沉香挥发油化学成分及药理活性研究进展

姚　诚,钟芙蓉,廖海浪,马云桐*

成都中医药大学药学院,成都 611137

摘　要:沉香既是传统中药,又是著名的香料。挥发油是沉香发挥药效和呈香的关键物质基础,被广泛应用于医药、宗教仪式、美容和香料等行业。现代研究表明不同提取方法获得的沉香挥发油种类与含量具有差异,主要含有倍半萜类与芳香族类化合物,其中某些标志化合物与其品质分级密切相关。药理研究证明沉香挥发油具有抗氧化和抑菌、镇痛及镇静、抗炎、抗癌等药理活性。目前关于沉香挥发油部位的研究尚处于基础阶段,其药效物质基础及质量指标价值亟需进一步的探索。笔者通过查阅、整理近 10 年关于沉香挥发油研究的国内外文献,对其提取方法、化学成分及药理活性研究进行综述,以期为沉香挥发油的进一步研究和应用开发提供参考借鉴。

关键词:沉香挥发油;倍半萜类;芳香族类;标志化合物;药理活性

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Research progress on chemical constituents and pharmacological activities of agarwood volatile oil

YAO Cheng,ZHONG Fu-rong,LIAO Hai-lang,MA Yun-tong*

Pharmacy School of Chengdu University of Traditional Chinese Medicine,Chengdu 611137,China

Abstract:Agarwood is both a traditional Chinese medicine and a famous spice. The volatile oil is the key material basis for agarwood to exert its medicinal effects and present fragrance,which is widely used in medicine,religious ceremonies,beauty and fragrance industries. Modern research indicates that varied extraction methods had influences on the type and contents of compound in agarwood volatile oils. These volatile oils mainly contain sesquiterpenoids and aromatic compounds,some marker compounds of which are closely related to its quality classification. Pharmacological research found that agarwood volatile oil has antioxidant and antibacterial,analgesic and sedative,anti-inflammatory and anti-cancer activities. At present,the study of agarwood volatile oil is still at the basic stage,and its medicinal substance basis and quality index value urgently need further exploration. This paper reviews the extraction methods,chemical composition and activity research of agarwood volatile oil by reviewing the literature on agarwood volatile oil in the past ten years,in order to provide a reference for further research,application and development of agarwood volatile oil.

Key words:agarwood volatile oil;sesquiterpenoids;aromatics;marker compounds;pharmacological activities

瑞香科植物白木香(*Aquilaria sinensis* Lour. Gilg)含树脂的木材为《中国药典》2015 版收载的中药沉香;味辛、苦,性微温,具行气止痛、温中止呕、纳气平喘的功效,用于治疗胸腹胀闷疼痛、胃寒呕吐呃逆、肾虚气逆喘[1]。沉香药用历史悠久,梁代陶弘景著《名医别录》首次收录并将其列为"上品",是沉香化气丸、沉香降气散等经典方剂的主要组成药物,被广泛使用于临床[2]。

全世界约有 19 种沉香属植物,主要分布于中国、印度、老挝、越南、缅甸、印尼、马来西亚、柬埔寨、菲律宾和巴布亚新几内亚等国家[3]。国产沉香仅有瑞香科白木香一种基原植物,其主产地在海南、广西和广东等地。沉香属植物只有在受到自然因素(雷劈、火烧、微生物入侵等)或人为因素(砍伤、打洞、接菌等)的作用,才有可能在受伤处分泌产生多种次级代谢产物,经复杂的结香过程后,沉积于木质部而形成沉香[4,5]。

沉香含有色酮类、挥发油类、脂肪酸类和甾体类

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*通信作者　Tel:86-013980598196;E-mail:mayuntong06@163.com

衍生物等多种化学成分,其中挥发油是沉香的主要有效成分群及芳香物质。沉香挥发性成分具有抗氧化、抑菌、镇痛、镇静、抗炎及抗癌等多种药理活性,因为其独特的香气,同时被广泛用于香水工业、宗教仪式等领域,具有很高的经济价值[6]。目前关于沉香的研究大多集中在其质量相关的2-(2-苯乙基)色酮类化学成分,对于挥发油类活性成分群关注较少。但研究表明其挥发性成分具有广泛的药理活性,且与品质密切相关。为此,笔者查阅主要是近十余年来沉香国内外相关文献报道,对其挥发油类化学成分的提取方法、化学成分及药理活性的研究进行梳理,以期为该类成分的进一步开发利用提供参考。

1 沉香挥发油不同提取方法比较研究

有效的提取方法是保证沉香挥发油质量和临床疗效的有效渠道。目前沉香挥发油的提取方法主要有水蒸气蒸馏法、溶剂提取法、酶辅助提取法、微波辅助法、超临界 CO_2 流体萃取法、亚临界水萃取法及固相微萃取法等。

