

Genus *Lantana*: chemical aspects and biological activities

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Abstract: Species of the genus *Lantana*, belonging to the family Verbenaceae, is among the various species studied scientifically. These species are mainly native to the tropical and subtropical regions of the Americas. Currently, they are present in various countries, where they are often grown as ornamental plants. For decades, species of *Lantana* have been of great interest for phytochemical, biological and pharmacological studies, which have been recently intensified. The components isolated from different species of *Lantana* cited in the literature constitute the focus of this review. Information ethnopharmacology of *Lantana*, as well as the activities of their different phytochemicals are discussed. In this review, it was observed that the genus *Lantana* has been widely studied in relation to its phytochemical components and terpenoids, flavonoids and phenylpropanoids are the more common secondary metabolites in *Lantana*. All these aspects, considered in this review, allow an evaluation of the ethnopharmacological potential of *Lantana* for the utilization of the large biomass of these plants.

Introduction

Although the curative potential of plants has been known for a long time, only in the last decades has there been an intensified interest from the pharmaceutical industry, institutes and research groups in chemical and pharmacological studies of plants in search of knowledge with respect to their therapeutic properties and to new active principles (Novais et al., 2003).

Among the innumerable species studied scientifically are the species of the genus *Lantana*, which belong to the family Verbenaceae. The family Verbenaceae comprises one hundred genus and about 2600 species distributed in tropical and subtropical regions around the world (Joly, 1993). Many genera belonging to this family appear to possess various biological and pharmacological properties, among which the genus *Lantana* has been widely studied.

The genus *Lantana* was described by Linnaeus in 1753 and contained seven species, six from South America and one from Ethiopia (Munir, 1996). The term *Lantana* probably comes from the old Latin name of the genus *Viburnum*, which resemble a little in leaves and inflorescence. Taxonomically, this genus shows difficult classification, because normally, the species are not stable, hybridization is very widespread, the shape of the inflorescence changes with age, and color of the flowers varies with age and maturity (Ghisalbert, 2000).

Due to this characteristic, species of this *Lantana* have been much studied with respect to cytogenetics within the family Verbenaceae.

Lantana is mainly native to the tropical and subtropical Americas, but a few taxa are originally from tropical Asia and Africa; currently, they occur in approximately fifty countries with a very large number of species and subspecies. This genus includes herbaceous and shrubby plants, which can reach a height of over 2 m, where they are very often planted for decorative purposes due to the beauty of their flowers (Joly, 1993).

Some species of *Lantana*, mainly varieties of *L. camara*, are responsible for clinical pictures of secondary photosensitization, a disease of seasonal nature, related to clinical episodes in ruminants, with the majority of cases of intoxication occurring in the winter (Ranjhan & Pathak, 1992). The principal factor for intoxication to occur is related to feeding on pastures with the presence of some toxic variety of *L. camara*. The toxic effects of the leaves have usually been attributed to a series of pentacyclic triterpenes, in which lantadenes A and B are typical members (Sharma et al., 1988). The nontoxic species do not contain these lantadenes or possess them in low quantities.

Species of genus *Lantana* are plants practically immune to attack by herbivores, due to the presence of a great diversity of secondary metabolites (Kohli et al., 2006). They also have anti-rheumatic, stimulant



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and sudorific properties, and are used to treat bronchopulmonary disorders, and some species are utilized in biological control as a pesticide (Ghisalbert, 2000; Dua et al., 2003; 2010). Organic extracts and essential oils of *Lantana* have shown a wide variety of biological and pharmacological activities.

Phytochemical studies conducted by various research groups have resulted in the isolation of various constituents from different parts of species of the genus *Lantana*. Therefore, the aim of the present review is to provide a complete compilation of the phytochemical components of *Lantana* recorded in the literature. The botanical classification and ethnopharmacology of *Lantana* have been included.

The aim of this review was to summarize the main chemical, biological and pharmacological aspects of species of the genus *Lantana*, indicating when possible the compounds identified in each species, as well as the biological and/or pharmacological actions described in the literature. We believe that this review can be used in innovative applications and investigative incentives in the search for more details of the plants of this important botanical genus.

Material and Methods

The study was conducted using data obtained from a bibliographic search, using mainly the science search engines “Web of Science”, “Science@direct”, “Pubmed”, “Scielo” and “Scirus”, with findings updated up to April 2011. The following key words were utilized, alone or in combinations: *Lantana*, chemical constituents, biological or pharmacological activities, and natural products.

Occurrence and distribution

This and the next section will cover only species of *Lantana* that were more studied with respect to phytochemical properties and biological and pharmacological activities. *Lantana hispida* Kunth is a widely distributed Mexican ornamental plant (Jiménez-Arellanes et al., 2007). *Lantana cujabensis* Schauer is a shrub that grows at an elevation of up to 1000 m and is found in both the Amazon and Andean forests of South America (Brako & Zarucchi, 1993). *Lantana viburnoides* var. *kisi* is indigenous to Tanzania (Innocent et al., 2008). *Lantana lilacina* Desf., a 50- to 120 cm tall native Brazilian shrub, which produces pink or purple flowers, is regarded as a weed and an ornamental plant (Lorenzi, 2002; Pereira et al., 2008). *Lantana salvifolia* Jacq is found growing wild from Ethiopia to the Congo (Ouamba et al., 2006). *Lantana indica* Roxb., a wild perennial shrub, native to India, is regarded both as notorious weed and a popular ornamental garden plant (Kumar et

al., 2010). *Lantana montevidensis* Briq., a shrub native to Brazil and Uruguay, is popularly known as “cambara”, and it was introduced to many countries as an ornamental plant (Nagão et al., 2002; Barreto et al., 2010). *Lantana achyranthifolia* Desf. is a shrub found in the Americas (Hernández et al., 2005). *Lantana tiliifolia* Cham. is the most common *Lantana* in Brazil, but it is not considered a weed because it is controlled by a complex of natural predators including insects and fungi (Rwangabo et al., 1988). *Lantana canescens* Kunth is listed as a rare species in Florida, U.S.A. and is used mainly for xeriscaping, as it is drought-tolerant. Efforts are being made to propagate this species in residential areas by local gardening groups (Sena Filho et al., 2010). *Lantana trifolia* L. is a small shrub that occurs in all regions of Brazil (Julião et al., 2010). *Lantana fucata* Lindl. and *Lantana radula* Sw. are small shrubs distributed in Southeast Brazil and grow in higher elevation fields (Julião et al., 2009). *Lantana camara* L., commonly known as wild sage, is the most widespread species of this genus, growing luxuriantly at elevations up to 2000 m in tropical, sub-tropical and temperate regions (Ghisalberti, 2000).

Traditional application

L. hispida Kunth traditionally is used in Mexico to treat tuberculosis, bronchitis, cough, cold, asthma, stomach ailments, kidney pain and diarrhea (Jiménez-Arellanes et al., 2007). In Bolivia, leaves of *L. cujabensis* Schauer are crushed between fingers and sniffed to treat head colds (Okunade & Lewis, 2004). *L. viburnoides* var *kisi* has ethnobotanical importance in Tanzania, where it is used to repel mosquitoes and in traditional medicine for stomach ache relief (Innocent et al., 2008). *L. lilacina* Desf. it has been used in traditional medicine to treat colds and bronchitis (Lorenzi, 2002). *L. salvifolia* Jacq is a plant widely used in the Congo as an herbal tea. The decoction of the leaves is used against typhoid fever (Ouamba et al., 2006). *L. indica* Roxb. is used as a sudorific, intestinal antiseptic and diaphoretic, and in treatment of tetanus, rheumatism and malaria in Indian medicine (Ghisalberti, 2000). A previous ethnobotanical study showed that *L. achyranthifolia* Desf. was recognized as one of the most important among the 44 species used for the treatment of gastrointestinal illnesses in Zapotitlan de las Salinas, Puebla (Mexico). Infusions of the aerial part of these plants have been used by native people to treat this type of disorder (Hernández et al., 2003). *L. canescens* Kunth is used mainly for xeriscaping, as it is drought-tolerant. In Northeast Brazil, the local community in Timbauba city (Pernambuco State) uses this species as an analgesic (Sena Filho et al., 2010). The concoction from the leaves of *L. radula* Sw. is used in Brazil as a tea to treat coughs, influenza and bronchitis (Sena Filho et al., 2010). *Lantana trifolia* L. is popularly used to treat colds, flu and sore

throat (Silva et al., 2005). *L. fucata* Lindl. is a Brazilian species used in folk medicine for the treatment of respiratory disorders (Julião et al., 2009). *L. camara* has been used for the treatment of various human ailments, such as ulcers, malaria, influenza, tumors, swellings, bilious fever, eczema eruptions, stomach ache, toothache and as antiseptic for wounds (Ghisalberti, 2000). *L. montevidensis* Briq. have been used in folk medicine for the same purposes as *L. camara* (Nagão et al., 2002).

