THE FLAVONOIDS OF *PARTHENIUM* L.

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ABSTRACT.—The distribution of 34 flavonoids detected in the North American species of *Parthenium* L. is presented. Of the 27 flavonoids identified (some tentatively) all are flavonols: eight are based on kaempferol, seven on quercetin, four on 6-hydroxykaempferol and eight on the quercetagetin skeleton. Of the 34 flavonoids detected, 19 are glycosides and 15 are aglycones, primarily highly methylated compounds.

Parthenium L. is a genus of the Asteraceae (Compositae) long considered to be part of the Melampodiinae but recently included with the ragweeds in the Ambrosiinae (1). The biology and chemistry of *Parthenium* has been of interest because *P. argentatum* Gray (guayule) is a desert species which is a source of natural rubber (2) and *P. hysterophorus* L. (Santa Maria feverfew, muleweed) causes severe contact dermatitis (3, 4, 5). The sesquiterpene lactone chemistry of the genus has been well summarized (6, 7, 8), and several papers (9, 10, 11) have provided information about flavonoids of several species of the genus. Here the results of an examination of the flavonoid constituents of all the North American species of *Parthenium* are correlated with the earlier published data.

RESULTS

The distribution of 34 flavonoids detected in North American *Parthenium* species is shown in table 1. The proposed structures of 27 of the flavonoids are indicated in figure 1.

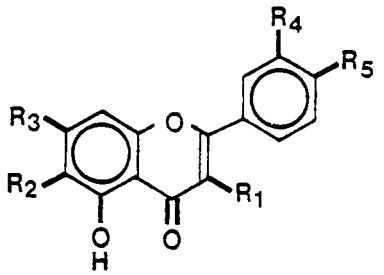
All the proposed structures are flavonols: derivatives of kaempferol (XIII, XIV, XIX–XXII, XXVII, XXVIII), quercetin (IX, XV, XVIII, XXIII-XXVI), 6-hydroxykaempferol (II, VII, VIII, XVI), and quercetagetin (III–VI, X–XII, XVII).

Parthenium tomentosum DC. is characterized here as a species of two varieties: *P. tomentosum* var. *tomentosum* and *P. tomentosum* var. *stramonium* (Greene) Rollins. Only a few derivatives of quercetin and quercetagetin were detected in var. *tomentosum*, although Rodriguez (11) reports other minor components. Minor components were detected in many taxa but are not included here unless they occurred sufficiently frequently to be regarded as dependable taxonomic units. Two unidentified glycosides were also detected in var. *tomentosum*. Similarly, only a few derivatives of kaempferol and quercetagetin were detected in var. *stramonium*.

Parthenium fruticosum Less is also composed of two varieties (12): var. *fruticosum* and var. *trilobatum* Rollins. One aglycone derivative of quercetagetin and three glycoside derivatives of kaempferol and quercetin were detected in var. *fruticosum*. Six aglycones, derivatives of quercetagetin, quercetin, 6-hydroxykaempferol, kaempferol and kaempferol 3-methyl ether, and three glycosides, derivatives of quercetagetin and quercetin, were detected in var. *trilobatum*. *Parthenium lozanianum* Blake, which is very closely related to *P. fruticosum* var. *trilobatum*, produces much the same pattern as *P. fruticosum* var. *trilobatum*, except that kaempferol 3-methyl ether was not detected in *P. lozanianum*.

Parthenium schottii Greenman, which is endemic to limestone in Yucatan, was found to produce only one flavonoid, quercetagetin 3,7-dimethyl ether; however, it is possible that fresher material would result in a richer species pattern.

FIGURE 1. Proposed structures of flavonoids of *Parthenium*.



Compounds	R_1	R_2	R_3	R_4	R_5
II	OCH_3	OCH_3	OH	H	OH
III	OCH_3	OH	OCH_3	OH	OH
IV	OCH_3	OCH_3	OCH_3	OH	OH
V	OCH_3	OCH_3	OH	OCH_3	OCH_3
VI	OCH_3	OH	OHC_3	OCH_3	OH
VII	OCH_3	OH	OCH_3	H	OH
VIII	OCH_3	OCH_3	OCH_3	H	OH
IX	OCH_3	H	OH	OCH_3	OH
X	OCH_3	OCH_3	OCH_3	OH	OCH_3
XI	OCH_3	OCH_3	OCH_3	OCH_3	OH
XII	OCH_3	OCH_3	OCH_3	OCH_3	OCH_3
XIII	OH	H	OCH_3	H	OH
XIV	OCH_3	H	OH	H	OH
XV	OCH_3	H	OCH_3	OCH_3	OCH_3
XVI	OCH_3	OCH_3	OGLY	H	OH
XVII	OCH_3	OCH_3	OGLY	OH	OH
XVIII	OGLY	H	OH	OCH_3	OH
XIX-XXII	OGLY	H	OH	H	OH
XXIII-XXVI	OGLY	H	OH	OH	OH
XXVII-XXVIII	OCH_3	H	OGLY	H	OH