1.1 不同提取方法得油率比较

水蒸气蒸馏法因其设备简单、易操作、低成本和污染小等优点,早期被广泛应用于沉香挥发油的提取。Pornpunyapat 等[7]在不同温度下进行水蒸气蒸馏,发现沉香挥发油在高温(120 ℃)下获得较高的出油率,品质较好且具有更好的物理性质,例如颜色较深,香味强度较高,对人体皮肤的黏附时间较长等。Chen 等[8]利用该法提取三批不同沉香药材,其精油得率分别为0.042%、0.32%、0.012 8%。但是该提取方法耗时较长,提取效率低,同时提取温度较高,易造成沉香挥发油中不稳定成分的损失。溶剂提取法不仅可以避免热不稳定活性成分的损失(主要是沉香中的特征性成分:2-(2-苯乙基)色酮类化合物),同时也具有能耗低、得率高的优点。Lin 等[9]采用乙醚冷浸法提取三批人工结香所产沉香挥发油,其得油率分别为9.7%、1.8%、2.9%。但是该提取方法存在溶剂用量大且难以去除残留的提取溶剂等缺点。

随着现代仪器分析技术及相关学科技术的迅猛发展,一些辅助提取技术逐渐兴起。酶辅助提取可在温和的条件下使细胞内有效成分充分溶解,是近年出现的一种新型植物精油提取方法。Gong 等[10]对经过纤维素酶预先处理的沉香进行精油提取,发现提取得率可达到1.621%,与未添加纤维素酶处理的样品相比,沉香挥发油提取得率增加了257%。微波辅助提取法利用微波加热打破植物的细胞壁,使挥发油溶出,可以加快反应速度,缩短反应时间及有效提高得油率。Chen 等[11]采用动态-微波辅助法对市售沉香进行精油提取,得率为0.68%。除上述沉香挥发油新型提取方法外,近年还出现了一些处于探索研究阶段的其他新型提取方法,如超临界流体萃取法[12]、亚临界流体法萃取法[13]和固相微萃取法[14,15]等技术。这些新型提取方法具有提取时间短、效率高且质量好等优点,但是大多成本昂贵,不适于大规模实际生产。

1.2 不同提取方法所得挥发油的组分及含量比较

研究表明,不同提取方法提取的沉香挥发油类化学成分在含量、组成上存在一定差异。表1总结了沉香挥发油提取方法相关研究中代表性文献的结论。发现水蒸气蒸馏法提取的化学成分多是相对分子质量较小且遇热结构稳定的倍半萜类成分,而超临界 CO_2 萃取法由于萃取过程短、温度低等特点所得成分以相对分子质量大且遇热不稳定的成分居多,能提取出更多的色酮类成分。微波辅助萃取和溶剂提取法能够得到较为丰富的芳香族类化合物。酶辅助提取法尽管增加了细胞内挥发性成分的溶出和节省提取时间,但同时使得脂肪酸及脂肪酸衍生物的含量较高,降低了精油质量。相对而言,亚临界流体法萃取沉香挥发油所得成分丰富,且特征呈香性成分提取率较高,对于沉香精油的制备有着独特优势。综合来看,为有效获得高品质的沉香挥发油,多种提取方法联用以实现提取效率的最大化,将是未来沉香挥发油提取工艺发展的方向。

2 沉香挥发油化学成分研究

沉香挥发油香气浓烈且成分复杂,是沉香主要次生代谢产物。近年来多采用气相色谱-质谱联用(GC-MS)技术进行成分分析研究。沉香挥发油中的主要活性成分是倍半萜化合物和芳香族化合物,与沉香的香味和品质息息相关[20,21]。

2.1 沉香挥发油化学成分的骨架类型

2.1.1 倍半萜化合物

倍半萜类化合物在沉香挥发油中广为存在,是主要的活性成分,按骨架可以分为沉香呋喃型(agarofurans)、沉香螺旋烷型(agarospiranes)、桉烷型(eudesmanes)、艾里莫酚烷型(eremophilanes)、愈创木烷型(guaianes)、杜松烷型(cadinanes)和前香草烷型(prezizanes)[22]。国内外研究人员已经相继对

表 1　不同提取方法沉香挥发油中的化学成分及含量

Table 1　Chemical components and contents of volatile oil of Agarwood by different extraction methods

