	化合物 Compound	来源 Source	参考文献 Ref.
175	反式-对羟基桂皮酸 <i>Trans-p-hydroxycinnamic acid</i>	PC	51
176	反式-对羟基桂皮酸甲酯 <i>Trans-p-Hydroxycinnamic acid methyl ester</i>	PC	51
177	咖啡酸 3,4-Dihydroxycinnamic acid	PC	51

续表 7 (Continued Tab. 7)

编号 No.	化合物 Compound	来源 Source	参考文献 Ref.
178	松柏醛 4-Hydroxy-3-methoxycinnaldehyde	PC	51
179	皮树脂醇 (+)-Medioresinol	PC	24
180	松脂素 (+)-Pinoresinol	PS	49
181	丁香脂素 Syringaresinol	PS、PC	49
182	蛇菰素 B Balanophorin B	PC	51
183	鹅掌楸苷 Liriodendrin	PS	58
184	(+)-Syringaresinol-O-β-D-glucopyranoside	PS、PC	58
185	(+)-Pinoresinol-O-β-D-glucopyranosyl(1→6)β-D-gluco-pyranoside	PS	42
186	黄精新木脂素苷 A Polygonlignanose A	PS	57
187	Solaricresinol 9'-O-β-D-glucopyranoside	PS	57

注:PS:黄精;PC:多花黄精;PK:滇黄精

Note:PS:*P. sibiricum.*; PC:*P. cyrtonea.*; PK:*P. kingianum.*

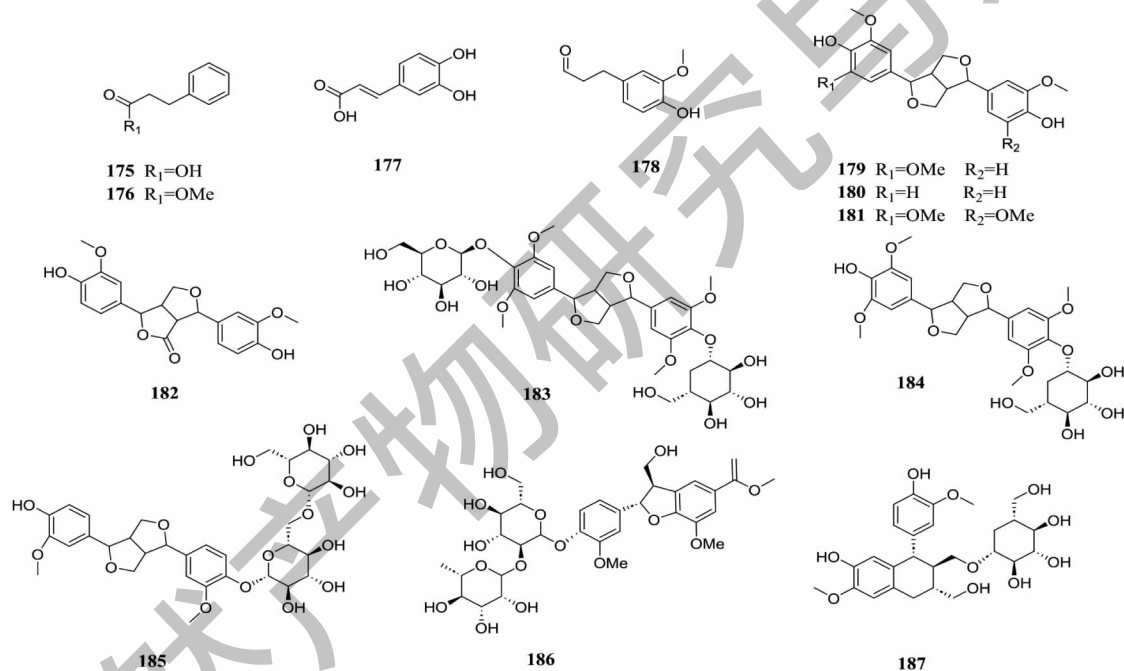


图 6 苯丙素类结构

Fig. 6 Structures of phenylpropanoid compounds

1.6 挥发性成分

近年来,挥发性成分被越来越广泛地用于医药、食品、化妆品、香料等行业,已成为创新资源开发研究的热点。挥发性成分也是黄精药理活性物质之一,相关研究主要集中在成分分析方面,方法包括气相色谱法、气质联用法和电子鼻技术,学者们分别从不同药用部位、不同产地、不同炮制方法及炮制前后等方面对其种类和含量进行了比较分析。据报道,黄精含有丰富的挥发性成分及较强的生物活性,但其提取、分离及药理方面的研究尚需进一步深入。

目前,从黄精中分离鉴定的挥发性成分仅有 50 种,且大部分来源于黄精的茎^[59],其中多花黄精中以庚烷、葵烷和正十二烷为主^[60]。

1.7 其他成分

除了上述成分,黄精还含有丰富的氨基酸和微量元素。Wang^[61]等分离得到了 16 种氨基酸和 18 种微量元素,其中丙氨酸和苏氨酸含量最高,微量元素中钙、镁、铝元素含量丰富^[62]。此外,黄精还含有赖氨酸、苯丙氨酸、组氨酸、缬氨酸、亮氨酸和异亮氨酸 6 种人体必需氨基酸^[63]。