Chemical constituents

The search for new chemotherapeutic compounds in species of the genus *Lantana* has led to the isolation of various constituents with varying structural patterns and belonging mainly to the terpenoids, flavonoids, phenylethanoid glycosides, furanophenanthroquinones, iridoid glycosides and steroids. Phytochemical investigations have reported many constituents and are classified as described in the following subsections.

Monoterpenes and sesquiterpenes

Various studies have reported the chemical composition of essential oils of species of the genus *Lantana* collected in different places and origins. By means of surveys, it was observed that the essential oil of aerial parts obtained by hydrodistillation shows a yield of 0.01-0.7%. Various constituents, namely mono- and sesquiterpenes, were identified in the essential oils of *Lantana*, but with a greater predominance of the latter (Oliveira et al., 2008; Dambolena et al., 2010). Cited among the common major constituents identified in the oils are the sesquiterpenes, caryophyllene, β -caryophyllene, *E* and *Z*-caryophyllene, isocaryophyllene,

caryophyllene oxide, caryophyllene epoxide, germacrene D and bicyclogermacrene (Sena Filho et al., 2010). The caryophyllene isomers (*Z*, *E* and β -caryophyllene) were present among the main constituents of the essential oil of *L. camara* from Northeast Brazil at different times of day (Sousa et al., 2010a). In the seasonal evaluation of the essential oil of *L. camara* from Madagascar, the concentration of β -caryophyllene was found to be consistently high throughout the year, independent of sampling seasons (Randrianalijaona et al., 2005).

Triterpenoids

Studies of different *Lantana* species have shown that a total of seventy-four triterpenoids were isolated from this genus (Table 1). The structure of the different types of triterpenoids are shown in structures 1-74 and given below. The compounds 1-69 possess a pentacyclic triterpene structure, while the compounds 70-74 possess a tetracyclic triterpene structure. Most of the compounds, namely 1-39, are based on the oleanane nucleus. Among the triterpenes with an oleanane nucleus, nineteen (1-19) have a common skeleton (Skeleton-I), ten (25-34) have Skeleton-II, two compounds (36, 37) have a common skeleton (Skeleton-III), and the other two (38, 39) have Skeleton-IV, while others have individual structures. Several other compounds (40-64) incorporate an ursane nucleus. Three compounds (40-42) have Skeleton-V, five compounds (43-47) have a common skeleton (Skeleton-VI), and ten compounds (54-63) have Skeleton-VII, while others have individual structures. Compounds (66-69) possess a lupane nucleus. Among them, three compounds (65-67) have Skeleton-VIII and others have individual structures. Five compounds (70-74) incorporate a euphane nucleus. Four of them (70-73) possess Skeleton-IX.

Table 1. Triterpenes from the genus *Lantana* informed in the literature.

Compound	Species (parts used)	Reference
lantadene A (1)	<i>L. camara</i> (leaves, ¹ stems, ² roots ³)	Louw (1948, 1949); ¹ Sastry & Mahadevan (1963); ¹ Hart et al. (1976a, 1976b); ^{1,2} Sharma et al. (1987); ¹ Sharma & Dawra (1991); ¹ Pan et al. (1993a); ¹ Begum et al. (1995); ¹ Wollenweber et al. (1997); ¹ Sharma et al. (1999); ¹ Kong et al. (2005); ¹ Litaudon et al. (2009) ¹
lantadene B (2)	<i>L. camara</i> (leaves, ¹ stems ²)	Sharma et al. (1987); ¹ Hart et al. (1976a, 1976b); ^{1,2} Sharma & Dawra (1991); ¹ Pan et al. (1993a); ¹ Inada et al. (1995); ¹ Kong et al. (2005); ¹ Litaudon et al. (2009) ¹
lantadene C (3)	<i>L. camara</i> var. <i>aculeate</i> (leaves, ¹ stems ²)	Johns et al. (1983a); ^{1,2} Sharma et al. (1990); ¹ Sharma & Dawra (1991); ¹ Sharma et al. (1992); ² Litaudon et al. (2009) ¹
lantadene D (4)	<i>L. camara</i> (leaves)	Sharma et al. (1990); Sharma & Dawra (1991); Sharma et al. (2000)
22 β -angeloyloxy-3 β -hydroxyolean-12-en-28-oic acid (5)	<i>L. camara</i> (leaves, ¹ stems ²), <i>L. hispida</i> (aerial parts ³)	Hart et al. (1976a, 1976b); ^{1,2} Sharma & Dawra (1991); ¹ Jiménez-Arellanes et al. (2007) ³
22 β -dimethylacryloyloxy-3 β -hydroxyolean-12-en-28-oic acid (6)	<i>L. camara</i> (leaves, ¹ stems, ² roots ³)	Hart et al. (1976a, 1976b); ^{1,2} Sharma & Dawra (1991); ¹ Pan et al. (1993b) ³

22 β -hydroxyoleanonic acid (7)	<i>L. camara</i> (leaves)	Pan et al. (1993a); Sharma et al. (2000); Sharma & Sharma (2006)
oleanonic acid (8)	<i>L. camara</i> (aerial parts, ¹ leaves, ² stems ³), <i>L. indica</i> (roots ⁴)	Hart et al. 1976b); ^{2,3} Singh et al. (1990); ⁴ Begum et al. (1995); ¹ Huang & Huang, (2004); ³ Misra et al. (2007); ³ Ghosh et al. (2010) ²
oleanolic acid (9)	<i>L. camara</i> (aerial parts, ¹ leaves, ² stems, ³ roots ⁴), <i>L. hispida</i> (aerial parts ⁵), <i>L. indica</i> (roots ⁶)	Hart et al. (1976b); ^{2,3} Singh et al. (1990); ⁶ Begum et al. (1995); ¹ Siddiqui et al. (1995); ¹ Misra et al. (1997); ³ Lai et al. (1998); ³ Jiménez-Arellanes et al. (2007); ⁵ Misra et al. (2007); ³ Banik & Pandey (2008); ⁴ Shikha et al. (2010) ⁴
oleanolic acid acetate (10)	<i>L. camara</i> (leaves)	Begum et al. (2003)
oleanenoic acid (11)	<i>L. hispida</i> (aerial parts)	Jiménez-Arellanes et al. (2007)
3 β -24-dihydroxyolean-12-en-28-oic acid (12)	<i>L. indica</i> (roots)	Singh et al. (1990)
24-formyl-3-oxoolean-12-en-28-oic acid (13)		Singh et al. (1991)
22 β -hydroxy-3-oxoolean-12-en-28-oic acid (14)	<i>L. camara</i> (leaves, ¹ stems, ² roots ³)	Pan et al. (1993b); ³ Hart et al. (1976a, 1976b) ^{1,2}
24-hydroxy-3-oxoolean-12-en-28-oic acid (15)	<i>L. camara</i> (leaves, ¹ stems ²), <i>L. indica</i> (aerial parts ³)	Hart et al. (1976a e 1976b); ^{1,2} Singh et al. (1989a); ³ Mahato & Kundu (1994) ^{1,2}
icterogenin (16)	<i>L. camara</i> (leaves, ¹ stems ²)	Pan et al. (1993a); ¹ Lai et al. (1998); ² Wollenweber et al. (1997); ¹ Litaudon et al. (2009) ¹
22 β -dimethylacryloyloxy-24-hydroxy-3-oxo-olean-12-en-28-oic acid (17)	<i>L. camara</i> (leaves)	Litaudon et al. (2009)
22 β - <i>O</i> -angeloyl-oleanoic acid (18), 22 β - <i>O</i> -senecioid-oleanoic acid (19)	<i>L. camara</i> (roots)	Pan et al. (1993b)
hederagenin (20), 25-hydroxy-3-oxoolean-12-en-28-oic acid (21)		Singh et al. (1996)
21,22 β -epoxy-3 β -hydroxyolean-12-en-28-oic methyl ester (22)		Misra & Laatsch (2000)
camarin (23), lantanone (24)	<i>L. camara</i> (leaves)	Begum et al. (2006, 2008b)
22 β -tigloyloxylantanolic acid (25)		Mahato et al. (1994)
camarilic acid (26)	<i>L. camara</i> (aerial parts)	Begum et al. (1995)
lantanic acid (27)	<i>L. camara</i> L. (leaves, ¹ stems, ² roots ³), <i>L. cujabensis</i> (leaves ⁴)	Pan et al. (1993b); ³ Barre et al. (1997); ¹ Siddiqui et al. (1995); ¹ Saleh et al. (1999); ² Okunade & Lewis (2004) ⁴
lantanic acid (28)	<i>L. camara</i> (aerial parts, ¹ roots ²)	Barua et al. (1966; 1971); ¹ Pan et al. (1993b); ² Siddiqui et al. (1995); ¹ Begum et al. (2003, 2008b) ¹
camaric acid (29)	<i>L. camara</i> (aerial parts ¹ , stems ²) <i>L. viburnoides</i> var <i>kisi</i> (roots ³) <i>L. cujabensis</i> Schauer (leaves ⁴)	Siddiqui et al. (1995) ¹ ; Begum et al. (2000) ¹ ; Misra et al. (1997) ² ; Saleh et al. (1999) ² ; Okunade & Lewis (2004) ⁴ ; Innocent et al. (2008) ³
camarolic acid (30), lantrigloylic acid (31)	<i>L. camara</i> (leaves)	Begum et al. (2008b)
22 β -dimethylacryloyloxy-lantanolic acid (32)		Barre et al. (1997)
3 β ,25-epoxy-3 α -hydroxy-22 β -isobutanoyloxyolean-12-eno-28-ic acid (33)	<i>L. cujabensis</i> (leaves)	Okunade & Lewis (2004)
ursangilic acid (34), lancamaric acid (35), camangeloyl acid (36)	<i>L. camara</i> (aerial parts)	Begum et al. (2003)
camarinin (37)	<i>L. camara</i> (aerial parts, ¹ stems ²)	Huang & Huang (2004); ² Begum et al. (2008b) ¹
lantadienone (38), camaradienone (39)	<i>L. camara</i> (aerial parts)	Begum et al. (2008c)
pomonic acid (40), 3 β ,19 α -dihydroxy-ursan-28-oic acid (41)	<i>L. camara</i> (roots)	Misra & Laatsch (2000)