提取方法 Extraction method	分析组分数 Detect the number of chemical compositions	成分及含量 Composition and content	文献 Ref.
水蒸汽蒸馏法 Hydrodistillation	53	倍半萜类占 68.68%,芳香族类占 9.7%,未鉴定出 2-(2-苯乙基)色酮类。包括 α-sntalol(3.9%)、10-epi-γ-eudesmol(2.39%)、γ-eudesmol(5.63%)、agarospirol(5.29%)、valerianol(4.99%)、guaiol(23.17%)、7-isopropenyl-1,4a-dimethyl-4,4a,5,6,7,8-hexahydro-3*H*-naphthalen-2-one(2.32%)、methyl ionone(5.92%)。	16
溶剂提取法 Solvent extraction	37	倍半萜类和芳香族类成分含量较高,包括 β-agarofuran(13.20%)、valerianol(5.88%)、β-eudesmol(5.48%)、jinkoh-eremol(5.19%)、dihydrokaranone(5.15%)、agarospirol(4.72%)、α-eudesmol(4.71%)、*n*-hexadecanoic acid(3.94%)、epoxybulnesene(3.21%)、γ-eudesmol(2.66%)、10-epi-γ-eudesmol(2.19%)。	17
酶辅助提取法 Enzyme-assisted extraction	37	脂肪酸及脂肪酸衍生物的含量较高,包括 hexadecanoic acid(16.06%)、oleic acid(4%)。	17
微波辅助萃取 Microwave-assisted extraction	26	倍半萜类和芳香族类成分含量较高,包括 neopetasane(7.58%)、valenca-1(10),8-dien-11-ol(6.22%)、jinkoh-eremol(5.53%)、valerianol(5.38%)、agarospirol(4.55%)、α-eudesmol(2.93%)、β-eudesmol(2.77%)、selina-3,11-dien-9-ol(2.67%)、dihydrokaranone(2.57%)。	17
超临界流体萃取 Supercritical fluid extraction	44	色酮类成分比例高达 29.42%。包括 2-phenethyl-4*H*-chromen-4-one(9.5%)、6-methoxy-2-phenethyl-4*H*-chromen-4-one(12.91%)、6,7-dimethoxy-2-phenethyl-chromone(6.85%)。	16
亚临界水萃取 Subcritical water extraction	60	倍半萜类占 10.66%,芳香族类占 1.51%。其中沉香特征呈香性成分愈创木醇(5.49%)、沉香螺萜醇(0.65%)、苄基丙酮(0.51%)等占总量的 14.65%。	18
固相微萃取 Solid phase microextraction	37	鉴别出优质精油的 5 种标志化合物 10-epi-γ-eudesmol(3.12%)、aromadendrane(1.08%)、β-agarofuran(5.28%)、α-agarofuran(2.96%)、γ-eudesmol(1.40%)。	19

沉香挥发油中的倍半萜类成分进行一定的研究。据有关文献不完全统计,沉香中的倍半萜类化合物迄今已分离并鉴定出 180 余种[23-25]。目前,随着提取分离技术和检测设备的不断优化升级,更多新成分被发现和确认。笔者主要对自 2010 年以来国内外研究中新分离鉴定沉香挥发油中的倍半萜类成分(**1**~**74**)[26-47]进行归纳总结,共有 74 种化合物。其骨架类型、名称见表 2,化学结构见图 1。

表 2　近年分离发现的沉香中的倍半萜类化合物

Table 2　Sesquiterpenoids in agarwood isolated in recent years

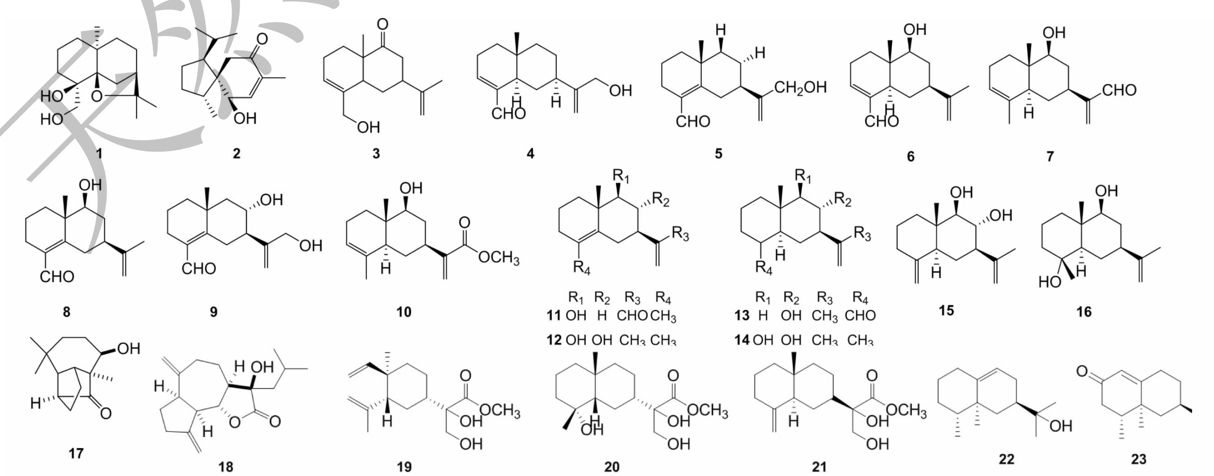
骨架类型 Skeleton type	编号 No.	化合物 Compound	参考文献 Ref.
Agarofurans 沉香呋喃型	**1**	4-Hydroxyl-baimuxinol	26
Agarospiranes 沉香螺旋烷型	**2**	4-epi-10-Hydroxyacoronene	27
Eudesmanes 桉烷型	**3**	Selina-3,11-dien-9,15-diol	28
	4	(4aβ,7β,8aβ)-3,4,4a,5,6,7,8,8a-Octahydro-7-[1-(hydroxymethyl) etenyl]-4a-methylnaphthalene-1-carboxaldehyde	29
	5	12-Hydroxy-4(5),11(13)-eudesmadien-15-al	29
	6	(5*S*,7*S*,9*S*,10*S*)-(-)-9-Hydroxy-selina-3,11-dien-14-al	30
	7	(5*S*,7*S*,9*S*,10*S*)-(+)-9-Hydroxy-selina-3,11-dien-12-al	30
	8	(7*S*,9*S*,10*S*)-(+)-9-Hydroxy-selina-4,11-dien-14-al	30
	9	(7*S*,8*R*,10*S*)-(+)-8,12-Dihydroxy-selina-4,11-dien-14-al	30