2 药理作用

现代药理学研究发现,黄精具有降血糖、降血脂、抗肿瘤、抗氧化、抗菌和免疫调节等药理作用,且发挥上述药理作用的主要成分是多糖类、皂苷类和黄酮类成分。

2.1 降血糖与降血脂

黄精在降血糖方面的研究主要集中在多糖成分,偶有报道显示其皂苷和黄酮成分也有一定的降糖作用^[64]。与模型组相比,黄精多糖给药 28 d 后,小鼠血清总胆固醇(total serum cholesterol, TC)、甘油三酯(triglyceride, TG)和肝组织丙二醛(malondialdehyde, MDA)水平均降低^[65]。另,黄精知母三七胶囊可能通过促进胰岛素分泌,降低胰岛素的抵抗,进而改善小鼠的糖代谢水平^[66]。将黄精与青钱柳配伍,可显著降低糖尿病大鼠空腹血糖,且血清中超氧化物歧化酶(superoxide dismutase, SOD)和谷胱甘肽过氧化酶(glutathione peroxidase, GSH-Px)活性显著提高^[67]。上述研究结果表明,单味黄精即可降低小鼠血糖,与其他药材配伍后,其降糖作用更为显著。此外,尚有研究发现黄精炮制后,降血糖活性尤为突出,这为其药理作用研究及中药传承发展提供了新的研究思路。

目前,相关黄精多糖及复方降血脂方面的研究较多^[68],黄精可通过调节脂质代谢、改善氧化应激损伤程度、减轻炎症反应、抑制凋亡信号通路激活等发挥降血脂功效。相比给予硝苯地平^[69],黄精益阴汤在 TC、TG、丙氨酸氨基转移酶(alanine aminotransferase, ALT)水平及不良反应上表现更优。复方多花黄精提取物高剂量组(30 g 生药/kg)小鼠给药第 2 周后,TC 和 TG 显著降低($P < 0.01$)^[68]。另,经红曲菌发酵后,黄精的色泽和口感得到改善,且降血脂和免疫作用也有所提高。经红曲菌发酵和炮制后均能达到对咽喉刺激性降低,麻舌感减弱的效果,同时

生物活性有所提高。因此,还可在中药配伍和炮制研究的基础上,应用现代药理学对其降血糖与降血脂机制进行富有中医药文化底蕴的分析和阐释。综上,目前黄精降血糖与降血脂方面的研究多而杂,目前已明确黄精降血糖作用机制主要包括改善血液流动性、影响糖原合成与分解、调节脂肪与蛋白质代谢、增强胰岛素受体敏感性及促进胰岛素的分泌等,但大多缺乏深层次分析和探讨,尤其是在促进胰岛素受体表达、减轻炎症反应和抗氧化等方向应进行更深入更系统的研究。

2.2 抗肿瘤

近年来,黄精抗肿瘤作用方面的研究逐渐深入,通过 H₂₂ 实体瘤、S180 腹水瘤和动物移植性肿瘤 Heps、Eac 方面的研究,已明确黄精多糖、皂苷和黄酮成分是其抗肿瘤活性的物质基础。多糖能显著抑制小鼠移植性肿瘤 Heps、Eac 的生长繁殖($P < 0.01$)^[70],也对肝癌 H₂₂ 移植瘤有明显的抑制作用;黄酮类化合物可抑制癌细胞生长并诱发凋亡^[71]。Wang 等^[72]从黄精中分离得到 2 种甾体皂苷,分别为薯蓣皂苷(51 号)和甲基原薯蓣皂苷(88 号),并发现薯蓣皂苷对肺癌、乳腺癌和宫颈癌细胞的增殖有抑制作用,且效果与剂量存在良好的线性关系。在上述研究的基础上,学者们还进一步研究了抗肿瘤机制。例如,黄精多糖抗肿瘤作用机制主要包含激活 Caspase 系统诱导肿瘤细胞凋亡、通过 TLR4/NF- κ B 和 TLR4-MAPK/NF- κ B 信号通路抑制肿瘤细胞生长以及免疫调节。黄精薯蓣皂苷抗肿瘤机理如图 7 所示。此外,黄精根状茎含有丰富的内生菌,其菌胞外多糖与原植物多糖有着相似甚至相同的生物活性,这为黄精抗肿瘤研究提供了新的研究思路和方向。另外,通过查阅古籍医书以及临床经验发现,以黄精为君药的抗肿瘤药方较多,且效果好、毒性低,这为中医理论指导下的新型抗癌药物研发奠定了坚实的理论和实践基础。

