

Pectolinarin and Pectolinarigenin

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Flavonoids are metabolites widely distributed in plants and commonly present in foods, such as fruits and vegetables. Pectolinarin, which belongs to the flavone subclass, has attracted considerable attention due to its presence in many medicinal plants. It has turned out to be a good biological agent especially due to its antioxidant, anti-inflammatory, antidiabetic, and antitumor activities, evaluated both in vitro and in vivo. Its aglycone, the metabolite pectolinarigenin, is also known for a series of biological properties including anti-inflammatory and antidiabetic effects. In the first overview on the two metabolites here presented, their collection, isolation and the results of their biological evaluation are reported

flavonoids

flavones

anticancer

1. Definition

Flavonoids are metabolites widely distributed in plants and commonly present in foods, such as fruits and vegetables. Based on several evidences, flavonoids have been associated with the role of preventing and managing current diseases such as cancers, diabetes, and cardiovascular disorders.

Pectolinarin, which belongs to the flavone subclass, has attracted considerable attention due to its presence in many medicinal plants. It has turned out to be a good biological agent especially due to its antioxidant, anti-inflammatory, antidiabetic, and antitumor activities, evaluated both in vitro and in vivo. Its aglycone, the metabolite pectolinarigenin, is also known for a series of biological properties including anti-inflammatory and antidiabetic effects.

2. Introduction

The glycosylated flavone pectolinarin was first isolated from *Linaria vulgaris* ^[1], a known medicinal Chinese herb used for the internal treatment of digestion problems and urinary disorders, in the external treatment of haemorrhoids, venous skin ulcer, as well as for the washing of festering wounds and skin rashes. It has also displayed anti-inflammatory effect ^[2] and has been used to treat coughs and asthma ^[3]. The structure of pectolinarin was determined to be a rutinoside conjugate of pectolinarigenin (=5,7-dihydroxy-4,6-dimethoxyflavone, C₁₇H₁₄O₆) at the 7-O position (pectolinarigenin-7-O-rutinoside, C₂₉H₃₄O₁₅) (Figure 1).

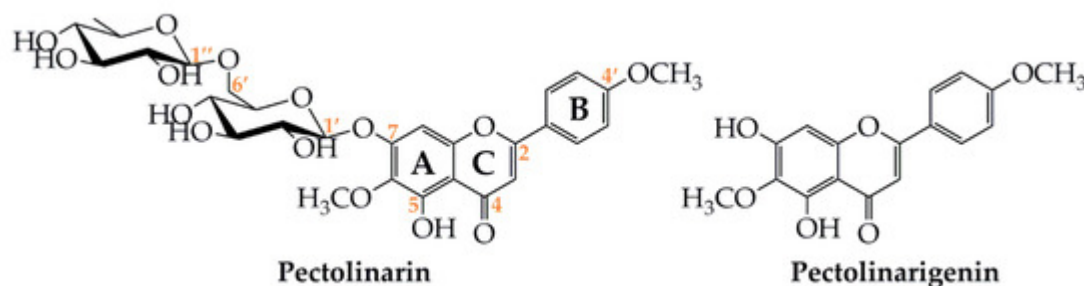


Figure 1. Molecular structures of pectolinarin and pectolinarigenin.

Later, pectolinarin and its aglycone pectolinarigenin were identified as the major constituents in many medicinal herbs from different genera around the world. Several studies reported so far prove that the presence of these two flavones has an important role in affecting the biological properties of the following herbs: i) the Korean herb *Cirsium setidens* (Dunn) Nakai employed for the treatment of hemostasis, hematemesis, hematuria and hypertension [4]; ii) the Chinese herb *Cirsium chanroenicum* used for detoxification, to treat fever and to enhance blood circulation [5]; iii) *Cirsium japonicum* DC. employed as an anti-hemorrhagic and uretic agent, as well as prescribed to treat liver and uterine tumours, and leukemia [6]; iv) *Kickxia ramosissima* (Wall.) Janch., used in Pakistan folk medicine as diuretic and against kidney stones [7], fever and rheumatism [8], and during management of snake and scorpion bites [9]; v) *Lantana camara* L., used for the treatment of various human ailments, such as ulcers, malaria, influenza, tumors, swellings, bilious fever, eczema eruptions, stomach ache, toothache, and as antiseptic for wounds [10]; and vi) *Picnemon acama* (L.) Cass., used in Greek folk medicine as hemostatic and spasmolytic agent [11].