Parthenium rollinsianum Rzedowski morphologically links the sections *Parthenichaeta* and *Bolophytum* of Rollins (12). Although Rodriquez (11)detected five flavonoid aglycones and eleven glycosides, the samples analyzed here showed no glycosides. The aglycones are all derivatives of quercetagetin, 6-hydroxykaempferol, and quercetin. Rodriguez also reported (11) glycosides of quercetin and quercetagetin derivatives.

In northern Mexico and western Texas *Parthenium incanum* HBK. hybridizes with *P. argentatum* Gray. Many of the desert populations show some signs of combinations of the characters which distinguish mesic forms of *P. incanum* from the desert limestone forms of *P. argentatum*. The few samples of *P. incanum* which showed little morphological evidence of influence by *argentatum* characters produced a flavonoid pattern with only one aglycone, kaempferol 3-methyl ether, and with eight flavonoid glycosides, derivatives of quercetin, quercetagetin and kaempferol. The several samples of *P. argentatum* showing little evidence of influence by *P. incanum* characters produced a flavonoid pattern rich in aglycones and glycosides: derivatives of quercetagetin, 6-hydroxykaempferol, quercetin, kaempferol and kaempferol 3-methyl ether. The many intermediate samples showed individually and collectively a strongly complementary pattern of seven aglycone derivatives of quercetagetin, 6-hydroxykaempferol, quercetin, kaempferol and kaempferol 3-methyl ether and thirteen glycoside derivatives of all those structural types except 6-hydroxykaempferol.

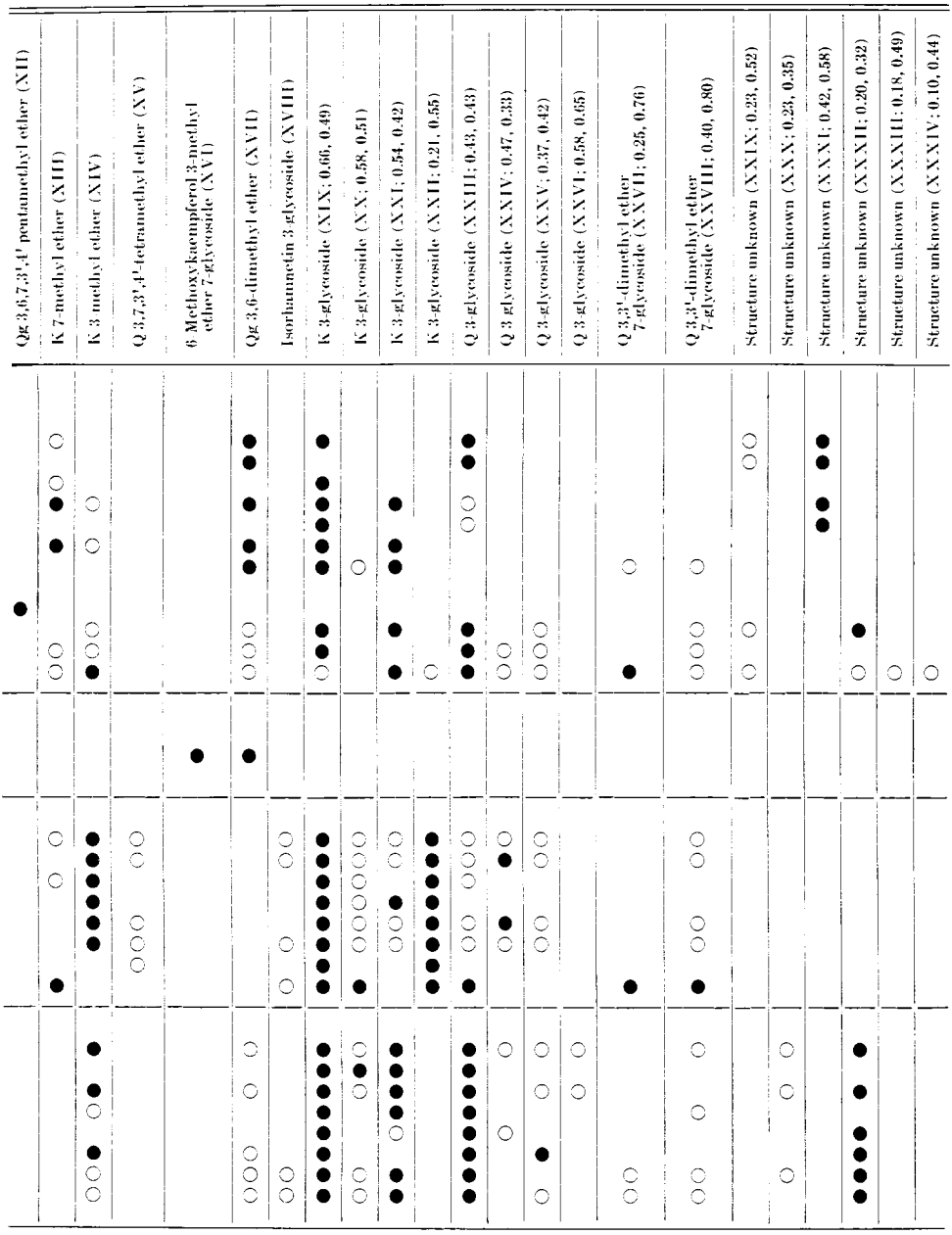
TABLE 1. Distribution of 34 flavonoids detected in North American *Parthenium*[1]

