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鹅掌楸属植物化学成分及其生物活性研究进展

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摘　要:本文综述了鹅掌楸属植物化学成分以及该属植物及其部位成分的生物活性,其化学成分包括生物碱、倍半萜、苯丙素、黄酮类等化合物。生物活性包括抗菌、抗疟疾、抗肿瘤等活性。

关键词:鹅掌楸;生物碱;倍半萜;生物活性

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Advances in the Study on Chemical Constituents and Biological Activities in *Liriodendron* Genus

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Abstract: The study on chemical constituents and biological activities of *liriodendron* was reviewed in this paper. Chemical constituents were investigated here including alkaloids, sesquiterpenes, phenylpropanoids, flavonoid, and others. Biological activities were also given including anti-microbial, anti-malarial, antineoplastic, and others.

Key words: *Liriodendron*; alkaloids; sesquiterpenes; biological activities

木兰科鹅掌楸属植物是在中生代侏罗纪就已经出现的一种被子植物,目前全球仅存两个种:北美鹅掌楸(*Liriodendron tulipifera* L.),主要分布于美国东部和加拿大东南部[1]。中国鹅掌楸[*Liriodendron Chinense* (Hemsl.) sarg.],星散分布于长江流域以南区域,如江西(庐山)、福建(武夷山)、湖北(房县)等[2],是首批列入《中国珍稀濒危保护植物名录》的国家二类濒危植物。这两个种又被称之为"洲际种对"(Vicariad Species Pairs)[3]。为保护濒危植物,1963 年,我国林木育种学家叶培忠教授首次以中国鹅掌楸为母本,与北美鹅掌楸杂交成功选育得到种间杂交种--杂交鹅掌楸[*L. chinense* (Hemsl.)Sarg. x *L. tulipifera* L.][4,5],又称杂交马褂木。

鹅掌楸属植物作为传统的药用植物,具有很高的药用价值。《全国中草药汇编》记载以中国鹅掌楸的树皮和树根入药,可祛风除湿,止咳消喘,用于治疗风寒咳嗽,风湿关节痛等病症。北美鹅掌楸树皮亦早期曾被作印第安人用于辅助用药、兴奋剂和退烧药,并且美国内战中北美鹅掌楸树皮的粗提物曾作为喹啉的替代物,用于治疗疟疾[6]。国内外学者对北美鹅掌楸中所含有的化合物及其药理活性进行了较为深入系统的研究,而对中国鹅掌楸植物的研究则相对较少,尤其迄今未见杂交鹅掌楸中化学成分的研究报道。本文对鹅掌楸属植物中分离鉴定得到多种生物碱类、倍半萜内酯类、黄酮类及苯丙素类等化学成分及该属植物部位成分可能的生物活性做一综述。

1　化学成分

1.1　生物碱类(Alkaloids)

生物碱类化合物广泛存在鹅掌楸属植物中。目前,国内外学者已经从北美鹅掌楸的不同部位分离得到 46 个生物碱,其中大部分为阿朴啡类生物碱及其脱氢、氧化的衍生物,只有少量的生物碱是原阿朴啡类生物碱和四氢小檗碱,见表 1。

1.2　倍半萜(Sesquiterpenes)

倍半萜类化合物也存在鹅掌楸属植物中。目前,该属植物中已经发现十余种愈创木烷型、吉马型、桉叶烷型构型的倍半萜类化合物,见表 2。

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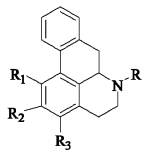
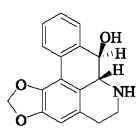
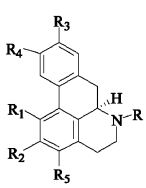
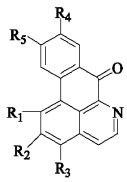
表 1 鹅掌楸属植物的生物碱

