

国产芸香科九里香属化学分类

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摘要 九里香是芸香科的一个小属,主要分布于我国南部及中南半岛,少数个别品种向西南延伸至印度和斯里兰卡及向东南伸展至澳洲东北部。我国境内共有 8 种和 1 亚种。九里香属植物含丰富的生物碱和香豆精,其中包括不少生物活性成分,民间亦每每选用该属植物作传统草药。最近又从千里香的根部分离得一种新的双吲哚生物碱,命名为月橘烯碱;该成分有强效的抗着床活性,对计划生育有重大意义。在发掘月橘烯碱的自然资源的研究过程中,作者分析了国产的 8 种九里香属植物,发现该属植物可以划分为两组,即九里香组和棕茎组。九里香组之成员跟棕茎组的在形态上有明显分别,而且前者之根部含抗着床成分月橘烯碱和 8-戊烯化香豆精,但后者之根部则含咪唑生物碱。初步分析了澳洲的卵叶九里香和泰国的暹罗九里香,其形态及化学成分亦支持将该属分为两组。作者据此发表新组合。

关键词 化学分类;月橘烯碱;咪唑生物碱;8-戊烯化香豆精;九里香属;九里香组;棕茎组

引 言

九里香属 (*Murraya*) 同亲缘关系接近的黄皮属 (*Clausena*) 和山小桔属 (*Glycosmis*) 一起组成了芸香科的柑桔亚科 (Aurantioidae) 黄皮族 (Clauseneae) 中的黄皮亚族 (Clauseninae)。九里香属主要分布于我国南部和中南半岛,少数特有种类和变种延伸到斯里兰卡和新喀里多尼亚岛以及澳大利亚东北部。Swingle^[1] 认为,本属有 11 个种和 4 个变种,其中中国有 6 个种和 2 个变种。黄成就通过对中国九里香属植物的研究,增加了 2 个新种和一个变种,即四数花九里香 (*Murraya tetramera*)、广西九里香 (*M. kwangsiensis*) 和大叶九里香 (*M. kwangsiensis* var. *macrophylla*); 但四数花九里香后来被鉴定与豆叶九里香 (*M. euchrestifolia*) 同种^[4-5]。黄成就又认为九里香 (*M. exotica*) 这个种有别于千里香 (*M. paniculata*), 而将前者恢复回种的等级^[4-5];我们在这两个分类群的化学、生态学和形态学特征的研究成果,亦支持这样的处理(未发表)。另外,由 Swingle 确认的两个变种,即:脐果九里香 (*M. paniculata* var. *omphalocarpa*) 和毛翼叶九里香 (*M. alata* var. *hainanensis*) 也被分别降为相应种的同物异名^[5]。因此,目前,中国的九里香属植物总共有 8 个种和 1 个变种。

在经济价值方面,九里香属植物为园艺珍品,而调料九里香 (*M. koenigii*) 的鲜叶更是调制咖喱粉的主要成分。本属植物的多个部分也广泛用作民间草药,具有止痛、收敛、抗痢疾及退热等效用。千里香的根和茎也有用作妇女分娩时的催产药^[1]。在化学成分研究方面,这属植物含有许多香豆精和生物碱化合物(其中包括吲哚酮类、咪唑类、咪唑啉类和吲哚类化合物)^[46]。最近,江润祥等^[7-11] 研究确定,千里香根具有调节生育的活性。

