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Our phytochemical research on *Jatropha* species

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This paper is dedicated to the memory of the late Professor (Mrs) Asima Chatterjee, a pioneer organic chemist of India, on the occasion of her 100th anniversary

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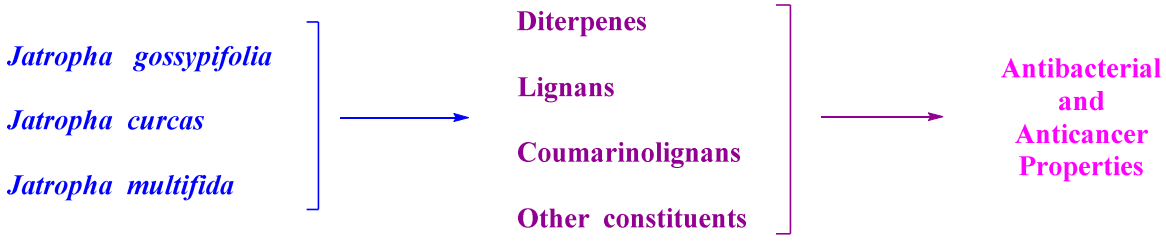
Abstract

Jatropha is an important genus of the family Euphorbiaceae. The plants of this genus contain complex chemical constituents which are structurally impressive. The medicinal properties of the plants and their various constituents are valuable. We carried out phytochemical investigation on three *Jatropha* species, viz., *Jatropha gossypifolia*, *Jatropha curcas* and *Jatropha multifida*. We isolated several constituents: diterpenes, lignans, coumarinolignans and other compounds. Some of the isolates possess significant antibacterial and anticancer properties. Here, we discuss our phytochemical research on *Jatropha* species informing of the isolation, structures and bioactivity of their chemical constituents.



Keywords: *Jatropha* species, phytochemistry, diterpenes, lignans, coumarins

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1. Introduction

Jatropha is a genus of flowering plants in the family *Euphorbiaceae*. The name "*Jatropha*" is derived from the Greek word "Jatros" (meaning "physician") and "trophe"(meaning "food"). Since ancient time, the plants of this genus have been used in ethno-medicine. The genus comprises around 170 species of shrubs and small trees. The plants are naturally distributed mainly in the tropical and sub-tropical regions of the Americas and Africa but they are now cultivated around the world. The species have attracted much attention in recent years due to their impressive medicinal properties, such as, antimicrobial, antidiabetic, anti-inflammatory, antimalarial, antioxidant, anti-HIV and anticancer activities. Other potential benefits include their applications for bio-diesel production, insecticide preparation and plastic formulation. The chemical structures and bio-properties of the constituents of these species are of considerable interest.[1–11]

We conducted phytochemical research on three *Jatropha* species: *Jatropha gossypifolia*, *Jatropha curcas* and *Jatropha multifida.* The plant materials were collected from the local areas. Our investigation resulted in the isolation of various novel constituents. The biological activities of some of these constituents were also examined. Here, we briefly review our phytochemical studies on *Jatropha* species.

2. Discussion

We successfully isolated and characterized several diterpenes, lignans, coumarinolignans and other constituents from three investigated *Jatropha* species. The structures of the new compounds were settled by extensive studies of their spectroscopic data. The X-ray crystallographic analysis of some of the complex compounds were also performed. The known compounds were characterized by comparison of their spectral properties with those reported in the literature. The transformations and syntheses of various constituents have been carried out.

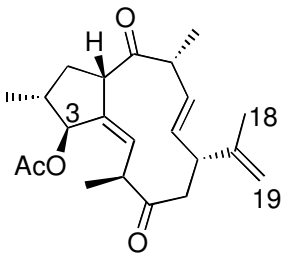
2.1 Diterpenes

Diterpenes are the major isolated constituents of the *Jatropha* species. Thirty diterpenes have been obtained from these species. Fourteen of these compounds are new. These thirty compounds are listed in Table 1, with their source(s) and references to our group's work.

Table 1. Diterpenes isolated from *Jatropha* species

No	Name (structure)	Source	Comment	Reference
1	Jatrophenone (**1**)	*Jatropha gossypifolia* *Jatropha multifida*	New	12 13,14
2	15-*O*-acetyl-15-*epi* 4(*E*)-jatrogrossidentadione (**2**)	*Jatropha curcas*	New	15
3	Epoxylathyrane diterpene (**3**)	*Jatropha curcas*	New	15
4	3β-Acetoxy-12-methoxy-13-methyl-podocarpa-8,10,13-trien-7-one (**4**)	*Jatropha curcas* *Jatropha multifida*	New	15 14,16
5	3β,12-Dihydroxy-13-methyl-podocarpane-8,11,13-triene (**5**)	*Jatropha curcas* *Jatropha multifida*	New	15 14
6	Multifolone (**6**)	*Jatropha multifida*	New	16
7	4(*E)*-Jatrogrossidentadione acetate (**7**)	*Jatropha multifida*	New	16
8	15-*epi*-4(*E*)-Jatrogrossidentadione acetate (**8**)	*Jatropha multifida*	New	17
9	Multifidone (**9**)	*Jatropha multifida*	New	18
10	15-*O*-Acetyljapodragrone (**10**)	*Jatropha multifida*	New	14
11	Hydroxylathyrane diterpene (**11**)	*Jatropha multifida*	New	14
12	Multifidanol (**12**)	*Jatropha multifida*	New	13
13	Multifidenol (**13**)	*Jatropha multifida*	New	13
14	Multidione (**14**)	*Jatropha multifida*	New	19
15	Citlalitrione (**15**)	*Jatropha gossypifolia* *Jatropha multifida*	Known	20 13,16,18
16	Heudolotinone (**16**)	*Jatropha curcas*	Known	15,21
17	*epi*-Isojatrogrossidione (**17**)	*Jatropha curcas*	Known	15
18	2-Hydroxy-*epi*-isojatrogrossidione (**18**)	*Jatropha curcas*	Known	15
19	Curcasone A (**19**)	*Jatropha curcas*	Known	15
20	Curcasone B (**20**)	*Jatropha curcas*	Known	15
21	Curcasone C (**21**)	*Jatropha curcas*	Known	15
22	Curcasone D (**22**)	*Jatropha curcas*	Known	15
23	Jatropholone A (**23**)	*Jatropha curcas* *Jatropha multifida*	Known	15 13,14
24	Jatropholone B (**24**)	*Jatropha curcas* *Jatropha multifida*	Known	15 14
25	Jatrophol (**25**)	*Jatropha curcas*	Known	15
26	4(*E*)-Jatrogrossidentadione (**26**)	*Jatropha multifida*	Known	14,16,17
27	15-*epi*-4(*E*)-Jatrogrossidentadione (**27**)	*Jatropha curcas* *Jatropha multifida*	Known	15 14,16,17,18
28	Jatrophone (**28**)	*Jatropha multifida*	Known	16,17,18
29	Japodagrone (**29**)	*Jatropha multifida*	Known	13,14
30	Jatrothrin (**30**)	*Jatropha multifida*	Known	13

From *Jatropha gossypifolia* two macrocyclic diterpenes, jatrophenone (**1**)[12] and citlalitrione (**15**)[20] were isolated. The first compound is a novel diterpene while the other was isolated from the species for the first time. The structure of jatrophenone (**1**) was established mainly by detailed studies of its 1D and 2D NMR spectra. 2D NMR spectra clearly showed that A ring of the molecule is saturated and it contains an acetoxy group (β-configuration) at C-3 [δ 2.09 in the ^{1}H NMR spectrum and δ 170.8, 21.3 in the ^{13}C NMR spectrum]. The macrocyclic B ring contains two keto groups and two olefinic double bonds (one is trisubstituted and the other is disubstituted) having *trans-E* stereostucture. The side chain is an isopropenyl moiety (H_3-18: δ 1.72, 3H, s; C-18: δ 21.3; H_2-19: δ 4.80,1H, s; 4.73, 1H, s; C-19: δ 110.1) having the α – configuration.