TAXA	Structure unknown (I; 0.48, 0.04)	6-Methoxykaempferol 3-methyl ether (II)	Qg 3,7-dimethyl ether (III)	Qg 3,6,7-trimethyl ether (IV)	Qg 3,6,3',4'-tetramethyl ether (V)	Qg 3,7,3'-trimethyl ether (VI)	6-Hydroxykaempferol 3,7-dimethyl ether (VII)	6-Hydroxykaempferol 3,6,7-trimethyl ether (VIII)	Q 3,3'-dimethyl ether (IX)	Qg 3,6,7,4'-tetramethyl ether (X)	Qg 3,6,7,3'-tetramethyl ether (XI)
SECT. *PARTHENICHAETA*											
P. tomentosum[2]			●								
var. *tomentosum*			●								
var. *stramonium*											
P. fruticosum[2]	○		●				○	○	○		
var. *fruticosum*			●								
var. *trilobatum*	○		●				○	○	○		
P. lozanianum			●				○		○		
P. schottii			●								
P. rollinsianum				●				●	●		●
P. incanum											
P. argentatum	○		●				●	●	●		
P. argentatum X *incanum*			●				●	●	●		
SECT. *BOLOPHYTUM*											
P. alpinum						○				●	●
P. tetraneuris						●				●	●
P. ligulatum					●					●	
SECT. *PARTHENIASTRUM*											
P. integrifolium[2]						○	○				
var. *integrifolium*						○	●				
var. *henryanum*						○	●				
var. *mabryanum*											
var. *auriculatum*											
var. *hispidum*						○					
f. *repens*											
P. radfordii							●				
SECT. *ARGYROCHAETA*											
P. confertum[2]	○	○	●			●	●				
var. *confertum*			●			●					
var. *divaricatum*	○	○	●				●				
var. *lyratum*			●			●	○				
var. *microcephalum*		○	●			○					
P. densipilum			●				●				
P. bipinnatifidum		○	●			○	○			●	
P. hysterophorus		○	●			○	○			○	

[1]Filled circles indicate compounds regularly detected in a taxon as a major component; hollow circles indicate compounds detected as minor components or often missing in a taxon. R_f values (TBA, 15% HOAc) are given for all unknown and incompletely identified compounds. In the names of the flavonoids, K, Q, and Qg are used for kaempferol, quercetin and quercetagetin, respectively.

[2]The use of filled and hollow circles to indicate patterns for those species in which varieties were studied represents a synthesis of the data for the varieties studied.