1)2)3) 见英文摘要的脚注

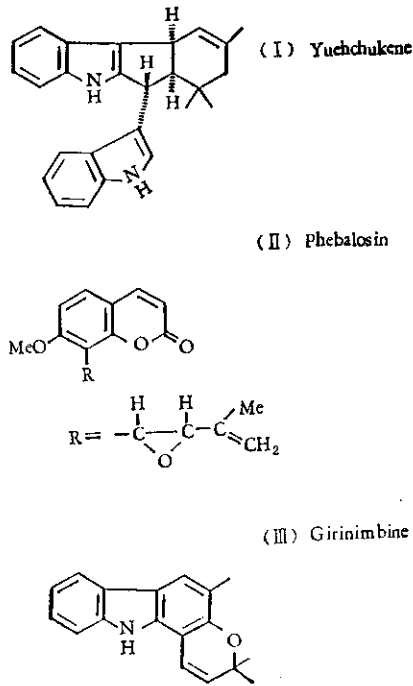


图 1 (I) 月橘烯碱, (II) Phebalosin 一种 8-戊烯化香豆精,
(III) Girinimbine, 一种咔唑生物碱

Fig. 1 (I) Yuehchukene, (II) Phebalosin, an 8-prenylated coumarin, and
(III) Girinimbine, a carbazole.

而且,分离出一个新类型的二聚戊烯化的吲哚类生物碱月橘烯碱 (Yuehchukene) (I)。这个二聚体对大鼠有显著的抗着床活性。大鼠在交配后怀孕的第二天喂服这种单味药(每次每公斤 3mg)可完全抑制受孕。然而,千里香中的月橘烯碱含量很低。为了寻找这个抗着床成分的更多来源,作者研究了我国九里香属所有种类的根部的化学成分除了月橘烯碱外,亦探索了根部其它化合物,从而希望化学的数据能够显示出这个属内的亲缘关系,为分类学提供新的见解。

材料与方 法

材料: 从我国野外采集九里香属 8 个种的根样品,洗净后,阴干,然后磨碎或切成长 1—2 cm 的小块。凭据标本存于广州中山大学生物系标本室。

月橘烯碱的提取、分离、鉴定和定量: 每种样品 100g, 用苯浸提两次, 每次用苯 400 ml, 前后时间共 3 天。合并浸提物, 并在 40℃ 减压浓缩。将苯的总提取物置于硅胶柱上分离, 用苯洗脱。用硅胶薄层板检出含月橘烯碱部分 (溶剂: 己烷: 二氯甲烷: 异丙醇; 9: 1: 0.5), 并进行合并。用高压液相色谱定量检测浸膏内的月橘烯碱, 色谱柱用 Ultrasphere-Si 柱, 溶剂用石油醚(沸点 60—80℃): 二乙基醚(7:3), 流速每分钟 1.5ml, 在 280mm 处检测。

香豆精的提取、分离和鉴定:按照提取月橘烯碱的步骤取得根部的苯提取物,将月橘烯碱从硅胶柱上洗脱下来后,洗脱剂改用丙酮,从而将香豆精洗脱下去。于是,将含香豆精较多的部分再进行硅胶柱层析,用苯:丙酮(7:3)作洗脱剂,得到了几个单体化合物,用光谱分析或根据标准样品进行层析比较,这些化合物被鉴定为:香豆九里素(Coumurrayin)、异梅九里香素(Isomexoticin)、梅九里香素(mexoticin)、莫潘尼定(mupanidin)、九里香亭(murrangatin)、番巴洛辛(Phebalosin)(II)和西伯里素(Sibiricin)。

咔巴唑类的提取、分离和鉴定:用硅胶柱,以苯作洗脱剂,将浓缩的苯提取物分成几个部分。柱层析各部分中的咔巴唑生物碱用薄层检测(用硫酸并加热显色)。结果分离出三个咔巴唑生物碱,其中两个经光谱分析鉴定为吉尼宾(Girinimbine)(III)和九里香叶素-A(Murrayafoline-A)第三个咔巴唑生物碱尚待鉴定。

结果和讨论

化学上的差异

分析的结果显示月橘烯碱仅在三个种的根样品中发现,即:翼叶九里香(*M. alata*)、九里香和千里香(还包括采自台湾的凸叶九里香的两个样品)。另外从同样的材料中还分离出多个 8-戊烯化的香豆精,但未见有咔巴唑类化合物。其余有四个种,即兰屿九里香(*M. crenulata*)、豆叶九里香、调料九里香和小叶九里香(*M. microphylla*)均含有咔巴唑化合物吉尼宾;并从兰屿九里香和豆叶九里香中分离出九里香叶素-A。在余下的一个种,广西九里香中则发现含有一个未被鉴定的咔巴唑化合物。然而,在上述这五个含咔巴唑类化合物的种中,既没有发现含香豆素,也未发现含月橘烯碱(检测的最低限量为 0.1mg/100g)。这些类型的化学成分在国产九里香属植物中分布情况已总结于表 1。

表 1 国产九里香属各种之根部化学成分类型分布

Table 1 Distribution of yuehchukene, carbazoles and 8-prenylated coumarins in *Murraya* species found in China.