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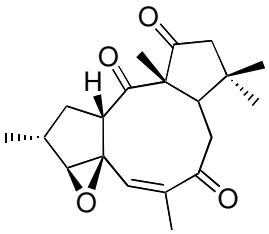
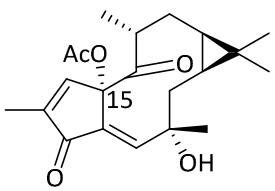


15

Jatrophenone (**1**) was found to exhibit significant antibacterial activity against *Staphylococcus aureus*; the activity was comparable to that of penicillin G.[12]

Citlalitrione (**15**) and related diterpenes were reported earlier from other *Jatropha* species. These compounds are considered as the useful taxonomic markers within the genus.[20] Both the compounds **1** and **15** were isolated from *Jatropha multifida*.[13,14,16,18]

Investigation on *Jatropha curcas* yielded a large number of diterpenes (Table 1).[15,21] Four of these constituents, **2**-**5**, are new compounds. Two of them, **2** and **3**, are of lathyrane type while the other two, **4** and **5** are of podocarpane type. From careful analysis of the spectral data compound **2** was characterized as 15-*O*-acetyl-15-*epi*-4(*E*)-jatrogrossidentadione and **4** and **5** as 3β-acetoxy-12-methoxy-13-methyl-podocarpa-8,11,13-trien-7-one and 3β,12-dihydroxy-13-methylpodocarpa-8,10,13-triene respectively. Compound **3** is an epoxylathyrane diterpene related to **2**.[15] The molecule **2** contains a cyclopropane moiety, a hydroxyl, an acetoxy and five methyl groups. All the signals for the protons and carbons in the ^{1}H and ^{13}C NMR spectra respectively were assigned from 2D NMR (^{1}H –^{1}H COSY, NOESY, HSQC and HMBC) and APT experiments. The NOESY experiment clearly supported the placement of the acetoxy group in the epimeric form at C-15. Both the compounds **2** and **3** possess a similar general structure. However, the compound **3** contains an epoxide ring at C-5, C-6 (instead of a double bond at C-4, C-5). The other difference is that the latter contains a tetrasubstituted double bond at C-14, C-15 with an acetoxy group at C-14. The trans *E* configuration of the C-14 - C-15 double bond was established from a NOESY experiment.



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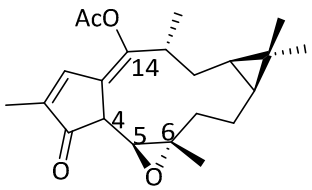

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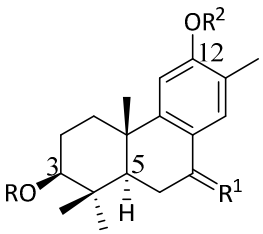
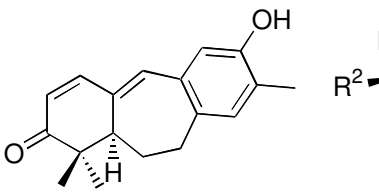


4, R=Ac, R^1=O, R^2=Me

5, R=R^2=H, R^1=H_2

The molecule **4**[15] contains an acetoxy and a methoxy group. The acetoxy group (δ 2.08, 3H, s in the ^{1}H NMR spectrum) was placed at C-3 as the proton at this position resonated as a doublet of a doublet. This was also supported from the NOESY experiment which showed a clear correlation between the protons of C-3 and C-5. On the other hand, the methoxy group (δ 3.88, 3H, s in the ^{1}H NMR spectrum) was placed at C-12 in the ring C as suggested by HMBC and NOESY experiments. The general structure of both the compounds **4** and **5**[15] is similar. However, **5** contains no acetoxy or methoxy group or any carbonyl function. The acetoxy group of **4** has been deacetylated and methoxy group demethylated in **5** which contains two hydroxyl groups at C-3 and C-12. The compound produces a diacetate by acetylation. Compounds **4** and **5** were also found later to be the constituents of *Jatropha multifida*.[14,16]

Along with the new constituents, **2**-**5**, different other known macrocyclic diterpenes, *viz*., heudolotinone (**16**), *epi*-isojatrogrossidione (**17**), 2-hydroxy-*epi*-isojatrogrossidione (**18**), curcasones A (**19**), B (**20**), C (**21**) and D (**22**), jatropholones A (**23**) and B (**24**), jatrophol (**25**) and 15-*epi*-4(*E*)-jatrogrossidentadione (**27**) were also obtained from *Jatropha curcas* (Table 1).[15] The first three diterpenes, **16–18**, were reported for the first time from the species. Compounds **23**, **24** and **27** are also diterpenoid constituents of *Jatropha multifida.*[13,14,16–18]



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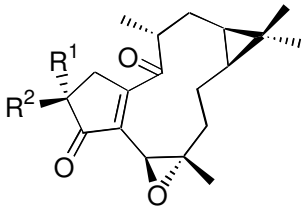
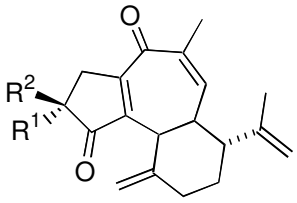


17, R^1=Me, R^2=H

18, R^1=Me, R^2=OH

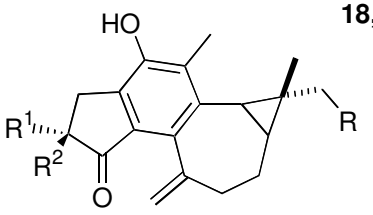


19, R^1=Me, R^2=H

20, R^1=H, R^2=Me

21, R^1=Me, R^2=OH

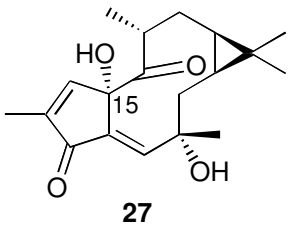
22, R^1=OH, R^2=Me



23, R^1=R=H, R^2=Me

24, R^1=Me, R^2=R=H

25, R^1=Me, R^2=H, R=OH



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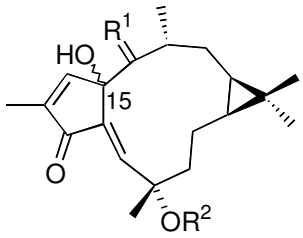
Several novel macrocyclic diterpenes, viz., multifolone (**6**),[16] 4-(*E*)-jatrogrossidentadione acetate (**7**),[16] 15-*epi*-4(*E*)-jatrogrossidentadione acetate (**8**),[17] multifidone (**9**),[18] 15-*O*-acetyljapodragrone (**10**),[14] hydroxy-lathyrane diterpene (**11**),[14] multifidanol (**12**),[13] multifidenol (**13**)[13] and multidione (**14**)[19] were obtained from the chemical investigation of *Jatropha multifida* (Table 1). The structures of the compounds were confirmed from their spectral properties. The NMR data revealed that multifolone (**6**) contains one carbonyl and three hydroxy groups. The ^{1}H-^{1}H COSY and HMBC experiments suggested to place the carbonyl group at C-3 and the hydroxy groups at C-6, C-14 and C-15. The ^{1}H-^{1}H COSY experiment indicated the sequence : H-7 – H-8 – H-9 – H-11 – H-12 – H -13 – H-14 and the HMBC experiment showed that H-14 was related to C-1, C-4 and C-20. In fact, the structure of multifolone (**6**) was similar to 4*E*-jatrogrossidentadione (**26**) but the only difference is that the position C-14 contains a hydroxy group for the former while a keto group for the latter.[16] The relative stereochemistry of multifolone (**6**) was established by NOESY correlations and was proved to be similar to that