Table 1 Alkaloids of *Liriodendron* Genus

分类 Classifications	名称 Names	结构 Structures	来源 Sources	参考文献 References
Aporphines				
		R / R_1 / R_2 / R_3		
	Anonaine	H / CH_2O_2 / H	*L. tulipifera* (Barks)	[6, 7]
	N – Acetylanonaine	$COCH_3$ / CH_2O_2 / H	L. tulipifera (Barks)	[7]
	Remerine	CH_3 / CH_2O_2 / H	*L. tulipifera* (Leaves)	[7 – 9]
	Remerine N – Oxide		*L. tulipifera* (Leaves)	[7]
	Caaverine	H / OH / OCH_3 / H	*L. tulipifera* (Leaves)	[7, 9, 10]
	Lirinidine	CH_3 / OH / OCH_3 / H	*L. tulipifera* (Barks)	[7, 9, 10]
	Lirine	CH_3 / OCH_3 / OCH_3 / OH	*L. tulipifera* (Barks)	[7]
	O – Methylirine	CH_3 / OCH_3 / OCH_3 / OCH_3	*L. tulipifera* (Leaves)	[7, 9, 11]
	Liridine	CH_3 / OCH_3 / OH / OCH_3	*L. tulipifera* (Leaves)	[7, 11]
	O – Methylnorlirine	H / OCH_3 / OCH_3 / OCH_3	*L. tulipifera* (Barks)	[7]
	Asimilobine	H / OCH_3 / OH / H	*L. tulipifera* (Barks)	[6, 7]
	N – Acetylasimilobine	$COCH_3$ / OCH_3 / OH / H	*L. tulipifera* (Barks)	[7]
	Nornuciferine	H / OCH_3 / OCH_3 / H	*L. tulipifera* (Leaves)	[7, 9]
	N – Acetylnornuciferine	$COCH_3$ / OCH_3 / OCH_3 / H	*L. tulipifera* (Barks)	[7]
	Nuciferine	CH_3 / OCH_3 / OCH_3 / H	*L. tulipifera* (Barks)	[7]
	Tuliferoline	$COCH_3$ / OCH_3 / OCH_3 / OCH_3	*L. tulipifera* (Seeds)	[7, 12]
	O – Acetyliridinine	CH_3 / OCH_3 / OCH_3 / $COCH_3$	*L. tulipifera* (Barks)	[7]
	Norushinsunine		*L. tulipifera* (Barks)	[6, 7]
				
		R / R_1 / R_2 / R_3 / R_4 / R_5		
	Thalicmidine	CH_3 / OH / OCH_3 / OCH_3 / OCH_3 / H	*L. tulipifera* (Barks)	[7]
	Isolaureline	CH_3 / O_2CH_2 / OCH_3 / H / H	*L. tulipifera* (Leaves)	[7, 9, 13, 14]
	N – Acetyl – 3 – metho – xynornantenine	$COCH_3$ / OCH_3 / OCH_3 / O_2CH_2 / OCH_3	*L. tulipifera* (Woods)	[7, 15]
	Lirinine	CH_3 / OH / OCH_3 / OCH_3 / H / H	*L. tulipifera* (Leaves)	[9, 16, 17]

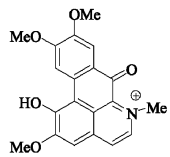
	Lirinine N – oxide						*L. tulipifera* (Leaves)	[7]
	O – Methyllirinine	CH_3	OCH_3	OCH_3	OCH_3	H	H	*L. tulipifera* (Leaves)	[17]
	Apoglaziovine	CH_3	OH	OCH_3	H	OH	H	*L. tulipifera* (Flowers)	[18]
	Perdicentrine	CH_3	OCH_3	OH	OCH_3	OCH_3	H	*L. tulipifera* (Flowers)	[7]
	N – Methyllaurotetanine	CH_3	OCH_3	OCH_3	OH	OCH_3	H	*L. tulipifera* (Leaves)	[7, 19]
	Lirioferine	CH_3	OCH_3	OCH_3	OCH_3	OH	H	*L. tulipifera* (Barks)	[7]
	Norglaucine	H	OCH_3	OCH_3	OCH_3	OCH_3	H	*L. tulipifera* (Barks)	[6, 7]
	Glaucine	CH_3	OCH_3	OCH_3	OCH_3	OCH_3	H	*L. tulipifera* (Woods)	[7, 20, 21]
	Boldine	CH_3	OH	OCH_3	OCH_3	OH	H	*L. tulipifera* (Leaves)	[7]
	N – Acetylnormantenine	$COCH_3$	OCH_3	OCH_3	O_2CH_2		H	*L. tulipifera* (Leaves)	[7, 15]
	Liriotulipiferine	CH_3	OCH_3	OH	OCH_3	OH	H	*L. tulipifera* (Leaves)	[7]

