

¹³C-NMR Data from Coumarins from Moraceae Family

Raphael F. Luz^{1,2*}, Ivo J. C. Vieira¹, Raimundo Braz-Filho¹, Vinicius F. Moreira¹

¹Sector of Natural Products Chemistry, Universidade Estadual do Norte Fluminense Darcy Ribeiro, Campos dos Goytacazes, Brazil

²Sector of Chemistry, Instituto Federal Fluminense, Campos dos Goytacazes, Brazil

Email: *phaelluz@gmail.com

Received 7 September 2015; accepted 16 October 2015; published 19 October 2015

Copyright © 2015 by authors and Scientific Research Publishing Inc.

This work is licensed under the Creative Commons Attribution International License (CC BY).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Species from Moraceae family stand out in popular medicine and phytotherapy, have been for example used as expectorants, bronchodilators, anthelmintics and treatment of skin diseases, such as vitiligo, due to the presence of compounds with proven biological activity, as the coumarins. Coumarins are lactones with 1,2-benzopyrone basic structure, and are widely distributed in the plant kingdom, both in free form, and in glycosylated form. This work reports a literature review, describing the data of ¹³C NMR from 53 coumarins isolated from the family Moraceae, and data comparison between genera who presented photochemical studies, in order to contribute to the chemotaxonomy of this family.

Keywords

Moraceae, Coumarin, Furocoumarin, Pyranocoumarin, NMR Spectral Data

1. Introduction

The Moraceae family has 6 tribes, 63 genera and about 1500 species found in the tropics, subtropics and, in a smaller proportion, in temperate regions. Among the main genera are the *Ficus*, with about 600 species and *Dorstenia*, with about 125 species [1].

Moraceae representatives can be found as shrub, tree, herb or subshrub, feature woody stem, alternate leaves, unisexual flowers and fruits in small nuts form [2]. Some of its species have great importance in fruit growing, in the production of heavy wood, in the textile industry, in the production of latex and also for ornamental purposes [3] [4].

Species from Moraceae family also stand out in popular medicine and phytotherapy, have been for example,

*Corresponding author.

used as expectorants, bronchodilators, in the treatment of Chagas disease, anthelmintics and treatment of skin diseases such as vitiligo, for example [5]. Those therapeutic effects are due to the presence of compounds with proven biological activity, such as flavonoids and coumarins [6] [7]. The *Brosimum* genus, for example, features species high in coumarin, as is the case of *Brosimum rubescens*, whose wood owns xanthyletin, a coumarin with antiplatelet, antifungal and herbicide activities [8]. The isolation and the study of coumarins biological effects like this one, has been of great importance for the understanding of the results obtained in folk medicine use of these plants, as well as the development of treatment in some diseases [9].

Coumarins

Coumarins are lactones with 1,2-benzopyrone basic structure, and are widely distributed in the plant kingdom, both in free form, and in glycosylated form [10]. Biosynthesized via the shikimic acid, with cinnamic acid as an intermediate, simple coumarins, by the addition of a furan ring in the process can become the furocoumarins, which could be linear, such as psoralen, or angular, such as angelicin. However, if a pyran ring is added instead of a furan ring in the process, it generates a pyranocoumarin, such as for example the xanthyletin (**Figure 1**). Structures containing two or three simple coumarins linked to each other are named *bis*-coumarins and *tris*-coumarins, respectively. The name coumarin, originated from coumarou, a Caribbean name of the tree Tonka (*Dipteryx odorata*), from which was isolated the compound in 1820 [11].

The coumarins hold several biological activities such as anticoagulant, antimicrobial, vasodilatory, sedative, analgesic and photosensitizer, been the last one more frequent in linear furocoumarins, also known as psoralens. The photosensitizing activity intensity varies according to the furocoumarin structure, having the psoralen as more active than the hydroxylated molecules or with less unsaturation [11]. This effect arises by the interaction of these compounds with ultraviolet radiation and can be an issue for humans, causing severe burns. However, its proper medical use can be useful for the treatment of diseases such as vitiligo, which causes a gradual skin depigmentation. Psoralens, due to their extended chromophore group, absorb in the UV region and allow this radiation to stimulate the melanin formation. The oral administration of a xanthotoxin dose, for example, following by the patient's exposure to ultraviolet radiation, causes pigmentation of the skin. This type of treatment is called PUVA (psoralen + UV-A), and is also efficient in the psoriasis treatment, a disease characterized by reddened lesions and increase in cell proliferation. In this case, the reaction inhibits DNA replication and consequently reduces the cell division rate (**Figure 2**) [9] [10].

Due to their flat nature, psoralens intercalate into DNA, and this allows a cycloaddition reaction initiated by UV between the pyrimidine bases, mainly thymine and the furan ring in the psoralens. The second cycloaddition can then occur, involving now the psoralens pyran ring, promoting interchain cross-links in nucleic acid [10].

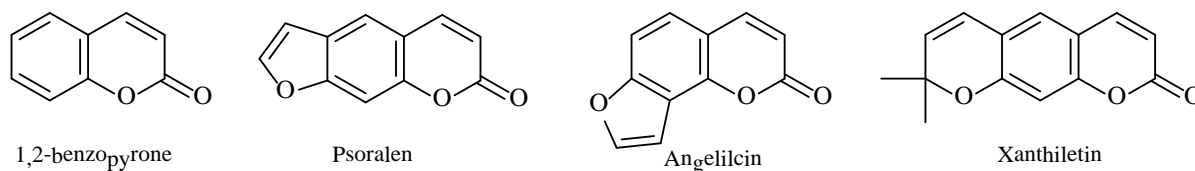


Figure 1. Types of coumarins.

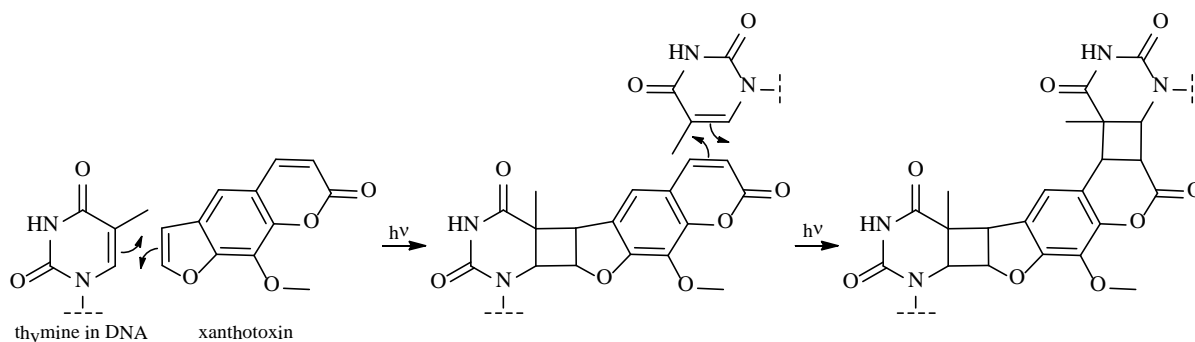


Figure 2. Xanthotoxin intercalation in DNA.

In Moraceae family, coumarins feature more than 135 occurrences in its main genera, been more frequent the presence of linear furocoumarins [12]. From the species *Brosimum gaudichaudii*, for example, were isolated so far 10 coumarins, been 8 linear furocoumarins and two pyranocoumarins, in addition to other compounds [13] [14].

This paper reports a literature review, describing the data of ^{13}C NMR from 53 coumarins isolated from the Moraceae family. From this group, several appear repeatedly in different species, such as psoralen (27), for example. **Table 1** lists the coumarins obtained in each gender without mentioning the duplicate cases. The structures are shown in **Figures 3-6**.