19 α -hydroxy ursolic (42), lantaiursolic acid (43)		Pan et al. (1993b)
ursonic acid (44)	<i>L. camara</i> (aerial parts)	Begum et al. (1995)
lantacin (45)		Begum et al. (2006, 2008b)
pomolic acid (46)	<i>L. camara</i> (aerial parts, ¹ stems, ² roots ³)	Pan et al. (1993b); ³ Siddiqui et al. (1995); ¹ Huang & Huang (2004); ² Begum et al. (2008b) ¹
ursolic acid (47)	<i>L. indica</i> (roots)	Singh et al. (1990)
24-hydroxy-3-oxours-12-en-28-oic acid (48)	<i>L. trifolia</i> (leaves)	Rwangabo et al. (1988)
3,24-dioxo-urs-12-en-28-oic acid (49)	<i>L. camara</i> (leaves)	Yadav & Tripathi (2003)
α -amyrin (50)	<i>L. camara</i> (leaves, flowers and stems)	Ahmed et al. (1972a; 1972b)
methyl 3-oxours-late (51)	<i>L. camara</i> (leaves)	Barua et al. (1969)
methyl-24-hydroxy-3-oxoursolate (52)	<i>L. indica</i> (aerial parts)	Singh et al. (1989a)
camaranoic acid (53)	<i>L. camara</i> (aerial parts)	Begum et al. (2008a)
lantoic acid (54)		Begum et al. (2008b); Roy & Barua (1985)
camarinic acid (55)	<i>L. camara</i> (leaves, ¹ stems ²)	Siddiqui et al. (1995) ¹ ; Barre et al. (1997) ¹ ; Saleh et al. (1999) ²
22 β -dimethylacryloyloxylantic acid (56)	<i>L. camara</i> (leaves)	Mahato et al. (1994)
lantic acid (57)		Barua et al. (1969); Saleh et al. (1999)
camaracinic acid (58)	<i>L. camara</i> (aerial parts)	Begum et al. (1995)
methyl ursoxylate (59), ursoxy acid (60), ursethoxy acid (61), methylcamaralate (62), camariolic acid (63), camarolide (64)		Begum et al. (2003)
betulinic acid (65)	<i>L. camara</i> (aerial parts, ¹ stems ²), <i>L. viburnoides</i> var. <i>kisi</i> (roots ³)	Begum et al. (1995) ¹ ; Hart et al. (1976b) ^{1,2} ; Lai et al. (1998) ² ; Innocent et al. (2008) ³
betulonic acid (66)	<i>L. camara</i> (leaves, ¹ stems ²)	Hart et al. (1976a, 1976b) ^{1,2} ; Lai et al. (1998) ²
betulonol (67)	<i>L. camara</i> (stems)	Lai et al. (1998)
lantabetulic acid (69)	<i>L. camara</i> (leaves and stems)	Hart et al. (1976a, 1976b)
lupeol analogue (68)	<i>L. camara</i> L. (leaves)	Hart et al. (1976a)
euphane lactone B (70-71), euphane lactone C (73-73), euphane lactone A (74)		O'Neill et al. (1998)

Flavonoids

Thirty-three flavonoids (compounds **75-107**), all based on a flavone or flavonol nucleus, have been isolated from *Lantana* species (Table 2). Two flavonoids (**75, 76**) have Skeleton-X and the flavonoids (**77-107**) have a common skeleton (Skeleton-XI).

Phenylethanoid glycosides

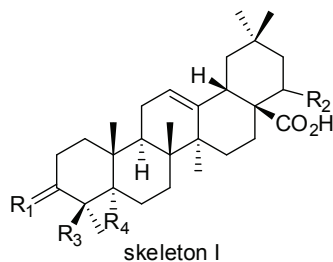
Sixteen phenylethanoid (**108-123**) have been reported from different *Lantana* species and are listed in Table 3. Among them, two compounds (**108, 109**) have Skeleton XII, five compounds (**112-116**) have a common skeleton (Skeleton-XIII), two (**117, 118**) have Skeleton-XIV, and four compounds (**120-123**) have a common skeleton (Skeleton-XV), whereas three others have individual structures.

Furanonaphthoquinones

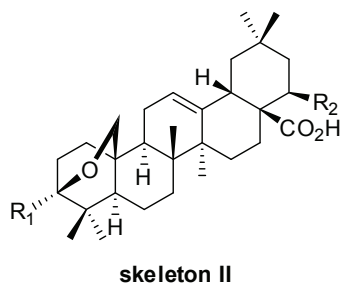
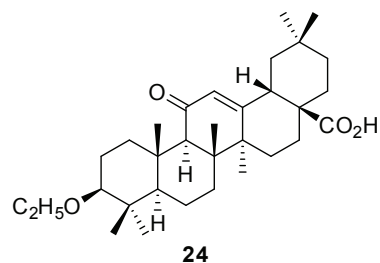
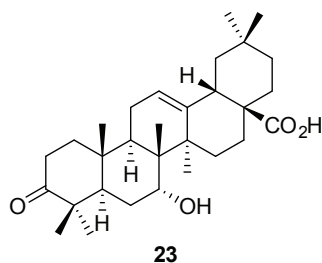
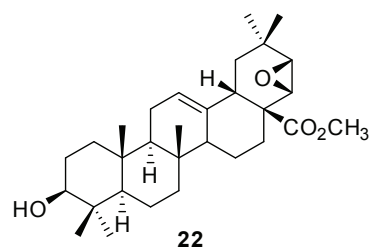
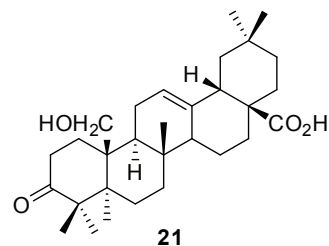
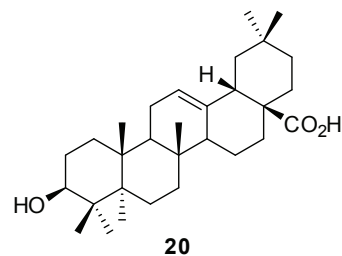
The structures of ten (**124-133**) furanonaphthoquinones isolated from *Lantana* are shown in Table 4. Among the furanonaphthoquinones, two compounds (**124, 125**) have Skeleton XVI, but two compounds (**126, 127**) have a common skeleton (Skeleton-XVII) and six others have individual structures.

