

黑老虎木脂素化学成分及药理作用研究进展

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摘要: 黑老虎是一种具有药用、食用、观赏等多种价值的经济植物。黑老虎的化学成分及药理作用研究进展较快, 目前已分离出 200 余种化合物, 其中木脂素类化合物 121 种, 具有抗炎、抗肿瘤、抗 HIV、抗凝血、抗氧化、保肝等多种药理作用。现对黑老虎中木脂素类化学成分和药理作用进行综述, 为黑老虎的深入开发利用提供参考。

关键词: 黑老虎; 木脂素; 化学成分; 药理作用

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Advances in chemical constituents and pharmacological activities of lignans from *Kadsura coccinea*

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Abstract: *Kadsura coccinea* is an economic plant with medicinal, edible, ornamental and other values. The research on chemical constituents and pharmacological effects of *Kadsura coccinea* has achieved rapid progress. More than 200 compounds have been reported so far, including 121 lignans. These lignans have various pharmacological effects, such as anti-inflammatory, anti-tumor, anti-HIV, anti-coagulation, anti-oxidation, liver-protection, ect. The chemical constituents and pharmacological effects of lignans in *Kadsura coccinea* are reviewed here to provide a reference for the further development and utilization.

Key words: *Kadsura coccinea*; lignan; chemical constituents; pharmacological activity

黑老虎 (*Kadsura coccinea* Lem. A. C. Smith) 是五味子科南五味子属植物, 别名冷饭团、过山龙藤、臭饭团、布福娜等, 主要分布于我国湖南、云南、福建、广西、四川、江西等地。生长在海拔 1 500~2 400 m 的山地疏林中, 喜弱光照、湿润环境^[1]。黑老虎的根、果均具有药用价值。黑老虎根曾收载于 1977 版《中国药典》中和 2010 版《中国药典》第四部附录 III 中^[2], 目前收载于湖南省、山西省、广东省中药材标准等地方标准中。黑老虎根性味辛、微苦, 性温, 具有行气活血, 消肿止痛的功效, 主要用于治疗胃病, 风湿骨痛, 跌打瘀痛^[1]。黑老虎果收载于湖南中药材标准中, 主要用于治疗月经不调、妇女围绝经期综合征、女性不孕。海南黎族地区还将其用作香料, 用于肉类保鲜、改善风味^[3]。

目前已从黑老虎中发现了 200 多种化合物, 有木脂素类、三萜类、倍半萜类、生物碱类等, 其中木脂素类为其主要化学成分。现代药理研究表明黑老虎中的木脂素类化学成分具有广泛的药理作用。本文全面总结了黑老虎中的木脂素类化学成分及其药理作用, 以期为黑老虎的药效物质基础研究及开发利用提供参考。

1 黑老虎木脂素类化学成分

目前已从黑老虎中分离鉴定出 121 种木脂素化合物（见图 1、表 1），以联苯环辛二烯型木脂素类为主，此外还有少量的芳基萘型和二苄基丁烷型木脂素。联苯环辛二烯型木脂素根据碳骨架和结构的不同又分为 3 种类型：联苯环辛二烯型、螺苯骈呋喃型、6, 9 氧桥联苯环辛二烯型^[4]。联苯环辛二烯木脂素具有较多立体异构，其中辛环的构象多为船椅式或船式^[4]。

关于黑老虎木脂素类成分的定量分析研究较少。Guo 等^[5]采用甲醇热回流的方法得到不同产地的黑老虎根茎粗提物，并以五味子酯甲作为对照测得黑老虎根的总木脂素含量在 1.599 3%~7.675 5%之间，其中以湖南怀化产的含量最高。Yang 等^[6]用高效液相色谱法（high performance liquid chromatography, HPLC）法测定了中国广西和越南产黑老虎根总提物中 binankadsurin A、qcetylbinankadsurin A、(2'S)-kadsuralignan J 的含量，质量分数分别为 0.021 9%~0.159 5%、0.031 8%~0.176 7% 和 0.036 4%~0.702 8%，三种化合物均表现为越南产比广西产的含量高、木质部比皮质部的含量高。Xu 等^[7]采用 HPLC 法测得贵州剑河、锦屏产黑老虎根 binankadsurin A 的含量在 0.74%~6.93%，认为其可作为标志性成分用于质量评价。