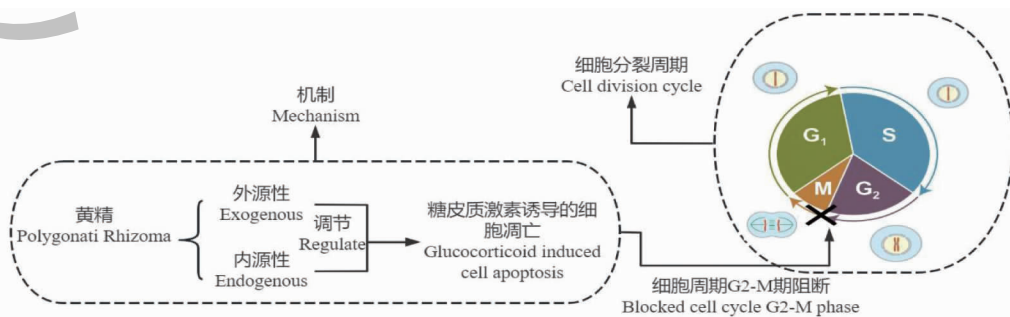


图 7 黄精薯蓣皂苷抑瘤机制流程图

Fig. 7 Flow chart of antitumor mechanism of diosgenin of Polygonati Rhizoma

2.3 抗菌

相关研究者发现,黄精的抗菌活性主要源于其内生菌,其次是甾体皂苷^[73]和多酚类成分。最新研究成果表明,黄精内生菌 HJ-12、HJ-3 对常见的植物病原真菌均表现出良好的拮抗活性。Lv 等^[74]研究显示,HJ-3 发酵产物对金黄色葡萄球菌、大肠杆菌、苏云金杆菌和枯草芽孢杆菌均有一定的抑制作用,其中对金黄色葡萄球菌的抑菌效果最好(发酵产物浓度为 40 mg/mL,抑菌圈直径达 16 mm)。Wang 等^[75]从黄精根中分离得到两种甾体皂苷化合物,(25R)-Spirost-5-ene-3 β -ol-3-O- α -L-rhamnopyranosyl(1 \rightarrow 2)-[α -L-rhamnopyranosyl(1 \rightarrow 4)] β -D-glucopyranoside(43 号)和(25R)-Spirost-5-ene-3 β -ol-3-O- α -L-rhamnopyranosyl(1 \rightarrow 4)- β -D-glucopyran

oside(42 号)对植物病原菌和细菌均有显著的抑制效果,黄精甾体皂苷发挥抗菌活性的主要途径为诱导细菌膜胆固醇产生分子复合物。另,通过黄精多酚体外抗菌研究发现,其提取液对枯草芽孢杆菌和大肠杆菌都表现良好的抑菌效果,最小抑菌浓度为 50 mg/mL^[76],为黄精进一步开发为天然抗菌药物和植物杀虫剂提供理论依据。

2.4 抗氧化及抗衰老

黄精优异的抗氧化作用基于其庞大的化学成分集群,如多糖^[77]、黄酮^[78]、皂苷^[79]和多酚^[80]。滇黄精的中性和酸性多糖对 ABTS 自由基的清除有显著活性,半清除浓度分别为 0.825 mg/mL 和 0.444 mg/mL^[81]。多花黄精总皂苷可有效清除 DPPH 和 ABTS 自由基,半抑制浓度分别为 91.90 μ g/mL 和 60.42 μ g/mL^[82]。另外,酒制可使黄精多糖结构发生改变,对 DPPH 自由基的清除能力增强,半数抑制浓度为酒制前的 6 倍^[83]。酒制黄精中含大量总黄酮,对 DPPH、ABTS 和羟自由基表现出强抗氧化活性,半抑制浓度分别为 19.4、31.57 和 4.46 μ g/mL^[84]。基于黄精优异的抗氧化效果,后续可将黄精开发为抗衰老药物、护肤保健品和功能性食品,提高黄精的综合利用,实现价值最大化。

2.5 其它作用

除了上述药理作用外,黄精还有保肝^[85]、抗骨质疏松^[86]、改善记忆^[87]等活性。持续灌胃黄精水提取物 3 个月后,大鼠体内血清谷丙转氨酶、谷草转氨酶、肝组织丙二醛、髓过氧化物酶和肝组织 CYP2E1 蛋白表达量显著上升,而超氧化物歧化酶和谷胱甘肽水平显著降低^[88]。黄精多糖可通过上

调 Wnt/ β -catenin 信号通路,加强小鼠脂肪干细胞的成骨分化能力^[89]。黄精和地龙配伍后,小鼠自发活动、探索能力、海马神经元水平和 Bcl-2 表达均有所提高,显著改善衰老小鼠的学习记忆^[90]。研究发现黄精可以降低东莨菪碱拮抗胆碱能神经系统以及竞争性抑制 M 型胆碱受体,降低胆碱能神经系统的损伤,进一步调节内侧隔核-海马 GABA 能神经投射通路,促进恢复长久记忆;与此同时改善皮层胆碱能系统,降低对短期记忆的损伤。进一步研究发现,黄精加强小鼠记忆机制还与小鼠海马神经元 Tau 和 P-Tau、Wnt/ β -catenin 信号通路影响蛋白 α 7 nAChR 和 PS-1 表达以及 CA1 区超微结构等有关。

3 Q-Marker 的预测分析

《中国药典》2020 年版以黄精多糖的总量不得少于 7.0% 作为其质量标准,上述大量研究表明,仅以多糖作为质量标准,尚不能更准确和全面地反映黄精质量的优劣及有效性,不利于其质量控制和临床用药。网络药理学可有效的建立药物成分与机体靶点互作的多维网络模型,其多成分、多靶点、多途径的研究思维与中医理论的“整体观”相一致。因此,本文通过网络药理学对其 Q-Marker 进行了预测,旨在建立更加全面和科学的质量控制体系。