Iridoid glycosides

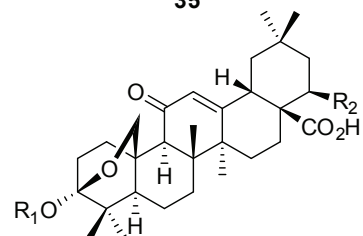
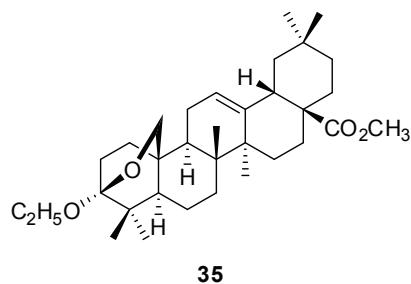
Eight iridoid glycosides isolated from *Lantana* species are characterized by the structures **134-141** (Table 5). Three compounds (**134-136**) have Skeleton XVIII, three other compounds (137-139) have a common skeleton (Skeleton-XIX) and two (140, 141) have individual structures.



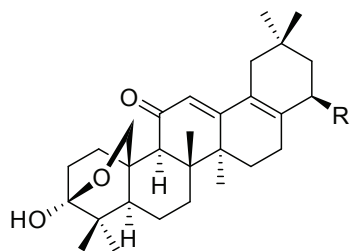
- 1 $R_1=O$; $R_2=\beta\text{-OCOC}(\text{CH}_3)=\text{CHCH}_3$; $R_3=\text{CH}_3$; $R_4=\text{H}$
- 2 $R_1=O$; $R_2=\beta\text{-OCOCH}=\text{C}(\text{CH}_3)_2$; $R_3=\text{CH}_3$; $R_4=\text{H}$
- 3 $R_1=O$; $R_2=\beta\text{-OCOCH}(\text{CH}_3)\text{CH}_2\text{CH}_3$; $R_3=\text{CH}_3$; $R_4=\text{H}$
- 4 $R_1=O$; $R_2=\beta\text{-OCOCH}(\text{CH}_3)_2$; $R_3=\text{CH}_3$; $R_4=\text{H}$
- 5 $R_1=\text{H}$, $\beta\text{-OH}$; $R_2=\beta\text{-OCOC}(\text{CH}_3)=\text{CHCH}_3$; $R_3=\text{CH}_3$; $R_4=\text{H}$
- 6 $R_1=\text{H}$, $\beta\text{-OH}$; $R_2=\beta\text{-OCOCH}=\text{C}(\text{CH}_3)_2$; $R_3=\text{CH}_3$; $R_4=\text{H}$
- 7 $R_1=O$; $R_2=\beta\text{-OH}$; $R_3=\text{CH}_3$; $R_4=\text{H}$
- 8 $R_1=O$; $R_2=R_4=\text{H}$; $R_3=\text{CH}_3$
- 9 $R_1=\text{H}$, $\beta\text{-OH}$; $R_2=R_4=\text{H}$; $R_3=\text{CH}_3$
- 10 $R_1=\text{H}$, OCOCH_3 ; $R_2=R_4=\text{H}$; $R_3=\text{CH}_3$
- 11 $R_1=\text{H}$, OCOCH_3 ; $R_2=\text{OCOC}(\text{CH}_3)=\text{CHCH}_3$; $R_3=\text{CH}_3$; $R_4=\text{H}$
- 12 $R_1=\text{H}$, OCOCH_3 ; $R_2=\text{H}$; $R_3\text{-CH}_2\text{OH}$; $R_4\text{-CH}_3$
- 13 $R_1=O$; $R_2=\text{H}$; $R_3=\text{CHO}$; $R_4=\text{CH}_3$
- 14 $R_1=O$; $R_2=\beta\text{-OH}$; $R_3=R_4=\text{CH}_3$
- 15 $R_1=O$; $R_2=\text{H}$; $R_3=\text{CH}_2\text{OH}$; $R_4=\text{CH}_3$
- 16 $R_1=O$; $R_2=\beta\text{-OCOC}(\text{CH}_3)=\text{CHCH}_3$; $R_3=\text{CH}_2\text{OH}$; $R_4=\text{H}$
- 17 $R_1=O$; $R_2=\beta\text{-OCOCH}=\text{C}(\text{CH}_3)_2$; $R_3=\text{CH}_2\text{OH}$; $R_4=\text{CH}_3$
- 18 $R_1=\text{H}$, H ; $R_2=\beta\text{-OCOC}(\text{CH}_3)=\text{CHCH}_3$; $R_3=\text{CH}_3$; $R_4=\text{H}$
- 19 $R_1=\text{H}$, H ; $R_2=\beta\text{-OCOCH}=\text{CHCH}_3$; $R_3=\text{CH}_3$; $R_4=\text{H}$



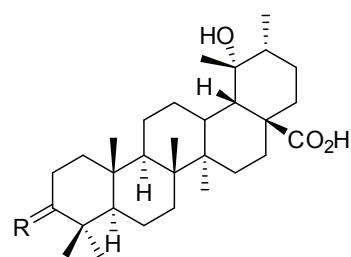
- 25 $R_1=\alpha\text{-OH}$; $R_2=\beta\text{-OCOC}(\text{CH}_3)=\text{CHCH}_3$
- 26 $R_1=\alpha\text{-OCH}_3$; $R_2=\beta\text{-OCOC}(\text{CH}_3)=\text{CHCH}_3$
- 27 $R_1=\alpha\text{-OH}$; $R_2=\beta\text{-OCOCH}=\text{C}(\text{CH}_3)_2$
- 28 $R_1=\alpha\text{-OH}$; $R_2=\text{H}$
- 29 $R_1=\alpha\text{-OH}$; $R_2=\beta\text{-OCOC}(\text{CH}_3)=\text{CHCH}_3$
- 30 $R_1=\alpha\text{-OH}$; $R_2=\beta\text{-OCOC}(\text{CH}_3)=\text{CHCH}_3$
- 31 $R_1=\alpha\text{-OH}$; $R_2=\beta\text{-OCOCH}=\text{C}(\text{CH}_3)_2$
- 32 $R_1=\beta\text{-OH}$; $R_2=\beta\text{-OCOCH}=\text{C}(\text{CH}_3)_2$
- 33 $R_1=\alpha\text{-OH}$; $R_2=\beta\text{-OCOCH}(\text{CH}_3)_2$
- 34 $R_1=\alpha\text{-OCH}_2\text{CH}_3$; $R_2=\beta\text{-OCOC}(\text{CH}_3)=\text{CHCH}_3$



- 36 $R_1=\text{CH}_3$; $R_2=\text{OCOC}(\text{CH}_3)=\text{CHCH}_3$
- 37 $R_1=\text{H}$; $R_2=\text{OCOCH}(\text{CH}_3)_2$

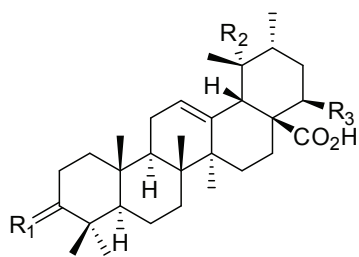


38 R= β -OCOCH(CH₃)₂
39 R=H



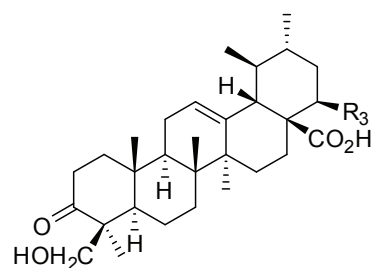
skeleton V

40 R=O
41 R=H, β -OH
42 R=H, H

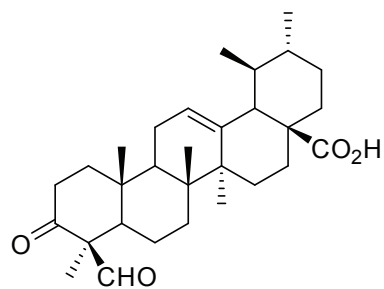


skeleton V

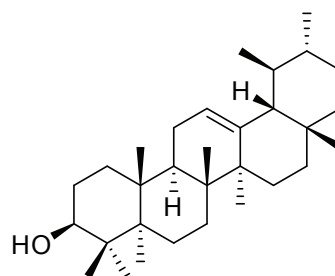
43 R₁=OCOCH₂CH(CH₃)₂; R₂=OH; R₃=H
44 R₁=O; R₂=R₃=H
45 R₁=H, β -OH; R₂=OH; R₃= β -OCOCH=C(CH₃)₂
46 R₁=H, β -OH; R₂=OH; R₃=H
47 R₁=H, β -OH; R₂=R₃=H