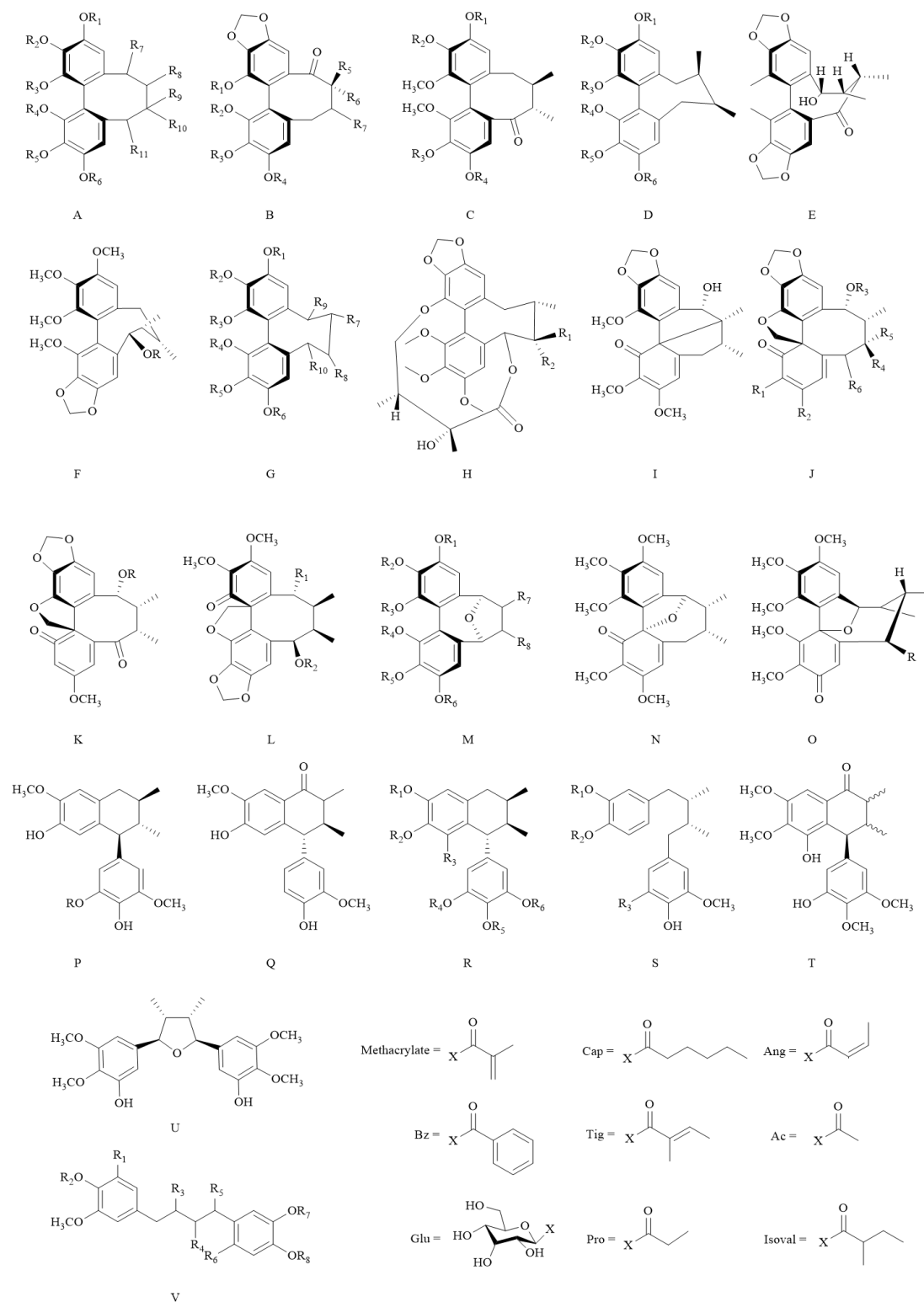


图 1 黑老虎中木脂素类化合物骨架 (A~V)

Fig. 1 Structure skeletons of lignans from *Kadsura coccinea* (A-V)

表 1 黑木老虎中脂素类化合物

Table 1 The chemical constituents of lignans from *Kadsura coccinea*

序号	化合物名称	骨架	取代基	参考文献
No.	Compound name	Skeleton	Substituent group	Ref.
联苯环辛二烯型木脂素				
1	戈米辛 M1 Gomisin M1	A	$R_1 + R_2 = R_5 + R_6 = \text{CH}_2$, $R_3 = R_{11} = \text{H}$, $R_7 = \alpha\text{-H}$, $R_4 = \text{CH}_3$, $R_8 = R_9 = \alpha\text{-CH}_3$, $R_{10} = \beta\text{-H}$	67
2	南五味子灵 A Kadusurain A	A	$R_1 + R_2 = R_5 + R_6 = \text{CH}_2$, $R_3 = \text{CH}_3$, $R_4 = \text{Tig}$, $R_7 = \alpha\text{-OH}$, $R_8 = R_9 = \alpha\text{-CH}_3$, $R_{10} = \beta\text{-H}$, $R_{11} = \text{H}$	85
3	南五味子灵 B Kadusurain B	A	$R_1 + R_2 = R_5 + R_6 = \text{CH}_2$, $R_3 = \text{CH}_3$, $R_4 = \text{Tig}$, $R_7 = \alpha\text{-OAc}$, $R_8 = R_9 = \alpha\text{-CH}_3$, $R_{10} = \beta\text{-H}$, $R_{11} = \text{H}$	85
4	南五味子灵 C Kadusurain C	A	$R_1 + R_2 = R_5 + R_6 = \text{CH}_2$, $R_3 = \text{CH}_3$, $R_4 = \text{Tig}$, $R_7 = \alpha\text{-OCH}_3$, $R_8 = R_9 = \alpha\text{-CH}_3$, $R_{10} = \beta\text{-H}$, $R_{11} = \text{H}$	85
5	五味子酯 L Schisantherin L	A	$R_1 + R_2 = R_5 + R_6 = \text{CH}_2$, $R_3 = R_4 = \text{CH}_3$, $R_7 = \alpha\text{-OH}$, $R_8 = R_9$ $= \alpha\text{-CH}_3$, $R_{10} = \beta\text{-H}$, $R_{11} = \alpha\text{-OAng}$	93
6	五味子酯 M Schisantherin M	A	$R_1 + R_2 = R_5 + R_6 = \text{CH}_2$, $R_3 = R_4 = \text{CH}_3$, $R_7 = \alpha\text{-OTig}$, $R_8 = R_9$ $= \alpha\text{-CH}_3$, $R_{10} = \beta\text{-H}$, $R_{11} = \beta\text{-OAng}$	93
7	五味子酯 N Schisantherin N	A	$R_1 + R_2 = R_5 + R_6 = \text{CH}_2$, $R_3 = R_4 = \text{CH}_3$, $R_7 = \alpha\text{-OAng}$, $R_8 = R_9$ $= \alpha\text{-CH}_3$, $R_{10} = \beta\text{-H}$, $R_{11} = \beta\text{-OAng}$	93
8	Acetylschisantherin L	A	$R_1 + R_2 = R_5 + R_6 = \text{CH}_2$, $R_3 = R_4 = \text{CH}_3$, $R_7 = \alpha\text{-OAc}$, $R_8 = R_9 = \alpha\text{-CH}_3$, $R_{10} = \beta\text{-H}$, $R_{11} = \beta\text{-OAng}$	67
9	Schizanrin F	A	$R_1 + R_2 = \text{CH}_2$, $R_3 = R_4 = R_5 = R_6 = \text{CH}_3$, $R_7 = \beta\text{-OAc}$, $R_8 = R_9$ $= \beta\text{-CH}_3$, $R_{10} = \text{OH}$, $R_{11} = \alpha\text{-OBz}$	20
10	Kadsurindutin A	A	$R_1 + R_2 = R_5 + R_6 = \text{CH}_2$, $R_3 = R_4 = \text{CH}_3$, $R_7 = \alpha\text{-OAc}$, $R_8 =$ $\alpha\text{-CH}_3$, $R_9 = \beta\text{-CH}_3$, $R_{10} = \alpha\text{-OH}$, $R_{11} = \beta\text{-OAng}$	67
11	Acetylepigomisin R	A	$R_1 + R_2 = R_5 + R_6 = \text{CH}_2$, $R_3 = R_4 = \text{CH}_3$, $R_7 = \text{H}$, $R_8 = R_9 =$ $\alpha\text{-CH}_3$, $R_{10} = \beta\text{-H}$, $R_{11} = \alpha\text{-OAc}$	35
12	戈米辛 R Gomisin R	A	$R_1 + R_2 = R_5 + R_6 = \text{CH}_2$, $R_3 = R_4 = \text{CH}_3$, $R_7 = \alpha\text{-H}$, $R_8 = \alpha\text{-CH}_3$, $R_9 = \text{CH}_3$, $R_{10} = \text{H}$, $R_{11} = \beta\text{-OAng}$	20
13	Kadsuphilin A	A	$R_1 + R_2 = \text{CH}_2$, $R_3 = R_4 = R_5 = R_6 = \text{CH}_3$, $R_7 = \alpha\text{-OPhenyl}$, R_8	94