of (**26**). Me-20 (δ 1.21) was clearly related to H-14 (δ 3.82). Thus the structure of multifolone (**6**) was established as 14-deoxy-14β-hydroxy-4(*E*)-jatrogrossidentadione.[16]

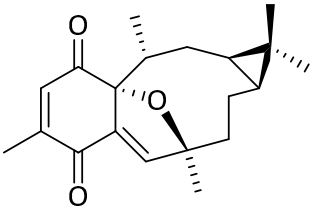


6, R^1=H, β-OH, R^2=H, 15β-OH
7, R^1=O, R^2=Ac, 15β-OH
8, R^1=O, R^2=Ac, 15α-OH
26, R^1=O, R^2=H, 15β-OH

In the new molecule 4(*E*)-jatrogrossidentadione acetate (**7**)[16] the acetoxy group (δ 2.05, 3H, s, in the ^{1}H NMR spectrum and δ 170.0, 22.1 in the ^{13}C NMR spectrum) was placed at C-6 because a comparision of the ^{1}H NMR spectra of this compound and of 4(*E*)-jatrogrossidentadione(**26**) showed that Me-17 (δ 1.75 for **7** and 1.48 for **26**) appeared at a downfield region in **7**. The ^{13}C NMR spectra (C-6: δ 84.4 for **7** and 73.5 for **26**) also supported this. The X-ray crystallographic analysis of **7** was accomplished.[16] The structure of **8**[17] is similar to that of **7**; the only difference is that in the former the hydroxy group at C-15 is with α-configuration while in the latter with β-configuration.[17]

Multifidone (**9**)[18] another constituent of *Jatropha multifida*, is structurally interesting as it possesses a six membered A ring in contrast to cyclopentane ring generally found in lathyrane-type diterpenes. The A ring contains two carbonyl groups at C-1 and C-4 and a trisubstituted double bond at C-2 – C-3 .The macrocyclic B ring was found to possess a dihydrofuran ring. The *E*–configuration of the double bond present in the furan ring was suggested from the ^{13}C NMR spectrum of the molecule. The sructure of **9** was confirmed from X-ray crystallographic analysis.[18]

Multifidone (**9**) was examined for *in vitro* cytotoxic activity against four different cancerous cell lines: THP-1 (human acute monocytic leukaemia), HL-60 (human promyelocytic leukaemia), A-375 (human malignant melanoma) and A-549 (human lung carcinoma) using etoposide as the positive control. The compound **9** showed significant decrease in cell viability in all the tested cell lines in a concentration dependent manner.[18]



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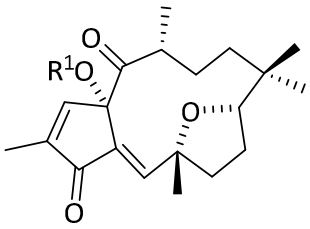
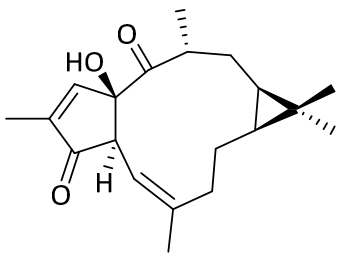


10, R^1 = Ac
29, R^1 = H

15-*O*-Acetyljapodragrone (**10**),[14] a new constituent of *Jatropha multifida*, contains a tetrahydrofuran moiety in the ring B but it contains no cyclopropane ring. The acetyl group (δ 2.09, 3H, s in the ^{1}H NMR spectrum) at C-15 is in the α-configuration. The compound is the acetyl derivative of japodagrone (**29**)[14] which contains a hydroxy group at C-15. The ^{13}C NMR spectrum suggested the placement of this acetoxy group at C-

15 as this carbon (δ 88.9) showed a downfield shift compared to the corresponding carbon (δ 82.4) of japodagrone. In the ^{1}H NMR spectrum H-1 showed a downfield shift (δ 7.30 in **10** and 6.80 in **29**). 2D NMR spectra also supported the structure of **10**.[14]

In other new constituent, a lathyrane type diterpene **11**,[14] a trisubstituted double bond is situated at C-5–C-6 position instead of C-4–C-5 position and the other at C-1–C-2. The structure is related to that of 4E-jatrogrossidentadione (**26**).[17] The compound contains a hydroxy group at C-15. From the NOESY experiment H-4 and OH-15 was suggested to be α and β oriented respectively.[14]



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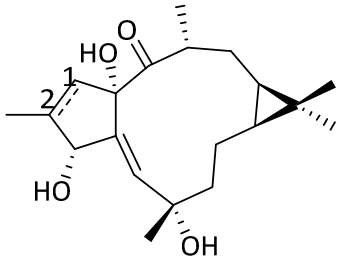


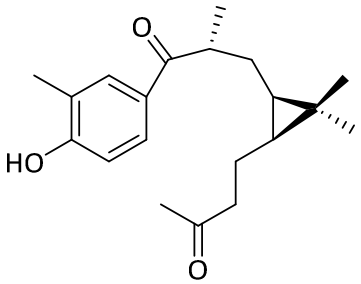
12, C_1-C_2 Saturated, C_2-β Me

13, C_1-C_2 double bond

Multifidanol (**12**)[13] and multifidenol (**13**)[13] two new diterpenes of *Jatropha multifida,* possess cyclopentanol A ring (instead of cyclopentanone). The structures of these two compounds are closely related. In multifidanol (**12**) C-1, C-2-bond is saturated while this bond is unsaturated in multifidenol (**13**). Both the compounds contain other two hydroxyls and a keto group. On the basis of 1D and 2D NMR spectral correlations these two hydroxyls were placed at C-6 and C-15 positions while the keto group at C-14. All the three –OH groups were found to have α - configuration.[13]

Multifidanol (**12**) and multifidenol (**13**) were evaluated for cyctotoxic activity (*in vitro*) against different cancerous cell lines using doxorubicin as the positive control. Both the compounds exhibited promising activity against some of these cell lines. It was observed that the absence of the double bond at C-1, C-2 enhanced the activity of multifidanol (**12**) against A-549 and MCF-7cell lines but the presence of a double bond at this position increased the activity of multifidenol (**13**) against Neuro-2aHeLa and MDA-231 cell lines.[13]