Oxoaporphines



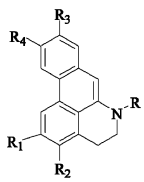
	R_1	R_2	R_3	R_4	R_5		
Liriodenine		O_2CH_2	H	H	H	*L. tulipifera* (Leaves)	[6, 7, 22]
Lysicamine	OCH_3	OCH_3	H	H	H	*L. tulipifera* (Woods)	[7, 9]
Liriodendronine	OH	OH	H	H	H	*L. tulipifera* (Barks)	[7, 20]
Liridrine	OCH_3	OCH_3	OCH_3	H	H	*L. tulipifera* (Leaves)	[11, 23]
Lanuginosine	O_2CH_2		H	OCH_3	H	*L. tulipifera* (Barks)	[7]
N – Methylatheroline	OCH_3	OCH_3	OCH_3	OCH_3	H	*L. tulipifera* (Barks)	[6]

Corunnine



L. tulipifera (Leaves) [7]

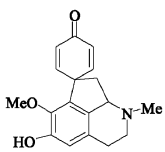
Dehydro-aporphines



	R	R_1	R_2	R_3	R_4		
Dehydroremerine	CH_3	O_2CH_2		H	H	*L. tulipifera* (Woods)	[7]
Dehydroisolaurenine	CH_3	O_2CH_2		OCH_3	H	*L. tulipifera* (Flowers)	[7]
Dehydroglaucine	CH_3	OCH_3	OCH_3	OCH_3	OCH_3	*L. tulipifera* (Woods)	[7, 15]

Proaporphine

N-Methylcrotsparine



L. tulipifera (Leaves) [24]

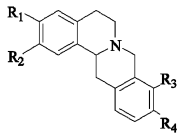
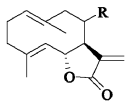
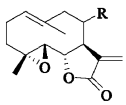
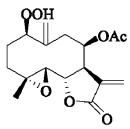
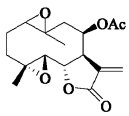
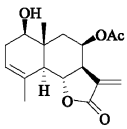
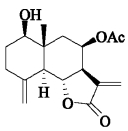
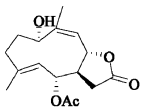
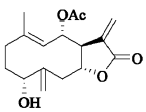
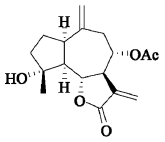
Tetrahydropro-toberberine							
		R_1	R_2	R_3	R_4		
	Isocorypalamine	OCH_3	OH	OCH_3	OCH_3	*L. tulipifera* (Leaves)	[19]
	Stepholidine	OCH_3	OH	OCH_3	OH	*L. tulipifera* (Flowers)	[18]

表 2 鹅掌楸植物中的倍半萜

Table 2 Sesquiterpenes of *Liriodendron* genus

名称 Names	结构 Structures	来源 Sources	参考文献 References
			
	R		
Tulipinolide	OAc	*L. tulipifera* (Roots), *L. chinense* (Woods)	[25,26]
Epitulipinolide	OAc	*L. tulipifera* (Roots)	[27]
Costunolide	H	*L. tulipifera* (Roots)	[26,28]
			