			$= R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \text{H}$	
14	Kadsuralignan B	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_4 = R_5 = R_6 = \text{CH}_3, R_7 = \alpha\text{-OAc}, R_8 = \alpha\text{-CH}_3, R_9 = \beta\text{-CH}_3, R_{10} = \alpha\text{-OH}, R_{11} = \beta\text{-OAc}$	20
15	Kadsuralignan F	A	$R_1 + R_2 = R_5 + R_6 = \text{CH}_2, R_3 = R_4 = \text{CH}_3, R_7 = R_{11} = \text{OH}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}$	95
16	Kadsuralignan G	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = \text{H}, R_7 = \alpha\text{-OCOC}(\text{CH}_3)=\text{CHCH}(\text{OCH}_3)_2, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \text{H}$	96
17	Kadsuralignan I	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = \text{Ang}, R_7 = \alpha\text{-OH}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \text{H}$	19
18	Kadsuralignan J	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = \text{Isoval}, R_7 = \alpha\text{-OH}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \text{H}$	19
19	Kadsuralignan K	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = \text{Bz}, R_7 = \alpha\text{-OH}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \text{H}$	19
20	五味子酯 O Schisantherin O	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = \text{H}, R_7 = \alpha\text{-OAc}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \text{H}$	93
21	乙酰基日本南五味子木脂素 A Acetylbinankadsurin A	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = R_{11} = \text{H}, R_7 = \alpha\text{-OAc}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}$	95
22	当归酰日本南五味子木脂素 A Angeloylbinankadsurin A	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = R_{11} = \text{H}, R_7 = \alpha\text{-OAng}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}$	95
23	异戊酰日本南五味子木脂素 A Isovaleroylbinankadsurin A	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = R_{11} = \text{H}, R_7 = \alpha\text{-OIsoval}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}$	95
24	异丁酰日本南五味子木脂素 Isobutyroylbinankadsurin A	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = R_{10} = R_{11} = \text{H}, R_7 = \alpha\text{-OIsobut}, R_8 = \alpha\text{-CH}_3, R_9 = \text{CH}_3$	95
25	Kadsurarin	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = R_{10} = \text{H}, R_7 = \alpha\text{-OAc}, R_8 = \alpha\text{-CH}_3, R_9 = \text{CH}_3, R_{11} = \alpha\text{-OAng}$	95
26	Heilaohulignan A	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = \text{Prop}, R_7 = \alpha\text{-OH}, R_8 = \alpha\text{-CH}_3, R_9 = \text{CH}_3, R_{10} = \alpha\text{-H}, R_{11} = \text{H}$	35
27	Longipedunin B	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = \text{H}, R_7 = \alpha\text{-OProp}$	95

			$R_8 = \alpha\text{-CH}_3, R_9 = \text{CH}_3, R_{10} = R_{11} = \text{H}$	
28	南五味子素 Kadsurin	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_4 = R_5 = R_6 = \text{CH}_3, R_7 = \alpha\text{-OAc}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = R_{11} = \beta\text{-H}$	67
29	异南五味子素 B Heteroclitin B	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_4 = R_5 = R_6 = \text{CH}_3, R_7 = \alpha\text{-OAng}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = R_{11} = \beta\text{-H}$	67
30	黑老虎素 A Heilaohusu A	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = \text{Ang}, R_7 = \beta\text{-OH}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \text{H}$	15
31	黑老虎素 B Heilaohusu B	B	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = \text{Isoval}, R_7 = \beta\text{-OH}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \text{H}$	15
32	Heilaohulignan B	A	$R_1 = R_3 = R_4 = \text{CH}_3, R_2 = \text{Isoval}, R_5 = \beta\text{-CH}_3, R_6 = \alpha\text{-OH}, R_7 = \alpha\text{-CH}_3$	35
33	Yunnankadsurin B	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_4 = R_5 = R_6 = \text{CH}_3, R_7 = \alpha\text{-OH}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \text{H}$	89
34	Heilaohuguosu A	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = \text{CH}_3, R_7 = \alpha\text{-OAng}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-OH}, R_{11} = \beta\text{-H}$	56
35	Heilaohuguosu B	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = \text{CH}_3, R_7 = \alpha\text{-OH}, R_8 = \alpha\text{-CH}_3, R_9 = \beta\text{-CH}_3, R_{10} = \alpha\text{-OH}, R_{11} = \beta\text{-OAng}$	56
36	Heilaohuguosu C	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = \text{H}, R_7 = \alpha\text{-OAc}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \beta\text{-OAng}$	56
37	Heilaohuguosu D	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = \text{CH}_3, R_7 = \alpha\text{-Methacrylate}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \beta\text{-OAng}$	56
38	Heilaohuguosu E	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = \text{CH}_3, R_7 = \alpha\text{-OH}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \beta\text{-OAng}$	56
39	Heilaohuguosu F	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = \text{CH}_3, R_7 = \alpha\text{-OIsobut}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \beta\text{-H}$	56
40	Heilaohuguosu G	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = \text{CH}_3, R_7 = \alpha\text{-OBz}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \beta\text{-H}$	56
41	Heilaohulignan C	A	$R_1 + R_2 = \text{CH}_2, R_3 = R_5 = R_6 = \text{CH}_3, R_4 = \text{H}, R_7 = \alpha\text{-OAng}, R_8 = \beta\text{-CH}_3, R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \text{H}$	35