续表 1(Continued Tab. 1)

骨架类型 Skeleton type	编号 No.	化合物 Compound	参考文献 Ref.
	10	(5*S*,7*S*,9*S*,10*S*)-(+)-9-Hydroxy-eudesma-3,11(13)-dien-12-methyl ester	30
	11	(+)-9β-Hydroxyeudesma-4,11(13)-dien-12-al	31
	12	(+)-Eudesma-4,11(13)-dien-8α,9β-diol	31
	13	(+)-8α-Hydroxyeudesma-3,11(13)-dien-14-al	31
	14	(+)-Eudesma-3,11(13)-dien-8α,9β-diol	31
	15	(+)-Eudesma-4(14),11(13)-dien-8α,9β-diol	31
	16	(4*R*,5*R*,7*S*,9*S*,10*S*)-(-)-Eudesma-11(13)-en-4,9-diol	31
	17	(+)-8β-Hydroxy-longicamphenylone	32
	18	11β-Hydroxy-13-isopropyl-dihydrodehydrocostus lactone	32
	19	5β,7β-*H*-Elema-1,3-dien-11,13-dihydroxy-11-methyl ester	33
	20	5β,7β-*H*-4α-Hydroxy-eudesma-11,13-dihydroxy-11-methyl ester	33
	21	5α,7α-*H*-4(14)-Ene-eudesma-11,13-dihydroxy-11-methyl ester	33
Eremophilanes 艾里莫酚烷型	**22**	Jinkoh-eremol	34
	23	11-Hydroxy-valenc-1(10)-en-2-one	34
	24	Nootkatone	34
	25	Eremophila-9,11-dien-8-one	34
	26	(rel)-4β,5β,7β-Eremophil-9-en-12,8β-olide	34
	27	7β-*H*-9(10)-Ene-11,12-epoxy-8-oxoeremophilane	34
	28	7α-*H*-9(10)-Ene-11,12-epoxy-8-oxoeremophilane	26
	29	2β,8aα-Dihydroxy-11-en-eremophilane	35
	30	(+)-9β,10β-Epoxyeremophila-11(13)-en	31
	31	(+)-11-Hydroxyvalenc-1(10),8-dien-2-one	31
	32	(-)-Eremophila-9-en-8β,11-diol	31
	33	2-[(2β,8α,8aα)-8,8a-Dimethyl-1,2,3,4,6,7,8,8a-octahydronaphthalen-2-yl] propane-1,2-diol	36
	34	(1β,3α,4aβ,5β,8aα)-4a,5-Dimethyl-3-(prop-1-en-2-yl) octahydronaphthalene-1,8a(1*H*)-diol	36
	35	Methyl-15-oxo-eudesmane-4,11(13)-dien-12-oate	36
	36	2-[(2β,8β,8aα)-8,8a-Dimethyl-1,2,3,4,6,7,8,8a-octahydronaphthalen-2-yl]-3-hydroxy-2-methoxpropanoic acid	36
	37	Methyl 2-(9,10-dimethyl-1,2,3,4,7,8,9,10-octahydronaphthalen-2-yl)-2,3-dihydroxypropanoate	37
	38	7β-*H*-9(10)-Ene-emophane-11,13-dihydroxy-11-methyl ester	33
	39	7α-*H*-11α,13-Dihydroxy-9(10)-ene-8α,12-epoxyemophane	33
	40	11,13-Dihydroxy-9(10)-ene-8β,12-epoxyemophilane	38
	41	(7β,8β,9β)-8,9-Epoxycalamenen-10-one	38
	42	(4*S*,5*R*,7*R*)-11,12-Dihydroxy-eremophila-1(10)-ene-2-oxo-11-methyl ester	38
Guaianes 愈创木烷型	**43**	Longifolene	39
	44	1α-Hydroxy-4α,10α-dimethyl-5β*H*-octahydro-azulen-8-one	40
	45	7β*H*-Guaia-1(10)-en-12,8β-olide	40
	46	1,10-Dioxo-4α*H*-5α*H*-7β*H*-11α*H*-1,10-secoguaia-2(3)-en-12,8β-olide	40
	47	1α-Hydroxy-4β*H*-5β*H*-7β*H*-11α*H*-8,9-secoguaia-9(10)-en-8,12-olide	40
	48	1,5;8,12-Diepoxy-guaia-12-one	41

续表 1(Continued Tab. 1)