The antibacterial activity of **12** and **13** was also tested against some bacterial organisms using neomycin as the positive control. Compound **12** showed impressive activity against *Bacillus subtilis* and *Escherichia coli* but compound **13** showed selective activity against *Staphylococcus aureus*.[13]

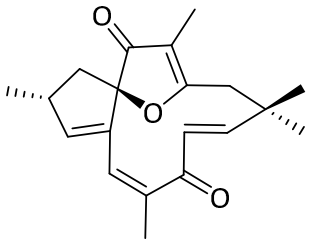


14

From *Jatropha multifida* another novel diterpene, multidione (**14**)[19] was isolated. The structure of the compound was settled from 1D and 2D NMR spectra. The spectra indicated that multidione possess a 2,4-disubstituted phenolic moiety containing a methyl group at C-2 and a long side chain at C-4. The side chain

was found to have four methyl groups, two carbonyl groups and a cyclopropane ring which were properly placed in the molecule by spectral correlations.The relative stereochemistry of the side chain was established from NOESY experiment and interproton or heteronuclear coupling constants. Ring B of the lathyrane skeleton has been cleaved to produce the side chain. Multidione (**14**) has possibly been derived biogenetically from a related diterpene.[19]

Along with the new diterpenes several known diterpenes were also isolated for the first time from *Jatropha multifida*. These compounds included jatropholones A (**23**)[13,14] and B (**24**),[14] 4-(*E*)-jatrogrossidentadione (**26**),[14,16,17] 15-*epi*-4-(*E*)-jatrogrossidentadione (**27**),[14,16–18] jatrophone (**28**),[16-18] japodagrone (**29**)[13,14] and jatrothrin (**30**).[13] jatrophone (**28**) was reported earlier to exhibit promising antileukemic activity against P-388 lymphocytic leukemia and also cytotoxicity against KB cell culture.[22]



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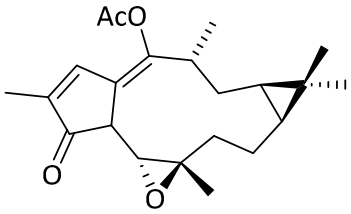

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2.2 Lignans

From *Jatropha gossypifolia* several lignans have been isolated (Table 2; Figure 1). These lignans are dibenzyl and arylnaphthalide types. Some of the molecules contain butyrolactone and butyrolactol moieties. Both *trans* (*E*)- and *cis* (*Z*)- configurations of the olefinic double bonds present in the molecules are observed. They also possess (*S*) as well as (*R*) stereochemistry.

Table 2. Lignans isolated from *Jatropha gossypifolia*[a]

No	Name	Structure	Reference
1	Jatrophan	**31**	23, 24
2	Gadain	**32**	24
3	Prasanthaline	**33**	25
4	Dihydroprasanthaline	**34**	26
5	Arylnaphthalide lignan	**35**	27
6	Gossypifan	**36**	28
7	Isogadain	**37**	29
8	Gossypiline	**38**	30
9	Jatrodien	**39**	31
10	Gossypidien	**40**	32
11	4´-*O*-Demethylretrochinensin	**41**	33
12	Jatrolactol	**42**	34

[a] All the lignans are new compounds.

Jatrophan (**31**) is the first lignan reported from the genus *Jatropha*.[23,24] Its structure was deduced from its spectral data and X-ray crystallographic analysis. The compound contains a trans (*E*)-olefinic double bond. On the other hand, gadain (**32**), another new lignan constituent of the same plant contains a cis (*Z*)-olefinic double bond.[24] In the ^{1}H NMR spectra the olefinic proton of jatrophan (**31**) appeared at δ 7.54 (1H, d, *J* =1.6 Hz) while that of gadain (**32**) at δ 6.59 (1H, d, *J* =1.6 Hz). An interesting *cis-trans* isomerisation of gadain (**32**) was observed when its NMR spectra in $CDCl_3$ were studied. This transformation was assumed to be catalyzed by the usual trace of HCl present in $CDCl_3$. In fact, when **32** was kept in HCl (1.0 M) for 72 h it changed to its *trans* (*E*) isomer. The structure as well as stereochemistry [(*S*)] of gadain was confirmed from its synthesis from jatrophan (**31**) (Scheme 1). The latter was demethylated with BBr_3 to produce a dihydoxy derivative which on treatement with bromochloromethane afforded the *trans* (*E*)-isomer (**37**) of gadain (**32**). This isomeric compound yielded gadain (**32**) by UV irradiation.[24] Isogadain (**37**) was also isolated later from *Jatropha gossypifolia*.[29]