3.1 基于药理活性预测 Q-Marker

黄精为常用传统中医用药,治疗脾胃虚弱、体倦乏力、口干食少等,现代药理学研究证明,其多糖、皂苷类和黄酮类为主要药理活性成分,用于降血糖、降血脂、抗肿瘤、抗氧化、抗菌和免疫调节等。大量研究已证实,黄精多糖具有上述全部药理活性,尤其在降血糖、增强免疫功能及神经系统方面活性显著;黄精黄酮类成分甘草素、异甘草素、黄芩素和汉黄芩素等对肿瘤细胞的转移、增殖和侵袭有抑制作用,同时诱导癌细胞凋亡和自噬;黄精皂苷类成分薯蓣皂苷元和甲基原薯蓣皂苷等具有降血脂、抗肿瘤、抗菌、抗血小板聚集等活性,甲基原薯蓣皂苷可将细胞周期阻断在 G2/M 期,达到抑瘤效果;黄精甾醇类成分 β -谷甾醇和谷甾醇等对肝癌、食管癌、白血病等具有防治作用^[91]。分析次生代谢产物与药理作用的效应关系是预测质量标志物的关键所在,表 8 为黄精化学成分对应的药理活性。由此,建议将黄精多糖、薯蓣皂苷元、甲基原薯蓣皂苷、甘草素、异甘草素、黄芩素和汉黄芩素、 β -谷甾醇、谷甾醇作为黄精药理作用的 Q-Marker。

表 8 黄精化学成分与药理活性

Table 8 Chemical constituents and pharmacological activities of Polygonati Rhizoma

化学成分 Compound	药理活性 Pharmacological effect
多糖 Polysaccharide	抗阿尔兹海默病、抗脂肪肝、抗糖尿病、抗肿瘤、抗衰老、抗菌、保护心脏肾脏骨骼、增强免疫、促进睡眠、改善记忆
薯蓣皂苷元 Diosgenin	降血脂、抗血小板聚集、促进胆汁分泌、抗肿瘤、防治白血病
甲基原薯蓣皂苷 Methylprotodioscin	抗肿瘤、抗炎、抗氧化、抑菌、镇痛
甘草素 Liquiritigenin	抗氧化、抗肿瘤、抗炎、抗辐射、抗心律失常、抑菌、免疫调节
β -谷甾醇 β -sitosterol	抗炎、抗氧化、抗菌、抗肿瘤、抗动脉粥样硬化、抗衰老、抗抑郁、降血脂、调节免疫、调节骨代谢
黄芩素 Baicalein	解热镇痛抗炎、抗菌、抗病毒、抗肿瘤、抑制新生血管形成、抗氧化、降血糖、护肝
汉黄芩素 Wogonin	抗病毒、抗氧化、调节炎症反应、免疫调节
异甘草素 Isoliquiritigenin	抗肿瘤、抗氧化、抗炎、心血管和气管作用
谷甾醇 Sitosterol	抗炎、抗癌、抗血脂、抗糖尿病、抗神经退行性疾病、护肤保养

3.2 基于网络药理学预测 Q-Marker

网络药理学是基于系统生物学理论,对生物系统的网络分析,选取特定信号节点,进行多靶点药物分子设计的方法,对于分析中药材多种化合物与多靶点相互作用的特点具有明显优势。本文利用该方

法分析预测了黄精的主要活性成分及其作用靶点。通过对 TCMSP、TCMID 数据库和文献报道,收集黄精化学成分共 84 种。首先根据 OB 值(口服生物利用度) $\geq 30\%$ 和 DL 值(类药性) ≥ 0.18 对化合物进行筛选,见表 9。

表 9 黄精效应成分化合物相关信息

Table 9 Related information of Polygonati Rhizoma effector compounds

化合物 Compound	TCMSP 编号 Mol ID	口服生物利用度 Oral bioavailability (%)	血脑屏障 Blood-brain barrier	类药性 Drug-likeness	肠上皮通透性 Intestinal epithelial permeability
新甘草苷 DFV	MOL001792	32.76	-0.29	0.18	0.51
黄芩素 Baicalein	MOL002714	33.52	-0.05	0.21	0.63
3'-甲氧基大豆苷 3'-Methoxydaidzein	MOL002959	48.57	-0.32	0.24	0.56
β -谷甾醇 β -Sitosterol	MOL000358	36.91	0.99	0.75	1.32
甲基原薯蓣皂苷 Methylprotodioscin	MOL003889	35.12	-0.45	0.86	0.20
甘草素 Liquiritigenin	MOL004941	71.12	-0.25	0.18	0.41
5,4'-二羟基黄酮 5,4'-Dihydroxyflavone	MOL006331	48.55	-0.03	0.19	0.76
薯蓣皂苷元 Diosgenin	MOL000546	80.88	0.27	0.81	0.82
刺五加甙 Acanthoside B	MOL009763	43.35	-1.83	0.77	-0.97

续表 9 (Continued Tab. 9)

化合物 Compound	TCMSP 编号 Mol ID	口服生物利用度 Oral bioavailability (%)	血脑屏障 Blood-brain barrier	类药性 Drug-likeness	肠上皮通透性 Intestinal epithelial permeability
谷甾醇 Sitosterol	MOL000359	36.91	0.87	0.75	1.32
黄精皂苷 A Sibiricoside A	MOL009760	35.26	-0.75	0.86	0.16
Zhonghualiaoine 1	MOL009766	34.72	-0.38	0.78	0.31

药理研究表明以上黄酮类成分具有抑菌、抗肿瘤、抗氧化等药理活性,皂苷类成分具有镇痛、解热、改善心血管等功效。传统中医药认为黄精具有补气养阴、清热解毒、化痰止咳的功效。借助网络药理学的手段,可以分析中草药的多种成分与人体受体的相互作用,预测其中有可能对疾病有治疗效果的成分,为中草药有效成分的发现提供了新思路和方法。因此,利用网络药理学技术预测了它们作用的蛋白靶点,见图 8。菱形为黄精化学成分、椭圆形为蛋白靶