Due to the structural similarity of pectolinarigenin to known potent flavonoids such as acacetin (5,7-dihydroxy-4'-methoxyflavone, $C_{16}H_{12}O_5$), hispidulin (4',5,7-trihydroxy-6-methoxyflavone, $C_{16}H_{12}O_6$) and scutellarein (5,6,7,4'-tetrahydroxyflavone, $C_{15}H_{10}O_6$) and based on the numerous data reported for both pectolinarin and pectolinarigenin, the aim of this work is to provide a comprehensive overview focusing on their isolation.

3. Isolation of Pectolinarin and Pectolinarigenin

Over the last 113 years from its first report [1], pectolinarin was isolated in most cases from the aerial parts of 87 plants belonging to 29 different genera distributing widely around the world. Most of these plants are used in folk medicine in different parts of the world. Table 1 gathers the 87 plants from which pectolinarin was isolated.

Table 1. Isolation of pectolinarin from the indicated plants, classified according to family, genus and species, and place of collection.

Genus	Species	Collection Place	Reference
Family: Adoxaceae			
<i>Viburnum</i>	<i>V. cotinifolium</i>	Kashmir/India	[12]

Genus	Species	Collection Place	Reference
	<i>V. mullaha</i>	Indian Himalayan region	[13]
Family: Asteraceae			
<i>Cirsium</i>	<i>C. subcoriaceum</i>	Pahuatlan/Mexico	[14]
	<i>C. japonicum</i>	Daejeon/S. Korea, Oberndorf/Austria, Chengdu/China, Henan/China	[6][15][16][17][18][19]
		Oberndorf/Austria	
		Bialystok/Poland	
		Daejeon/S. Korea	
	<i>C. setosum</i>	Daejeon/S. Korea	[17]
	<i>C. rivulare</i>	Daejeon, Wonju, Pyongchang-gun, Gangwondo, Jeongseon-gun, Yanggu/S. Korea	[20]
	<i>C. lineare</i>	Daejeon/S. Korea	[18]
	<i>C. nipponicum</i>	Daejeon, Sancheong/S. Korea	[18][21]
	<i>C. setidens</i>	Jeongseon-gun, Jeju Island/S. Korea	[18][22][23][24][25]
		Laramie/USA	
		Laramie/USA, Vitebsk/Belarus	
	<i>C. pendulum</i>	Nemuro, Hatimandake, Memanbetsu, Onsen Kyushu, Hokkaido/Japan	[18]
	<i>C. chanroenicum</i>		[18][25][26]
	<i>C. rhinoceros</i>		[27][28]
	<i>C. coloradense</i>	Wyoming/USA, Japan	[29]
	<i>C. arisanense</i>	Mount Akaishi, Mount Senmai, Shizuoka, Takanomori, Nekura Valley/Japan, Vitebsk/Belarus,	

Genus	Species	Collection Place	Reference
	<i>C. tioganum</i>	Mount Shirouma/Japan	
	<i>C. oleraceum</i>	Ia Dotze/Switzerland	[29][30][31]
		Hsien/Taiwan	
	<i>C. microspicatum</i>	Nemuro, Mount Shirouma /Japan, Mount Ali, Chiayi Hsien/Taiwan	[15]
	<i>C. babanum</i>	Ku Kuan, Taichung Haien/Taiwan	
	<i>C. kagamontanum</i>	Mount Shirouma, Mount Hakusan ad pedem/Japan	
	<i>C. inundatum</i>	Vancouver/Canada	
	<i>C. dipsacolepis</i>	Seongnam/Korea	
	<i>C. brevicaule</i>		
	<i>C. yezoense</i>		
	<i>C. kamtschaticum</i>		
	<i>C. pectinellum</i>		
	<i>C. bitchuense</i>		[32][33]
	<i>C. senjonse</i>		[16][30][34][35] [36]
	<i>C. spicatum</i>		
	<i>C. yezonese</i>		
	<i>C. vallis-demonii</i>		
	<i>C. gratiosum</i>		
	<i>C. indundatum</i>		
	<i>C. otayae</i>		[34]
	<i>C. purpuratum</i>		
	<i>C.</i>		[37]