骨架类型 Skeleton type	编号 No.	化合物 Compound	参考文献 Ref.
	49	3-Oxo-7-hydroxylholosericin A	41
	50	Qinanlactone	27
	51	Qinan-guaiane-one	27
	52	Qinanol A	42
	53	Qinanol B	42
	54	Qinanol C	42
	55	Qinanol D	42
	56	Qinanol E	42
	57	(4*R*)-3-Oxo-gweicurculactone	43
	58	(4*R*,5*S*)-3-Oxo-5,6-dihydro-gweicurculactone	43
	59	1(5)-Ene-7,10-epoxy-guaia-12-one	43
	60	1,8-Epoxy-5*H*-guaia-9-en-12,8-olide	43
Cadinanes 杜松烷型	**61**	*cis*-7-Hydroxycalamenene	44
	62	Malacinone A	45
	63	Malacinone B	45
Prezizanes 前香草烷型	**64**	Aquilarene A	46
	65	Aquilarene B	46
	66	Aquilarene C	46
	67	Aquilarene D	46
	68	Aquilarene E	46
	69	Aquilarene F	46
	70	Aquilarene G	46
	71	Aquilarene H	46
	72	Aquilarene I	46
	73	Aquilarene J	46
Unknown	**74**	Aquilarin B	47



续图 1(Continued Fig.1)