点,节点之间的连线越多、字体和节点图形越大意味着化学成分引起的生物活性越显著,药理作用越明显。综上,筛选出新甘草苷、黄芩素、甘草素、甲基原薯蓣皂苷、薯蓣皂苷元、3'-甲氧基大豆苷、5,4'-二羟基黄酮、 β -谷甾醇和刺五加甙共 9 个化合物。由于 β -谷甾醇作为黄精质量标记物缺乏特异性,因此上述 9 个化合物除 β -谷甾醇外其余成分建议作为黄精的潜在 Q-Marker。

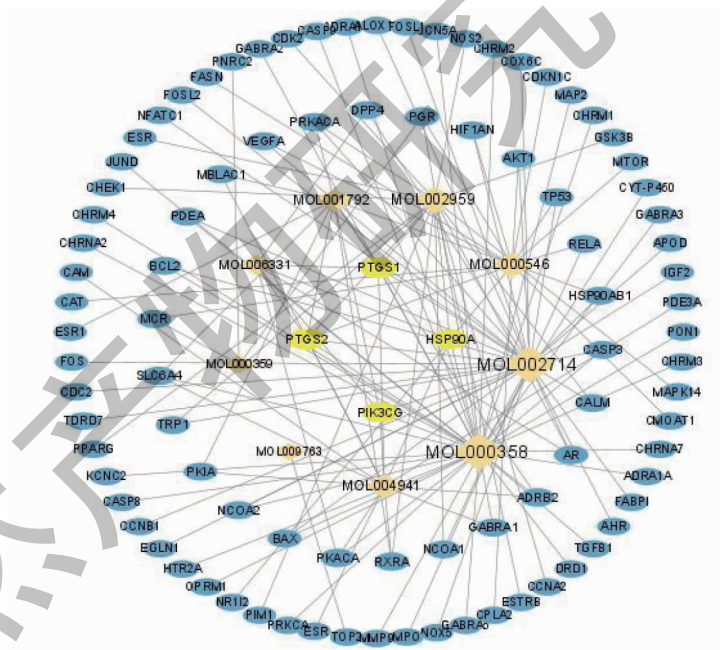


图 8 “成分-靶点”网络图

Fig. 8 Network diagram of “component-target”

4 结语与展望

黄精医用记载始于《名医别录》:“黄精,味甘、性平,无毒。长久服用身体轻盈,多年不饥饿”。历代医药名著《证类本草》《本草图经》和《本草纲目》等均记载黄精具有补气益阴和调补脾胃的功效,用于治疗倦怠乏力、腰膝酸软、遗精滑精等症。现代药理研究表明,黄精在治疗心脑血管疾病,抗衰老、抗炎、抗病原微生物、抗动脉粥样硬化、改善记忆、免疫

调节、降血脂和降血糖等都具有良好的效果,且发挥上述药效的物质基础主要是多糖、皂苷和黄酮类成分。因此,仅以黄精多糖作为指标性成分,尚不能全面反映黄精的质量标准。

本文首先系统地总结了黄精的活性成分和药理作用,其次通过网络药理学预测黄精的活性成分与作用靶点,最后从黄精的特征性成分、药理活性物质和网络药理学分析三个方面预测黄精的 Q-Marker,

建议将大类成分多糖、皂苷类和黄酮类作为质量标志物;单一成分:黄芩素、甘草素、薯蓣皂苷元、5,4'-二羟基黄酮、3'-甲氧基大豆苷、新甘草苷和黄精多糖 PSP 作为黄精潜在的 Q-Marker。旨在更科学、客观地对黄精进行质量评价,为其生产、加工、流通和应用等过程中的质量控制提供参考依据。