Genus	Species	Collection Place	Reference
	<i>spinosissimum</i>		
	<i>C. spinosum</i>		[33]
	<i>C. ferum</i>		[38]
	<i>C. kawakamii</i>		[15][39][40]
	<i>C. wallichii</i>		[40]
	<i>C. yoshizawae</i>		[34]
	<i>C. matsumurae</i>		[33]
	<i>C. brevistylum</i>		[41]
	<i>C. chlorolepis</i>		[42]
<i>Duranta</i>	<i>D. plumieri</i>	Rajshahi/Bangladesh	[43]
<i>Hemistepta</i>	<i>H. lyrata</i>	Kangwon/S. Korea	[44]
<i>Picnomon</i>	<i>P. acarna</i>	Mount Hortiatis/Greece	[45]
Family: Bignoniaceae			
<i>Distictella</i>	<i>D. elongata</i>	Minas Gerais State/Brazil	[46]
<i>Markhamia</i>	<i>M. lutea</i>	Benguluru/India	[47]
Family: Buddlejaceae			
<i>Buddleja</i>	<i>B. officinalis</i>	Anhui/China	[48]
Family: Ericaceae			
<i>Rhododendron</i>	<i>R. arboreum</i>	Aligarh/India	[49]
Family: Gesneriaceae			
<i>Corallodiscus</i>	<i>C. flabellate</i>	Kunming/China	[50]
<i>Aeschynanthus</i>	<i>A. moningeriae</i>	Jinhua/China	[51]
Family: Lamiaceae			
<i>Leucosceptrum</i>	<i>L. canum</i>	Tibet/China	[52]
<i>Teucrium</i>	<i>T. hyrcanicum</i>	Sicily/Italy	[53]

Genus	Species	Collection Place	Reference
Family: Lythraceae			
<i>Lawsonia</i>	<i>L. inermis</i>	Thanjavur/India	[54]
Family: Moraceae			
<i>Clerodendrum</i>	<i>C. phlomides</i>	Tamil Nadu/India	[55]
Family: Orchidaceae			
<i>Oncidium</i>	<i>O. baueri</i>	Londrina/Brazil	[56][57]
Family: Orobanchaceae			
<i>Melampyrum</i>	<i>M. roseum</i>	Suwon/S. Korea	[58]
Family: Plantaginaceae			
<i>Scoparia</i>	<i>S. dulcis</i>	Nanning/China	[59]
Family: Poaceae			
<i>Oryza</i>	<i>O. sativa</i>	a)	[60]
Family: Ranunculaceae			
<i>Trollius</i>	<i>T. ledebourii</i>	Hebei/China	[61]
Family: Rosaceae			
<i>Kerria</i>	<i>K. japonica</i> var.	Chongqing/China	[62]
<i>Crataegus</i>	<i>C. laevigata</i>	Bremen/Germany	[63]
Family: Santalaceae			
<i>Thesium</i>	<i>T. chinense</i>	Anhui/China	[64]
Family: Scrophulariaceae			
<i>Linaria</i>	<i>L. vulgaris</i>	Sofia/Bulgaria, Tachkent/Uzbekistan	[1][65][66][67]
	<i>L. japonica</i>	Heilongjiang/China	[68][69][70]
	<i>L. reflexa</i>	Tottori Prefecture/Japan	[71][72][73][74]
	<i>L. vulgariformis</i>	Constantine/Algeria, Calabria/Italy	[65]

Genus	Species	Collection Place	Reference
	<i>L. popovii</i>	Tachkent/Uzbekistan	
	<i>L. kurdica</i>		
	<i>L. sessili</i>		[75]
	<i>L. kokanica</i>	Pamir/Tajikistan	
	<i>L. haelava</i>		[76]
	<i>L. simplex</i>	Mansoura/Egypt	[66]
	<i>L. genistifolia</i>	Sofia/Bulgaria	
	<i>L. dalmatica</i>		
	<i>L. scariosa</i>	Msila/Algeria	[77]
	<i>K. elatine</i>	Dustlik/Uzbekistan	[78]
	<i>K. heterophylla</i>	Mansoura/Egypt	[79]
	<i>K. ramosissima</i>	Ankara/Turkey	[80][81]
<i>Kickxia</i>	<i>K. abhaica</i>	Baljurashi/Saudi Arabia	[82]
		Appennines hills/Italy	
	<i>K. spuria</i>	Saudi Arabia	[83]
	<i>K. aegyptiaca</i>		[84]
Family: Verbenaceae			
<i>Morus</i>	<i>M. alba</i> L.	Hongseong/Korea	[85]
<i>Lantana</i>	<i>L. camara</i>	Taichung/Taiwan, Palampur/India, Karachi/Pakistan, Ceará state/Brazil, Manado/Indonesia, Okinawa/Japan	[86][87][88][89][90][91]
<i>Lippia</i>	<i>L. rubella</i>	Minas Gerais/Brazil	[92]
Family: Winteraceae			
<i>Tasmannia</i>	<i>T. lanceolata</i>	Go Wild Harvest/Australia	[93]

^a Not found.