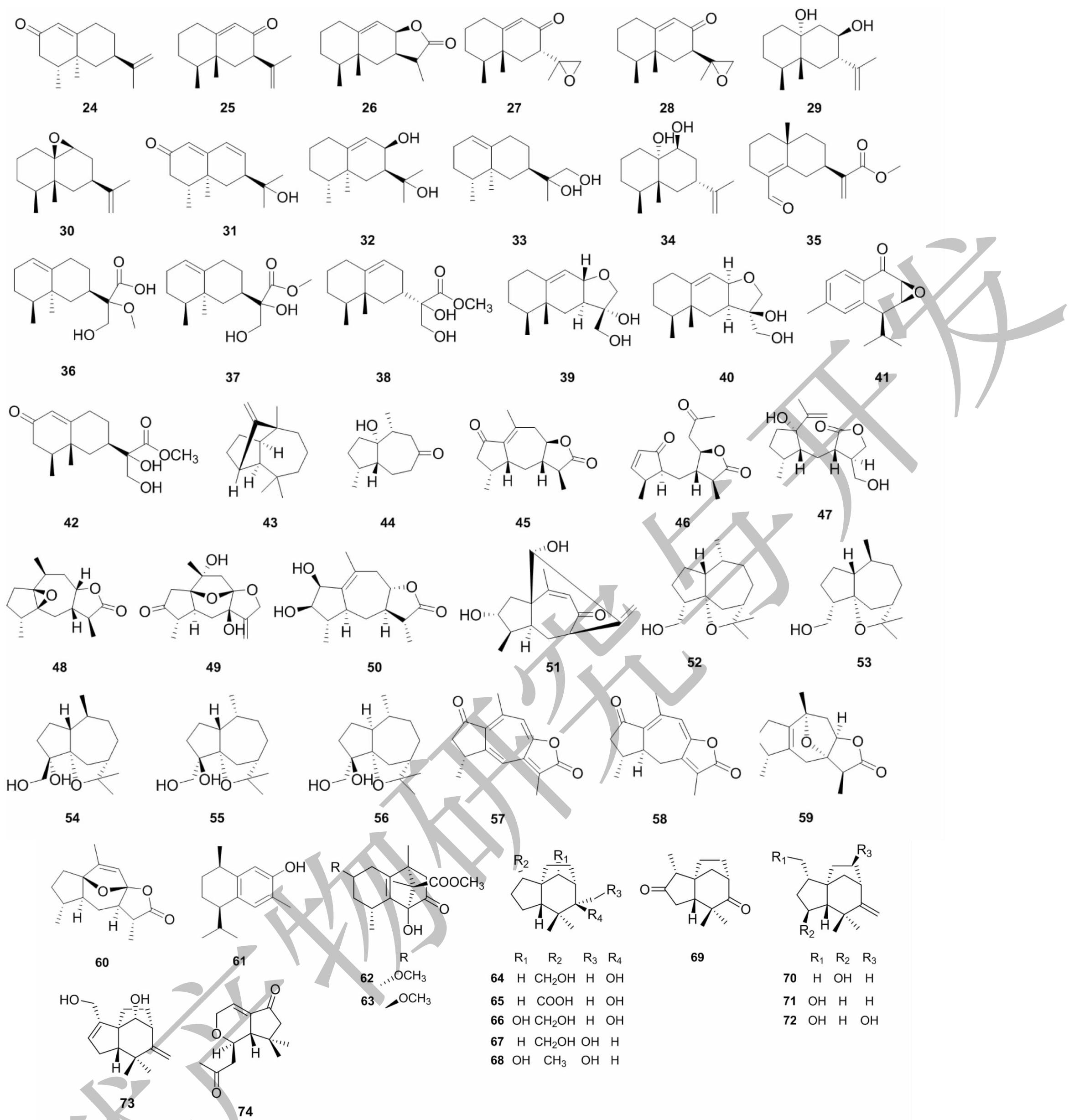


图 1 沉香挥发油中倍半萜类化合物结构

Fig. 1 Structure of sesquiterpenoids in volatile oil of agarwood

2.1.2 芳香族化合物

芳香族类化合物是沉香中的另一类特征成分，在沉香挥发油中所占比例较小。1998 年，Yang 等[48]从沉香中分离得到苄基丙酮(**75**)、对甲氧基苄基丙酮(**76**)和茴香酸(**77**)。近年来，Mei 等[49]应用 GC-MS 分析技术测定国产沉香挥发油化学成分，报道发现了 2,4-二叔丁基苯酚(**78**)和苯基丙酸(**79**)。Lin 等[9]采用乙醚浸提法在 3 种人工结香法所产沉香的挥发性成分中检测到苯甲醛(**80**)、3-苯基-2-丁酮(**81**)、4-甲基-2,6-二叔丁基苯酚(**82**)和 3,5-二叔丁基苯酚(**83**)。Chen 等[50]发现三氯甲烷能有效提取出沉香挥发油中的芳香族类化合物，从中得到苯甲酸(**84**)、4-甲氧基-苯甲醛(**85**)、2-甲基-萘(**86**)、苯丙酸(**87**)、香草醛(**88**)、3-(4-甲氧基苯基)丙酸(**89**)、4-羟基-3,5-二甲基苯甲醛(**90**)和 4-羟基-3-甲氧基苯丙酸(**91**)。Li 等[3]从国产人工打洞沉香的乙酸乙酯提取物中分离鉴定出 3 个挥发性芳香族化合物:3-羟基-4-甲氧基苯丙酸甲基酯(**92**)、姜油酮(**93**)和对甲氧基苯丙酸(**94**)。化学结构见图 2。

2.2 沉香挥发油分级主要标志化合物

传统上沉香挥发油等级的分类是人为的依据颜色和气味等物理感觉，但无法处理大量样品，且存在

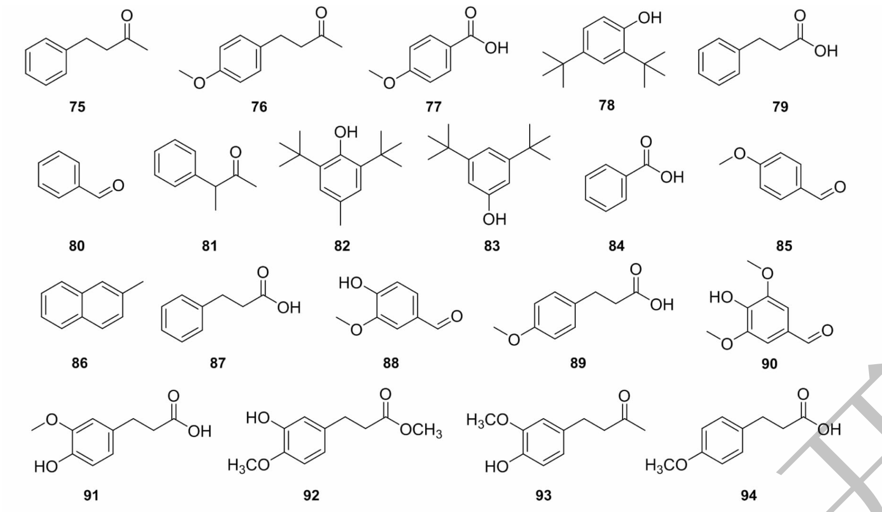


图 2　沉香挥发油中芳香族类化合物结构

Fig. 2　Structure of aromatic compounds in volatile oil of agarwood

主观性强、重复性差等缺点,使得沉香挥发油的质量分级难以实现标准化[25]。随着对沉香挥发油化学成分的深入研究,发现倍半萜类和芳香族化合物在一定程度上可以决定沉香挥发油的品质,作为质量分级的标志化合物。