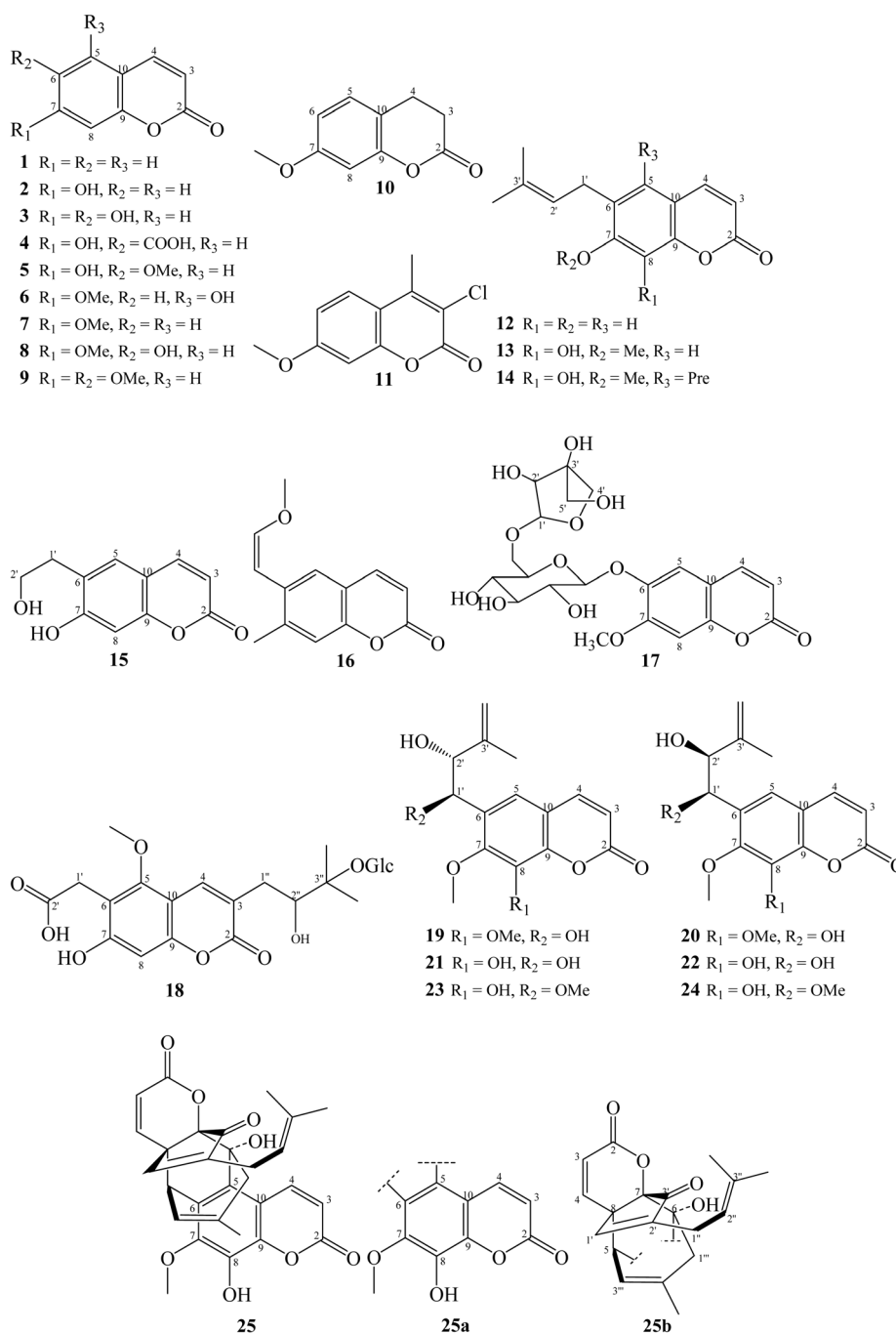


Figure 3. Simple coumarins isolated from Moraceae family.

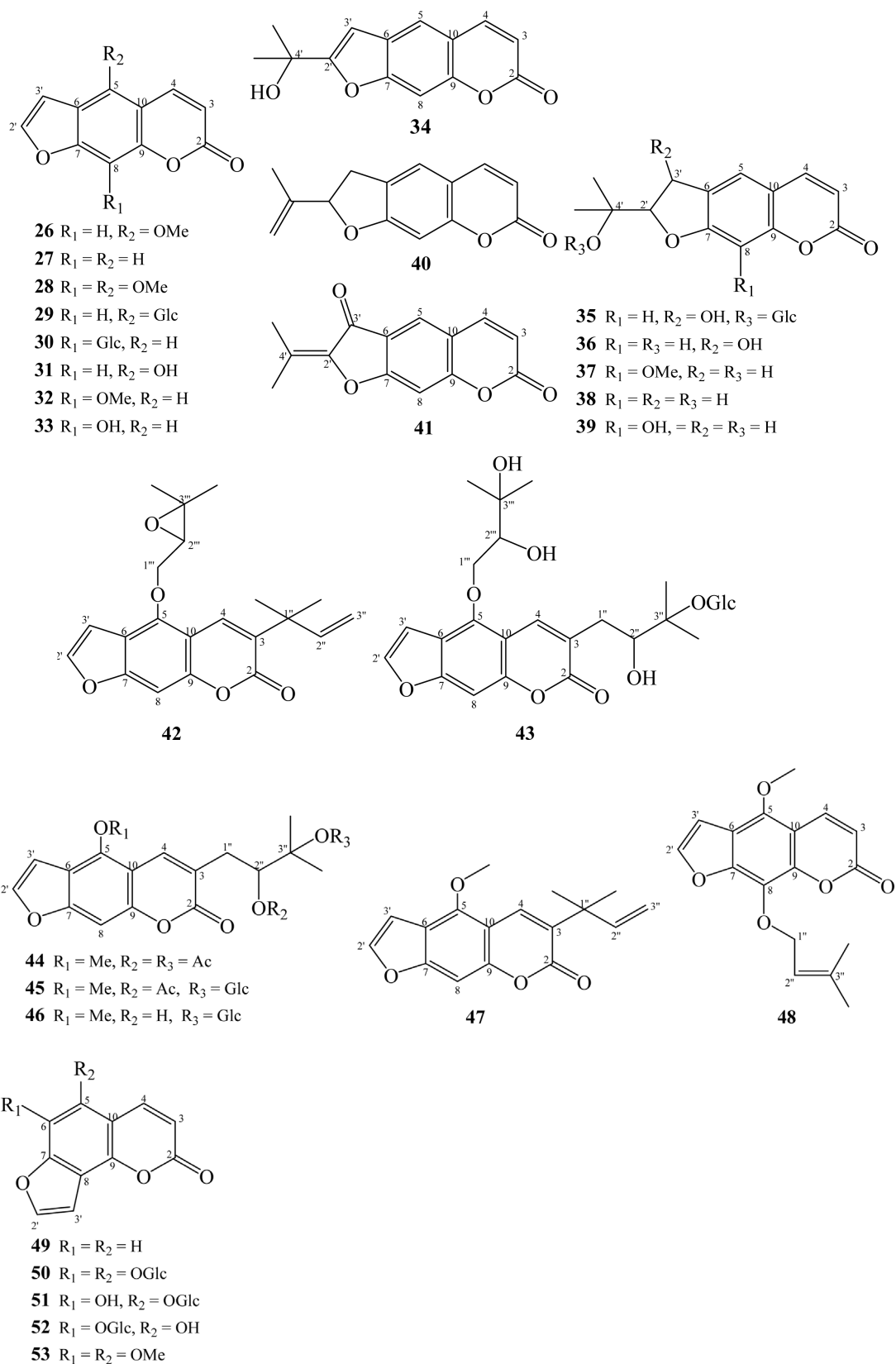


Figure 4. Furocoumarins isolated from Moraceae family.

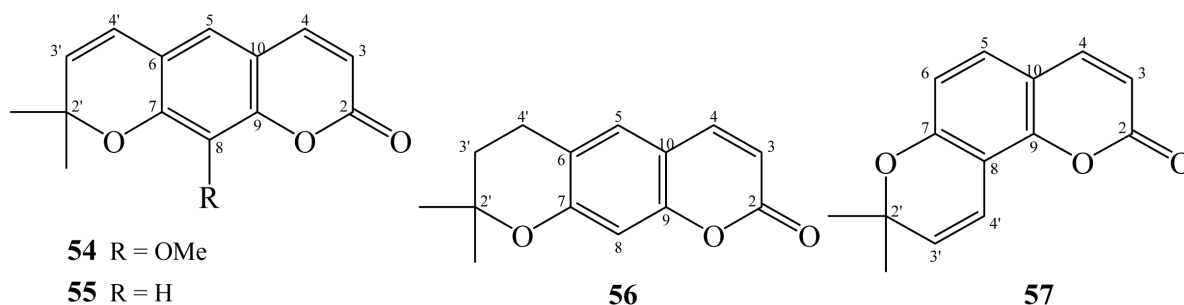


Figure 5. Pyranocoumarins isolated from Moraceae family.