种 Species	样品次数 Number of samples analysed	月橘烯碱 Yuehchukene (mg/100g)	咔巴唑生物碱 Carbazoles	8-戊烯化香豆精 8-Prenylated Coumarins
九里香组 <i>Murraya</i> section <i>Murraya</i>				
翼叶九里香 <i>M. alata</i>	3	+(2.06±4.4)	-	+
九里香 <i>M. exotica</i>	4	+(2.61±0.53)	-	+
千里香 <i>M. paniculata</i>	18	+(1.39±0.38)	-	+
(var. <i>omphalocarpa</i> 凸果九里香)	2	+(1.01)	-	+
棕荃组 <i>Murraya</i> section <i>Bergera</i>				
兰屿九里香 <i>M. crenulata</i>	2	-	+	-
豆叶九里香 <i>M. euchrestifolia</i>	1	-	+	-
调料九里香 <i>M. koenigii</i>	2	-	+	-
广西九里香 <i>M. kwangsiensis</i>	1	-	+	-
小叶九里香 <i>M. microphylla</i>	2	-	+	-

形态上的差异

在几个形态特征的组合上,这两大类型的种也是相互不同的。第一类型的植物,含月橘烯碱和 8-戊烯化香豆精,但不含咔巴唑,具有淡灰黄色的茎和根皮,花瓣较大(长 1—2

cm), 果椭圆状, 红色。另一方面, 另一个类型的植物, 则含有咔巴唑类, 而不含月橘烯碱和 8-戊烯化香豆精, 茎和根皮黑棕色, 花瓣较小(长 4—7mm), 果球形至椭圆状, 紫黑色。

分类学处理

对九里香属的分类处理, Swingle^[14]提到, 这个属的植物大概可以分成 2 个或 3 个组, 但有待更充分的研究。然而, 在这个观察基础上, 他并没有进一步阐明如何划分他所提到的几个组。我们的结果证明, 中国的 8 种九里香植物可以分成两个组(sections)。这两个组的植物在外部形态和化学成分上是有明显分别的。因此, 为了反映中国 8 种九里香植物的亲缘关系, 我们认为应把这个属分成两个组。Tanaka^[15]亦有同一想法, 他在一篇关于这个属(属名为 *Chalcas*)的较老的专论中根据植物的形态特征也提出同样的结论。这篇专论发表于日本占领时期台湾出版的一本不出名的杂志上。所以我们一直未有机会拜读, 直到我们完成了化学分析和提出了分类学上的结论后, 才收到胡秀英教授影印寄来 Tanaka 的这篇文章。Tanaka 的分类, 基本上与我们建议的两个组(sections)相吻合。

组 1 九里香组

Murraya sect. *Murraya*

Chalcas sect. *Euchalcas* Tanaka, J. Soc. Trop. Agric., 1, 41 (1929).

Radix et caulis stramineus vel alutaceus; fructus ellipsoideus, ruber; petala 1—2 cm longa. Radix yuehchukinum et coumarinum, 8-prenylatum sed non carbazolum continens.

Typus: *Murraya paniculata* (L.) Jack

根和茎皮稻秆黄带白色或淡黄白色; 果椭圆球形, 红色; 花瓣 1—2cm 长; 根部含月橘烯碱和 8-戊烯化香豆精, 不含咔巴唑生物碱。

这个组包括: 翼叶九里香(*M. alata* Drake), 九里香(*M. exotica* L.)和千里香(*M. paniculata*(L.)Jack), 其中包括脐果九里香 *M. paniculata* var. *omphalocarpa*; 国外的 *M. alternans*(kurz) Swingle, *M. glenici* Thwaites ex Oliv 和 *M. ovatifoliolata* (Engl.) Domin 也应隶属于这个组。

组 2 棕茎组(新组合)

Murraya sect. *Bergera* (Koenig ex L.) But et Kong, comb. nov.