TABLE 1. Distribution of 34 flavonoids detected in North American *Parthenium*[1]



The forementioned species are all the species of Rollins' section *Parthenichaeta* DC. except *P. cineraceum* Rollins of Bolivia. Rodriguez (11) noted the occurrence of both aglycones and glycosides in *P. cineraceum*, but no structural types have been reported. Section *Parthenichaeta* is characterized by a wide variety of aglycone and glycoside derivatives of methylated and unmethylated derivatives of

TABLE 2. Spectrophotometric and chromatographic data for the flavonoids of North American *Parthenium*

	R_f x 100		MeOH max, nm	NaOMe max, nm	$AlCl_3$ max, nm	$AlCl_3$/HCl max, nm	NaOAc max, nm	NaOAc/H_3BO_3 max, nm
	TBA	15% HOAc						
6-Methoxykaempferol 3-methyl ether (II) (18)[1]	54	12	337 270	398 320 279	402sh 369 276	400sh 361 272	390 320 272	340 269
Quercetagetin 3,7-dimethyl ether (III)[2, 3] (10)	56	4	348 280 261sh	395 268	430 375sh 296sh 280	370 298 271	402 375 264	370 285sh 269
Quercetagetin 3,6,7-trimethyl ether (IV)[2,3] (10)	60	5	347 278	388 268	433 375sh 294sh 278	372 297sh 270	400 370 262	368 285sh 269
Quercetagetin 3,6,3',4'-tetramethyl ether (V)[2] (9)	61	10	344 276 255	375 305 267	384 293sh 271 245sh	376 291sh 264 242sh	338 281	341 280
Quercetagetin 3,7,3'-trimethyl ether (VI)[2] (10)	68	10	349 278 260sh	395 272	430sh 390 292sh 267	375 292sh 262	410 255	351 282
6-Hydroxykaempferol 3,7-dimethyl ether (VII)[2, 3] (10)	72	13	340 276	380 295sh 269sh	372 300	364 295	340 275	339 284
6-Hydroxykaempferol 3,6,7-trimethyl ether (VIII)[2, 3] (13)	80	30	340 279	380 322 282	369 308sh 283	364 306sh 289 267	309 279	400sh 338 282
Quercetin 3,3'-dimethyl ether (IX)[2] (21)	82	20	369 267sh 255	407 330 272	405 368 300 269	402 361 292 266	379 319 274	360 267 252
Quercetagetin 3,6,7,4'-tetramethyl ether (X)[2] (9, 13)	87	30	347 270sh 258	376 273	404sh 387 300sh 280sh 268	400sh 367 295sh 281 265	354 270sh 257	350 271sh 257
Quercetagetin 3,6,7,3'-tetramethyl ether (XI)[2] (9, 10)	75	40	346 269sh 254	402 284sh 272	380 296sh 277sh 266	373 296sh 275sh 263	412sh 350 268sh 253	348 268sh 254
Quercetagetin 3,6,7,3',4'-pentamethyl ether (XII)[2] (9, 13)	86	34	347 275 255	386sh 325sh 290	375 280sh 267	365 285 267	343 275	347 273 255
Kaempferol 7-methyl ether (XIII) (22)	68	10	365 320sh 265 251sh	410 dec 265 243	423 350 265	420 350 264	415 dec 370 320sh	368 320sh 260sh
Kaempferol 3-methyl ether (XIV)[2] (21)	55	20	345 261	395 325 273	395 350 302sh 371	395 345 300sh 273	385 300sh 290	346 302sh 263
Quercetin 3,7,3',4'-tetramethyl ether (XV)[2] (21)	80	15	355 330sh 255	365 307sh 284	400 300sh 274	398 300sh 275	357 271sh 257	356 306sh 258
6-Methoxykaempferol 3-methyl ether 7-glycoside (XVI)[2]	45	70	338 279 236sh	382 248sh	373 298 240	366 294 238	390 281	338 238
6-Methoxykaempferol 3-methyl ether (hydrolyzed XVI) (18)	NA		337 255sh	400 330sh 250sh	375 296sh 252sh	367 300sh 255sh	393sh 335 297sh	330sh 285sh
Quercetagetin 3,6-dimethyl ether 7-glycoside (XVII)[2] (9)	30	60	352 278 260	398 270	434 342sh 308sh 279	377 290 267 242sh	404 298sh 273	357 280sh 268
Quercetagetin 3,6-dimethyl ether (hydrolyzed XVII) (9)	NA		355 278sh 246sh	408 335sh 281sh	426 313sh 279sh	374 296	NA	NA

Isorhamnetin 3-glycoside (XVIII)[1] (13)	73	40	361	300sh	417	320	405	322sh	400	322sh	385	312	365	300sh
			287sh	258	274		275		275		274		267sh	260
Kaempferol 3-glycoside (XIX)[4,5] (13)	66	49	345	300	395	325	400	350	395	350	391	310	352	300
			265		275		305	275	303	275	275		268	
Quercetin 3-glycoside (XXIII)[1,5]	43	43	352	265	407	330	413	352	403	360	398	325	370	260
					277		399	268	300sh	270	266			
Quercetin 3,3[1]-dimethyl ether 7-glycoside (XXVII)[4]	25	76	350	266	406	272	397	352	398	350	418	355	352	265
							274		274		265			
Quercetin 3,3[1]-dimethyl ether 7-glycoside (XXVIII)[4]	40	80	349	262	405	265	395	349	396	346	418	350	347	262
							274		273		257			

[1]References are to earlier reports of flavonoids, for comparison.