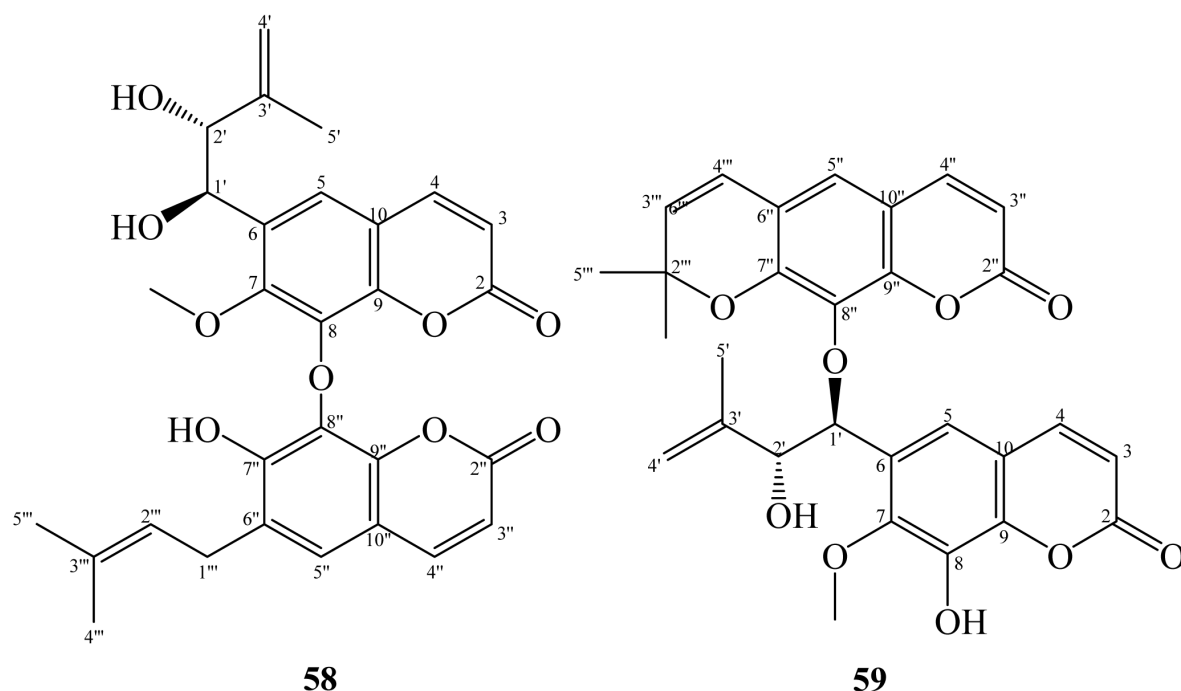


Figure 6. Bis-coumarins isolated from Moraceae family.

2. Results and Discussion

The simple coumarin isolated from Moraceae family (**Figure 3**), have their ^{13}C NMR chemical shift data listed in **Table 2**. The C-2 of most structures presents indicative signs of carbon α -carbonyl, β -unsaturated, δ_{C} 158.9 to 162.9, characteristic of lactone ring without substituent in the C-3 and C-4 carbon atom. The exceptions are the compound **18**, which has the C-3 replaced, presenting C-2 with δ_{C} 164.5, and the compound **10**, where C-3 and C-4 are methylene carbons. This way, because there are fewer resonance structures in the molecule, C-2 becomes more unprotected, presenting δ_{C} 177.0. The signs of C-5 (δ_{C} 127.8), C-6 (δ_{C} 124.3), C-7 (δ_{C} 131.3) and C-8 (δ_{C} 116.8) from coumarins (**1**), are characteristic for the benzene ring from the benzopyran nucleus. As these carbons are replaced in other molecules shown in **Figure 3**, the signals diversify, for example, the C-5 from substance **18**, with δ_{C} 157.5 due to the unprotection caused the presence of the methoxyl group attached to this carbon.

Table 3 lists the ^{13}C NMR data from the Moraceae family isolated furocoumarins. This kind of coumarin is the one that appears most often in the studied species, highlighting the linear furocoumarins such as psoralen (**27**). In this case, the signals to C-2' (δ_{C} 147.0) and C-3' (δ_{C} 106.6) evidence the presence of methine carbons typical from furan ring. The sign for the C-2', higher than the C-3', explained by the fact that this carbon is directly linked to the oxygen atom and so, more unprotected. In the molecules **35** to **39** C-2' is further substituted

Table 1. Coumarins isolated from Moraceae family.

Compound	Genus	References	¹³ C NMR Data
Simple Coumarins			
Coumarin (1)	<i>Dorstenia</i>	[15]	[17]
	<i>Ficus</i>	[16]	
	<i>Brosimum</i>	[18]	
Umbelliferone (2)	<i>Dorstenia</i>	[19]	[22]
	<i>Fatoua</i>	[20]	
	<i>Ficus</i>	[21]	
esculetin (3)	<i>Ficus</i>	[21]	[23]
6-carboxy-umbelliferone (4)	<i>Ficus</i>	[21]	[24]
S copoletin (5)	<i>Fatoua</i>	[20]	[25]
	<i>Ficus</i>	[21]	
5-hydroxy-7-methoxycoumarin (6)	<i>Morus</i>	[26]	[27]
7-methoxycoumarin (7)	<i>Dorstenia</i>	[19]	[29]
	<i>Ficus</i>	[28]	
6-hydroxy-7-methoxycoumarin (8)	<i>Streblus</i>	[30]	[31]
6,7-dimethoxycoumarin (9)	<i>Streblus</i>	[30]	[32]
7-methoxy-dihydrocoumarin (10)	<i>Ficus</i>	[28]	[28]
3-chloro-7-methoxy-4-methyl-chromen-2-one (11)	<i>Ficus</i>	[33]	*
Demethylsuberosin (12)	<i>Brosimum</i>	[8]	[34]
Brosiparin (13)	<i>Brosimum</i>	[8]	*
Brosiprenin (14)	<i>Brosimum</i>	[8]	*
Phellodenol-A (15)	<i>Fatoua</i>	[20]	[20]
6-(2-methoxy-Z-vinyl)-7-methyl-piranocoumarin (16)	<i>Ficus</i>	[35]	*
Isoscopoletin 6-(6-O-β-apiofuranosyl-β-glucopyranoside) (17)	<i>Morus</i>	[36]	[36]
7-hydroxy-5-methoxy-6-carboxy-methyl-3-[3-(β-D-glucopyranosyloxy)-2-hydroxy-3-methyl-butyl]-coumarin (18)	<i>Dorstenia</i>	[37]	[37]
Fatouain-A (19)	<i>Fatoua</i>	[38]	[38]
Fatouain-B (20)	<i>Fatoua</i>	[38]	[38]
Fatouain-C (21)	<i>Fatoua</i>	[38]	[38]
Fatouain-D (22)	<i>Fatoua</i>	[38]	[38]
Fatouain-E (23)	<i>Fatoua</i>	[38]	[38]
Fatouain-F (24)	<i>Fatoua</i>	[38]	[38]
Fatouapilosin (25)	<i>Fatoua</i>	[20]	[20]