Basionym: *Bergera* Koenig ex L. Mant. Pl., p. 563(1771). — *Chalcas* sect. *Bergera* Tanaka, J. Soc. Trop. Agric., 1, 41(1929).

Radix et caulis fuliginosus; fructus globosus vel ellipsoideus, purpureo-niger; petala brevissima, 4—7mm longa. Radix carbazolum continens, non yuehchukinum necque coumarinum 8-prenylatum inventa.

Typus: *Murraya koenigii* (L.) Spreng.

根和茎皮污棕色; 果球形或椭圆球形, 紫黑色; 花瓣短, 长 4—7mm。根部含咔巴唑生物碱, 未见有月橘烯碱或 8-戊烯化香豆精。

这个组包括: 兰屿九里香(*M. crenulata* (Turcz.) Oliver)、豆叶九里香(*M. euchrestifolia* Hayata)、调料九里香(*M. koenigii* (L.) Spreng.)、广西九里香(*M. kwangsiensis* (Huang) Huang)、小叶九里香(*M. microphylla*(Merr. et Chun)Swingle)以及暹罗九里香(*M. siamensis* Craib)。另外的两个种 *M. glabra* (Guill.) Swing 和 *M. stenocarpa* (Drake) Swin-

gle 暂时被包括在这个组里,有待于进一步研究。

将国产九里香属植物分成两个组的观点又得到了中国以外两个其它种的化学成分研究结果的支持。这两个种是澳大利亚昆士兰的卵叶九里香(*M. ovatifoliolata*)和泰国的暹罗九里香(*M. siamensis*)。我们的研究表明,凭形态关系来说,前一个种与千里香较为密切,它也含月橘烯碱和香豆精(未发表);而后一个种与调料九里香相近,也同样缺乏月橘烯碱和香豆精,但含有吉尼宾^[12-13]。近来,关于斯里兰卡特有的 *M. gleniei* 这个种的研究报告,也倾向于支持我们的分类结论。在这个种中亦发现含有 8-戊烯化香豆精^[17]和吡喃喹啉类生物碱,但不含咔巴唑^[6]。虽然月橘烯碱还未见报道由 *M. gleniei* 中找到(也许受到技术上的限制),但估计它会存在于这个种中。将九里香属分成两个组具有重要的实际意义。它可以指导民族药的筛选。以后进一步开发这个属以及探索抗着床成分月橘烯碱的天然来源就应集中在九里香属的九里香组植物上。另一方面,九里香属棕茎组成员可作为一种新抗癌药咔巴唑的来源(Soejarto, Pers. comm. 1985)。另外,这种分类上的划分也许会表明咔巴唑生物碱和戊烯化吡啶类化合物的生源。

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A CHEMOTAXONOMIC STUDY OF MURRAYA (RUTACEAE) IN CHINA

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Abstract 1. *Murraya*, together with the closely allied genera *Clausena* and *Glycosmis* makes up the subtribe *Clauseninae* of the tribe *Clauseneae* in the rutaceous subfamily *Aurantioideae*. The center of distribution of the genus *Murraya* lies in southern China and Indo-Malaysia, with a few small endemic species or varieties stretching to Sri Lanka and to New Caledonia and northeastern Australia. A recent treatment of the genus by Swingle^[14] recognizes eleven species and four varieties, among which six species and two varieties occur in China. Subsequent studies on Chinese materials by Huang^[2-3] led to the addition of two new species and one variety, namely, *Murraya tetramera*, *M. Kwangsiensis*, and *M. kwangsiensis* var. *macrophylla*; the former species, *M. tetramera*, has since been found to be identical with *M. euchrestifolia*^[4-5]. Huang also reinstated *M. exotica* as a species distinct from *M. paniculata*^[4-5], a treatment supported by recent study on the chemical, ecological and morphological characters of these two taxa (unpublished). Moreover, two of the varieties recognised by Swingle, namely, *M. paniculata* var. *omphalocarpa* and *M. alata* var. *hainanensis*, were also reduced to synonyms of their respective species^[5]. Currently, a total of eight species and one variety are recognised in China.