[2]Demethylation gave the expected aglycone.

[3]Comparison of Rf's of homologous series of 6-hydroxylated flavonoids, with and without methylation at C_6, indicated that for the pairs III and IV and VII and VIII, where the spectral data does not discriminate methylation of the C_6 hydroxyl, the more highly methylated compounds should have the higher Rf's in 15% HOAc.

[4]Hydrolysis gave the expected aglycone.

[5]Three additional 3-glycosides each of kaempferol (XX, XXI, XXII) and quercetin (XXIV, XXV, XXVI) gave UV spectra essentially identical to those observed for XIX and XXIII, respectively. See Table 1 for their Rf's.

quercetagetin, quercetin, 6-hydroxykaempferol, kaempferol and kaempferol 3-methyl ether.

Parthenium alpinum (Nuttall) Torrey & Gray, *P. ligulatum* (Jones) Barneby and *P. tetraneuris* Barneby, three species of the temperate (western U.S.) section *Bolophytum* (Nuttall) Torrey & Gray, were characterized earlier (9) as producing methylated aglycones and glycosides of quercetagetin and 6-hydroxykaempferol. Compound XVII, detected in *P. tetraneuris* and *P. alpinum*, is a flavonol, 3,6-O-methylquercetagetin 7-O-glycoside; it was earlier reported erroneously to be a flavone, 6-methoxyluteolin 7-O-glycoside. A previously undetermined constituent of *P. alpinum* and *P. tetraneuris* has been identified tentatively, on the basis of chromatographic data, with 3,7,3′-tri-O-methylquercetagetin, which was reported by Rodriguez (11) from *P. bipinnatifidum* and *P. hysterophorus*.

The two species and five other subspecific taxa of section *Partheniastrum* DC. are very similar in flavonoid chemistry, with the more widespread varieties showing more minor constituents: aglycones of quercetagetin, 6-hydroxykaempferol, quercetin and kaempferol derivatives and glycosides of 6-hydroxykaempferol, quercetin and kaempferol derivatives. Some of the varieties and forms of *P. integrifolium L.* produce very few detectable flavonoids. Var. *integrifolium* produces five aglycones and nine glycosides; var. *henryanum* Mears, four aglycones and four glycosides; var. *mabryanum* Mears, one aglycone and four glycosides of kaempferol; var. *auriculatum* (Britton) Cornelius ex Cronquist, two aglycones and eight glycosides; var. *hispidum* (Rafinesque) Mears f. *hispidum*, three aglycones and nine glycosides; and var. *hispidum* f. *repens* (Eggert) Mears, one aglycone and two glycosides of kaempferol. Some varieties and forms of *P. integrifolium* do not produce detectable amounts of flavonoids oxygenated at C_6. *Parthenium radfordii* Mears produces two aglycones (6-hydroxy-3,7-di-O-methyl kaempferol and kaempferol 3-methyl ether) and six glycosides (glycosides of kaempferol, kaempferol 3-methyl ether and quercetin).

Section *Argyrochaeta* (Cavanilles) DC. of Rollins (12) contains four North American species, *P. confertum* (Gray) Gray, *P. densipilum* Wooton, *P. hysterophorus* L., and *P. bipinnatifidum* (Ortega) Rollins, as well as *P. glomeratum* Rollins, which is endemic to northwestern Argentina and Bolivia. *Parthenium confertum* consists of several varieties: var. *confertum*, characterized by two flavonoid aglycones and four glycosides, derivatives of quercetagetin and kaempferol; var. *divaricatum* Rollins, by five aglycones (derivatives of quercetagetin, 6-hydroxykaempferol and quercetin) and no glycosides (derivatives of 6-hydroxykaempferol, quercetin and kaempferol); var. *lyratum* (Gray) Rollins, by four aglycones (derivatives of quercetagetin, 6-hydroxykaempferol and kaempferol 3-methyl ether) and four glycosides (derivatives of kaempferol and quercetin); var. *microcephalum* Rollins, by three aglycones (derivatives of quercetagetin and 6-hydroxykaempferol) and five glycosides (derivatives of quercetin and kaempferol). *Parthenium densipilum*, a very rare limestone endemic very closely related to *P. confertum*, is characterized by three aglycones (derivatives of quercetagetin, 6-hydroxykaempferol and kaempferol 3-methyl ether) and five glycosides of quercetin and kaempferol. *Parthenium bipinnatifidum* is characterized by seven aglycones (derivatives of quercetagetin, 6-hydroxykaempferol and kaempferol 3-methyl ether) and ten glycosides of quercetagetin, quercetin, and kaempferol derivatives. Its very close relative *P. glomeratum* Rollins, which was not examined in this study, was reported by Shen *et al.* (10) to produce a subset of the flavonoids of *P. bipinnatifidum*. *Parthenium hysterophorus*, which is very closely related to both *P. bipinnatifidum* and