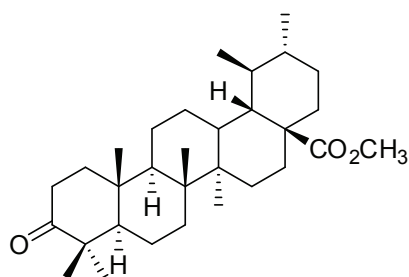
48



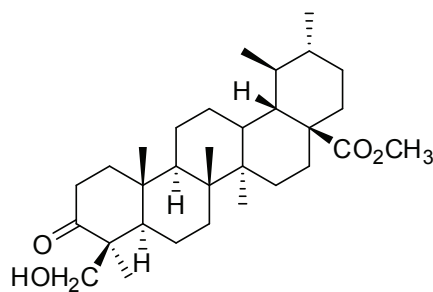
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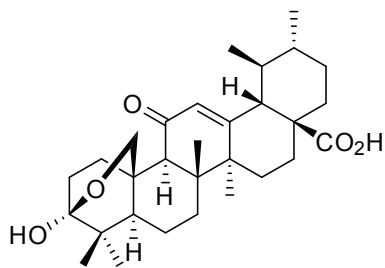
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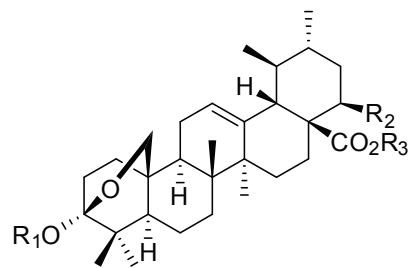
51



52

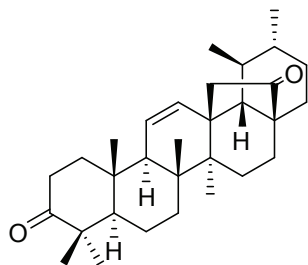


53

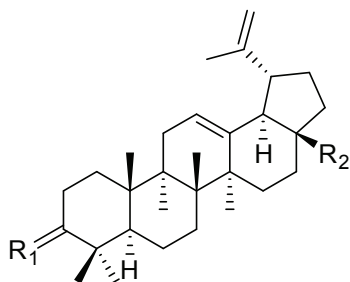


skeleton VII

- 54 $R_1=H$; $R_2=\beta-OH$; $R_3=H$
 55 $R_1=H$; $R_2=\beta-OCOCH_3$; $R_3=H$
 56 $R_1=H$; $R_2=\beta-OCOCH=C(CH_3)_2$; $R_3=H$
 57 $R_1=R_2=R_3=H$
 58 $R_1=CH_3$; $R_2=\beta-OCOC(CH_3)=CHCH_3$; $R_3=H$
 59 $R_1=CH_3$; $R_2=H$; $R_3=CH_3$
 60 $R_1=CH_3$; $R_2=R_3=H$
 61 $R_1=C_2H_5$; $R_2=R_3=H$
 62 $R_1=H$; $R_2=\beta-OCOCH_3$; $R_3=CH_3$
 63 $R_1=CH_3$; $R_2=\beta-OCOCH=C(CH_3)_2$; $R_3=H$

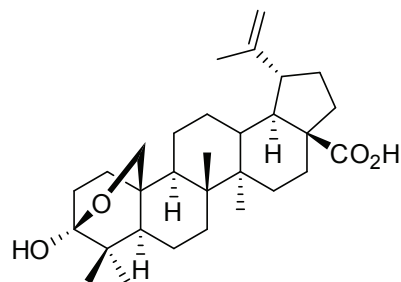


64

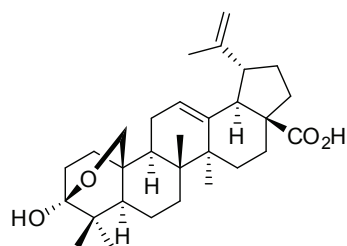


skeleton VIII

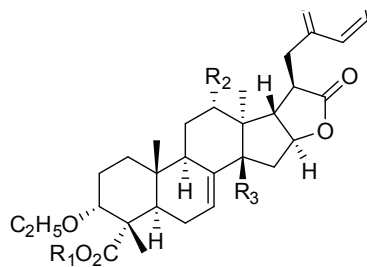
- 65 $R_1=H$, $\beta-OH$; $R_2=CO_2H$
 66 $R_1=O$; $R_2=CO_2H$
 56 $R_1=O$; $R_2=CH_2OH$



68

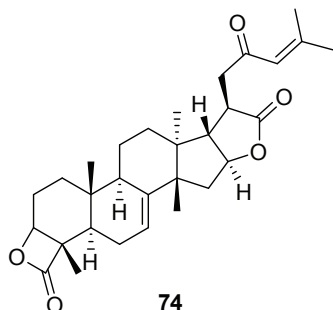


69



skeleton IX

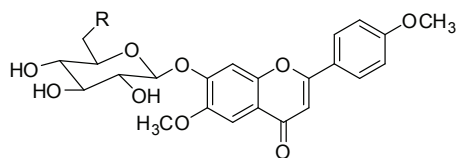
- 70 $R_1=R_2=H$; $R_3=CH_3$
 71 $R_1=H$; $R_2=OH$; $R_3=CH_3$
 72 $R_1=\beta-D-Glu$; $R_2=OH$; $R_3=CH_2OH$
 73 $R_1=\beta-D-Glu$; $R_2=OH$; $R_3=CH_2OC_2$



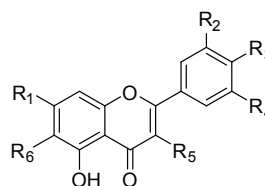
74

Table 2. Flavonoids from the genus *Lantana* informed in the literature.

Compound name	Species (parts used)	Reference
lantanoside (75), linaroside (76),	<i>L. camara</i> (aerial parts)	Begum et al. (2000)
luteolin (77), 7,3',4'-trimethoxyluteolin (78), 7,3'-dimethoxyluteolin (79), 5,6-dihydroxy-7,3',4'-trimethoxyflavone (80), 5,6,3'-trihydroxy-7,4'-dimethoxyflavone (81)	<i>L. montevidensis</i> (leaves)	Wollenweber et al. (1997)
3-methoxy-quercetin (82), 3-methoxy-3,7-dimethoxy-quercetin (83), 3,7,4'-trimethoxy-quercetin (84)	<i>L. camara</i> (leaves)	
scutellarein-7- <i>O</i> - β -D-apiofuranoside (85), apigenin-7- <i>O</i> - β -D-apiofuranosil-(1 \rightarrow 2)- β -D-apiofuranosideo (86), 5,6,4',5'-tetrahydroxi-7,3'-dimetoxiflavona (87), scutellarein-7- <i>O</i> - β -D-glucopiranoside (88), sorbifolin (89)	<i>L. trifolia</i> (leaves)	Julião et al. (2010)
apigenin (90), cirsilineol (91), eupatorin (92), hispidulin (93), 5,4'-dihydroxy-6,7,3',5'-tetramethoxyflavone (94), 5,3',4'-trihydroxy-6,7,5'-trimethoxyflavone (96), 5,6,4'-trihydroxy-7,3',5'-trimethoxyflavone (96)	<i>L. montevidensis</i> (leaves)	Nagão et al. (2002)
umuhengerin (97)	<i>L. tiliifolia</i> (leaves ¹), <i>L. trifolia</i> L. (leaves ²)	Johns et al. (1983b) ¹ ; Rwangabo et al. (1988) ²
cirsiliol (98)	<i>L. montevidensis</i> (leaves ¹), <i>L. fucata</i> (leaves ²)	Nagão et al. (2002) ¹ ; Julião et al. (2009) ²
eupafolin (99)		
penduletin (100), crysosplenetin (101)	<i>L. achyranthifolia</i> (roots)	Dominguez et al. (1983)
pectolarigenin (102), pectolarin (103),	<i>L. camara</i> (leaves)	Juang et al. (2005)
camaraside (104)		Pan et al. (1993a)
camaraside (105)		Mahato et al. (1994)
salvigenin (106), 5,3',5'-trihydroxy-6,7,4'-trimethoxyflavone (107)	<i>L. fucata</i> (leaves)	Julião et al. (2009)