Continued

Furocoumarins			
	<i>Brosimum</i>	[18]	
Bergapten (26)	<i>Dorstenia</i>	[34]	[4]
	<i>Fatoua</i>	[20]	
	<i>Ficus</i>	[39]	
	<i>Brosimum</i>	[18]	
Psoralen (27)	<i>Dorstenia</i>	[34]	[4]
	<i>Fatoua</i>	[20]	
	<i>Ficus</i>	[39]	
Isopimpinellin (28)	<i>Dorstenia</i>	[37]	[40]
5-O- β -D-glucopyranosyl-8-hydroxypsoralen (29)	<i>Ficus</i>	[41]	*
8-O- β -D-glucopyranosyl-5-hydroxypsoralen (30)	<i>Ficus</i>	[41]	[41]
Bergaptol (31)	<i>Ficus</i>	[42]	[24]
Xanthotoxin (32)	<i>Ficus</i>	[43]	[43]
Xanthotoxol (33)	<i>Ficus</i>	[42]	[44]
2',3'-dehydromarmesin (34)	<i>Brosimum</i>	[13]	[4]
	<i>Fatoua</i>	[20]	
1'-hydroxy-3'-O- β -glucopyranosylmarmesin (35)	<i>Brosimum</i>	[13]	[4]
	<i>Ficus</i>	[21]	
2-S,3-R-1'-hydroxymarmesin (36)	<i>Brosimum</i>	[18]	[4]
8-methoxymarmesin (37)	<i>Brosimum</i>	[13]	[4]
	<i>Fatoua</i>	[20]	
Marmesin (38)	<i>Brosimum</i>	[13]	[4]
	<i>Fatoua</i>	[20]	
Rutaretin (39)	<i>Fatoua</i>	[20]	[45]
	<i>Ficus</i>	[43]	
Isoangenomalin (40)	<i>Ficus</i>	[21]	*
Gaudichaudine (41)	<i>Brosimum</i>	[46]	[46]
5-(2-3-epoxy-3-methyl-butoxy)-chalepensin (42)	<i>Dorstenia</i>	[37]	[37]
5-(3-methyl-2,3-dihydroxybutyloxy)-3-[3-(β -D-glucopyranosyloxy)-2-hydroxy-3-methyl-butyl-psoralen (43)	<i>Dorstenia</i>	[37]	[37]
5-methoxy-3-(3-methyl-2,3-dihydroxybutyl)-psoralen-diacetate (44)	<i>Dorstenia</i>	[37]	[37]
5-methoxy-3-[3-(β -D-glucopyranosyloxy)-2-acetyloxy-3-methyl-butyl]-psoralen (45)	<i>Dorstenia</i>	[37]	[37]
Turbinatocoumarin (46)	<i>Dorstenia</i>	[37]	[37]
5-methoxychalepensin (47)	<i>Dorstenia</i>	[37]	[37]
Phellopterin (48)	<i>Dorstenia</i>	[37]	[47]
Angelicin (49)	<i>Ficus</i>	[43]	[48]

Continued

5,6-O- β -D-diglucoopyranosylangelicin (50)	<i>Ficus</i>	[41]	[41]
5,-O- β -D-glucoopyranosyl-6-hydroxyangelicin (51)	<i>Ficus</i>	[41]	[41]
6-O- β -D-glucoopyranosyl-5-hydroxyangelicin (52)	<i>Ficus</i>	[41]	[41]
Pimpinellin (53)	<i>Ficus</i>	[43]	[49]
Pyranocoumarins			
Luvangetin (54)	<i>Brosimum</i>	[8]	[50]
	<i>Brosimum</i>	[8]	
Xanthyletin (55)	<i>Fatoua</i>	[10]	[8]
	<i>Ficus</i>	[21]	
Dihydroxanthyletin (56)	<i>Ficus</i>	[21]	[51]
Seselin (57)	<i>Ficus</i>	[43]	[50]
Bis-coumarins			
Fatouain-G (58)	<i>Fatoua</i>	[38]	[38]
Fatouain-H (59)	<i>Fatoua</i>	[38]	[38]

*Data not found.

with signs between δ_c 90.3 to 91.4, while in the compound **34**, the signal is δ_c 165.4, due to C-2' be a quaternary carbon. In the case of angular furocoumarins C-8 shows signs suggesting his involvement with the furan ring, in the C-6's place. In angelicin (**49**), for example, C-6 and C-8 are δ_c 108.0 and δ_c 117.0 signals respectively, while in the psoralen the displacements are δ_c 125.0 for C-6 and 93.8 to δ_c C-8.

Table 4 lists the 13 C NMR data from pyranocoumarins found until now in the Moraceae family. The luvangetin (**54**) and Xanthyletin (**55**), linear pyranocoumarins, show signals which indicate existence of a six-membered ring linked to the benzopyran nucleus benzene's section. In luvangetin, the methine carbon C-3' and C-4' feature chemical shift δ_c 131.3 and δ_c 121.1, respectively, while these signals on xanthyletin are δ_c 104.4 for C-3' and δ_c 113.0 for C-4'. This difference is due to the presence of methoxyl on luvangetin C-8, which makes these carbons more vulnerable. In dihydroxanthyletin (**56**), the carbons C-2' and C-3' feature signs δ_c 32.4 and δ_c 21.9, respectively, indicating that they are methylene and not methine as in other molecules. In the case of the only isolated angular pyranocoumarin, the seselin (**57**), the found signal for C-8 (δ_c 144.1) indicates that it is linked to the C-4' and not at the C-6, which signal is δ_c 113.8.

The only *bis*-coumarin found in Moraceae family so far are fatouain-G (**58**) and the fatouain-H (**59**), both isolated from *Fatoua* genus. The link between the simple coumarin which form the fatouain-G occurs between the carbons C-8 and C-8', through an oxygen atom. In the case of fatouain-H, the molecules links occurs between the C-8' carbon of a molecule and the C-1' carbon belonging to the side chain of other, also through an oxygen atom. Twenty-nine carbon atoms signals are identified in each compound, which are described in **Table 5**.

3. Conclusions

Until the present moment, coumarins were only found in 6 from the 63 genera from Moraceae family, mainly in *Ficus*, *Brosimum* and *Fatoua*. The simple coumarin representing 42.4% of the total, furocoumarines, found mainly in the genus *Ficus*, representing 47.4%, while the other 10.2% are consisted of pyranocoumarins, and *bis*-coumarin, been the latter found only in the genres *Fatoua* (**Figure 7(a)**).

From the genus *Ficus*, were isolated 27 from the 59 coumarins found so far, been 15 furocoumarins. In addition, 20 of these substances are exclusive to this genus. The genus *Brosimum* features 14 coumarins, been 9 furocoumarins while the genus *Dorstenia* features 10 furocoumarins and a total of 13 coumarins. The smallest number of occurrences is in the *Morus* and *Streblus* genera, having been isolated only 2 simple coumarins in each. The *Fatoua* genus features 17 coumarins from all kinds found in Moraceae, mainly simple coumarin. This

Table 2. ^{13}C NMR data from simple coumarins isolated from Moraceae family.

	1	2	3	4	5	6	7	8	9	10	12	15
C												
2	159.6	160.3	162.9	162.9	164.1	161.7	162.8	161.4	161.0	177.0	162.9	161.2
5	-	-	-	-	-	146.1	-	-	-	-	-	-
6	-	-	143.2	110.2	146.0	-	-	149.7	144.8	-	126.4	125.9
7	-	161.6	150.8	151.3	151.1	150.9	161.2	144.0	153.0	159.2	158.9	160.5
9	153.3	155.7	149.1	157.7	112.1	151.9	155.9	150.2	149.9	155.6	154.0	155.5
10	118.6	110.4	111.3	112.9	151.9	111.9	112.5	111.5	111.6	119.8	112.0	112.5
1'	-	-	-	178.7	-	-	-	-	-	-	-	-
3'	-	-	-	-	-	-	-	-	-	-	134.3	-
CH												
3	116.0	111.4	111.0	113.3	113.3	112.9	113.1	113.4	113.1	-	112.0	112.8
4	143.9	144.2	144.7	145.3	144.7	144.8	143.4	143.3	146.3	-	144.7	144.7
5	128.2	129.5	111.5	127.4	110.0	-	128.8	107.6	109.3	130.5	128.1	131.0
6	124.2	113.3	-	-	-	110.1	112.6	-	-	105.0	-	-
7	131.7	-	-	-	-	-	-	-	-	-	-	-
8	116.0	102.5	102.2	104.8	103.7	103.5	100.9	103.2	100.5	101.9	102.8	103.4
2'	-	-	-	-	-	-	-	-	-	-	121.2	-
CH₂												
3	-	-	-	-	-	-	-	-	-	34.5	-	-
4	-	-	-	-	-	-	-	-	-	24.9	-	-
1'	-	-	-	-	-	-	-	-	-	-	28.0	34.5
2'	-	-	-	-	-	-	-	-	-	-	-	62.7
CH₃												
Me	-	-	-	-	-	-	-	-	-	-	17.8	-
Me	-	-	-	-	-	-	-	-	-	-	25.8	-
O-Me	-	-	-	-	56.7	56.6	55.8	56.4	56.3	55.2	-	-
O-Me	-	-	-	-	-	-	-	-	56.6	-	-	-
	17	18	19	20	21	22	23	24	25a	25b		
C												
2	162.2	164.5	160.2	160.2	161.0	161.1	159.8	159.9	158.9	161.5		
3	-	122.9	-	-	-	-	-	-	-	-		
5	-	157.5	-	-	-	-	-	-	120.5	-		
6	150.6	114.6	130.5	130.1	134.1	134.2	128.7	128.6	129.6	81.4		
7	146.9	161.0	152.9	153.4	149.7	150.4	148.6	148.8	145.3	86.2		