参考文献

- 1 Yin SY, et al. Research progress in diversity of origin plants of Chinese medicinal Polygonati Rhizoma and its utilization [J]. Chin Wild Plant Resour(中国野生植物资源), 2022, 41:49-57.
- 2 Zhu BJ, et al. Prediction of suitable areas of *Polygonatum sibiricum* Red. under climatic background [J]. Pharm Clin Chin Mater Med(中药与临床), 2023, 14:6-9.
- 3 Tao HJ. Mingyi Bielu(名医别录) [M]. Beijing: People's Medical Publishing House, 1986:23.
- 4 Peng JY. Extraction characterization and applications in cosmetics of active ingredients of *Polygonatum cyrtonema* [D]. Guangzhou: South China University of Technology(华南理工大学), 2017.
- 5 Qi B. Extraction, isolation and identification of structures of active components reducing blood sugar in *P. sibiricum* Red-oute [D]. Wuxi: Jiangnan University(江南大学), 2005.
- 6 Chen HY, et al. Predictive analysis of quality marker in Zhuang medicine for deficiency conditioning prescriptions based on "Five Principles" [J]. Asia-Pac Tradit Med(亚太传统医药), 2022, 18:216-225.
- 7 Liu XC. Five-year review on development of quality markers of traditional Chinese medicine [J]. Chin Tradit Herb Drugs(中草药), 2021, 52:2511-2518.
- 8 Chen T, et al. Study on chemical composition changes of *Polygonatum sibiricum* before and after processing [J]. Shandong Chem Ind(山东化工), 2021, 50:103-104.
- 9 Yang MH, et al. Recent advances in *Polygonatum* polysaccharides: extraction, isolation, purification and bioactivities [J]. Sci Technol Food Ind(食品工业科技), 2022, 43:407-416.
- 10 Li YL, et al. Research progress on chemical and activities of Huangjing (*Polygonatum sibiricum* Red) [J]. Guid J Tradit Chin Med Pharm(中医药导报), 2019, 25:86-89.
- 11 Wang YJ, et al. Purification, structural characterization and in vivo immunoregulatory activity of a novel polysaccharide from *Polygonatum sibiricum* [J]. Int J Biol Macromol, 2020, 160:688-694.
- 12 Zhang H, et al. Microwave assisted degradation of polysaccharide from *Polygonatum sibiricum* and antioxidant activity [J]. J Food Sci, 2019, 4:754-761.
- 13 Wang K, et al. Sequential extraction and structural analysis of polysaccharides from *Polygonatum cyrtonema* Hua [J]. Nat Prod Res Dev(天然产物研究与开发), 2014, 26:364-369.
- 14 Wang Y, et al. Analysis on composition of *Polygonatum sibiricum* polysaccharide and its antioxidant activity [J]. Genomics Appl Biol(基因组学与应用生物学), 2019, 38:2191-2199.
- 15 Sun TT, et al. Physicochemical properties and immunological activities of polysaccharides from both crude and wine-processed *Polygonatum sibiricum* [J]. Int J Biol Macromol, 2020, 143:255-264.
- 16 Li RS, et al. Structural characterization, hypoglycemic effects and antidiabetic mechanism of a novel polysaccharides from *Polygonatum kingianum* Coll. et Hems [J]. Biomed Pharmacother, 2020, 131:110687.
- 17 Chen H, et al. Advances in studies on chemical constituents of three medicinal plants from *Polygonatum* Mill. and their pharmacological activities [J]. Chin Tradit Herb Drugs(中草药), 2015, 46:2329-2338.
- 18 Wang CX. Isolation and identification of triterpene saponins and active polysaccharides from *Polygonatum sibiricum* Red [D]. Wuxi: Jiangnan University(江南大学), 2008.
- 19 Hu CY, et al. Triterpenoid saponins from the rhizome of *Polygonatum sibiricum* [J]. Asian Nat Prod Res, 2010, 12:801-808.
- 20 Yu HS, et al. Two new steroidal saponins from the processed *Polygonatum kingianum* [J]. Helv Chim Acta, 2010, 93:1086-1092.
- 21 Yu HS, et al. Saponins from the processed rhizomes of *Polygonatum kingianum* [J]. Chem Pharm Bull, 2009, 57:1011-1014.
- 22 Zhang J. Studies chemical constituents of *Polygonatum kingianum* [D]. Zhengzhou: Henan College of Traditional Chinese Medicine(河南中医学院), 2006.
- 23 Ma BP, et al. NMR study on a triterpene saponin from *Polygonatum kingianum* [J]. J Nat Prod, 2007, 19:7-10.
- 24 Ning HH. Identification of chemical constituents from *Polygonatum cyrtonema* [J]. Chin J Exp Tradit Med Form(中国实验方剂学杂志), 2018, 24:77-82.
- 25 Zhao YL, et al. Accumulation of steroidal saponins and biomass in *Paris polyphylla* var. *yunnanensis* with different growth years [J]. Chin Tradit Herb Drugs(中草药), 2023, 54:7156-7165.
- 26 Liu FY. Establishment of tissue culture system and extraction of steroidal saponins from *Polygonatum cyrtonema* Hua [D]. Hefei: Anhui University(安徽大学), 2017.
- 27 Li XC, et al. Steroid saponins from *Polygonatum kingianum* [J]. Phytochemistry, 1992, 31:3559-3563.
- 28 Yu HS, et al. Three new saponins from the fresh rhizomes of