75 R=OH
76 R=OC₂H₅

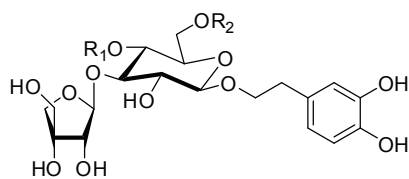
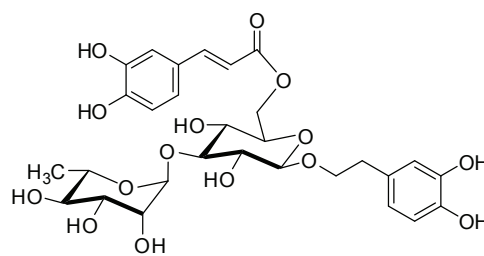


skeleton XI

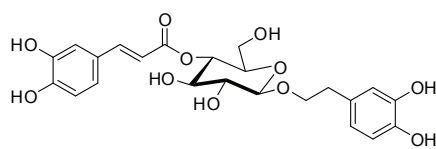
- 77 R₁=R₃=R₄=OH; R₂=R₅=R₆=H
78 R₁=R₃=R₄=OCH₃; R₂=R₅=R₆=H
79 R₁=OCH₃; R₂=R₄=R₅=R₆=H; R₃=OH
80 R₁=R₂=R₃=OCH₃; R₄=R₅=H; R₆=OH
81 R₁=R₃=OCH₃; R₂=R₆=OH; R₄=R₅=H
82 R₁=R₃=R₄=OH; R₂=R₆=H; R₅=OCH₃
83 R₁=R₅=OCH₃; R₂=R₆=H; R₃=R₄=OH
84 R₁=CH₃; R₂=R₆=H; R₃=R₆=OCH₃; R₄=OH
85 R₁=O- β -D-Api; R₂=R₄=R₅=H; R₃=R₆=OH
86 R₁=O- β -D-Api-(1 \rightarrow 2)- β -D-Api; R₂=R₄=R₅=R₆=H; R₃=OH
87 R₁=R₂=OCH₃; R₃=R₄=R₆=OH; R₅=H
88 R₁=O- β -D-Glu; R₂=R₄=R₅=H; R₃=R₆=OH
89 R₁=OCH₃; R₂=R₄=R₅=HR₃=R₆=OH
90 R₁=R₃=OH; R₂=R₄=R₅=R₆=H
91 R₁=R₂=R₄=R₆=OCH₃; R₃=OH; R₅=H
92 R₁=R₃=R₆=OCH₃; R₂=R₅=H; R₄=CH₃
93 R₁=R₄=R₆=OCH₃; R₂=R₃=OH; R₅=H
94 R₁=R₃=R₆=OCH₃; R₂=OH; R₄=R₅=H
95 R₁=R₂=R₄=OCH₃; R₃=R₆=OH; R₅=H
96 R₁=R₃=OH; R₂=R₄=R₅=H; R₆=OCH₃
97 R₁=R₂=R₃=R₄=R₆=OCH₃; R₅=H
98 R₁=R₆=OCH₃; R₂=R₅=H; R₃=R₄=OH
99 R₁=R₂=R₃=OH; R₄=R₅=H; R₆=OCH₃
100 R₁=R₅=R₆=OCH₃; R₂=H; R₃=R₄=OH
101 R₁=R₂=R₅=R₆=OCH₃; R₃=R₄=OH
102 R₁=OH; R₂=R₄=R₅=H; R₃=R₆=OCH₃
103 R₁=O- β -D-Glu-(1 \rightarrow 2)- β -D-Glu; R₂=R₄=R₅=H; R₃=R₆=OCH₃
104 R₁=R₆=OCH₃; R₂=R₄=R₆=H; R₃=O- β -D-Glu
105 R₁=O- β -D-Glu; R₂=R₄=H; R₃=R₆=OCH₃; R₅=OH
106 R₁=R₃=R₆=OCH₃; R₂=R₄=R₅=H
107 R₁=R₃=R₆=OCH₃; R₂=R₄=OH; R₅=H

Table 3. Phenylethanoid glycosides from the genus *Lantana* informed in the literature.

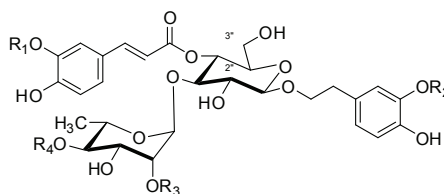
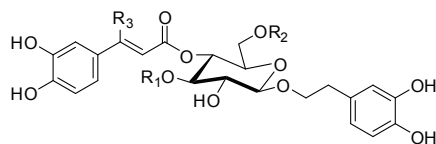
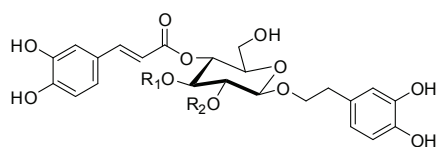
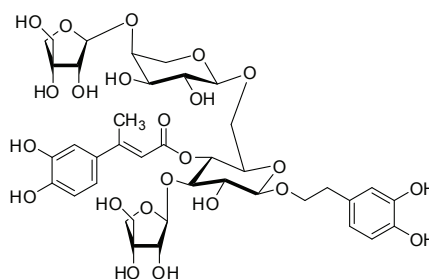
Compound name	Species (parts used)	Reference
calceolarioside E (108). isonuomioside A (109)	<i>L. camara</i> (leaves ¹), <i>L. radula</i> (roots ²)	Taoubi et al. (1997) ¹ ; Sena Filho et al. (2009) ²
isoverbascoside (110), derhamnosylverbascoside (111), lantanaside (112)	<i>L. camara</i> L. (leaves)	Taoubi et al. (1997) Mahato et al. (1994)
verbascoside (113)	<i>L. camara</i> (leaves ¹ , stems ²), <i>L. lilacina</i> (leaves ³), <i>L. radula</i> (roots ⁴), <i>L. trifolia</i> (leaves ⁵)	Herbert et al. (1991) ¹ ; Taoubi et al. (1997) ¹ ; Syah et al. (1998) ² ; Takeda et al. (1998) ¹ ; Pereira et al. (2008) ³ ; Sena Filho et al. (2009) ⁴ ; Julião et al. (2010) ⁵
betonioside F (114)	<i>L. trifolia</i> (leaves)	Julião et al. (2010)
samioside (115)	<i>L. radula</i> (roots ¹), <i>L. trifolia</i> (leaves ²)	Sena Filho et al. (2009) ¹ ; Julião et al. (2010) ²
martynoside (116)	<i>L. camara</i> (leaves and stems) ¹ , <i>L. trifolia</i> (leaves ²)	Syah et al. (1998) ¹ ; Julião et al. (2010) ²
arenarioside (117)	<i>L. canescens</i> Kunth (roots)	Sena Filho et al. (2009)
alyssonoside (118), raduloside (119)	<i>L. radula</i> Sw. (roots)	
parvifloroside A (120), fucatoside A (121), fucatoside C (122), fucatoside B (123)	<i>L. fucata</i> (leaves)	Julião et al. (2009)

**skeleton XII**108 R₁=Caffeoyl; R₂=H109 R₁=H; R₂=Caffeoyl

110



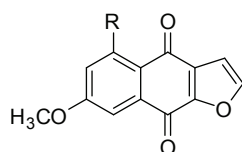
111

**skeleton XIII**112 R₁=R₂=R₃=H; R₄=H 2''Z113 R₁=R₂=R₃=H; R₄=H 2''E114 R₁=R₂=H; R₃=β-D-Api; R₄=H 2''E115 R₁=R₂=R₃=H; R₄=β-D-Api 2''E116 R₁=R₂=CH₃; R₃=H; R₄=H 2''E**skeleton XIV**117 R₁=α-L-Rha; R₂=β-D-Api; R₃=CH₃118 R₁=α-L-Rha; R₂=β-D-Xyl; R₃=H**skeleton XV**120 R₁=H; R₂=α-L-Rha121 R₁=H; R₂=β-D-Api122 R₁=α-L-Api; R₂=α-L-Api123 R₁=β-D-Api; R₂=β-D-Xyl

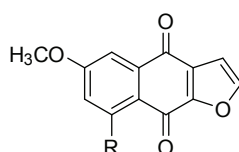
119

Table 4. Furanonaphthoquinones from the genus *Lantana* informed in the literature.