Continued

8			139.5	139.5	138.1	138.4	135.7	135.7	136.4	42.7
9	149.1	155.6	147.9	147.8	144.4	144.4	143.0	142.4	143.4	-
10	113.1	108.0	115.1	115.3	116.4	116.5	114.5	114.6	114.0	-
2'	-	175.6	-	-	-	-	-	-	-	135.3
2'''	-	-	-	-	-	-	-	-	-	140.2
3'	-	-	143.9	144.3	146.8	147.3	143.0	144.1	-	196.3
3''	-	81.4	-	-	-	-	-	-	-	135.6
CH										
3	113.1	-	114.7	114.8	115.6	115.5	114.4	114.4	113.5	122.4
4	144.4	138.5	143.8	143.8	146.0	146.0	144.1	144.3	144.3	148.7
5	109.5	-	120.9	121.0	118.1	118.7	117.0	117.4	-	39.2
8	104.2	98.9	-	-	-	-	-	-	-	-
1'	109.7	-	69.8	70.0	70.7	70.9	79.0	78.8	-	136.7
2'	76.8	-	77.8	78.8	79.9	80.0	79.2	77.7	-	-
2''	-	76.3	-	-	-	-	-	-	-	118.4
3'''	-	-	-	-	-	-	-	-	-	120.9
CH₂										
1'	-	29.9	-	-	-	-	-	-	-	-
1''	-	34.0	-	-	-	-	-	-	-	27.3
1'''										38.2
4'	73.6	-	112.9	114.4	113.1	113.8	113.9	113.5	-	-
5'	61.0	-	-	-	-	-	-	-	-	-
CH₃										
Me	-	22.8	18.9	18.5	19.6	19.5	18.3	18.8	-	17.6
Me	-	23.5	-	-	-	-	-	-	-	21.8
Me	-	-	-	-	-	-	-	-	-	25.5
O-Me		63.7	61.2	61.4	61.7	61.9	60.8	61.0	61.0	-
O-Me	55.7	-	61.5	61.5	-	-	57.3	57.4	-	-
Glc-1	100.7	98.6	-	-	-	-	-	-	-	-
Glc-2	73.3	75.3	-	-	-	-	-	-	-	-
Glc-3	76.6	78.1	-	-	-	-	-	-	-	-
Glc-4	70.4	71.6	-	-	-	-	-	-	-	-
Glc-5	75.8	77.8	-	-	-	-	-	-	-	-
Glc-6	67.5	62.7	-	-	-	-	-	-	-	-

Table 3. (a) ^{13}C NMR data from furocoumarins isolated from Moraceae family. (b) ^{13}C NMR data from furocoumarins isolated from Moraceae family.

(a)													
	26	27	28	30 ^a	31	32	33	34	35 ^b	36	37	38	39
C													
2	161.2	161.2	160.3	160.0	161.1	160.4	160.0	161.1	160.6	161.2	160.8	161.6	160.2
3	-	-	-	-	-	-	-	-	-	-	-	-	-
5	149.6	-	146.5	142.7	149.6	-	-	-	-	-	-	-	-
6	112.7	125.0	126.0	113.6	114.3	126.1	125.2	125.8	123.6	128.2	125.9	125.1	125.2
7	158.4	156.6	147.4	148.4	158.2	147.6	145.3	156.3	162.0	162.6	153.8	163.2	151.3
8	-	-	132.5	121.9	-	133.7	130.1	-	-	-	131.0	-	128.0
9	152.7	152.2	139.6	143.1	152.8	142.9	139.8	151.9	156.9	156.6	147.1	155.1	143.6
10	106.4	115.6	116.3	104.2	107.5	116.4	116.2	115.3	113.5	113.4	113.5	112.2	112.7
2'	-	-	-	-	-	-	-	165.4	-	-	-	-	-
4'	-	-	-	-	-	-	-	69.3	78.6	71.8	71.4	71.1	69.9
CH													
3	112.6	114.7	114.4	110.9	112.6	114.7	113.7	114.5	113.0	113.0	112.0	111.3	110.8
4	139.2	144.2	144.3	140.1	139.3	144.3	145.3	144.1	143.5	144.2	143.8	143.9	144.9
5	-	120.0	-	-	-	112.9	110.1	119.5	126.4	125.2	117.1	123.1	113.9
8	93.8	99.9	-	-	94.2	-	-	100.0	98.8	99.3	-	97.3	-
2'	144.8	147.0	145.0	145.3	144.8	146.6	147.2	-	90.3	91.1	91.4	90.9	90.5
3'	105.0	106.6	106.6	104.9	105.1	106.7	106.9	99.7	71.2	72.2	-	-	-
CH₂													
3'	-	29.0	-	-	-	-	-	-	-	-	29.7	29.0	29.4
CH₃													
Me	-	-	-	-	-	-	-	28.7	23.2	25.9	-	24.4	-
Me	-	-	-	-	-	-	-	28.7	22.8	28.6	-	25.1	-
Me	-	-	-	-	-	-	-	-	-	-	-	-	25.9
Me	-	-	-	-	-	-	-	-	-	-	-	-	24.5
O-Me	59.9	-	60.6	-	-	61.3	-	-	-	-	60.7	-	-
O-Me	-	-	61.1	-	-	-	-	-	-	-	-	-	-

^asinaisGlc: 102.3 (Glc-1); 73.9 (Glc-2); 76.6 (Glc-3); 69.7 (Glc-4); 77.4 (Glc-5); 60.7 (Glc-6); ^bsinaisGlc: 95.1 (Glc-1); 71.3 (Glc-2); 72.6 (Glc-3); 68.4 (Glc-4); 71.5 (Glc-5); 62.1 (Glc-6).

(b)													
	41	42	43	44 ^a	45 ^b	46	47	48	49	50 ^c	51	52	53
C													
2	159.9	159.7	164.3	161.9	163.9	164.3	160.0	160.5	160.7	159.7	163.1	163.2	160.7
3	-	131.8	124.0	121.3	123.2	123.9	131.0	-	-	-	-	-	-
5	-	147.8	150.1	149.0	150.6	150.6	149.1	144.3	-	140.7	138.3	146.8	144.5
6	114.8	114.3	115.4	112.8	114.3	114.3	112.3	114.5	-	131.3	135.2	128.5	114.1
7	165.9	157.2	159.1	157.8	159.4	159.9	157.6	150.7	157.3	148.8	148.2	151.6	149.1