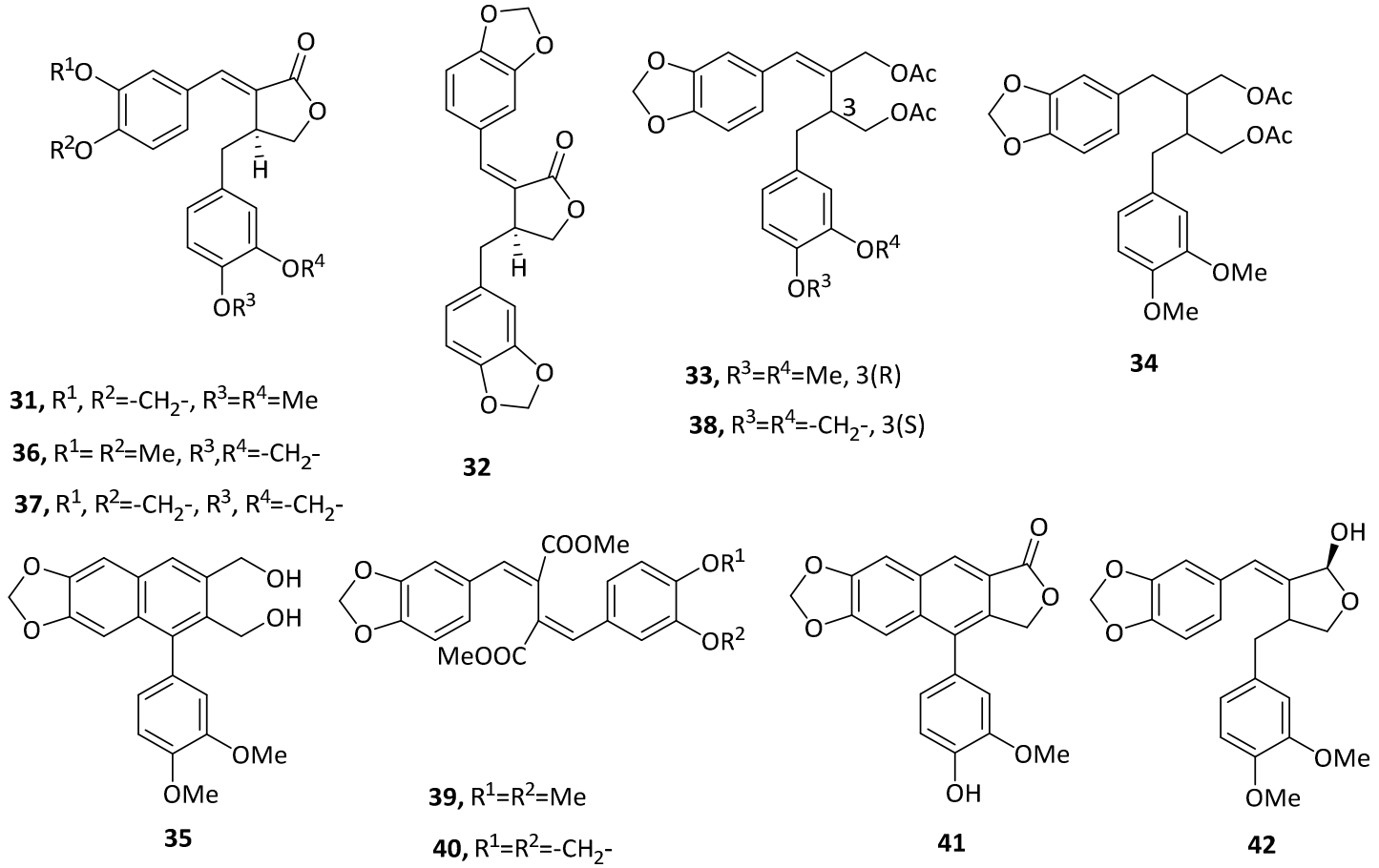


Figure 1. Structures of the lignans of *Jatropha gossypifolia.*

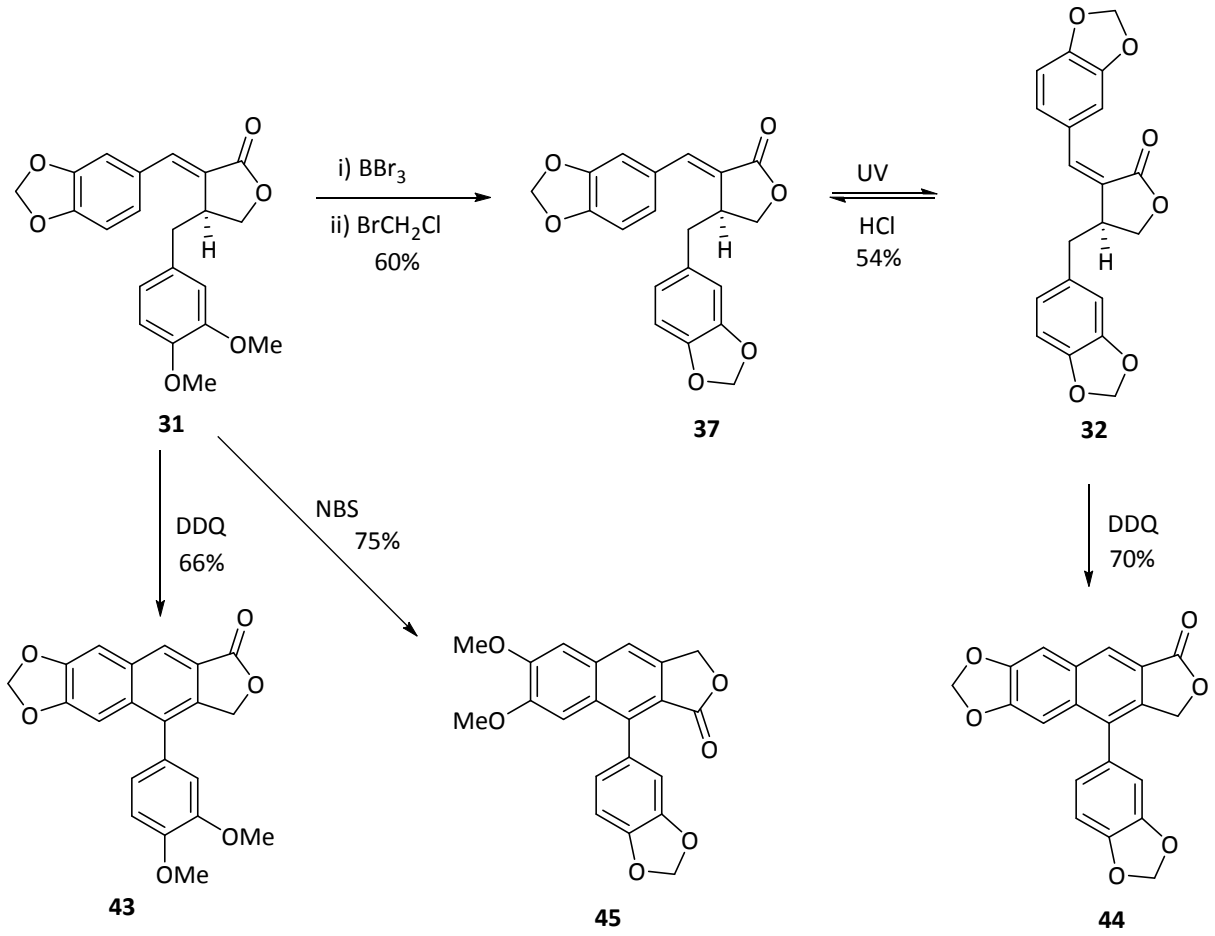
Various chemical conversions and synthetic studies of jatrophan (**31**) and gadain (**32**) were performed (Scheme 1).[24,35,36] On treatment with DDQ the former yielded retrochinensin (**43**) while the latter produced justicidin *E* (**44**), both the products are naturally occurring aryl naphthalide lignans. Another natural aryl naphthalide lignan, justicidin B (**45**) was also prepared from jatrophan (**31**) by NBS treatment.[24]

A total synthesis of jatrophan in racemic form started with the Stobbe condensation of piperonal (**46**) with dimethyl succinate followed by methylation to yield a diester (**48**) (Scheme 2). A second Stobbe

condensation of this diester with veratraldehyde and subsequent Bouveault-Blanc reduction generated (±)-jatrophan.[35]

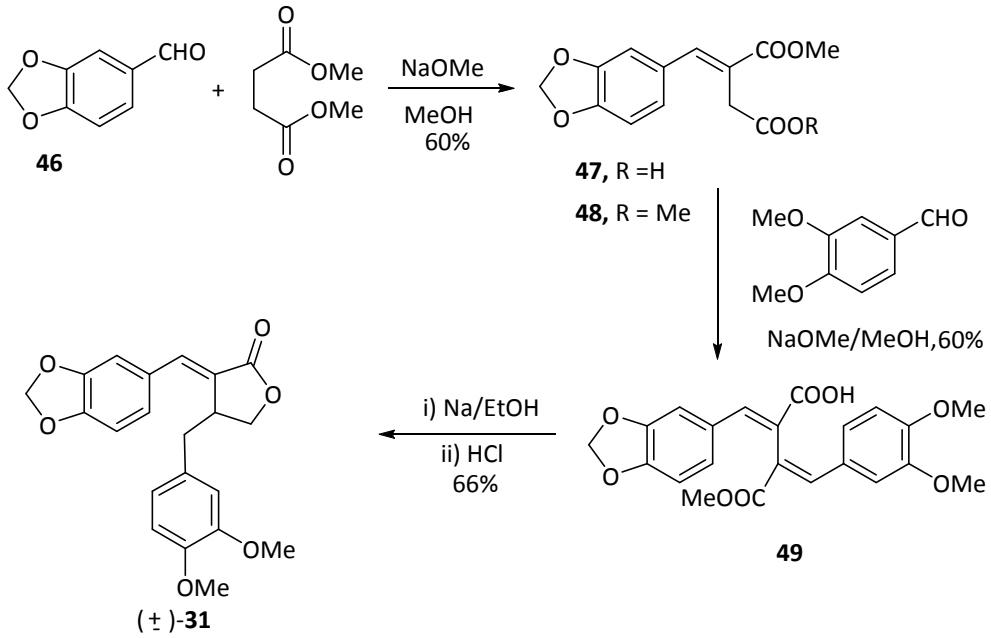
Another butyrolactone lignan, gossypifan (**36**), structurally related to jatrophan (**31**), was isolated from the aerial parts of *Jatropha gossypifolia*. The compound also possesses an olefinic trans (*E*)- double bond and (*S*)-stereoconfiguration. Two aromatic rings with their functionalities have been interchanged in **36**.[28]