42	Kadsuralignan L	A	$R_1 = H, R_2 = R_3 = R_5 = R_6 = CH_3, R_4 = \alpha\text{-Isoval}, R_7 = \alpha\text{-OH},$ $R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = H$	96
43	五味子酯 F Schisantherin F	A	$R_1 = R_{10} = R_{11} = H, R_2 = R_3 = R_5 = R_6 = CH_3, R_4 = \text{Ang}, R_7 =$ $\alpha\text{-OH}, R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \alpha\text{-CH}_3,$	95
44	Schizanrin H	A	$R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = CH_3, R_7 = \alpha\text{-OAc}, R_8 = \alpha\text{-CH}_3,$ $R_9 = CH_3, R_{10} = OH, R_{11} = \beta\text{-OBz}$	20
45	五味子醇甲 Schizandrin	A	$R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = CH_3, R_7 = \alpha\text{-H}, R_{11} = H, R_8 =$ $\alpha\text{-CH}_3, R_9 = CH_3, R_{10} = OH,$	95
46	(6 <i>R</i> ,7 <i>R</i> ,8 <i>R</i>)-1,2,10,11,12-Pentamethoxy-6,7-dimethyl-5,6,7,8-tetrahydrodibenzo [a,c][8]annulene-3,8-diol	A	$R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = CH_3, R_7 = \alpha\text{-OH}, R_8 = R_9 =$ $\alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = H$	94
47	Deangeloylschisantherin F	A	$R_1 + R_2 = CH_2, R_3 = R_5 = R_6 = CH_3, R_4 = H, R_7 = \alpha\text{-OH}, R_8 =$ $R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = H$	15
48	黑老虎素 D Heilaohusu D	A	$R_1 = H, R_2 = R_3 = R_4 = R_5 = R_6 = CH_3, R_7 = \alpha\text{-OAc}, R_8 =$ $\beta\text{-CH}_3, R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \beta\text{-OBz}$	15
49	Heilaohuguosu H	A	$R_1 = R_2 = R_3 = R_5 = R_6 = CH_3, R_4 = \text{Cap}, R_7 = \alpha\text{-OH}, R_8 = R_9$ $= \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \beta\text{-OAc}$	56
50	Heilaohuguosu I	A	$R_1 = R_2 = R_3 = R_5 = R_6 = CH_3, R_4 = \text{Ang}, R_7 = \alpha\text{-OH}, R_8 =$ $\beta\text{-CH}_3, R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \alpha\text{-OAc}$	56
51	Heilaohuguosu J	A	$R_1 = R_2 = R_3 = R_5 = R_6 = CH_3, R_4 = H, R_7 = \alpha\text{-OH}, R_8 = R_9 =$ $\alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \beta\text{-OCH}_3$	56
52	Heilaohuguosu K	A	$R_1 = R_2 = R_3 = R_5 = R_6 = CH_3, R_4 = CH_3, R_7 = \alpha\text{-OH}, R_8 = R_9$ $= \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \beta\text{-OCH}_3$	56
53	Heilaohuguosu L	A	$R_1 = R_2 = R_3 = R_5 = R_6 = CH_3, R_4 = CH_3, R_7 = \alpha\text{-OH}, R_8 = R_9$ $= \alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \beta\text{-OAc}$	56
54	Kadsuphilin B	A	$R_1 + R_2 = CH_2, R_3 = R_4 = R_5 = CH_3, R_6 = R_{11} = H, R_7 = \alpha\text{-H},$ $R_8 = R_9 = \alpha\text{-CH}_3, R_{10} = \beta\text{-H}$	94
55	Kadsuralignan A	A	$R_1 + R_2 = R_5 + R_6 = CH_2, R_3 = R_4 = CH_3, R_7 = \alpha\text{-H}, R_8 = R_9 =$ $\alpha\text{-CH}_3, R_{10} = \beta\text{-H}, R_{11} = \beta\text{-OH}$	95

56	Schizanrin D	A	$R_1 + R_2 = CH_2$, $R_4 = R_5 = R_6 = CH_3$, $R_3 = R_{10} = R_{11} = H$, $R_7 = \alpha\text{-OTig}$, $R_8 = \alpha\text{-CH}_3$, $R_9 = CH_3$	95
57	Kadsutherin A	A	$R_1 = R_2 = CH_3$, $R_5 + R_6 = CH_2$, $R_3 = R_4 = R_{10} = H$, $R_7 = \alpha\text{-H}$, $R_8 = \alpha\text{-CH}_3$, $R_9 = CH_3$, $R_{11} = OAng$	95
58	日本南五味子木脂素 A Binankadsurin A	A	$R_1 + R_2 = CH_2$, $R_3 = R_5 = R_6 = CH_3$, $R_4 = R_{11} = H$, $R_7 = \alpha\text{-OH}$, $R_8 = R_9 = \alpha\text{-CH}_3$, $R_{10} = \beta\text{-H}$	95
59	14-O-Demethyl polysperlignan D	A	$R_1 + R_2 = CH_2$, $R_4 = R_5 = R_6 = CH_3$, $R_3 = H$, $R_7 = \alpha\text{-OTig}$, $R_8 = R_9 = \alpha\text{-CH}_3$, $R_{10} = \beta\text{-H}$, $R_{11} = \beta\text{-OAng}$	67
60	Neglignan G	A	$R_1 + R_2 = CH_2$, $R_3 = H$, $R_4 = R_5 = R_6 = CH_3$, $R_7 = \alpha\text{-OIsobut}$, $R_8 = R_9 = \alpha\text{-CH}_3$, $R_{10} = \beta\text{-H}$, $R_{11} = H$	15
61	Neglectalignan D	A	$R_1 + R_2 = CH_2$, $R_3 = R_4 = R_6 = CH_3$, $R_5 = H$, $R_7 = H$, $R_8 = R_9 = \alpha\text{-CH}_3$, $R_{10} = \beta\text{-H}$, $R_{11} = \alpha\text{-OH}$	89
62	Heilaohuguosu M	A	$R_1 + R_2 = CH_2$, $R_3 = R_5 = R_6 = CH_3$, $R_4 = H$, $R_7 = \alpha\text{-H}$, $R_8 = R_9 = \alpha\text{-CH}_3$, $R_{10} = \beta\text{-H}$, $R_{11} = \alpha\text{-OH}$	56
63	(6 <i>R</i> ,7 <i>R</i> ,8 <i>R</i>)-2,10,11,12-Tetramethoxy-6,7-dimethyl-5,6,7,8-tetrahydrodibenz[<i>a,c</i>][8]annulene-3,8-diol	A	$R_1 = R_2 = R_3 = R_4 = R_5 = CH_3$, $R_6 = H$, $R_7 = \alpha\text{-OH}$, $R_8 = R_9 = \alpha\text{-CH}_3$, $R_{10} = \beta\text{-H}$, $R_{11} = H$	95
64	Diankadsurinone	B	$R_1 = R_2 = R_3 = R_4 = CH_3$, $R_5 = \beta\text{-CH}_3$, $R_6 = \alpha\text{-H}$, $R_7 = \beta\text{-CH}_3$	67
65	Kadoblongifolin A	B	$R_1 = R_3 = R_4 = CH_3$, $R_2 = H$, $R_5 = \alpha\text{-CH}_3$, $R_6 = \beta\text{-OH}$, $R_7 = \beta\text{-CH}_3$	15
66	黑老虎素 C Heilaohusu C	B	$R_1 = R_3 = R_4 = CH_3$, $R_2 = H$, $R_5 = \beta\text{-OAng}$, $R_6 = R_7 = \alpha\text{-CH}_3$	15
67	五味子酯 R Schisantherin R	C	$R_1 + R_2 = R_3 + R_4 = CH_2$	97
68	五味子酯 S Schisantherin S	C	$R_1 = R_2 = R_3 = R_4 = CH_3$	97
69	冷饭团素 Kadsutherin	D	$R_1 + R_2 = CH_2$, $R_3 = Tig$, $R_4 = R_5 = R_6 = CH_3$	98
70	戈米辛 M2 Gomisin M2	D	$R_1 = R_2 = R_3 = CH_3$, $R_4 = H$, $R_5 + R_6 = CH_2$	98
71	五味子甲素 Schizandrin A	D	$R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = CH_3$	98
72	五味子酯 P Schisantherin P	D	$R_1 + R_2 = R_5 + R_6 = CH_2$, $R_3 = R_4 = CH_3$	99
73	南五味子乙素 Schizandrin B	D	$R_1 = R_2 = R_3 = R_4 = CH_3$, $R_5 + R_6 = CH_2$	98
74	五味子酯 Q Schisantherin Q	E		99