- Polygonatum kingianum*[J]. Chem Pharm Bull,2009,57:1-4.
- 29 Wang S, et al. De novo assembly and analysis of *Polygonatum sibiricum* transcriptome and identification of genes involved in polysaccharide biosynthesis[J]. Int J Mol Sci,2017,18:1950.
- 30 Cui XW, et al. A Review: The bioactivities and pharmacological application of *Polygonatum sibiricum* polysaccharides[J]. Molecules,2018,23:2-12.
- 31 Yu YM. Studies on the active constituents of *Polygonatum sibiricum*[D]. Tianjin: Tianjin Medical University(天津医科大学),2017.
- 32 Zhang J, et al. Furostanol saponins from the fresh rhizomes of *Polygonatum kingianum*[J]. Chem Pharm Bull,2006,54:931-935.
- 33 Xu DP, et al. Two new steroidal saponins from the rhizome of *Polygonatum sibiricum*[J]. J Asian Nat Prod Res,2009,11:1-6.
- 34 Ma K, et al. Steroidal saponins from *Polygonatum cyrtonea*[J]. Chem Nat Compd,2013,49:888-891.
- 35 Tang C, et al. Steroidal saponins from the rhizome of *Polygonatum sibiricum*[J]. J Asian Nat Res,2019,21:197-206.
- 36 Son KH, et al. Steroidal saponins from the rhizomes of *Polygonatum sibiricum*[J]. J Nat Prod,1990,53:333-339.
- 37 Zhou D, et al. Antiproliferative steroidal glycosides from rhizomes of *Polygonatum sibiricum*[J]. Phytochemistry,2019,164:172-183.
- 38 Yu YM, et al. Rapid characterization on components of *Polygonatum sibiricum* based on HPLC-MS technology[J]. Lishizhen Med Mater Med Res(时珍国医国药),2016,27:794-796.
- 39 Ahn MJ, et al. Steroidal saponins from the rhizomes of *Polygonatum sibiricum*[J]. J Nat Prod,2006,69:360-364.
- 40 Zhai YF. Study on extraction, isolation and biological activities of saponins from *Polygonatum sibiricum*. [D]. Hangzhou: Zhejiang Sci-Tech University(浙江理工大学),2023.
- 41 Wang Q. Study on the transformation of the steroid saponins in processing of Rhizoma Polygonati[D]. Kunming: Kunming University of Science and Technology(昆明理工大学),2017.
- 42 Wang DM, et al. Research advances in chemical constituents and biological activity of *Polygonatum sibiricum*[J]. J Northwest For Univ(西北林学院学报),2006,21:142-145.
- 43 Tang PP. Isolation and structure determination of steroidal saponin from *Polygonatum sibiricum* Red[D]. Wuxi: Jiangnan University(江南大学),2009.
- 44 Wang DM, et al. Steroidal saponins from the rhizomes of *Polygonatum odoratum*[J]. Nat Prod Res,2009,23:940-947.
- 45 Gao Y, et al. Studies on the chemical constituents of fresh *Polygonatum sibiricum*[J]. Pharm Clin Res(药学与临床研究),2015,23:365-367.
- 46 Ma PC, et al. NMR Study on a triterpene saponin from *Polygonatum kingianum*[J]. Nat Prod Res Dev(天然产物研究与开发),2007,19:7-10.
- 47 You XJ. Studies on chemical constituents of the low polarity and antibacterial activity of *Polygonatum sibiricum*. Red[D]. Yangling: Northwest A&F University(西北农林科技大学),2009.
- 48 Sun LR, et al. Studies on chemical constituents of rhizome of *Polygonatum sibiricum*(II)[J]. Chin Tradit Herb Drugs(中草药),2001,32:12-14.
- 49 Chen H, et al. Chemical constituents of ethyl acetate extract from the Rhizomes of *Polygonatum sibiricum*[J]. J Chin Med Mater(中药材),2017,40:1345-1347.
- 50 Wang QL. Study chemical constituents and anti-inflammatory activity of the rhizome of *Polygonatum sibiricum* Red[D]. Beijing: Beijing University of Chemical Technology(北京化工大学),2017.
- 51 Xu JX, et al. Chemical constituents from aerial part of *Polygonatum cyrtonea*[J]. Chin Tradit Herb Drugs(中草药),2016,47:3569-3572.
- 52 Wang W, et al. Polygonatone H, a new homoisoflavanone with cytotoxicity from *Polygonatum cyrtonea* Hua[J]. Nat Prod Res,2019,33:1727-1733.
- 53 Chen H, et al. Homoisoflavanones with estrogenic activity from the rhizomes of *Polygonatum sibiricum*[J]. J Asian Nat Prod Res,2018,20:92-100.
- 54 Wang YF, et al. A new indolizinone from *Polygonatum kingianum*[J]. Planta Med,2003,69:1066-1068.
- 55 Wang YF, et al. Studies on chemical constituents from the root of *Polygonatum kingianum*[J]. China J Chin Mater Med(中国中药杂志),2003,28:47-50.
- 56 Sun LR, et al. Two new alkaloids from the rhizome of *Polygonatum sibiricum*[J]. J Asian Prod Res,2005,7:127-130.
- 57 Chen H, et al. A new benzofuran lignan from rhizomes of *Polygonatum sibiricum*[J]. Chin Tradit Herb Drugs(中草药),2020,51:21-25.
- 58 Fan SM. Study on chemical constituents and metabolomics of *Polygonatum sibiricum*[D]. Zhengzhou: Henan Agricultural University(河南农业大学),2023.
- 59 Lv Y, et al. GC-MS Analysis of volatile compounds in different parts of *Polygonatum sibiricum*[J]. J Anhui Agric Sci(安徽农业科学),2010,38:20619-20620.
- 60 Du LJ, et al. Changes of volatile substances in rhizome of *Polygonatum cyrtonea* processing by GC-MS[J]. J Anhui Agric Univ(安徽农业大学学报),2021,48:1035-1040.
- 61 Wang SD, et al. Analysis of trace elements and amino acid in rhizome and fibrous root of *Polygonatum cyrtonea* Hua[J]. Chin Tradit Pat Med(中成药),2001,23:59.