Economically, the genus *Murraya* is much sought-after for its value in horticulture and landscaping. The fresh leaf of *M. koenigii* is a constant and essential component in preparing curry. Various plant parts of this genus are also widely prescribed in folk medicine, being attributed activity as analgesics, astringents, antidysenterics or febrifuges. The root and stem of *M. paniculata* have also been used as an ecboic for delivery, at full term, in human subjects^[1]. Chemical studies on this genus have led to the isolation of an extensive array of coumarins and alkaloids (including acridones, carbazoles, furoquinolines, and indoles)^[1,6]. Recently, Kong and associates^[7-11] have con-

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firmed the fertility regulating activity of the root of *M. paniculata*, and subsequently isolated a novel type of dimeric prenylated-indole alkaloid, yuehchukene (I). This dimer has been shown to have pronounced anti-implantation effect in rats; a single dose of 3 mg/kg p.o. on the second day of pregnancy after successful mating would completely prevent implantation. However, the yield of yuehchukene obtained from *M. paniculata* is low and in an attempt to find better sources of this anti-implantation principle, a survey of the roots of all other *Murrraya* species available in China has been conducted. Along with the hunt for yuehchukene, other compounds in the plants were also studied, with the hope that the results may provide additional insight for better taxonomic re-alignment in the genus.

2. Yuehchukene was found in the root samples of three species, namely, *M. alata*, *M. exotica* and *M. paniculata* (including two samples of *M. paniculata* var. *omphalocarpa* from Taiwan). From the same sources of materials, a number of 8-prenylated coumarins, but no carbazole, were also isolated. Four of the remaining species, viz. *M. crenulata*, *M. cuchrestifolia*, *M. koenigii* and *M. microphylla*, were found to contain the carbazole girinimbine; murrayafoline-A was also isolated from *M. crenulata* and *M. euchrestifolia*. The last species, *M. kwangsiensis*, was found to contain an unidentified carbazole. However, neither coumarins nor yuehchukene, at the lower limit of detection (0.1 mg/100 g), were found in these five species. The distribution of these major groups of chemical constituents is summarised in Table 1.

3. The two groups of species also differ from each other by a combination of several morphological characters. Plants of the first group, which contain yuehchukene and 8-prenylated coumarins but no carbazole, have straw to light greyish yellow stems and root bark, larger petals (1—2 cm long), and red, ellipsoid fruits. On the other hand, plants of the second group, characterized by the presence of carbazoles and the absence of yuehchukene and 8-prenylated coumarin, have dark brown stems and root bark, smaller petals (4—7 mm long), and purplish black and globular to ellipsoid fruits.

4. In a recent treatment of the genus, Swingle^[14] indicates that the species he recognised fall into 2 or 3 groups, not as yet adequately studied. However, he did not expand further on this observation and shed light on where to delimit the groups he alluded to. Our results demonstrate that the eight species of *Murrraya* in China can be divided into two groups, which differ from each other in both external morphology and chemical constituents. Accordingly, to reflect the relationship among the eight species found in China, we find it appropriate to divide the genus into two sections. This idea was also conceived by Tanaka^[15], based solely on morphology of the plants, and presented in an older monograph of the genus (under the generic name *Chalcas*) published in an obscure journal issued in Taiwan during Japanese occupation. Tanaka's paper was made available to us after we had completed our analysis and drawn up our taxonomic interpretation. Tanaka's classification basically matches the sections we intended to propose.

Key words Chemotaxonomy; Yuehchukene; Carbazoles; Coumarins; *Murrraya*; *Murrraya* sect. *Murraga*; *Murrraya* sect. *Bergera*