Continued

8	-	-	-	-	-	-	-	126.8	117.0	114.2	116.2	110.7	135.1
9	158.9	151.6	153.1	152.0	153.2	153.2	151.8	144.3	148.9	142.6	141.6	145.7	143.2
10	105.1	107.9	109.1	106.7	107.9	108.2	106.5	107.5	114.0	110.9	111.4	107.7	109.4
1"	-	-	-	-	-	-	40.5	-	-	-	-	-	-
2'	145.9	-	-	-	-	-	-	-	-	-	-	-	-
3'	182.2	-	-	-	-	-	-	-	-	-	-	-	-
3"	-	-	81.1	82.3	79.5	81.2	-	139.5	-	-	-	-	-
3'''	-	58.4	72.6	-	-	-	-	-	-	-	-	-	-
4'	133.7	-	-	-	-	-	-	-	-	-	-	-	-
CH													
3	114.8	-	-	-	-	-	-	112.7	141.2	113.3	114.2	112.4	113.7
4	143.6	132.8	138.8	136.0	138.1	138.4	133.2	139.3	144.6	141.6	143.1	142.4	139.8
5	124.8	-	-	-	-	-	-	-	123.8	-	-	-	-
6	-	-	-	-	-	-	-	-	108.0	-	-	-	-
8	100.5	94.2	94.3	93.7	94.0	93.9	92.8	-	-	-	-	-	-
2'	-	145.0	146.6	144.7	146.6	146.5	145.5	145.0	145.9	147.4	148.0	146.1	145.3
2"	-	145.4	75.8	76.1	78.3	76.1	144.4	119.8	-	-	-	-	-
2'''	-	-	78.2	-	-	-	-	-	-	-	-	-	-
3'	-	104.3	-	104.9	106.3	106.3	104.9	105.0	104.1	103.7	104.7	104.6	104.3
CH₂													
1"	-	-	34.2	30.8	32.2	34.1	-	70.3	-	-	-	-	-
1'''	-	72.4	75.9	-	-	-	-	-	-	-	-	-	-
2'''	-	61.1	-	-	-	-	-	-	-	-	-	-	-
3"	-	112.1	-	-	-	-	112.0	-	-	-	-	-	-
CH₃													
Me	20.3	-	22.8	22.4	22.5	23.0	26.2	25.7	-	-	-	-	-
Me	17.5	-	23.4	22.4	24.3	23.3	26.2	18.0	-	-	-	-	-
Me	-	-	27.2	-	-	-	-	-	-	-	-	-	-
Me	-	-	24.8	-	-	-	-	-	-	-	-	-	-
O-Me	-	-	-	60.1	60.9	60.9	59.9	60.7	-	-	-	-	61.2
O-Me	-	-	-	-	-	-	-	-	-	-	-	-	62.3
Glc-1	-	-	98.3	-	99.0	98.5	-	-	-	104.0	108.3	106.9	-
Glc-2	-	-	75.4	-	75.3	75.3	-	-	-	73.9	75.4	75.3	-
Glc-3	-	-	78.1	-	78.2	78.1	-	-	-	76.3	77.9	77.8	-
Glc-4	-	-	71.7	-	71.7	71.7	-	-	-	69.7	70.9	70.9	-
Glc-5	-	-	77.9	-	77.8	77.8	-	-	-	77.2	78.6	78.5	-
Glc-6	-	-	62.8	-	62.7	62.8	-	-	-	60.7	62.2	62.1	-

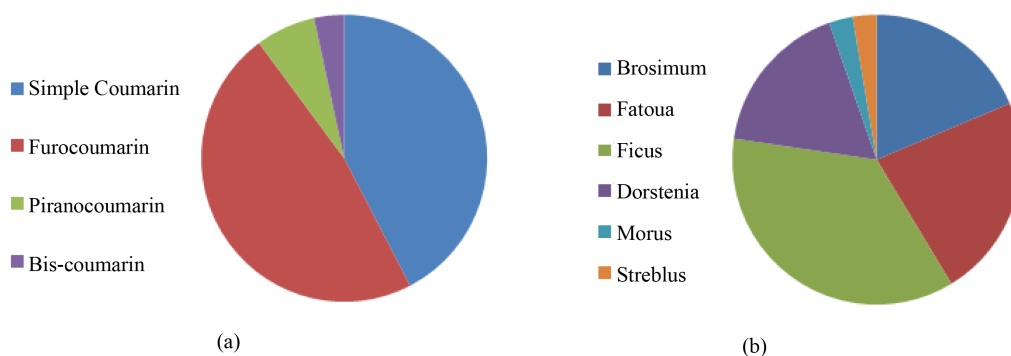
^agruposacetil: 170.2; 170.1 (CO); 20.8; 22.0 (Me); ^bgrupoacetil: 172.4 (CO); 20.9 (Me); ^csinaisGlc': 102.5 (Glc-1'); 73.9 (Glc-2'); 76.3 (Glc-3'); 69.7 (Glc-4'); 77.2 (Glc-5'); 60.7 (Glc-6').

Table 4. ^{13}C NMR data from pyranocoumarins isolated from Moraceae family.

	54	55	56	57		54	55	56	57
C					CH				
2	160.0	161.2	161.5	161.0	6	-	-	-	113.8
6	114.4	118.5	118.4	-	8	-	120.8	104.6	-
7	149.1	156.8	157.7	144.2	3'	131.3	104.4	-	130.6
8	135.8	-	-	144.1	4'	121.1	113.0	-	114.9
9	147.9	155.6	154.0	108.8	CH₂				
10	113.0	112.7	112.2	113.1	3'	-	-	32.4	-
2'	77.8	77.7	75.8	77.9	4'	-	-	21.9	-
CH					CH₃				
3	113.3	131.2	112.8	112.8	Me	28.2	28.3	26.9	28.1
4	143.6	143.3	143.3	144.2	Me	28.2	28.3	26.9	28.1
5	119.1	124.8	128.2	121.4	O-Me	61.5	-	-	-

Table 5. ^{13}C NMR data from *bis*-coumarins isolated from Moraceae family.

	58	59		58	59		58	59
C			CH			CH₂		
2	159.8	159.9	3	114.4	114.1	1'''	27.8	-
6	127.6	128.0	4	144.1	144.6	4'	116.0	114.8
7	148.1	147.8	5	119.0	119.2			
8	132.6	135.0	1'	84.7	82.0	4''	17.9	-
9	143.2	142.6	2'	79.5	80.0	5'	17.8	18.1
10	114.5	114.3	2'''	121.2	-	5''	25.8	28.3
2''	159.9	159.6	3''	112.2	113.4	6''	-	28.2
2'''	-	78.6	3'''	-	131.0	O-Me	61.0	60.6
3'	142.4	142.4	4''	143.8	143.3	-	-	-
3'''	133.8	-	4'''	-	120.9	-	-	-
6''	126.2	118.8	5''	123.1	119.7	-	-	-
7''	151.8	148.7	-	-	-	-	-	-
8''	135.9	133.2	-	-	-	-	-	-
9''	146.3	147.9	-	-	-	-	-	-
10''	111.6	112.9	-	-	-	-	-	-

**Figure 7.** (a) Types of coumarins isolated from Moraceae; (b) Coumarins isolated by genera of Moraceae.

genus, native to eastern Asia, contains only 3 species and all compounds were found in *Fatouapilosa* (Figure 7(b)).

The compounds with the highest number of occurrences in the family are the linear furocoumarins, especially the psoralen (27) and the bergapten (26), which together with the simple coumarin umbelliferone (2), appear in four from the six genera mentioned.

Since most Moraceae species has not yet been chemically studied, it is necessary to proceed these studies in order that it contributes to the family taxonomic classification. In this scenario, the coumarins can contribute as potential Moraceae genera chemotaxonomic markers.

Acknowledgements

The authors thank CNPq and FAPERJ for the financial support.