	R		
Parthenolide	H	*L. tulipifera* (Roots)	[29]
Lipiferolide	OAc	*L. tulipifera* (Leaves), *L. chinense* (Woods)	[6,25]
Peroxyferolide		*L. tulipifera* (Seeds)	[6,12]
Epitulipinolide diepoxide		*L. tulipifera* (Seeds), *L. chinense* (Woods)	[12,25]
α-Liriodenolide		*L. tulipifera* (Roots), *L. chinense* (Woods)	[25]
β-Liriodenolide		*L. tulipifera* (Roots), *L. chinense* (Woods)	[25]
Tulirinol		*L. tulipifera* (Leaves), *L. chinense* (Woods)	[25]
Dihydrochrysanolide		*L. tulipifera* (Leaves)	[26]

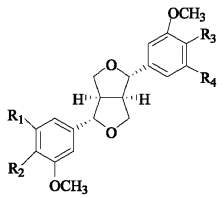
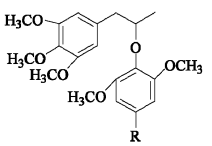
β-Cyclolipiferolide		*L. tulipifera* (Leaves)	[26]

1.3 苯丙素类(Phenylpropanoid)

苯丙素类化合物主要存在鹅掌楸属植物的茎、叶和种子中。目前,国内外学者已在北美鹅掌楸植物中已经发现木质素类和苯丙素类化合物,见表3。

表3 鹅掌楸属植物中的苯丙素类化合物

Table 3 Phenylpropanoids of *Liriodendron* Genus

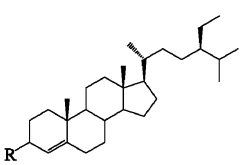
分类 Classifications	名称 Names	结构 Structures				来源 Sources	参考文献 References
Ligans							
		R_1	R_2	R_3	R_4		
	Liriodendrin	OCH_3	GlcO	GlcO	OCH_3	*L. tulipifera* (Stems, Leaves)	[28,30]
	(+)-Syringaresinol	OCH_3	OH	OH	OCH_3	*L. tulipifera* (Stems, Leaves)	[30,31]
	(+)-Pinoresinol	H	OH	OH	H	*L. tulipifera* (Stems, Leaves)	[30]
	(+)-Medioresinol	H	OH	OH	OCH_3	*L. tulipifera* (Stems, Leaves)	[30]
	Yangambin	OCH_3	OCH_3	OCH_3	OCH_3	*L. tulipifera* (Woods)	[31,32]
	Eudesmin	H	OCH_3	OCH_3	H	*L. tulipifera* (Seeds)	[31]
Phenylpro-panoids							
		R					
	β-O-Dilignol	CH_2-CH = CH_2				*L. tulipifera* (Seeds)	[24]
	Liriolignal	CHO				*L. tulipifera* (Seeds)	[28]

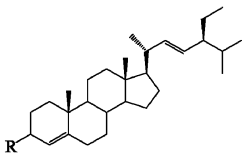
1.4 甾体类(Steroids)

在北美鹅掌楸植物的茎中发现了甾体类化合物,见表4。

表4 鹅掌楸属植物中的甾体类化合物

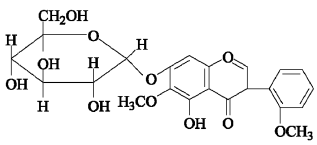
Table 4 Steroids of *Liriodendron* Genus

名称 Names	结构 Structures	来源 Sources	参考文献 References
			
	R		
β-Sitosterol	—OH	*L. tulipifera* (Stems)	[31]

β-Sitostenone	=O	*L. tulipifera* (Stems)	[31]
Stigmasterol		*L. tulipifera* (Stems)	[31]
Stigmastenone	=O	*L. tulipifera* (Stems)	[31]

1.5 黄酮类(Flavonoids)

仅在北美鹅掌楸植物中发现了一个黄酮类化合物 5-Hydroxy-6-2-dimethoxy isoflavone 7-*O*-β-D galacotopyranoside[33],其结构如图所示。