75	苯甲酰异五味子素 O Benzoylisogomisin O	F	R = Bz	95
76	戈米辛 J Gomisin J	G	R ₂ = R ₃ = R ₄ = R ₅ = CH ₃ , R ₁ = R ₆ = H, R ₇ = R ₈ = α -CH ₃ , R ₉ = R ₁₀ = H	98
77	五味子丙素 Schisandrin C	G	R ₁ + R ₂ = R ₅ + R ₆ = CH ₂ , R ₃ = R ₄ = CH ₃ , R ₇ = R ₈ = β -CH ₃ , R ₉ = R ₁₀ = H	5
78	Intermedin A	G	R ₁ = H, R ₂ = R ₃ = R ₄ = R ₅ = R ₆ = CH ₃ , R ₇ = α -CH ₃ , R ₈ = α -OH/ β -CH ₃ , R ₉ = α -OAng, R ₁₀ = β -OBz	95
79	戈米辛 D Gomisin D	H	R ₁ = CH ₃ , R ₂ = OH	98
80	戈米辛 E Gomisin E	H	R ₁ = H, R ₂ = CH ₃	98
螺苯骈呋喃联苯环辛二烯型木脂素				
81	异南五味子素 G Heteroclitin G	I		15
82	Schiarisanrin B	J	R ₁ = R ₂ = OCH ₃ , R ₃ = Ac, R ₄ = α -CH ₃ , R ₅ = β -H, R ₆ = H	70
83	异南五味子丁素 Heteroclitin D	J	R ₁ = R ₂ = OCH ₃ , R ₃ = Ang, R ₄ = α -CH ₃ , R ₅ = β -H, R ₆ = H	32
84	南五味子木脂素 H Kadsulignan H	J	R ₁ = R ₂ = OCH ₃ , R ₃ = But, R ₄ = α -CH ₃ , R ₅ = β -H, R ₆ = H	67
85	南五味子木脂素 I Kadsulignan I	J	R ₁ = R ₂ = OCH ₃ , R ₃ = Prop, R ₄ = α -CH ₃ , R ₅ = β -H, R ₆ = H	67
86	Schiarisanrin A	J	R ₁ = R ₂ = OCH ₃ , R ₃ = Isoval, R ₄ = α -CH ₃ , R ₅ = β -H, R ₆ = H	67
87	异南五味子素 E Heteroclitin E	J	R ₁ = H, R ₂ = OCH ₃ , R ₃ = H, R ₄ = α -CH ₃ , R ₅ = β -H, R ₆ = H	15
88	南五味子木脂素 E Kadsulignan E	J	R ₁ = R ₂ = OCH ₃ , R ₃ = Bz, R ₄ = β -CH ₃ , R ₅ = α -OH, R ₆ = β -OAc	5
89	南五味子木脂素 F Kadsulignan F	J	R ₁ = R ₂ = OCH ₃ , R ₃ = Bz, R ₄ = β -CH ₃ , R ₅ = α -OH, R ₆ = β -OAng	95
90	Kadsutherin C	K	R = Bz	15
91	异戊酰氧代南五味子烷 Isovaleroyl oxokadsurane	L	R ₁ = OH, R ₂ = Isoval	103
92	丙酰基氧代南五味子烷 Propoxyl oxokadsurane	L	R ₁ = H, R ₂ = Pro	103
93	乙酰基氧代南五味子烷 Acetoxyl oxokadsurane	L	R ₁ = H, R ₂ = Ac	103
94	苯甲酰氧代南五味子烷 Benzoyl oxokadsurane	L	R ₁ = H, R ₂ = Bz	103

	oxokadsurane			
95	异戊酰氧代南五味子醇	L	$R_1 = OH, R_2 = Isoval$	103
	Isovaleroyl oxokadsuranol			
96	Propoxyl oxokadsuranol	L	$R_1 = OH, R_2 = Pro$	103
97	Benzoyl oxokadsuranol	L	$R_1 = OH, R_2 = Bz$	103
6, 9 氧桥联苯环辛二烯型木脂素				
98	南五味子木脂素 L Kadsulignan L	M	$R_1 + R_2 = CH_2, R_3 = R_4 = R_5 = R_6 = CH_3, R_7 = R_8 = \alpha-CH_3$	5
99	南五味子木脂素 M Kadsulignan M	M	$R_1 + R_2 = CH_2, R_3 = R_4 = R_5 = CH_3, R_6 = H, R_7 = R_8 = \alpha-CH_3$	5,102
100	南五味子木脂素 N Kadsulignan N	M	$R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = CH_3, R_7 = R_8 = \alpha-CH_3$	5
101	5,8-Epoxy-6,7-dimethyl-2',3',2'',3''- dimethylenedioxy-4',1''-dimethoxy- 1,2,3,4-dibenzo-1,3-cyclooctadiene	M	$R_1 + R_2 = R_5 + R_6 = CH_2, R_3 = R_4 = CH_3, R_7 = R_8 = \alpha-CH_3$	95
102	南五味子木脂素 Q Kadsulignan Q	M	$R_1 = R_2 = R_3 = R_4 = CH_3, R_5 + R_6 = CH_2, R_7 = R_8 = \alpha-CH_3$	85
103	(5 <i>R</i> ,6 <i>R</i> ,7 <i>R</i>)-1,2,3,10,11,12-Hexamet hoxy-6,7-dimethyl-5,6,7,8-tetrahydr odibenzo[a,c][8]annulen-5-ol	M	$R_1 + R_2 = CH_2, R_3 = R_5 = R_6 = CH_3, R_4 = H, R_7 = R_8 = \beta-CH_3,$	101
104	Kadsuralignan D	N		46
105	南五味子木脂素 A Kadsulignan A	O	$R = H$	100
106	南五味子木脂素 B Kadsulignan B	O	$R = OAc$	100
芳基萘型木脂素				
107	Kadsuralignan C	P	$R = CH_3$	20
108	(7' <i>S</i> ,8' <i>S</i> ,8' <i>R</i>)-(8 <i>b</i> ,80 <i>a</i>)-Dimethyl-4,4'- dihydroxy-5,3-dimethoxy-50-cycloli gnanglucoside	P	$R = Glu$	95
109	Arisantetralone B	Q		89
110	黑老虎素 E Heilaohusu E	R	$R_1 = R_2 = R_5 = R_6 = CH_3, R_3 = OH, R_4 = H$	15
111	Heilaohuguosu O	R	$R_2 = R_4 = R_5 = CH_3, R_3 = OCH_3, R_1 = R_6 = H$	56