Pectolinarigenin is the aglycone part of pectolinarin, which is obtained by hydrolysis reaction [72]. It is also a natural product, isolated and identified from 136 plantes of 71 differents genera. The data are summarized in Table 2, indicating that pectolinarigenin was isolated from 20 different families, especially from Asteraceae with 33 genera and 64 species (47.1%), Lamiaceae with 9 genera and 19 species (14%) and Verbenaceae with 4 genera and 10 species (8%).

Table 2. Isolation of pectolinarigenin from the indicated plants, classified according to family, genus and species, and place of collection.

Genus	Species	Collection Place	Reference
Family: Apiaceae			
<i>Coriandrum</i>	<i>C. sativum</i>	Faisalabad/Pakistan	[94]
Family: Aspleniaceae			
<i>Asplenium</i>	<i>A. glaucophyllum</i>	West Malaysia	[95]
	<i>A. normale</i>	West Malaysia	[96]
Family: Asteraceae			
<i>Achillea</i>	<i>A. collina</i>	wet lowland meadows/UK	[97]
	<i>A. asplenifolia</i>		
<i>Ajania</i>	<i>A. potaninii</i>	Gansu/China	[98]
<i>Ambrosia</i>	<i>A. camphorate</i>	Baja California/Mexico	[99]
<i>Arnica</i>	<i>A. angustifolia</i>	northwest Canada and Alaska	[100]
	<i>A. Montana</i>	California/USA	[101]
	<i>A. chamissonis</i>	Graines Voltz/France	[102]
	<i>A. montana</i>	Šumava Mounts/Czech	[103]
<i>Artemisia</i>	<i>A. mongolica</i>	Gansu/China	[104]
	<i>A. judaica</i>	St. Catherine, Sinai/Egypt	[105]
	<i>A. monosperma</i>	Cairo/Egypt	
	<i>A. herba-alba</i>	Mount Moses/Egypt	

Genus	Species	Collection Place	Reference
	<i>A. xerophytica</i>	South Gobi Aimak/Mongolia	[106]
	<i>A. glabella</i>	Karaganda/Kazakhstan	[107]
	<i>A. vestita</i>	Lhasa/Tibet	[108]
<i>Baccharis</i>	<i>B. trinervis</i>	Costa Rica	[109]
	<i>B. decussata</i>	Venezuela	[110]
	<i>B. concave</i>		[111]
	<i>B. uncinella</i>	Campos do Jordão/Brazil	[112]
	<i>B. conferta</i>	Veracruz/Mexico	[113]
<i>Centaurea</i>	<i>C. alexandrina</i>	Alexandria/Egypt	[114]
	<i>C. aspera</i>	Ribera Baixa/Spain	[115]
	<i>C. cariensis</i>		[116]
	<i>C. collina</i>	Valencia/Spain	[117]
	<i>C. sadleriana</i>	Jakabszállás/Hungary	[118]
	<i>C. moesiaca</i>	Malashevskia planina/Bulgaria	[119]
	<i>C. behen</i>	Iran	[120]
<i>Chromolaena</i>	<i>C. odorata</i>	Chonburi/Thailand	[121]
<i>Chrysanthemum</i>	<i>C. pacificum</i>	Tsukuba/Japan	[26]
	<i>C. shiwogiku</i>	Muroto-misaki/Japan	
	<i>C. kinokuniense</i>	Tsukuba/Japan	
	<i>C. rupestre</i>	Mount Mikuni/Japan	
<i>Cirsium</i>	<i>C. setidens</i>	Jeongseon-gun, Halla of jejudo, Daejeon, Kangwon, Yanggu/S. Korea; Guerrero/Mexico;	[18][23][24][25][26][27] [122]
	<i>C. chanroenicum</i>	Daejeon, Ulsan,	[25][123]