Two dibenzyl lignans (without having butyrolactone moiety), prasanthaline (**33**)[25] and gossypiline (**38**)[30] are also the constituents of *Jatropha gossypifolia*. The occurrence of dihydroprasanthaline (**34**) in the plant was also reported.[26] The structures of the compounds, **33** and **38** (established from the spectral data) are related. The difference is that prasanthaline (**33**) contains one methylenedioxy and two methoxy groups while gossypiline (**38**) contains two methylenedioxy groups. However, the stereochemistry of these two compounds are opposite; compound **33** bears (*R*)- configuration but **38** (*S*)- configuration.

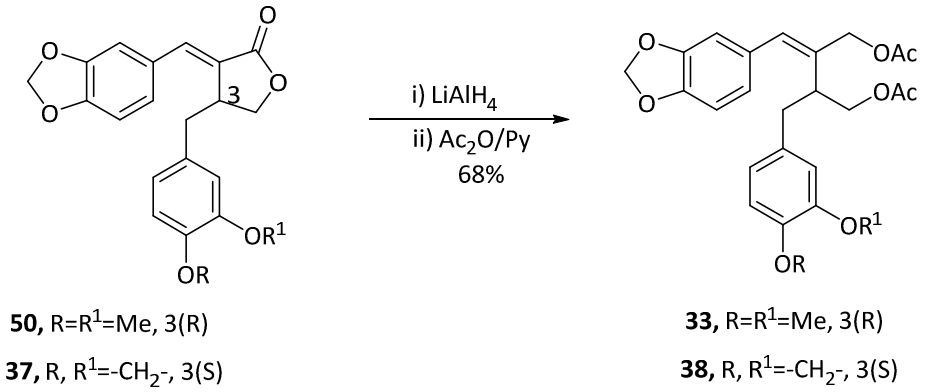


Scheme 1. Chemical conversions of jatrophan (**31**) and gadain (**32**).[24,35,36]

Prasanthaline (**33**)[25] and gossypiline (**38**)[30] were prepared from the natural lignans, suchilactone (**50**) and isogadain (**37**) respectively (Scheme 3) by reduction with lithium aluminium hydride followed by acetylation with acetic anhydride and pyridine. Thus the structures (along with the stereochemistry) of the two compounds were confirmed.

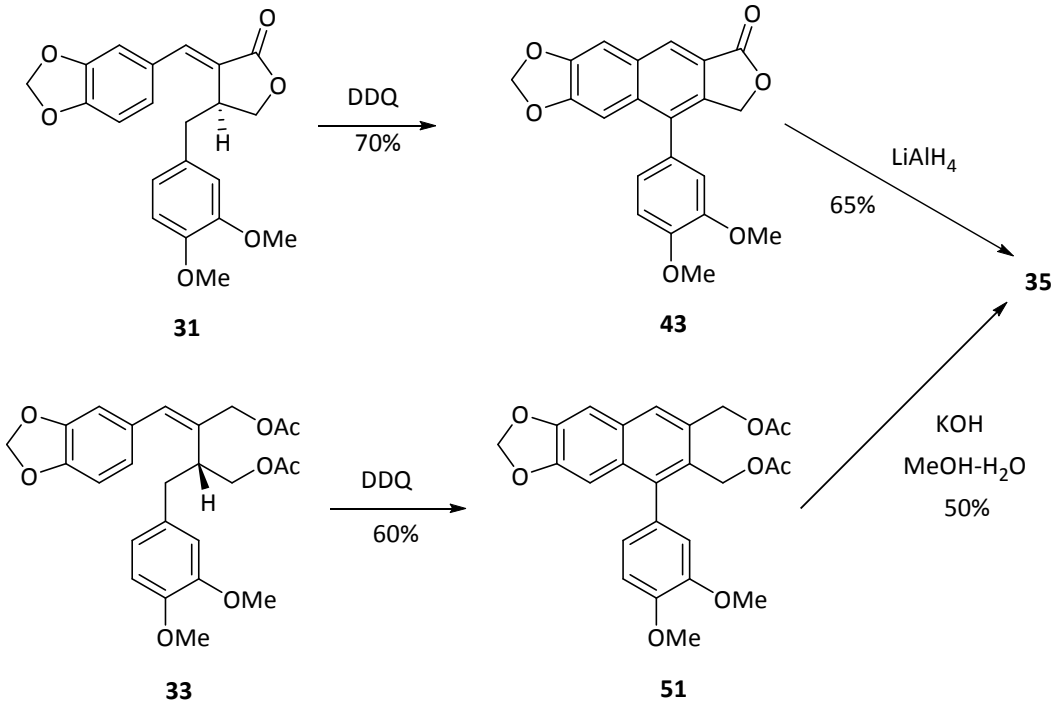


Scheme 2. Synthesis of (±)-jatrophan.[35]



Scheme 3. Preparation of prasanthaline (**33**) and gossypiline (**38**).[25,30]

Chemical investigation on the same plant, *Jatropha gossypifolia*, resulted in the isolation of two aryl naphthalide lignans, 2,3-bis(hydroxymethyl)-6,7-methylenedioxy-1-(3′,4′-dimethoxyphenyl)naphthalene (**35**)[27] and 4′-O-demethyl retrochinensin (**41**).[33] In the ^{1}H NMR spectrum of **35** two hydroxyls (δ 3.05) appeared as a broad signal. The methylene protons at C-2 and C-3 resonated at δ 4.55 (2H, s) and 4.85 (2H, s) indicating their association with the hydroxyls as –CH_2OH. The ^{13}C NMR spectral data (δ 60.71, C-2 ; 65.25, C-3) also supported this. The substitution pattern of the molecule **35** was confirmed from the analysis of its mass spectrum. The spectral data of **41** revealed that its sructure is similar to that of retrochinensin (**43**) but it contains a hydroxyl group at C-4' instead of a methoxy group present in the latter. The compound **35** was synthesised from jatrophan (**31**) (Scheme 4) by oxidative cyclization with DDQ followed by reduction with lithium aluminium hydride. The compound was also prepared from prasanthaline (**33**) by treatment with DDQ and subsequent deacetylation of the product with 10% aqueous methanolic KOH solution (Scheme 4).[35]



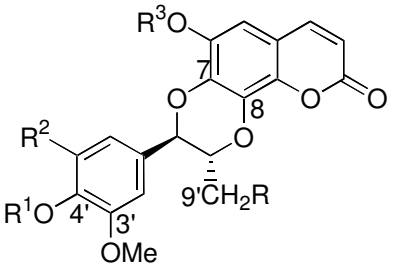
Scheme 4. Semisynthesis of the aryl naphthalide lignan **35.**[35]