112	Heilaohuguosu P	R	$R_1 = R_2 = R_4 = R_5 = \text{CH}_3, R_3 = \text{OH}, R_6 = \text{H}$	56
113	Heilaohuguosu Q	R	$R_1 = R_2 = R_4 = R_5 = \text{CH}_3, R_3 = \text{OH}, R_6 = \text{H}$	56
114	Heilaohuguosu R	R	$R_1 = R_4 = R_6 = \text{CH}_3, R_5 = R_2 = \text{H}, R_3 = \text{OCH}_3$	56
115	Kadsuralignan H	R	$R_1 = R_2 = R_4 = \text{CH}_3, R_3 = \text{OH}, R_5 + R_6 = \text{CH}_2$	19
二苯基丁烷型木脂素				
116	Kadsurindutin E	S	$R_1 + R_2 = \text{CH}_2, R_3 = \text{OH}$	95
117	内消旋二氢愈创木脂酸 Meso-dihydroguaiaretic acid	S	$R_1 = \text{CH}_3, R_2 = R_3 = \text{H}$	67
118	Coccilignan A	T		67
119	Heilaohuguosu S	U		56
120	安五脂素 Anwulignan	V	$R_1 = R_2 = R_5 = R_6 = \text{H}, R_3 = \alpha\text{-CH}_3, R_4 = \beta\text{-CH}_3, R_7 + R_8 = \text{CH}_2$	17
121	Kadcoccilignan	V	$R_1 = R_5 = R_6 = \text{OH}, R_2 = R_3 = R_4 = R_7 = R_8 = \text{CH}_3$	95

2 黑老虎木脂素类化合物的药理作用

黑老虎木脂类化合物拥有众多药理作用,其中很多是在研究其他天然药物的过程中发现的。既往综述没有完全纳入,本文进行了全面总结。

2.1 抗炎作用

抗炎作用是黑老虎有效成分活性研究中最早也是最多的作用。早在上个世纪 80 年代末就报道黑老虎乙醇提取物中含有抗炎活性成分^[8],此后陆续发现了许多具有抗炎作用的化合物,其中大部分为联苯环辛二烯型木脂素。五味子醇甲、五味子甲素、五味子乙素、五味子丙素的抗炎作用有较多报道。Sun 等^[9]通过经典的耳肿胀度和足肿胀度模型证明了五味子醇甲具有抗炎作用,能抑制炎症部位肿瘤坏死因子(tumour necrosis factor- α , TNF- α)、白介素 6(interleukin-6, IL-6)、白介素 1 β (interleukin-1 β , IL-1 β)等炎症因子的生成。Li 等^[10]通过体内及体外实验证明五味子甲素的抗炎机制可能是抑制 TLR4/NF- κ B、MAPK 途径、NLRP3 炎性小体,从而抑制炎症因子释放。Ji 等^[11]证明五味子乙素可改善 LPS 诱导的脓毒症模型小鼠的症状,其机制可能是通过 miR-17-5p 下调 TLR4 mRNA 和蛋白水平的表达,进而降低 TNF- α 、IL-1 β 的表达水平。五味子丙素通过抑制 ERK、JNK、p38、NF- κ B 的磷酸化发挥抗炎作用^[12]。Meso-dihydroguaiaretic acid 能减少哮喘模型小鼠气道炎症和粘液的分泌,其机制与抑制 NF- κ B、MAPK 信号通路有关^[13]。Angeloylbinankadsurin A 和 heilaohusu A 具有抗关节炎活性,对类风湿性关节炎成纤维样滑膜细胞 RA-FLS 有抑制作用,其 IC₅₀ 值分别

为 11.70、14.57 μM ^[14]。Oh 等^[15]研究表明 20 μM 的 gomisin J 能显著抑制脂多糖 (lipopolysaccharides, LPS) 诱导的巨噬细胞 RAW 264.7 中 NO 的释放及 TNF- α 、IL-6、IL-1 β mRNA 表达, 其机制可能与抑制 p38、JNK 蛋白的磷酸化有关。Zhang 等^[16]近期研究发现 (+)-anwulignan 能抑制 COX-2 的蛋白表达水平, 有望用于炎症性疾病的治疗。Isovaleroylbinankadsurin A、kadsuralignan C、kadsuralignan H 和 kadsuralignan I 都能抑制 LPS 诱导的 RAW 264.7 巨噬细胞中 NO 生成, 其中 kadsuralignan C、kadsuralignan H 的 IC₅₀ 分别为 21.2、19.6 μM ^[17-19]。

2.2 抗肿瘤作用

抗肿瘤作用一直是天然产物的研究热点之一, 研究表明多种黑老虎木脂素具有抗肿瘤作用。Gomisin M2 可以抑制乳腺癌细胞及结肠癌细胞的增殖和迁移, 其机制可能与抑制 Wnt/ β -catenin 信号通路有关^[20-21]。Gomisin J 可通过诱导细胞程序性坏死或凋亡、降低神经胶质瘤细胞中己糖激酶 II (hexokinase II, HKII) 的表达, 抑制糖酵解, 最终抑制神经胶质瘤发展^[22]。五味子醇甲对 A549、MCF-7 和 DU-145 等多种肿瘤细胞具有抑制作用^[23]。体外研究表明五味子甲素对结肠癌、非小细胞肺癌、黑色素瘤、胰腺癌、胶质瘤等均有一定抑制作用, 其机制可能与抑制热休克因子 1 (heat shock factor 1, HSF1) 活化、抑制 NF- κ B、PI3K/AKT 通路有关^[24]。五味子乙素的抗肿瘤作用也有较多报道, 研究显示五味子乙素可通过调控 Trfa/TAK1、PI3K/AKT/mTOR、MAPK、Wnt/ β -catenin 信号通路, 阻滞细胞周期、诱导细胞凋亡、抑制肿瘤细胞侵袭及转移、抑制肿瘤血管生成以及促进氧自由基清除, 进而抑制肝癌、胆囊癌、黑色素瘤、前列腺癌和胶质瘤等肿瘤细胞的生长及转移^[25]。五味子乙素还能抑制耐药相关蛋白和 P-糖蛋白 (P-gp) 的表达和活性, 减少药物外排, 增强抗肿瘤药物的敏感性^[26]。五味子丙素主要通过诱导细胞凋亡、降低膜电位, 升高 ATP 诱导的钙离子浓度升高, 抑制小胶质瘤、白血病等肿瘤细胞增殖^[27,28]。Meso-dihydroguaiaretic acid 也能抑制多种肿瘤细胞, 如 HeLa (IC₅₀ = 30.0 μM)、HepG 2 (IC₅₀ = 15.1 μM)、MCF-7 (IC₅₀ = 16.9 μM)、H358 (IC₅₀ = 10.1 μM) 等^[29], 其机制可能是通过抑制 Src/EGFR/intergrin β 信号通路, 进而抑制细胞迁移、诱导细胞凋亡^[30]。体外研究显示 heteroclitin D 可以促进胃癌细胞凋亡, 抑制体内肿瘤生长, 明显下调胃癌裸鼠血清中趋化性细胞因子 IL-8 和细胞间黏附因子 s ICAM-1 等细胞因子水平^[31]。最新研究表明 anwulignan 可通过抑制 JAK1/STAT3 信号通路, 上调周期蛋白 p21 表达, 抑制 cyclin D1/3 表达, 发挥抑制非小细胞肺癌的作用^[32]。其他木脂素类化合物仅做了体外抗肿瘤测试: angeloylbinankadsurin A 可抑制鼻咽表皮样癌细胞 KB, IC₅₀ 为 30.2 μM ^[33]; heilaohulignan C (IC₅₀ = 9.92 μM)、kadsuralignan I (IC₅₀ = 21.72