在现代分级体系中,多种分析技术与统计方法相结合是实现沉香挥发油分级的重要手段[23]。比如利用 GC-MS 分析技术结合 K 最近邻(k-Nearest Neighbor)法[51]、Z-score 标准化[52]和人工神经网络(ANN)[53]等近年较为流行的算法,研究人员实现了沉香油品质的分级,准确率高达 83% 以上,且发现 10-epi-γ-eudesmol(**95**)、β-agarofuran(**96**)、α-agarofuran(**97**)、γ-eudesmol(**98**)、longifolol(**99**)、oxo-agarospirol(**100**)、hexadecanol(**101**)和 eudesmol(**102**)在沉香挥发油中含量相对较高且稳定,可以作为沉香油分类的标志化合物。直接热脱附法(direct thermal desorption,DTD),是近年新兴的一种获取香气成分的方法,节省样品且效率高,Ismail 等[54]利用此法提取不同等级沉香的挥发油化学成分进行分析发现 α-guaiene(**103**)、β-selinene(**104**)、guaia-1(10),11-dien-15-al(**105**)和 guaia-1(10),11-dien-15,2-olide(**106**)对于沉香油品质分级具有重要意义。Tajuddin 等[55]采用气相色谱-火焰离子化检测器(GC-FID)和气相色谱-质谱联用仪(GC-MS)对沉香挥发油成分进行化学分析,发现 jinkoh-eremol(22)、kusunol(**107**)和 selina-3,11-dien-9-one(**108**)可作为沉香油的分类标志化合物。Pripdeevech 等[56]采用固相微萃取法提取沉香挥发性成分,并结合气相色谱-质谱联用和气相色谱-嗅闻技术对萃取成分进行鉴定,发现 4-phenyl-2-butanone(**75**)、furfural(**109**)和 benzaldehyde(**80**)3 种芳香族化合物是沉香精油中主体香气成分。此外研究发现 caryophellene oxide(**110**)、α-copaene(**111**)、β-guaiene(**112**)、α-bulnesene(**113**)、valencene(**114**)和 aromadendrene(**115**)也是重要的沉香挥发油分级的标志化合物[57-59]。化学结构见图 3。

近年来刘昌孝院士提出关于中药质量控制标志物的新概念[60],明确指出质量标志物是中药材及中药产品具有特异性的、固有存在的有效化学成分,可作为质量控制鉴定及临床用药有效性、安全性的评价依据。通过对沉香挥发油标志化合物的研究,笔者认为可以为今后沉香挥发油质量标志物预测分析提供有益参考。

3　沉香挥发油的药理活性

沉香在医药产品的开发利用方面有较大潜力,与其挥发油广泛的药理作用密切相关。研究表明沉香挥发香油具有抗氧化、抑菌、镇痛、镇静、抗炎和抗癌等多种药理活性。

3.1　抗氧化、抑菌作用

研究表明,沉香挥发油具有显著的抗氧化、抑菌作用。Xiong 等[61]研究发现沉香挥发油在一定程度上能减少细胞内活性氧水平,显著增强细胞内抗氧化酶 SOD、GSH-Px 的活力,对 H_2O_2 诱导的 PC12 细胞氧化损伤具有保护作用。Wang 等[62]通过 1,1-二

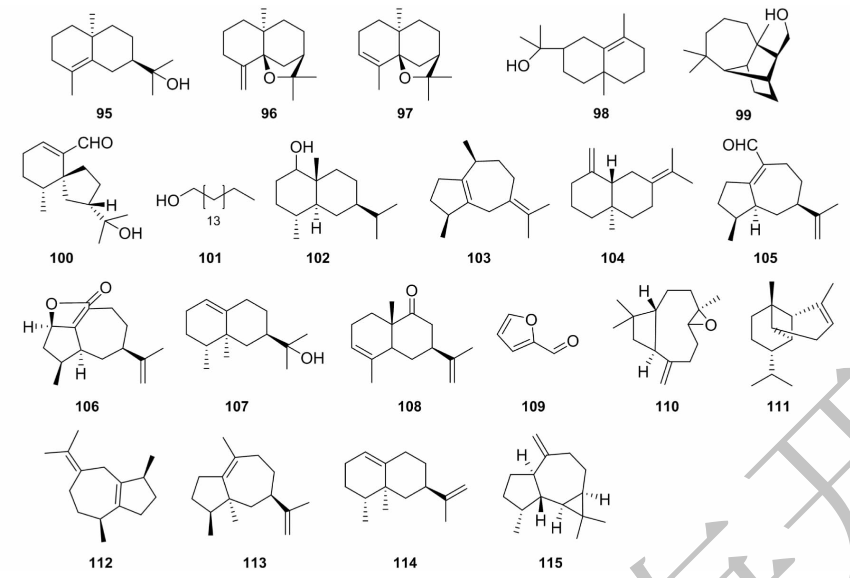


图3 沉香挥发油中主要标志化合物结构

Fig. 3 Structure of main marker compounds in volatile oil of agarwood

苯基-2-三硝基苯肼(DPPH)自由基清除和铁离子还原/抗氧化能力法(FRAP)测定沉香精油抗氧化活性,结果显示具有较好的体外抗氧化能力。抗菌活性试验表明,沉香精油对革兰氏阴性菌和革兰氏阳性菌均有较好抑制效果,且对革兰氏阳性菌(金黄色葡萄球菌、枯草芽孢杆菌)的抑菌作用较明显。Dahham 等[63]进一步研究发现沉香挥发油中的倍半萜类化合物β-石竹烯具有显著的抗氧化、抗菌性能。