5-hydroxy-6,2-dimethoxy isoflavone 7-O-β-D-galacotopyranoside

2 生物活性

鹅掌楸属植物及其部位成分含有各种生物活性成分,《全国中草药编汇》中记载鹅掌楸属植物具有祛风除湿,止咳,可用于风湿关节痛,风寒咳嗽。文献报道有抗菌、抗疟疾,抗肿瘤等。

2.1 抗菌活性

李书华和曾超珍分别采用滤纸片观察法和杯碟法表明:中国鹅掌楸的正丁醇部位抑菌性最强,且中国鹅掌楸提取物对金色葡萄球菌(*Staphylococcus aureus*)、枯草芽孢杆菌(*Bacillus subtilis*)、大肠埃希杆菌(*Escherichia coli*)的生长均有较强的抑制效果,其 MIC 值分别为 0.0313、0.0625、0.0625 mg/mL[34,35]。

Anonaine 对三种革兰氏阳性菌:蜡样芽孢杆菌(*Bacillus cereus*)、微球菌属(*Micrococcus*)、金黄色葡萄球菌具有显著的抑菌作用(MIC 值 ≥ 50 mg/mL)。同时 Anonaine 也能够有效的抑制真菌如白色念珠菌(*Candida albicans*)、新型隐球菌(*Cryptococcus neoformans*)及其他念珠属菌类的生长(MIC 值在 62.5 ~ 1000 mg/mL 之间)[36]。

Liriodenine 能够抑制多种革兰氏阳性菌如枯草芽孢杆菌、金黄色葡萄球菌及 β-溶血链球菌(*Beta hemolytic streptococcus*)等和革兰氏阴性菌如大肠埃希杆菌、铜绿假单胞菌(*Pseudomonas aeruginosa*)和志贺痢疾杆菌(*Shigella shigae*)等的生长。Liriodenine 对黄曲霉(*Aspergillus flavus*)、白色念珠菌、杂色曲霉(*Aspergillus versicolor*)和黑曲霉(*Aspergillus niger*)等真菌亦具有显著的细胞毒性[37]。同时,Lysicamine 和 Liriodenine 对表皮葡萄球菌(*Staphylococcus epidermidis*)和都柏林念珠菌(*Candida dubliniensis*)具有细胞毒性(MIC 值在 12.5 ~ 100 mg/mL 之间)[36]。

2.2 抗疟疾活性

Graziose R 等研究发现北美鹅掌楸树皮及树皮的乙醇提取物和叶子的氯仿提取物均具有抗疟原虫活性,其 IC_{50} 值分别为 10.9 μg/mL,2.0 μg/mL[6]。

Liriodenine 能够抑制利什曼原虫(*Leishmania braziliensis* 和 *Leishmania donovani*)和恶性疟原虫(*Plasmodium falciparum*)的生长(其 IC_{50} 值分别为 21.5、26.16、15 mM)[38,39]。Graziose R 等人从北美鹅掌楸树皮中分离纯化得到六种阿朴啡类生物碱:Asimilobine、Norushinsunine、Norglaucine、Liriodenine、Anonaine、Oxoglaucine,并在体外进行抗疟疾活性实验,实验显示这六种生物碱均具有抗疟疾活性。并且研究显示 Dehydroremerine 在体外能够抑制恶性疟原虫 *Plasmodium falciparum* W2 的生长,其 IC_{50} 值为 0.36 mM。Caaverine 亦对利什曼原虫和克氏锥虫具有显著的抑制效果[6]。

2.3 抗肿瘤活性

Jin-Hui Chen 等人研究表明中国、北美及杂交鹅掌楸的茎、叶的粗体物对人体乳腺癌细胞 MDAMB-231 和 MCF-7、胃癌细胞 SGC-7901、肝癌细胞 HuH-7 及结肠癌细胞 HCT-15 都有不同程度的抑制活性[40]。Rao 等人亦研究显示北美鹅掌楸根部树皮的醇提物对人的鼻咽癌细胞 KB 细胞具有强烈的抑制活性[35]。