μM)、longipedunin B ($\text{IC}_{50} = 18.72 \mu\text{M}$)、neglignan G ($\text{IC}_{50} = 16.41 \mu\text{M}$)、heilaohusu C ($\text{IC}_{50} = 13.04 \mu\text{M}$)可抑制肝癌细胞 HepG-2 增殖^[34,141]；heilaohulignan C 还能抑制胃癌细胞 BGC-823、结肠癌细胞 HCT-116 增殖， IC_{50} 分别为 16.75、16.59 μM ^[34]；kadsulignan H、I 对白血病细胞 P-388 有抑制作用， IC_{50} 分别为 85.02、21.91 μM ^[35]；schisantherin F 可诱导 A375 人黑色素瘤细胞凋亡^[36]；intermedin A 对淋巴瘤、白血病有一定抑制作用^[37]。

2.3 心血管作用

Gomisin J 有较好的抗高血压治疗前景。Park 等^[38]研究表明 gomisin J 具有扩血管作用，其机制可能是通过促进内皮型一氧化氮合酶 (endothelial nitric oxide synthase, eNOS) 活化和 AKT (又称 protein kinase B, PKB) 磷酸化，促进一氧化氮 (nitric oxide, NO) 生成。动物实验进一步显示，gomisin J 可以抑制血管紧张素 II (angiotensin II, Ang-II) 诱导的小鼠高血压^[39]。五味子醇甲与五味子乙素呈现有心脏保护作用。Yang 等^[40]研究表明五味子醇甲具有心脏保护作用，可减轻去甲肾上腺素诱导的心肌细胞损伤，其机制与下调心肌肌钙蛋白-T (cardiac troponin T, CT-T)、心肌肌钙蛋白 I (cardiac troponin I, CT-I) 和内皮素-1 (endothelin-1, ET-1) 蛋白表达、抑制炎症及心肌细胞凋亡有关。五味子乙素可通过激活 Nrf2、AMPK 信号通路、抑制 ATR、TGF- β /Smad 信号通路，防治心脏氧化损伤^[41]。五味子丙素也可以通过抑制 keap/Nrf2、NF- κ B 信号通路，减少炎症反应、氧化应激和细胞凋亡，改善 Ang-II 诱导的小鼠心肌重构^[42, 43]，五味子丙素还可缓解高脂饮食喂养 ApoE^{-/-}小鼠的动脉粥样硬化^[44]。Zuo 等^[45]研究表明 isovaleroylbinankadsurin A 能直接激动糖皮质激素受体，激活 RISK 信号通路，抑制氧化应激及细胞凋亡，改善心肌缺血再灌注损伤。五味子甲素通过促进 AMPK 蛋白磷酸化和激活 Nrf2 信号通路，减少炎症反应和氧化应激，进而发挥防治脑缺血再灌注损伤作用^[46]。Song 等^[47]研究发现 meso-dihydroguaiaretic acid 可以通过抑制 ERK1/2、p38、JNK 以及血小板衍生生长因子受体 β (platelet derived growth factor, PDGFR β) 磷酸化，抑制血小板衍生生长因子 (platelet derived growth factor, PDGF) 诱导的血管平滑肌细胞增殖。通过膜片钳技术发现 1、10 μM 的 heteroclitin D 以及 10 μM 的 gomisin J 对豚鼠心室肌细胞 L 型钙离子通道具有阻断作用^[48]。

2.4 保肝作用

五味子木脂素的保肝作用广为人知，五味子醇甲、五味子甲素、五味子乙素作为五味子的主要有效成分，三者的保肝作用已广泛报道^[10,49,50]，本文不再赘述。Lee 等^[51]和 Park 等^[52]的研究表明 meso-dihydroguaiaretic acid 可通过激活 AMPK 信号通路、抑制 α 平滑肌肌动蛋白 (α smooth muscle Actin, α -SMA) 表达及 TGF- β 1 mRNA 表达水平改善肝细胞纤维化和

脂质聚集。体内实验证实 1 mg/kg meso-dihydroguaiaretic acid 治疗高脂饮食小鼠 2 周后确能改善非酒精性肝脂肪变性，并发现 meso-dihydroguaiaretic acid 是 LXR α 的选择性拮抗剂^[53]。Gao 等^[54]研究表明 anwulignan 能改善 D-半乳糖诱导的小鼠肝脏损伤，抑制肝细胞凋亡，降低外周血 AST 和 ALT 水平，其机制可能与上调 MAPK、Nrf2/HO-1 通路有关。Kadsurin 能清除氧自由基，改善 CCl₄ 诱导的小鼠肝脏过氧化损伤^[55]，并且能浓度依赖性地抑制大鼠肝细胞和微粒体 CYP3A，其 IC₅₀ 小于 10 μ M^[56]。体外实验显示 isovaleroylbinankadsurin A (EC₅₀ = 26.1 μ M)、heilaohuguosu A、heilaohuguosu L、binankadsurin A 和 acetylepigomisin R 能保护叔丁基过氧化氢诱导的肝细胞损伤，其中 isovaleroylbinankadsurin A、binankadsurin A 和 acetylepigomisin R 的 EC₅₀ 分别为 26.1、26.1、79.3 μ M^[57,58]。

2.5 抗过敏及免疫调节作用

Dhakal 等^[59]研究表明 gomisin M2 可以抑制免疫球蛋白 E (immunoglobulin E, IgE) 刺激后肥大细胞脱颗粒和过敏介质 (如组胺、白介素 4) 释放，其机制主要是抑制 Fc ϵ RI-介导的 Lyn/Fyn 信号通路进而抑制细胞中钙离子内流。五味子醇甲也有一定的抗过敏作用，可显著抑制鸡卵白蛋白 (ovalbumin, OVA) 致敏小鼠血清中 IgE、IgG1 及 IL-4 水平，抑制 OVA 致敏小鼠脾脏中 IL-6、TNF- α 和 IL-1 β 的生成，抑制 caspase-1 (cysteiny l aspartate specific proteinase-1，含半胱氨酸的天冬氨酸蛋白水解酶-1) 和受体相互作用蛋白 2 (receptor-interacting protein 2, RIP-2) 的表达^[60]。Li 等^[61]研究表明 anwulignan 具有免疫调节功能，通过调节 Nrf2/HO-1 信号通路，抑制炎症反应，增加小鼠体内免疫球蛋白 IgG、IgM 和 IgA 水平。