- 62 Wang W, et al. Determination and analysis of the content of trace elements in *Polygonatum cyrtonea* and its prepared products from Majiang county[J]. J Kaili Univ(凯里学院学报), 2023, 41: 42-46.
- 63 Li H. Studies on the processing technology of instant tea of *Polygonatum*[D]. Hefei: Anhui Agricultural University(安徽农业大学), 2013.
- 64 Liu S, et al. Advances in chemical constituents and pharmacological effects of *Polygonati Rhizoma*[J]. Nat Prod Res Dev(天然产物研究与开发), 2021, 33: 1783-1796.
- 65 Long FJ, et al. Study on the components of *Polygonatum* mash fermentation broth and its inhibitory activity on α -glucosidase[J]. Cereals Oils(粮食与油脂), 2022, 35: 103-106.
- 66 Zhang XC, et al. Antidiabetic effect of polysaccharides from *Polygonatum kingianum* in streptozotocin-induced diabetic mice[J]. Chin J Ethnomed Ethnopharm(中国民族民间医药), 2022, 31: 19-24.
- 67 Bamodu OA, et al. Elevated PDK1 expression drives PI3K/Akt/MTOR signaling promotes radiation-resistant and dedifferentiated phenotype of hepatocellular carcinoma[J]. Cells, 2020, 9: 746.
- 68 Liu YJ, et al. Hypolipidemic effect of *Polygonatum cyrtonea* prescription extract[J]. Sci Technol Food Ind(食品工业科技), 2019, 40: 285-288.
- 69 Wu YX. The influence of the Huangjing Yiyin decoction on blood pressure, blood lipid and function of liver and kidney in elderly patients with hypertension[J]. Clin J Chin Med(中医临床研究), 2016, 8: 69-70.
- 70 Jiang H. The study of anti-tumour activity of *Rhizoma Polygonati*[J]. J Nanjing Univ Tradit Chin Med(南京中医药大学学报), 2010, 26: 479-480.
- 71 Yang JN, et al. Exploration of the material basis and molecular mechanism of *Rhizoma Polygonati* in the treatment of non-small cell lung cancer based on network pharmacology and molecular docking[J]. Chin Med Herald(中国医药导报), 2022, 19: 16-20.
- 72 Wang LJ, et al. Dioscin restores the activity of the anticancer agent adriamycin in multidrug-resistant human leukemia K562/adriamycin cells by down-regulating MDRI via a mechanism involving NF- κ B signaling inhibition[J]. J Nat Prod, 2013, 76: 909-914.
- 73 Wang DM. Studies on the chemical constituents and bioactivity of two *Polygonatum* plants of Qinling Mountains[D]. Yangling: Northwest A&F University(西北农林科技大学), 2008.
- 74 Lv CY, et al. Identification and antimicrobial activity of an antagonistic endophytic strain HJ-3 from *Polygonatum cyrtonea*[J]. Nat Prod Res Dev(天然产物研究与开发), 2022, 34: 399-406.
- 75 Wang DM, et al. Steroid saponins of *Polygonatum cirrhifolium* root and their antiseptic activity[J]. Sci Silv Sin(林业科学), 2007, 43: 91-95.
- 76 Chen KK, et al. Optimization of ultrasonic assisted extraction of polyphenols from *Polygonatum sibiricum* Red. using response surface methodology and its antibacterial activity[J]. J Shaanxi Normal Univ; Nat Sci(陕西师范大学学报: 自然科学版), 2018, 46: 91-96.
- 77 Pan LC, et al. Chemical structure and effects of antioxidation and against α -glucosidase of natural polysaccharide from *Glycyrrhiza inflata* Batalin[J]. Int J Biol Macromol, 2020, 155: 560-571.
- 78 Guo KL, et al. Enzymatic-ultrasonic assisted extraction of total flavonoids from Shaanxi *Polygonatum sibiricum* and *in vitro* evaluation of their anti-oxidant and anti-A549 proliferation activities[J]. Nat Prod Res Dev(天然产物研究与开发), 2022, 34: 630-638.
- 79 Zhao HY, et al. The main chemical constituents and antioxidant activities of *Polygonatum cyrtonea* Hua[J]. J Anhui Agric Univ(安徽农业大学学报), 2020, 47: 793-797.
- 80 Yang YB, et al. Optimization of the extraction technology and antioxidant activity of polyphenols from *Polygonatum kingianum* Coll. et Hemsl by response surface methodology[J]. Northwest Pharm J(西北药学杂志), 2021, 36: 537-541.
- 81 Xiao KM, et al. Extraction process and antioxidant activity of polysaccharides from *Polygonatum kingianum*[J]. J Southwest Forest Univ; Nat Sci(西南林业大学学报: 自然科学版), 2022, 42: 147-154.
- 82 Quan LN, et al. Study on extraction technology and *in vitro* antioxidant activity of total saponins from *Polygonatum multiflorum*[J]. Mod Chin Med(现代中医药), 2022, 42: 47-51.
- 83 Lu WJ, et al. Comparative study on polysaccharide monosaccharide composition and antioxidant activity of *Polygonatum sibiricum* before and after wine processing[J]. J Basic Chin Med(中国中医基础医学杂志), 2023, 29: 285-291 + 310.
- 84 Xue M, et al. Extraction optimization and antioxidant activities of total flavonoid from alcoholic *Polygonatum*[J]. Cent South Pharm(中南药学), 2023, 21: 351-356.
- 85 Li JJ. *Polygonatum sibiricum* aqueous extract prevents liver from CCl₄-induced acute injury by inhibiting macrophage M1 polarization[D]. Hefei: Anhui Medical University(安徽医科大学), 2022.
- 86 Shao YM, et al. Study on mechanism of action of Huangjing in the treatment of osteoporosis based on network pharmacology and molecular docking technology[J]. Henan Tradit Chin Med(河南中医), 2022, 42: 1676-1682.