Anonaine 能够抑制人肺癌细胞 H1299 增殖,扩

散迁移以及阻断 H1299 细胞周期,引起其 DNA 损伤,进而抑制癌细胞生长[41];同时 Anonaine 能够上调宫颈癌细胞 HeLa 细胞中 Bax 蛋白和 p53 蛋白表达,促使癌细胞迅速凋亡[42]。

Gerhardt D 等人指出 Boldine 能有效的抑制神经胶质瘤细胞系 U138MG、U87-MG 和 C6 的细胞生长,Boldine 可能成为治疗神经胶质瘤的一种潜在的抗癌药物[43]。

Liriodenine 对人的多种癌细胞生长具有抑制作用。Yang C 等人通过实验指出 Liriodenine 能够抑制癌细胞系 MCF-7、NCI-H460 和 SF-268 细胞的生长(其 IC_{50} 值分别为 2.19、2.38 和 3.19 mg/mL)[44],且 Liriodenine 可以诱导癌细胞凋亡。同时,Liriodenine 分别和金属离子 Mn^{2+}、Fe^{2+}、Co^{2+} 和 Zn^{2+} 形成复合物,增强对癌细胞株的毒性[45,46]。Liriodenine 碱银配合物($AgLA_2$)在体外能够抑制肺癌细胞 SPC-A-1 增殖,并诱导肺癌细胞凋亡[45]。

Lanuginosine 能够抑制肝细胞癌细胞系 HepG2 和脑癌细胞系 U251 的增殖[47],并诱导其凋亡,Caaverine 对 HepG2 细胞具有强烈的抑制活性[48]。

2.4 神经系统作用活性

Boldine 在体外和多巴胺受体结合能力非常强。Boldine 和 Glaucine 在大鼠神经具有抑制功效,表明它们对多巴胺受体可能有拮抗作用,研究显示 Boldine 在体外对 D1-和 D2-受体均具有良好的亲和力,但在体内却不能有效的显示对中枢系统多巴胺受体的拮抗作用;而 Glaucine 在体内有显著的多巴胺受体拮抗作用,但在体外实验中效果却并不明显[49]。

2.5 其他生物活性

除了上述活性外,鹅掌楸属中的阿朴啡生物碱还表现出许多其他生物活性。Lysicamine 、Glaucine 和 Nornuciferine 具有安眠镇静的功效[50,51];Glaucine 和 Oxoglaucine 显示出明显的消炎能力[52];Nuciferine 具有较强的抗 HIV 活性(IC_{50} 值为 0.8 mg/mL)[53];N-methylcrotsparine 能够抑制单纯性疱疹病毒 HSV-1、HSV-1-TK、HSV-2(IC_{50} 值分别为 8.3、7.7、6.7 mg/mL)[54];Anonaine 、Liriodenine、Norshinsunine 具有促使血管舒张作用[42,55],同时,Liriodenine 具有抗心率不齐和在心肌缺血再灌注损伤时对心脏和心血管保护的功效[56,57];Liriodenine、Lanuginosine、N-acetylnornuciferine 可以抑制由花生四烯酸等引发的血小板聚集[58-60];Boldine 能够通过清除活性氧和活性自由基,抑制次黄嘌呤-黄嘌呤氧化镁系统等机理发挥其抗氧化作用[61,62]。

3 结语

鹅掌楸属植物含有结构多样的植物化学成分以及潜在的生物活性成分,开发利用本属植物资源有良好的药学等应用前景。目前从鹅掌楸属植物中所分离得到的部位成分大多具有良好的生物活性,但该属植物尤其中国马褂木中化学成分以及可能的活性物质还没有被系统研究,另外中国马褂木和北美鹅掌楸均为孑遗濒危植物,通过对杂交马褂木中活性成分的研究显得更有意义。总结提出进一步创新性研究想法与思路!

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