References

- [1] Barooso, G.M., Peixoto, A.L., Ichaso, C.L.F., Guimarães, E.F. and Costa, C.G. (2002) Sistemática de angiospermas do Brasil. 2nd Edition, Universidade Federal de Viçosa, Viçosa.
- [2] Romaniuc Neto, S., Carauta, J.P.P., Vianna Filho, M.D.M., Pereira, R.A.S., da S. Ribeiro, J.E.L., Machado, A.F.P., dos Santos, A., Pelissari, G. and Pederneiras, L.C. (2015) Moraceae in List of Species of Flora of Brazil. <http://reflora.jbrj.gov.br/jabot/floradobrasil/FB167>
- [3] Castro, R.M. (2006) Flora da Bahia—Moraceae. Master's Thesis, Universidade Estadual de Feira de Santana, Feira de Santana.
- [4] Monteiro, V. (1999) Estudo fitoquímico de *Brosimum gaudichaudii* Trécul (Moraceae). Master's Thesis, Universidade Estadual do Norte Fluminense Darcy Ribeiro: Campos dos Goytacazes.
- [5] Pio-Correa, M. and Pena, L.A. (1984) Dicionário das plantas úteis do Brasil e das exóticas cultivadas. Vol. 2-3, Ministério da Agricultura, Instituto Brasileiro de Desenvolvimento Florestal, Rio de Janeiro.
- [6] Chang, M.A., Yang, Y. C., Kuo, Y.C., Kuo, Y.H., Chang, C., Chen, C.M. and Lee, T.H. (2005) Furocoumarin Glycosides from the Leaves of *Ficus ruficaulis* Merr. Var. *antaoensis*. *Journal of Natural Products*, **68**, 11-13. <http://dx.doi.org/10.1021/np0401056>
- [7] Diaz, M.G., Arruda, A.C., Arruda, M.S.P. and Muller, A.H. (1997) Methoxyflavones from *Ficus máxima*. *Phytochemistry*, **45**, 1697-1699.
- [8] Hayasida, W., Sousa, A.S., Lima, M.P., Nascimento, C.C. and Ferreira, A.G. (2008) Proposta de aproveitamento em resíduos de pau-rainha (*Brosimum rubescens*) descartados pelo setor madeireiro. *Acta Amazônica*, **38**, 749-752. <http://dx.doi.org/10.1590/S0044-59672008000400019>
- [9] Pozetti, G.L. (2005) *Brosimum gaudichaudii* Trécul (Moraceae): Da planta ao medicamento. *Revista de Ciências Farmacêuticas Básica e Aplicada*, **26**, 159-166.
- [10] Dewick, P.M. (2009) Medicinal Natural Products: A Biosynthetic Approach. 3rd Edition, John Wiley & Sons, New York. <http://dx.doi.org/10.1002/9780470742761>
- [11] Sardari, S., Nishibe, S. and Danessthalab, M. (2000) Coumarins, the Bioactive Structures Antifungal Property. *Studies in Natural Products Chemistry*, **23**, 335-393. [http://dx.doi.org/10.1016/s1572-5995\(00\)80133-7](http://dx.doi.org/10.1016/s1572-5995(00)80133-7)
- [12] Ribeiro, C.V.C. and Kaplan, M.A.C. (2002) Evolutionary Tendency of Coumarin-Bearing Families in Angiospermae. *Química Nova*, **25**, 533-538. <http://dx.doi.org/10.1590/S0100-40422002000400004>
- [13] Monteiro, V., Mathias, L.M., Vieira, I.J.C., Schripsema, J. and Braz-Filho, R. (2002) Prenylated Coumarins, Chalcone and New Cinnamic Acid and Dihydrocinnamic Acid Derivatives from *Brosimum gaudichaudii*. *Journal of the Brazilian Chemistry Society*, **13**, 281-287.
- [14] Lourenço, M.V. (2001) Estudo comparativo dos constituintes químicos de *Brosimum gaudichaudii* Trécul e do medicamento "V". PhD Thesis, Universidade Estadual Paulista, Araraquara.
- [15] Vouffo, B., Hussain, H., Eyong, K.O., Dongo, E., Folefoc, G.N., Nkengfack, A.E. and Krohn, K. (2008) Chemical Constituents of *Dorstenia picta* and *Newbouldia laevis*. *Biochemical Systematics and Ecology*, **36**, 730-732. <http://dx.doi.org/10.1016/j.bse.2008.06.004>
- [16] Lazreg-Aref, H., Mars, M., Fekih, A., Aouni, M. and Said, K. (2012) Chemical Composition and Antibacterial Activity of a Hexane Extract of Tunisian Caprifig Latex from the Unripe Fruit of *Ficus carica*. *Pharmaceutical Biology*, **50**, 407-412. <http://dx.doi.org/10.3109/13880209.2011.608192>
- [17] Chan, K.K., Giannini, D.D., Cain, A.H., Roberts, J.D., Porter, W. and Trager, W. (1977) Carbon-13 Nuclear Magnetic Resonance Studies of Coumarin and Related Compounds. *Tetrahedron*, **33**, 899-906.

- [http://dx.doi.org/10.1016/0040-4020\(77\)80043-4](http://dx.doi.org/10.1016/0040-4020(77)80043-4)
- [18] Poumale, H.M., Amadou, D., Shiono, Y., Kapche, G.D.W.F. and Ngadjui, B.T. (2011) Chemical Constituents of *Dorstenia convexa*. *Asian Journal of Chemistry*, **23**, 525-527.
- [19] Vilegas, W. and Pozetti, G.L. (1993) Coumarins from *Brosimum gaudichaudii*. *Journal of Natural Products*, **56**, 416-417. <http://dx.doi.org/10.1021/np50093a015>
- [20] Chiang, C.C., Cheng, M.J., Peng, C.F., Huang, H.Y. and Chen, I.S. (2010) A Novel Dimeric Coumarin Analog and Antimycobacterial Constituents from *Fatoua pilosa*. *Chemistry and Biodiversity*, **7**, 1728-1736. <http://dx.doi.org/10.1002/cbdv.200900326>
- [21] Wang, Y., Liang, H., Zhang, Q., Cheng, W. and Yi, S. (2014) Phytochemical and Chemotaxonomic Study on *Ficus tsiangii*. *Biochemical Systematics and Ecology*, **57**, 210-215. <http://dx.doi.org/10.1016/j.bse.2014.08.003>
- [22] Zolek, T., Paradowska, K. and Wawer, I. (2003) ¹³C MAS NMR and GIAO-CHF Calculations of Coumarins. *Solid State Nuclear Magnetic Resonance*, **23**, 77-87. <http://ncbi.nlm.nih.gov/pubmed/12633833>
- [23] Dudek-Makuch, M. and Matlawska, I. (2013) Coumarins in Horse Chestnut Flowers: Isolation and Quantification by UPLC Method. *Acta Poloniae Pharmaceutica—Drug Research*, **70**, 517-522.
- [24] Shults, E.E., Petrova, T.N., Shakirov, M.M., Chernyak, E.I., Pokrovskiy, L.M., Nekhoroshev, S.A. and Tolstikov, G.A. (2003) Coumarin Compounds from Roots of *Peucedanum morisonii* Bess.). *Chemistry of Sustainable Development*, **11**, 649-654.
- [25] Prabowo, W.C., Wirasutisna, K.R. and Insanu, M. (2013) Isolation and Characterization of 3-Acetylaleuritic Acid and Scopoletin from Stem Bark of *Aleurites moluccana* (L. Willd). *International Journal of Pharmacy and Pharmaceutical Sciences*, **5**, 851-853.
- [26] Oh, H., Ko, E.K., Jun, J.Y., Oh, M.H., Park, S.U., Kang, K.H., Lee, H.S. and Kim, Y.C. (2002) Hepatoprotective and Free Radical Scavenging Activities of Prenylflavonoids, Coumarin, and Stilbene from *Morus alba*. *Planta Medica*, **68**, 932-934. <http://ncbi.nlm.nih.gov/pubmed/12391560>
<http://dx.doi.org/10.1055/s-2002-34930>
- [27] Yue, M., Li, Y. and Shi, Y.P. (2007) Determination of Six Bioactive Components of *Saussurea katochaete* by Capillary Electrophoresis. *Biomedical Chromatography*, **21**, 376-381. <http://ncbi.nlm.nih.gov/pubmed/17236245>
<http://dx.doi.org/10.1002/bmc.765>
- [28] Naressia, M.A., Ribeiroa, M.A. dos S., Bersani-Amadob, C.A., Zamunerb, M.L.M., da Costa, W.F., Tanaka, C.M.A. and Sarragiottoa, M.H. (2012) Chemical Composition, Anti-Inflammatory, Molluscicidal and Free-Radical Scavenging Activities of the Leaves of *Ficus radicans* “Variegata” (Moraceae). *Natural Product Research*, **26**, 323-330. <http://dx.doi.org/10.1080/14786411003754223>
- [29] Boeck, F., Blazejak, M. and Anneser, M.R. and Hintermann, L. (2012) Cyclization of Ortho-Hydroxycinnamates to Coumarins under Mild Conditions: A Nucleophilic Organocatalysis Approach. *Beilstein Journal of Organic Chemistry*, **8**, 1630-1636. <http://dx.doi.org/10.3762/bjoc.8.186>
- [30] Li, L.Q., Li, J., Huang, Y., Wu., Q., Deng, S.P., Su, X.J., Yang, R.Y., Huang, J.G., Chen, Z.Z. and Li, S. (2012) Lignans from the Heartwood of *Streblus asper* and Their Inhibiting Activities to Hepatitis B Virus. *Fitoterapia*, **83**, 303-309. <http://dx.doi.org/10.1016/j.fitote.2011.11.008>
- [31] Ragasa, C.Y., Ng, V.A.S., Reyes, M.M. De L., Mandia, E.H. and Shen, C.C. (2014) Triterpenes and a Coumarin Derivative from *Kibatalia gitingensis* (Elm.) Woodson. *Der Pharma Chemica*, **6**, 360-364.
- [32] Gao, W., Li, Q., Chen, J., Wang, Z. and Hua, C. (2013) Total Synthesis of 3,4-Unsubstituted Coumarins. *Molecules*, **18**, 15613-15623. <http://dx.doi.org/10.3390/molecules181215613>
- [33] Parveen, M., Ali, A., Malla, A.M., Silva, P.S.P. and Silva, M.R. (2011) A Halogenated Coumarin from *Ficus krishnae*. *Chemical Papers*, **65**, 735-738. <http://dx.doi.org/10.2478/s11696-011-0055-9>
- [34] Patre, R.E., Shet, J.B., Parameswaran, P.S. and Tilve, S.G. (2009) Cascade Wittig Reaction-Double Claisen and Cope Rearrangements: One-Pot Synthesis of Diprenylated Coumarins Gravelliferone, Balsamiferone, and 6,8-Diprenylumbelliferone. *Tetrahedron Letters*, **50**, 6488-6490. <http://dx.doi.org/10.1016/j.tetlet.2009.09.017>
- [35] Yn, W., Chen, H., Wang, T. and Cai, M. (1997) A New Coumarin Compound with Anticancer Activity. *Chinese Traditional and Herbal Drugs*, **28**, 3-4.
- [36] Rivière, C., Krisa, S., Péchamat, L., Nassra, M., Delaunay, J.C., Marchal, A., Badoc, A., Waffo-Téguo, P. and Mérillon, J.M. (2014) Polyphenols from the Stems of *Morus alba* and Their Inhibitory Activity against Nitric Oxide Production by Lipopolysaccharide-Activated Microglia. *Fitoterapia*, **97**, 253-260. <http://dx.doi.org/10.1016/j.fitote.2014.06.001>
- [37] Heinke, R., Franke, K., Porzel, A., Wessjohann, L.A., Ali, N.A.A. and Schimidt, J. (2011) Furanocoumarins from *Dorstenia foetida*. *Phytochemistry*, **72**, 929-934. <http://dx.doi.org/10.1016/j.phytochem.2011.03.008>
- [38] Chiang, C.C., Cheng, M.J., Huang, H.Y., Chang, H.S., Wang, C.J. and Vhen, I.S. (2010) Prenyl Coumarins from *Fa-*