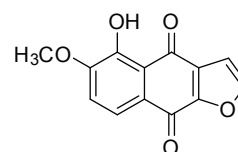
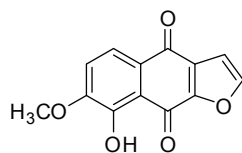
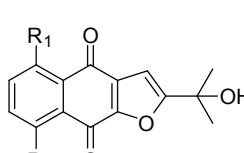
Compound name	Species (parts used)	Reference
6-methoxydiodantunezone (124), 6-methoxy-8-hydroxy-diodantunezone (125), 7-methoxydiodantunezone (126), 7-methoxy-5-hydroxy-isodiodantunezone (127), 7-methoxy-8-hydroxy-diodantunezone (128), 6-methoxy-7-hydroxy-diodantunezone (129), 8-hydroxy-13-(methyl-dimethyl-hydroxy)-diodantunezone (130), 5-hydroxy-13-(methyl-dimethyl-hydroxy)-diodantunezone (131)	<i>L. camara</i> (roots), <i>L. achyranthifolia</i> (roots)	Abeygunawardena et al. (1991)
diodantunezone (132), isodiodantunezone (133)	<i>L. camara</i> (roots ¹), <i>L. achyranthifolia</i> (roots ²)	Abeygunawardena et al. (1991) ^{1,2} ; Dominguez et al. (1983) ²

**skeleton XVI**

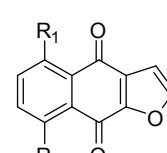
124 R=H
125 R=OH

**skeleton XVII**

126 R=H
127 R=OH

**128****129**

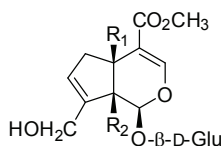
130 R₁=OH; R₂=H
131 R₁=H; R₂=OH



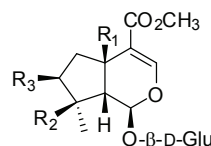
132 R₁=H; R₂=OH
133 R₁=OH; R₂=H

Table 5. Iridoid glycosides from the genus *Lantana* informed in the literature.

Compound name	Species (parts used)	Reference
geniposide (134)	<i>L. camara</i> (roots)	Miyokawa et al. (1992); Pan et al. (1992)
theviridoside (135)		Pan et al. (1992)
theveside (136)	<i>L. camara</i> (leaves ¹ , stems ² , roots ³)	Ford & Bendall (1980) ^{1,2} ; Pan et al. (1992) ³
lamiide (137), durantoside (138)	<i>L. viburnoides</i> var <i>kisi</i> (roots)	Rimpler & Sauerbier (1986)
8-epiloganin (139), lamiridoside (140), shanzhiside methyl ester (141)	<i>L. camara</i> L. (roots)	Pan et al. (1992)

**skeleton XVIII**

134 R₁=H; R₂=H
135 R₁=OH; R₂=H
136 R₁=OH; R₂=OH

**skeleton XIV**

137 R₁=R₂=R₃=OH
138 R₁=R₂=OH; R₃=*t*-cinnamoyl
139 R₁=R₂=H; R₃=OH

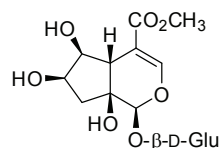
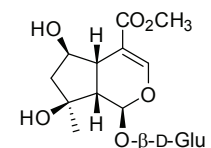
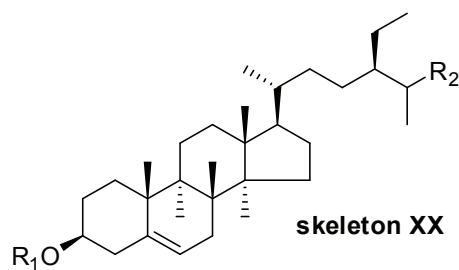
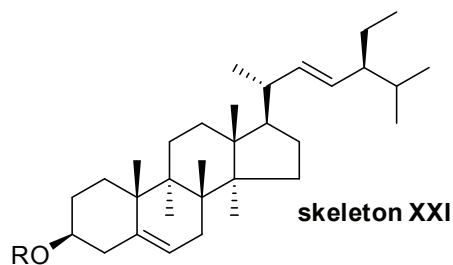
**140****141**

Table 6. Steroids from the genus *Lantana* informed in the literature.

Compound name	Species (parts used)	Reference
β -sitosterol (142)	<i>L. camara</i> (leaves ¹ , flowers ² , stems ³)	Ahmed et al. (1972a, 1972b) ^{1,2,3} ; Misra et al. (1997) ³
β -sitosterol-3- <i>O</i> - β -D-glucopyranoside (143)	<i>L. camara</i> (aerial parts)	Begum et al. (2003)
β -sitosterole (144), β -sitosterol-3- <i>O</i> - β -D-D-glicoside (145)	<i>L. camara</i> (stems)	Misra et al. (1997)
β -sitosterol acetate (146), stigmasterol acetate (147)	<i>L. camara</i> (leaves)	Ahmed et al. (1972b)
stigmasterol (148), 3 β -hydroxystigmast-5-en-7-one (149), campesterol (150)		Begum et al. (2008b)
lancomarone (151)		Siddiqui et al. (1995)
cholesterol (152)	<i>L. indica</i> (leaves)	Goyal & Kumar (1984)