2.6 治疗中枢神经退行性疾病

中枢神经退行性疾病是当前临床治疗的难点之一，黑老虎木脂素类有望为此类疾病的治疗带来希望。研究表明五味子醇甲可通过抑制中枢神经系统突触前膜的小分子可溶性 α -突触核蛋白 (α -synuclein, α -Syn) 的表达，延缓阿尔茨海默病进展^[62]。此外，五味子醇甲还可以通过抗氧化、抗炎减轻脑缺血再灌注损伤等作用，防治中枢神经 (缺血) 损伤后的认知障碍，改善学习记忆能力^[63,64]，这对于原发性及继发性阿尔茨海默病的防治具有重要价值。五味子丙素也能通过抑制胆碱酯酶和抗氧化作用，改善 β 淀粉样蛋白引起的小鼠认知及记忆功能减退，有望用于阿尔兹海默症防治^[65]。五味子甲素和 meso-dihydroguaiaretic acid 则能分别抑制谷氨酸诱导的原代大鼠神经细胞和帕金森综合征模型细胞的凋亡^[10,66]。另外 heteroclitin D、schiarisanrin A 和 schiarisanrin B 具有保护神经元损伤作用，能显著抑制 LPS 诱导 BV-2 细

胞中 NO 生成, IC₅₀ 分别为 18.6 ± 1.0、9.6 ± 0.5、26.4 ± 3.2 μM^[67,68]。

2.7 抗抑郁作用

五味子醇甲具有抗抑郁作用, 在 LPS 诱导的抑郁小鼠模型中, 可缩短模型小鼠强迫游泳实验和悬尾实验的不动时间, 其机制可能与抑制海马 TLR4/NF-κB 信号通路的表达有关^[69]。五味子甲素也呈现有抗抑郁的作用, 能抑制慢性不可预知性温和刺激 (chronic unpredictable mild stress, CUMS) 所致的模型大鼠海马内炎症损伤, 其机制可能是抑制 caspase-3 蛋白活化及炎症因子释放^[10]。

2.8 抗糖尿病作用

Hsu 等^[70]研究表明 schiarisanrin A 和 schiarisanrin B 具有促进胰岛素分泌的作用, 其机制可能与抑制大鼠胰腺 BRIN-BD11 细胞凋亡有关。Poornima 等^[71]证明 gomisin M1 能有效清除 DPPH、ABTs 自由基, 抑制合成糖基化终末产物, 降低糖尿病患者发生心血管疾病的风险。Gomisin J 可以抑制 α-葡萄糖苷酶的活性, IC₅₀ 为 77.69 μM^[72]。

2.9 抗衰老

Meso-dihydroguaiaretic acid 能抑制紫外线照射人永生化角质形成细胞 HaCaT 中基质金属蛋白酶 9 (matrix metalloprotein 9, MMP 9) 的表达^[73], 也可抑制热休克蛋白诱导的原代人成纤维细胞中 MMP-1 的表达, 证明其具有抗皮肤衰老的潜力^[74]。最新研究结果显示五味子丙素也具有抗皮肤衰老的活性, 能改善过氧化氢诱导的人永生化角质形成细胞 HaCaT 氧化应激损伤, 其机制可能是抑制 NF-κB、激活 Nrf2/HO-1 信号通路, 降低炎症因子表达水平, 进而抑制凋亡相关蛋白表达^[75]。

2.10 抗病毒作用

Gomisin M1、gomisin J、kadsurarin、binankadsurin A 和 acetoxyl oxokadsurane 都能抑制人类免疫缺陷病毒 (human immunodeficiency virus, HIV), 其中 gomisin J、kadsurarin 和 acetoxyl oxokadsurane 的 EC₅₀ 分别为 17.5、3.86、16.95 μM^[76-79]。五味子甲素、kadsulignan L 可抑制 HBV 病毒活性, 对 HBsAg 和 HBeAg 也具有抑制作用^[80,81], 另外 kadsulignan L 对鼻咽癌和儿童淋巴瘤相关的 EB 病毒也有抑制作用^[82]。

2.11 抗疲劳作用

Zhang 等^[83]研究表明 anwulignan 具有抗疲劳作用, 可通过激活 Nrf2 和 p38/MAPK-PGC-1α 信号通路, 抑制氧化应激和细胞凋亡, 改善小鼠血清中疲劳相关的生化指标, 增强小鼠运动耐力。

2.12 抗凝作用

黑老虎中多种联苯环辛二烯型木脂素成分具有抗凝血的活性。Wang^[84]研究发现 isoaleroylbinankadsurin A 和 acetylbinankadsurin A 能抑制血小板聚集。Kadsulignan L 及 meso-dihydroguaiaretic acid 能拮抗血小板活化因子, IC₅₀ 分别为 26、41 μM^[85]。另外 heteroclitin D、acetoxyl oxokadsurane、五味子甲素也具有抗凝血作用^[86、87]。

2.13 美白作用

Goh 等^[88]证明 kadsuralignan F 能诱导酪氨酸酶降解, 抑制大鼠黑素细胞 Melan-A 黑色素生成, 改善色素沉着。

2.14 抑菌作用

Duan^[89]研究发现 neglectalignan D 和 yunnankadsurin B 可以抑制金黄色葡萄球菌, 而 arisantetralone B 对金黄色葡萄球菌和大肠杆菌具有较强的抑制作用。Meso-dihydroguaiaretic acid 对结核分枝杆菌 H37Rv 以及伤寒沙门氏菌有较好的抑制作用^[90,91]。

2.15 其他

五味子醇甲具有抗肺纤维化作用, 还能改善勃起功能障碍^[50]。五味子甲素还有肾保护作用^[10]。五味子丙素可以通过促进 M1 型巨噬细胞向 M2 型转化, 发挥保护糖尿病肾病作用^[92]。Liu 等^[104]报道五味子醇甲和五味子乙素还有一定的杀虫效果。

3 总结与展望

黑老虎极具经济价值, 在湖南、福建等省部分地区已成为当地重点扶植的特色产业。然而由于对黑老虎的研究开发不足, 导致黑老虎相关产品种类不多、附加值不高, 产业发展受到一定制约。虽然我们对黑老虎的化学成分已有了较为全面的了解, 但对其药效及药效物质基础的研究仍十分薄弱: 一是很多化学成分还缺乏活性及机制研究; 二是药理研究不全面、不深入、不系统, 尚不能对黑老虎的临床应用与功效开发提供足够支撑; 三是对其化学成分定量研究明显缺乏, 导致标准研究受到较大限制; 四是缺乏体内代谢及代谢产物活性的研究。这些问题都需要我们在今后的研究工作中重点关注并加以解决。

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