Genus	Species	Collection Place	Reference
		Sancheong/S. Korea	
	<i>C. japonicum</i>	Jiang Xi/China	[124]
	<i>C. arvense</i>	Musa Khel Bannu/Pakistan	[125]
	<i>C. nipponicum</i>	Suwon/S. Korea	[126]
	<i>C. rhinoceros</i>		[127]
<i>Dichrocephala</i>	<i>D. integrifolia</i>	Shanghai/China	[128]
<i>Dugaldia</i>	<i>D. pinetorum</i>	Nuevo Lebn/Mexico	[129]
<i>Eriocephalus</i>	<i>E. giessii</i>	Aus-Koppies/Namibia	[130]
<i>Eupatorium</i>	<i>E. cannabinum</i>	Gronigen/Netherlands	[131]
	<i>E. odoratum</i>	Kuala Pilah/Malaysia	[132][133]
	<i>E. semiserratum</i>	Arkansas/USA	[134]
<i>Fragrant</i>	<i>F. Eupatorium</i>	Guangxi/China	[135]
<i>Grindelia</i>	<i>G. glutinosa</i>	Poconchile, Valle deLiuta, Tarapaca/Chile	[136]
<i>Gutierrezia</i>	<i>G. mandonii</i>	Salta/Argentina	[137]
<i>Helenium</i>	<i>H. integrifolium</i>		[138]
<i>Heterotheca</i>	<i>H. latifolia</i>	San Luis/Argentina	[139]
<i>Hemistepta</i>	<i>H. lyrata</i>	Kangwon/S. Korea	[44]
<i>Hymenoxys</i>	<i>H. jamesii</i>	Coconino/USA	[140]
<i>Iva</i>	<i>I. nevadensis</i>	Tonopah/USA	[141]
	<i>I. frutescens</i>	Franklin/USA	[142]
<i>Jungia</i>	<i>J. polita</i>	San Martin/Argentina	[143]
<i>Olearia</i>	<i>O. paniculata</i>	Dunedin/New Zealand	[144]
<i>Onopordon</i>	<i>O. corymbosum</i>	Barracas, Castellon/Spain	[145]
	<i>O. nervosum</i>	a)	[146]

Genus	Species	Collection Place	Reference
<i>Santolina</i>	<i>S. chamaecyparissus</i>	Lyon/France	[147]
	<i>S. pinnata</i>	Pisa/Italy	[148]
<i>Saussurea</i>	<i>S. elegans</i>	Murghab/Tajikistan	[149]
<i>Schkuhria</i>	<i>S. pinnata</i>	Cordoba/Argentina	[150]
<i>Seriphidium</i>	<i>S. santolium</i>	Xinjiang Uigour/China	[151]
<i>Stevia</i>	<i>S. laxiflora</i>	Cuernavaca, Morelos/Mexico	[152]
<i>Vernonia</i>	<i>V. cinerea</i>	Pahang/Malaysia	[153]
Family: Betulaceae			
<i>Alnus</i>	<i>A. glutinosa</i>	Darmstadt/Germany	[154]
	<i>A. japonica</i>		[155]
<i>Betula</i>	<i>B. ermanii</i>		[154]
	<i>B. verrucosa</i>	a)	[156]
	<i>B. pubescens</i>	Biebrza/Poland	[157]
	<i>B. pendula</i>		
Family: Bignoniaceae			
<i>Millingtonia</i>	<i>M. hortensis</i>	Khon Kaen/Thailand	[158]
Family: Blechnaceae			
<i>Brainea</i>	<i>B. insignis</i>	Yunnan/China	[159]
Family: Boraginaceae			
<i>Eriodictyon</i>	<i>E. tomentosum</i>	Placer Co./USA	[160]
Family: Fabaceae			
<i>Adesmia</i>	<i>A. grandiflora</i>	a)	[161]
	<i>A. trijuga</i>		
	<i>A. horrida</i>		

Genus	Species	Collection Place	Reference
	<i>A. retrofracta</i>		
<i>Ononis</i>	<i>O. fruticosa</i>	Los Castanõs/Spain	[162]
	<i>O. natrix</i>		
	<i>O. rotundifolia</i>	a)	[163]
<i>Trifolium</i>	<i>T. pratense</i>	Trout Lake/USA	[164]
Family: Lamiaceae			
<i>Leucosceptrum</i>	<i>L. canum</i>	a)	[165]
<i>Mentha</i>	<i>M. pulegium</i>	Petite Kabylie/Algeria	[166]
	<i>M. suaveolens</i>		
<i>Ocimum</i>	<i>O. americanum</i>	RoyalBotanic Gardens, Kew/England	[167]
<i>Otostegia</i>	<i>O. fruticosa</i>	St. Catherine/Egypt	[168]
<i>Salvia</i>	<i>S. trilobu</i>	Marmara island/Turkey	[169]
	<i>S. hypoleuca</i>	Elbruz moun/Russia	[170]
	<i>S. pedicellata</i>	a)	[171]
	<i>S. yosgadensis</i>	Sultanhani/Turkey	[172]
	<i>S. plebeia</i>	a)	[173]
	<i>S. pilifera</i>	Berit Mount/Turkey	[174]
	<i>S. tomentosa</i>	Sofia/Bulgaria	[175]
	<i>S. argentea</i>		
<i>Scutellaria</i>	<i>S. polyodon</i>	a)	[176]
	<i>S. przewalskii</i>	Susamyr/Kyrgyzstan	[177]
<i>Sideritis</i>	<i>S. gomerae</i>	Canary islands/Spain	[178]
<i>Teucrium</i>	<i>T. chamaedrys</i>	Eskisehir/Turkey	[179]
<i>Thymus</i>	<i>T. longicaulis</i>	Sar planina/Macedonia	[180]
	<i>T. glabrescens</i>	Skopje/Macedonia	