- toua pilosa*. *Journal of Natural Products*, **73**, 1718-1722. <http://dx.doi.org/10.1021/np100354c>
- [39] Juan, E.A., Rideout, J.A. and Ragasa, C.Y. (1997) Bioactive Furanocoumarin Derivatives from *Ficus pumila* (Moraceae). *Philippine Journal of Science*, **126**, 143-153.
- [40] Santana, L.L.B., Silva, C.V., Almeida, L.C., Costa, T.A.C. and Velozo, E.S. (2011) Extraction with Supercritical Fluid and Comparison of Chemical Composition from Adults and Young Leaves of *Zanthoxylum tingoassuba*. *Brazilian Journal of Pharmaceutical Science*, **21**, 564-567.
- [41] Chang, M.S., Yang, Y.C., Kuo, Y.C., Kuo, Y.H., Chang, C., Chen, C.M. and Lee, T.H. (2005) Furocoumarin Glycosides from the Leaves of *Ficus ruficaulis* Merr. var. *antaoensis*. *Journal of Natural Products*, **68**, 11-13. <http://dx.doi.org/10.1021/np0401056>
- [42] El-Khrisy, E.A.M., Khatlab, A.A. and Abu-Mustafa, E.A. (1980) Constituents of Local Plants. Part XXVIII. Constituents of *Ficus prima*, *F. hispida* and *F. carica*. *Fitoterapia*, **51**, 269-272.
- [43] Marrelli, M., Menichini, F., Statti, G.A., Bonesi, M., Duez, P., Menichini, F. and Conforti, F. (2012) Changes in the Phenolic and Lipophilic Composition, in the Enzyme Inhibition and Antiproliferative Activity of *Ficus carica* L. Cultivar Dottato Fruits during Maturation. *Food and Chemical Toxicology*, **50**, 726-733. <http://dx.doi.org/10.1016/j.fct.2011.12.025>
- [44] Elgamel, M.H.A., Elewa, N.H., Elkhisy, E.A.M. and Duddeck, H. (1979) ¹³C NMR Chemical Shifts and Carbon-Proton Coupling Constants of Some Furocoumarins and Furochromones. *Phytochemistry*, **18**, 139-143. [http://dx.doi.org/10.1016/S0031-9422\(00\)90932-4](http://dx.doi.org/10.1016/S0031-9422(00)90932-4)
- [45] Lemmich, J. and Shabana, M. (1984) Coumarin Sulphates of *Seseli libanotis*. *Phytochemistry*, **23**, 863-865. [http://dx.doi.org/10.1016/S0031-9422\(00\)85044-X](http://dx.doi.org/10.1016/S0031-9422(00)85044-X)
- [46] Vieira, I.J.C., Mathias, L., Monteiro, V. de F.F., Braz-Filho, R. and Rodrigues-Filho, E. (1999) A New Coumarin from *Brosimum Gaudichaudii* Trecul. *Natural Products Letters*, **13**, 47-52. <http://dx.doi.org/10.1080/10575639908048490>
- [47] Nizamutdinova, I.T., Jeong, J.J., Xu, G.H., Lee, S.H., Kang, S.S., Kim, Y.S., Chang, K.C. and Kim, H.J. (2008) Hesperidin, Hesperidin Methyl Chalone and Phellopterin from *Poncirus trifoliata* (Rutaceae) Differentially Regulate the Expression of Adhesion Molecules in Tumor Necrosis Factor- α -Stimulated Human Umbilical Vein Endothelial Cells. *International Immunopharmacology*, **8**, 670-678. <http://dx.doi.org/10.1016/j.intimp.2008.01.011>
- [48] Liu, R., Li, A., Sun, A. and Kong, L. (2004) Preparative Isolation and Purification of Psoralen and Isopsoralen from *Psoralea corylifolia* by High-Speed Counter-Current Chromatography. *Journal of Chromatography A*, **1057**, 225-228. <http://dx.doi.org/10.1016/j.chroma.2004.09.049>
- [49] Souri, E., Farsam, H., Sarkheil, P. and Ebadi, F. (2004) Antioxidant Activity of Some Furocoumarins Isolated from *Heracleum persicum*. *Pharmaceutical Biology*, **42**, 396-399. <http://dx.doi.org/10.1080/13880200490885077>
- [50] Oliveira, L.S. dos S. (2014) Chemical Constituents of *Conchocarpus cyrtanthus* (Rutaceae). Master's Thesis, Universidade Estadual do Norte Fluminense Darcy Ribeiro, Campos dos Goytacazes.
- [51] Elgamel, M.H.A., Shalaby, N.M.M., Duddeck, H. and Hiegemann, M. (1993) Coumarins and Coumarin Glucosides from the Fruits of *Ammi majus*. *Phytochemistry*, **34**, 819-823. [http://dx.doi.org/10.1016/0031-9422\(93\)85365-X](http://dx.doi.org/10.1016/0031-9422(93)85365-X)