P. glomeratum, differs from *P. bipinnatifidum* in a few details; *P. hysterophorus* is characterized by six aglycones (derivatives of quercetagetin, 6-hydroxykaempferol, kaempferol and kaempferol 3-methyl ether) and ten glycosides of quercetagetin, quercetin and kaempferol derivatives. Section *Argyrochaeta* DC. of Rollins, is therefore characterized by the presence of many aglycones of all four major structural types as well as by the presence of glycosides of quercetagetin, quercetin and kaempferol derivatives.

All of the sections of *Parthenium* recognized by Rollins (12) contain some species which produce many aglycones and many glycosides except section *Bolophytum*, which produces primarily aglycones, with a few glycosides in *P. tetraneuris*. Similarly, all the sections tend to produce both the usual flavonoids, kaempferol and quercetin derivatives, as well as the C_6-oxygenated types, except section *Bolophytum*, which does not produce flavonoids that are not oxygenated C_6. Some varieties and forms of *P. integrifolium* (section *Partheniastrum*) do not produce detectable amounts of 6-oxygenated flavonoids.

Although the flavonoid pattern of every taxon is distinct in some detail, there is little evidence of major differences in sectional trends in flavonoid structures. The tendency for forming methylethers and for 6-oxygenation in section *Bolophytum* is the most distinctive feature of the flavonoid chemistry of *Parthenium*.

PROCEDURES

Air-dried leaf material (100 g) of 1 to 20 population samples of each of the *Parthenium* taxa included in table 1 was ground in 85% aqueous methanol. After extraction (24 hr), the filtered solution was dried *in vacuo* and separated into a chloroform-soluble fraction and a methanol-water-soluble fraction. The fractions were separated into components by two-dimensional paper chromatography on Whatman 3 mm paper, developed first in TBA and second in 15% acetic acid. The color of the chromatographic components was recorded when viewed above a broad wave-length uv lamp with and without ammonia vapor present. Individual spots were eluted with methanol and were rechromatographed, cochromatographed or analyzed by standard uv spectral procedures (13, 14, 15). Glycosides were hydrolyzed with 6% aqueous HCl. The aglycones were analyzed spectrally as before or were demethylated with the pyridine-HBr method of Rösler (see 16) for co-chromatographic comparison with authentic samples or with demethylated types of known aglycones. Kilogram quantities of dried material of *P. bipinnatifidum*, *P. hysterophorus*, *P. incanum*, *P. integrifolium*, and *P. fruticosum* var. *trilobatum* were extracted for polyclar column chromatography with various combinations of chloroform, butanone, methanol, and water for elution. Identification of flavonoids and coumarins was by comparison of chromatographic and spectral data of both glycosides and aglycones with those reported for known structures. The chromatographic and uv spectral data for the 34 flavonoids are given in table 2.

ACKNOWLEDGMENTS

Some of this study of the flavonoids of *Parthenium* was accomplished during my graduate studies in the Phytochemistry Laboratories of the Botany Department of the University of Texas at Austin (directed by T. J. Mabry), but the greater part of this study was accomplished at the Phytochemical Laboratory of the Botany Department of The Academy of Natural Sciences of Philadelphia. These studies relate to several traineeships and grants: NIH traineeship 5 TO1 M-00789 (to T. J. Mabry) and NSF grants GB-26276 and GB-37666.

I thank Margaret Buckby, Helgard Niremberg, Elaine Bishop, Carole Ram, Roy Hill, and, particularly, Helen R. Mears, for laboratory assistance over a period of years. Helen R. Mears produced the figure for this paper.

Received 7 November 1979.

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