Genus	Species	Collection Place	Reference
Family: Lythraceae			
<i>Lawsonia</i>	<i>L. inermis</i>	Thanjavur/India	[148]
Family: Nothofagaceae			
<i>Nothofagus</i>	<i>N. dombeyi</i>	Altos de Lircay/Chile	[181]
Family: Orobanchaceae			
<i>Striga</i>	<i>S. passargei</i>	a)	[182]
	<i>S. aspera</i>	a)	[183]
Family: Padaliacea			
<i>Sesamum</i>	<i>S. indicum</i>	Gambang/Malaysia	[184]
Family: Plantaginaceae			
<i>Digitalis</i>	<i>D. trojana</i>	Kizilcahamam, DemirkOy/Turkey	[185]
	<i>D. orientalis</i>		
	<i>D. lanata</i>	a)	[186]
<i>Hebe</i>	<i>H. cupressoides</i>	Dunedin/New Zealand	[187]
<i>Veronica</i>	<i>V. chamaedrys</i>	Rila Mount/Bulgaria	[188]
<i>Veronicastrum</i>	<i>V. latifolium</i>	Yongkang/China	[189]
Family: Portulacaceae			
<i>Portulaca</i>	<i>P. oleracea</i>	Tianjin/China	[190]
Family: Ranunculaceae			
<i>Trollius</i>	<i>T. chinensis</i>	Hebei/China	[191]
Family: Rosaceae			
<i>Rosa</i>	<i>R. damascena</i>	Plovdiv/Bulgaria	[192]
	<i>R. rugosa</i>	Botanischer Garten der TU Darmstadt/Germany	[193]

Genus	Species	Collection Place	Reference
Family: Scrophulariaceae			
<i>Buddleia</i>	<i>B. macrostachya</i>	Sibsagar/India	[194]
<i>Kickxia</i>	<i>K. ramosissima</i>	Takht-e-Nusrati/Pakistan	[195][196][197]
<i>Limnophila</i>	<i>L. aromatica</i>	Ho Chi Minh/Vietnam	[198]
<i>Linaria</i>	<i>L. vulgaris</i>	Ukrania; China	[67][199]
	<i>L. reflexa</i>	Constantine/Algeria	[72]
	<i>L. kurdica</i>	Ukrania	[199]
	<i>L. scariosa</i>	Msila/Algeria	[77]
Family: Verbenaceae			
<i>Clerodendrum</i>	<i>C. siphonanthus</i>	Calcutta, Kalyani/India	[200][201]
	<i>C. phlomidis</i>	Pondicherry, Alanthurai/India	[200][201][202][203][204][205]
	<i>C. serratum</i>	Bhilai/India	[206]
	<i>C. inerme</i>	Pondicherry/India	[207][208]
	<i>C. neriifolium</i>	a)	[209]
	<i>C. indicum</i>	a)Khao Kho/Thailand	[210][211]
<i>Duranta</i>	<i>D. repens</i>	a)	[212]
	<i>D. plumieri</i>	a)	[43][213]
<i>Lantana</i>	<i>L. camara</i>	Taichung/Taiwan, Palampur/India, Karachi/Pakistan, Cear� state/Brazil, Manado/Indonesia, Okinawa/Japan	[86][87][88][89][90][91]
<i>Lippia</i>	<i>L. citriodora</i>	Athens/Greece	[214]
Family: Zosteraceae			
<i>Phyllospadix</i>	<i>P. japonica</i>	Omaezaki/Japan	[215]

1.

a) not found.

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