Two novel lignans, jatrodien (**39**)[31] and gossypidien (**40**)[32] each containing two olefinic trans (E)-double bonds, were isolated from *Jatropha gossypifolia*. The ^{1}H NMR spectrum of **39** showed the appearance of two deshielded olefinic protons at C-7 and C-7' at δ 7.76 and 7.72 (1H each, s). On the other hand, in the ^{1}H NMR spectrum of **40** the two deshielded olefinic protons appeared at δ 7.82 (s 2H, H-7 and H-7') The compound **40** is symmetrical and the ^{13}C NMR spectrum revealed the signals for only 11 carbons present in the half of the molecule. The total syntheses of **39** and **40** involving Stobbe condensation were also accomplished. These two compounds represent the intermediates in Haworth's biosynthetic scheme for the formation of lignans.[31,32]

Jatrolactol (**42**)[34] is an another new lignan of *Jatropha gossypifolia*. The ^{1}H and ^{13}C NMR spectral data suggested that the compound is structurally related to jatrophan (**31**). They possess two 1,3,4–trisubstituted aromatic rings, a trisubstituted olefinic double bond, one methylenedioxy and two methoxy groups. The difference is that jatrophan contains a lactone ring while jatrolactol a lactol group at C-9. The H-9 in jatrolactol (**42**) appeared at δ 5.32 in its ^{1}H NMR spectrum and C-9 at δ 108.4 in the ^{13}C NMR spectrum. The β-configuration of the hydroxyl at C-9 was settled from its 2D NMR spectra. The compound on oxidation with Fétizon's reagent yielded jatrophan (**31**) and thus its structure was confirmed.[34]

2.3 Coumarinolignans

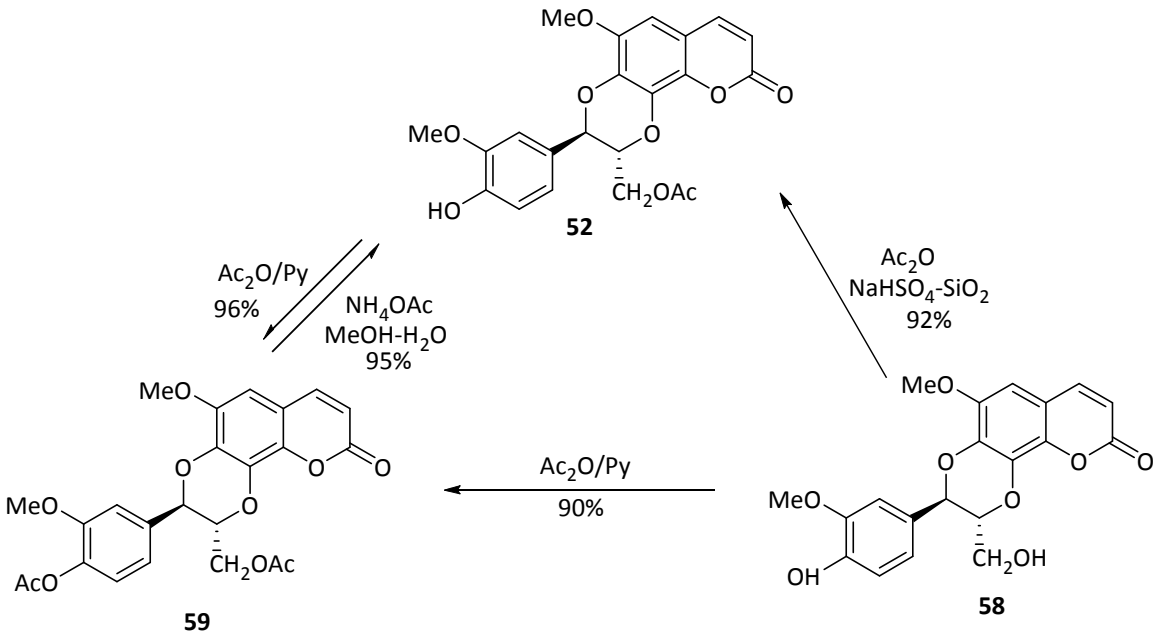
Coumarinolignans contain a coumarin moiety linked with a phenyl propanoid unit through a 1,4-dioxane bridge. From *Jatropha gossypifolia* five new coumarinolignans, viz., venkatasin (**52**),[37] jatrorins A (**53**) and B (**54**),[38] jatrocins A (**55**) and B (**56**)[39] along with the known compounds, propacin (**57**)[40] and cleomiscosin A (**58**)[41] were isolated (Figure 2).



52, R=OAc, R^1=R^2=H, R^3=Me
53, R=OH, R^1=R^2= R^3=H
54, R=OH, R^1= Me, R^2= R^3=H
55, R= R^1= R^2= R^3= H
56, R= R^1=H, R^2=OMe, R^3=Me
57, R= R^1= R^2=H, R^3=Me
58, R=OH, R^1=R^2=H, R^3=Me
59, R=OAc, R^1=Ac, R^2=H, R^3=Me

Figure 2. Structures of the coumarinolignans of *Jatropha gossypifolia* and of cleomiscosin A diacetate (**59**).

Venkatasin (**52**) is the first acetylated coumarinolignan obtained from nature.[37] The structure of the compound was established from its ^{1}H and ^{13}C NMR spectral data. The compound contains a hydroxyl group (phenolic) at C-4′and an acetoxy group at C-9′. A direct comparison of the ^{1}H NMR spectrum of venkatasin (**52**) with that of authentic cleomiscosin A (**58**) showed that the signals for H_2- 9' of **52** resonated at δ 4.42 – 4.28 (m) but the signals for these two protons of **58** appeared at δ 3.81 (1H, dd, *J* =13.0, 2.0 Hz and 3.56 (1H, dd, *J* =13.0, 3.0 Hz). This observation suggested to place the acetoxy group (δ2.04, 3H, s in the ^{1}H NMR spectrum and δ 20.62 in the ^{13}C NMR spectrum) at C-9' of venkatasin (**52**). The acetylated product of **52** was found to be identical to cleomiscosin A diacetate (**59**). The regioselective acetylation of the hydroxyl group (alcoholic) at C-9′ of cleomiscosin A (**58**) using $NaHSO_4{\cdot}SiO_2$ catalyst[42] afforded venkatasin (**52**), thus confirming the structure of the latter as 9′-*O*-acetyl cleomiscosin A. Venkatasin (**52**) was also directly synthesised[43] from cleomiscosin A diacetate (**59**) by applying NH_4OAc as the catalyst for selective deprotection of aromatic acetate group (Scheme 5).