3.2 镇痛、镇静作用

沉香在传统中药中作为行气药,具有行气止痛功效。Wang 等[64]比较不同年份沉香药材的镇痛作用,研究发现沉香挥发油可显著提高小鼠痛阈值和降低醋酸致小鼠扭体反应的扭体发生次数,证明其具有明确的镇痛作用。Wang 等[65]通过协同戊巴比妥钠催眠实验和自主活动实验评价了沉香不同部位在镇静催眠方面的药效学作用,发现沉香挥发油能显著延长戊巴比妥钠诱导的小鼠睡眠时间及增加阈下剂量小鼠进入睡眠的比例,综合实验结果进一步推断沉香挥发油中具有镇静催眠作用的活性分子可能为弱极性分子。Wang 等[66]通过动物行为学实验评价沉香精油的镇静催眠作用,探讨对 GABA 能系统的潜在作用机制,结果表明沉香挥发油具有显著的镇静催眠作用,其作用机制可能与调节 $GABA_A$ 受体的基因表达,增强 $GABA_A$ 受体功能,促进 Cl^{-1} 内流有关。

3.3 抗炎作用

体内和体外抗炎活性实验均表明沉香挥发油具有较强的抗炎活性[67]。Gao 等[68]研究发现沉香精油灌胃给药具有显著的抗炎活性,通过脂多糖(LPS)诱导 RAW264.7 细胞模型和 Western blot 方法发现其抗炎信号通路可能是通过抑制 p-STAT3 的表达,进而降低前炎症细胞因子 IL-1β 和 IL-6 的产生和释放,同时结合化学成分的分析结果推断与其主要成分倍半萜类有关。Zhao 等[37]从沉香 95% 乙醇提取物中分离得到 7 个倍半萜类化合物,研究发现化合物 **1**,10-dioxo-4αH-5αH-7βH-11αH-1,10-secoguaia-2(3)-en-12,8β-olide 具有明显的抗炎活性,其 IC_{50} 值为 8.4 μmol/L。Yadav 等[69]研究发现沉香精油可显著减少 TPA 诱导的小鼠耳炎症模型中小鼠耳厚度、耳重量和降低 MDA 水平及促炎细胞因子的产生,推测其抗炎机制可能与抑制促炎症细胞因子(IL-1β、IL-6 和 TNF-α)的水平和降低机体脂质过氧化程度(MDA)有关,同时通过分子对接研究结果发现倍半萜类化合物 jinkoh-eremol 和 10-epi-γ-eudesmol 具有较强的抗炎和免疫调节活性。这些研究结果初步阐明了沉香挥发油抗炎活性的物质基础及相关作用机制,证明其可以作为治疗炎症疾病的有效药物。

3.4 抗癌作用

此外,沉香挥发油还具有一定的抗肿瘤作用。Hashim 等[70]对沉香挥发油进行了细胞活力、细胞附着度和细胞毒性的测定,确定了其 IC_{50} 值为 900 g/mL,结果表明沉香精油对 MCF-7 乳腺癌细胞具有潜在的抗癌活性。Ibrahim 等[71]研究结果发现沉香

精油对人结肠癌细胞具有较强的抗癌活性,是治疗结肠癌的良好选择。此外 Dahham 等[72-74]研究了沉香挥发油对结肠癌细胞 HCT116 和胰腺癌细胞 MIAPaCa-2 的抑制活性,发现均有显著的抑制作用,并推测沉香挥发油的抗癌作用可能是由于多种生物活性成分协同作用所致。

3.5　其他作用

Wang 等[75]通过一系列的动物行为实验,证明了沉香挥发油具有抗焦虑和抗抑郁作用,推测可能与抑制促肾上腺皮质激素释放因子(CRF)和下丘脑-垂体-肾上腺(HPA)轴的过度活动有关。Rahman 等[76]采用吸入途径对小鼠给药,研究发现沉香精油具有一定的抗焦虑作用。在胃肠道调节作用方面,有研究发现[77,78],沉香挥发油中的主要活性化合物苄基丙酮具有增强食欲的作用。此外,沉香挥发油还有降血糖[79,80]、抗心肌缺血[81]等药理活性。

4　总结与展望

沉香药用历史悠久、疗效确切,是我国传统珍贵中药材。其挥发油作为香气的主要来源和主要活性部位群,所含化学成分种类多样且药理作用广泛,具有广阔的开发利用前景。近年来随着现代提取分离技术的飞速发展,不同提取方法所得沉香挥发油提取率和成分种类含量有较大差别。目前从沉香挥发油中分离得到的化合物主要包括倍半萜类、芳香族类等。现代药理学研究表明,沉香挥发油具有抗氧化、抑菌、镇痛、镇静、抗炎、抗癌等多种药理作用,具有良好的临床应用与新药研发价值。

然而,现代沉香品质评价研究主要集中在特征化学成分色酮类,对主要活性成分挥发油关注较少,对沉香挥发油整体质量控制的研究相对薄弱。笔者通过对沉香挥发油的提取方法、化学成分以及药理活性进行总结,有助于建立沉香挥发油质量评价体系。同时通过对挥发油中主要标志化合物进行总结,能够为沉香挥发油质量标志物的筛选和确定提供参考方向,具有指导意义。这将有助于后续深入挖掘沉香挥发油的药效物质基础,为其质量评价和临床用药奠定研究基础和理论依据。

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