Scheme 5. Interconversions of coumarinolignans of *Jatropha* species.[42,43]

Other two cleomiscosin A derivatives, jatrorins A (**53**) and B (**54**) were isolated from *Jatropha gossypifolia*. Jatrorin A (**53**) is 6-*O*-demethyl derivative while jatrorin B (**54**) is 6-*O*-demethyl-4´-*O*-methyl derivative of cleomiscosin A (**58**). The structures of these two compounds, **53** and **54** were clearly derived from detailed analysis of their ^{1}H and ^{13}C NMR spectra.[38]

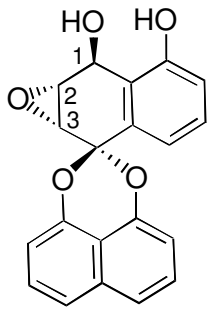
From the whole plant of *Jatropha gossypifolia* two new propacin analogues, jatrocins A (**55**) and B (**56**) were also isolated. Jatrocin A was characterized as 6-*O*-demethylpropacin and jatrocin B as 5´-methoxy-propacin.[39]

Cleomiscosin A (**58**) was also obtained from *Jatropha multifida*.[16-18] The compound is known to possess cytotoxic and anti-HIV properties. It also exhibits immunomodulatory and liver protective activities.[44]

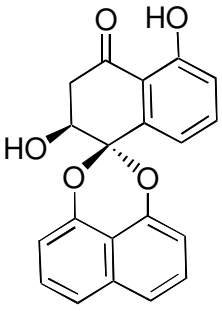
2.4 Other constituents

Besides diterpenes, lignans and coumarinolignans some other constituents were also isolated from the investigated *Jatropha* species.

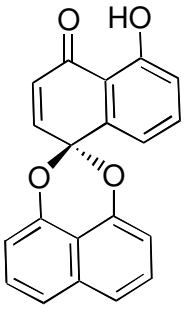
Three deoxypreussomerins, palmarumycins JC 1 (**60**), JC 2 (**61**) and CP 1 (**62**), were isolated from a collection of the stem of *Jatropha curcas* (Table 1).[45] The first two compounds, **60** and **61** are new deoxypreussomerins while **62** is a known compound. All these compounds were characterized from spectral evidence. The ^{1}H NMR spectrum of JC 1 showed the signals at δ 3.56 (1H, dd, *J* = 4.5, 3.0 Hz), 3.64 (1H, d, *J* = 4.5 Hz) and 5.47 (1H, d, *J* = 3.0 Hz) corresponding to three oxymethine protons. The ^{13}C NMR spectrum also revealed the signals of three oxymethine carbons (δ 53.3, 50.5 and 60.4). The ^{1}H–^{1}H COSY and HMBC experiments suggested the presence of a hydroxy group at C-1 and an epoxide ring at C-2, C-3. The β-configurations of HO-1, H-2 and H-3 were settled by comparision of the spectral data and optical property of JC-1 with those of related compounds. The X-ray crystallographic analysis of **60** was also performed.[45] The hydroxyl group at C-1 of JC-1 was oxidised to a keto group in JC-2 (**61**). The ^{1}H NMR spectrum of JC-2 showed the signal of a chelated –OH group (δ 12.27, 1H, brs). The spectrum also indicated that C-2 was not oxygenated but C-3 is oxygenated. A hydroxyl group was placed at this position. The β-configuration of this hydroxyl group was suggested from the observation that JC-2 showed almost opposite optical rotation to that of the compound of similar system having α-OH group at C-3.



60



61



62

The isolation of these compounds, **60**, **61** and **62** in reasonable quantities indicated their presence as constituents and excluded their occurrence in any endophytic fungus present in the plant. These compounds were examined to possess impressive antibacterial activity against the organism *Staphylococcus aureus.* Their activity was comparable to that of the standard compound, penicillin G.[45]

From the roots of *Jatropha gossypifolia* the phenolic compounds, tetradecyl-(*E*)-ferulate (**63**), ferulic acid (**64**) and fraxetin (**65**) were obtained (Figure 3).[46] The first compound (**63**) is a new natural product and the other

two compounds (**64** and **65**) were reported for the first time from the species. Compound **63** was also obtained from *Jatropha curcas* and *Jatropha multifida*.[13–15]

A new minor imidazole derivative, 4-butyl-2-chloro-5-formyl-1*H*-imidazole (**66**) was obtained from *Jatropha curcas*.[47] The molecule is structurally impressive as it is associated with various functionalities. Three functionalities (-Cl, -Bu and -CHO) were placed at C-2, C-4 and C-5 respectively on the basis of its 1D and 2D NMR spectral data. The compound was found to possess significant antibacterial activity. This imidazole derivative was also isolated from *Jatropha multifida*. [14]

Jatropha curcas also yielded 2-methoxyanthraquinone (**67**), scopoletin (**68**), 3-O-(*Z*)-coumaroyl oleanolic acid (**69**) and tomentin (**70**),[15] and *Jatropha multifida* yielded pictolinarigenin (**71**)[16,17] and fraxidin (**72**).[13]

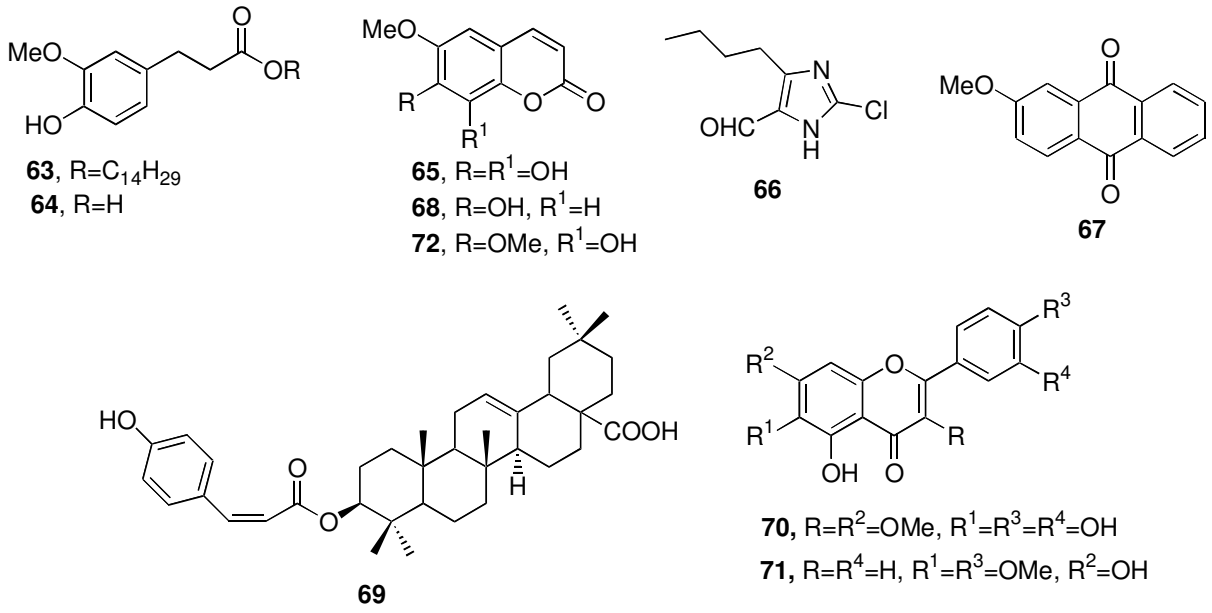


Figure 3. Structures of miscellaneous constituents of *Jatropha* species.

3. Conclusion

In the present article we have described our phytochemical investigation on three *Jatropha* species *viz*., *Jatropha gossypifolia. Jatropha curcas* and *Jatropha multifida* which resulted in the isolation of a large number of their chemical constituents. These constituents are of different types: diterpenes, lignans, coumarino-lignans, flavones, coumarins, simple phenolics etc. Some of the compounds possess novel interesting molecular structures. Various chemical transformations and synthetic studies on several constituents were performed. Antibacterial and anticancer activities of some of the isolates are impressive.

Acknowledgements

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