- 142** R₁=H; R₂=CH₃
143 R₁=D-Glu; R₂=CH₃
144 R₁=R₂=H
145 R₁=D-Glu; R₂=H
146 R₁=COCH₃; R₂=CH₃



- 147** R=CHOCH₃
148 R=H

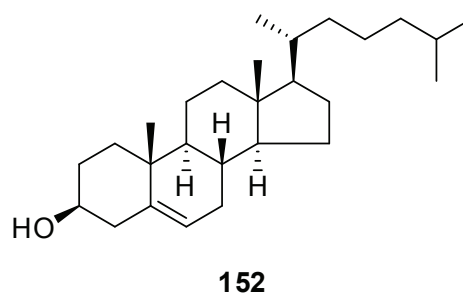
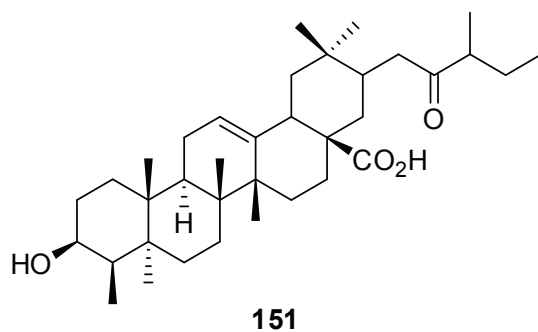
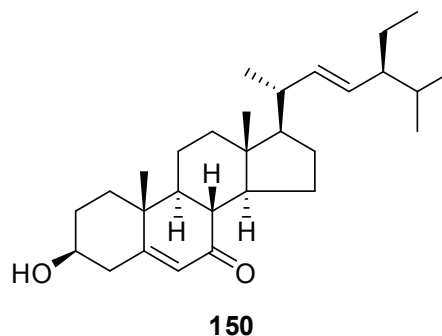
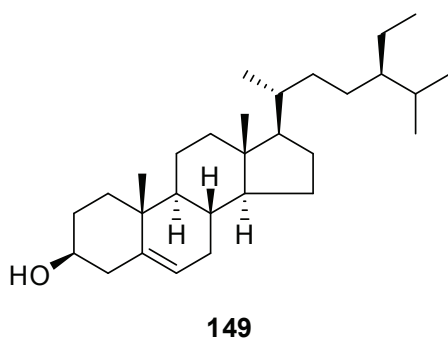
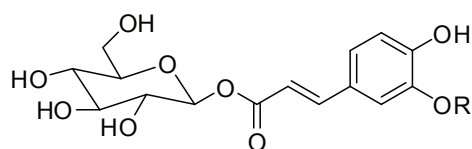
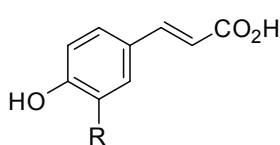
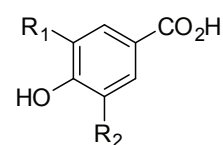
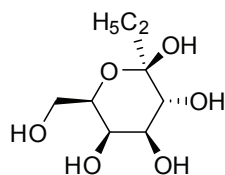
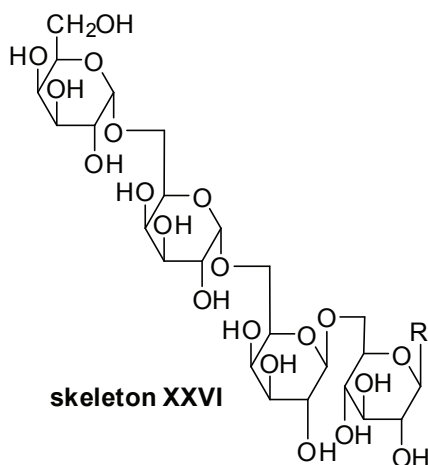
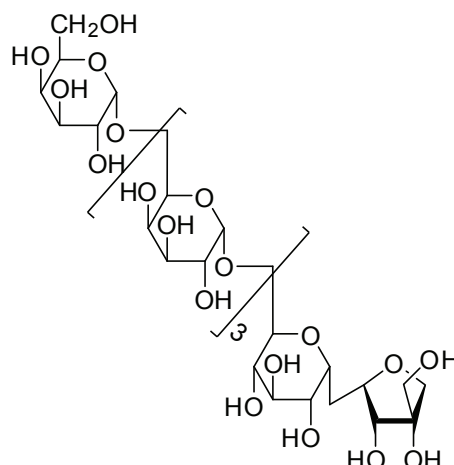
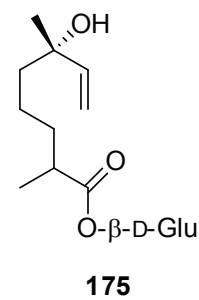
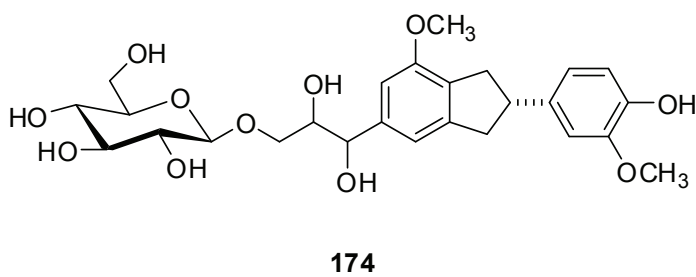
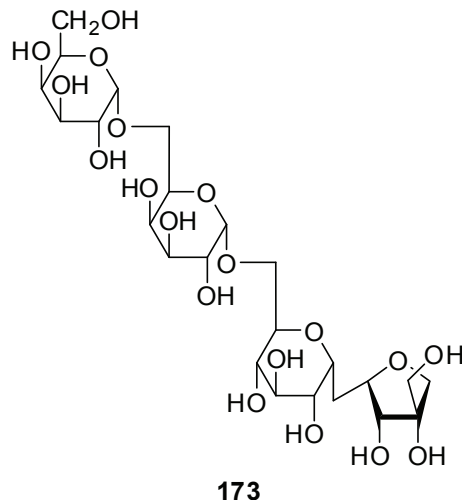
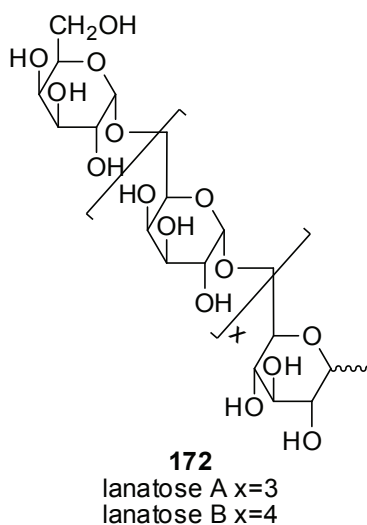


Table 7. Miscellaneous compounds from the genus *Lantana* informed in the literature.

Compound name	Species (parts used)	Reference
1-(3-glucosyloxy-4-hydroxycinnamyl) glucose (153)	<i>L. camara</i> var. <i>hybrida</i> (flowers)	Imperato (1967)
1-caFFEylrhamnose (154)		Imperato et al. (1975)
<i>p</i> -coumaric acid (155)	<i>L. camara</i> (leaves)	Jain et al. (1989)
caffeic acid (156), vanillic acid (157), protocatechuic acid (158), 4-hydroxybenzoic acid (159)	<i>L. trifolia</i> (leaves)	Julião et al. (2010)
ethyl- β -D-galactoside (160), octanoic acid (161)	<i>L. camara</i> (stems)	Misra et al. (1997)
cotriacontanoic acid (162), tetracosanoic acid (163), palmitic acid (164), docosanoic acid (165), octadecanoic acid (166)	<i>L. camara</i> (aerial parts)	Begum et al. (2003)
arachidic acid (167), 1-triacontanol (168)	<i>L. camara</i> (leaves, flowers and stems)	Ahmed et al. (1972a; 1972b)
ajugose (169), verbascose (170), verbascotetrose (171), lantanose A e B (172), stachyose (173)	<i>L. camara</i> (roots)	Pan et al. (1992)
radulignan (174)	<i>L. radula</i> (roots)	Sena Filho et al. (2009)
2- <i>trans</i> -2,6-dimethyl-6-hydroxyocta-2,7-dienoic acid (175)	<i>L. lilacia</i> (leaves)	Takeda et al. (1998)

**skeleton XXII****153** R=H**154** R= β -D-Glu**skeleton XXIII****155** R=H**156** R=OH**skeleton XXIV****157** R₁=H; R₂=CH₃**158** R₁=H; R₂=OH**159** R₁=H; R₂=H**160**CH₃(CH₂)_nCO₂H**161** n = 6**162** n = 30**163** n = 22**164** n = 14**165** n = 20**166** n = 16**167** n = 18CH₃(CH₂)₂₈CH₂OH**168****skeleton XXVI****169** R= α -(β -fructofuranosyl)**170** H**171**



Steroids

Ten steroidal compounds (**142-152**) have been reported from different *Lantana* species (Table 6) and all have the tetracyclic hydrocarbon derivative of the steroid nucleus. Among the steroids, five steroids (**142-146**) have a common skeleton (Skeleton-XX), and two (**147, 148**) have Skeleton-XXI, while three others have individual structures.

Miscellaneous compounds

Hydroxycinnamic acid-sugar derivatives, oligosaccharides, different types of organic acids and other compounds with varying structural patterns have been summarized under this category. They are characterized by the structures **153-175** (Table 7). Among the miscellaneous compounds, two compounds (**153, 154**) have Skeleton XXII, two other compounds (**155, 156**) have a common skeleton (Skeleton-XXIII), three (**157-159**) have Skeleton-XXIV, seven (**161-167**) have a common skeleton (Skeleton-XXV), and two (**169, 170**) have Skeleton-XXVI, whereas others have individual structures.

Activities attributed to the genus *Lantana*

Species of the genus *Lantana* are of great interest for phytochemical, biological and pharmacological studies. Phytochemical investigations have established the presence of terpenoids, phenylpropanoids and flavonoids, as the main class components with relevant biological activities (Ghisalbert, 2000). Studies on the biological and pharmacological activities of phytoconstituents isolated from the genus *Lantana*, as well as works related to the activities of extracts and/or essential oils are reported below.

Anthelmintic activity (anti-filarial activity and nematocidal activity)

Begum et al. (2008b) isolated seven compounds from the aerial parts of *L. camara* L., and tested them for nematocidal activity against the root-knot nematode *Meloidogyne incognita*. The lantanolic acid (**28**), pomolic acid (**46**), and lantoic acid (**54**) showed 100% mortality at 1.0% concentration after 24 h, while camarin (**23**), camarinin (**37**), lantacin (**45**) and ursolic acid (**47**) exhibited 100% mortality at 1.0% concentration after 48

h. Lantanoside (75), linaroside (76) and camaric acid (29) isolated from the aerial parts of *L. camara* L. showed 90, 85 and 100% mortality, respectively, at 1.0% concentration (Begum et al., 2000). All results were comparable with the conventional nematicide furadan (100% mortality at 1.0% concentration after 24 h).

In another study, extracts of stems and isolated compounds from seedlings of *L. camara* L. were assessed for anti-filarial activity *in vitro* and *in vivo* (Misra et al., 2007). The crude extract at 1 g/kg for five days, administered orally, killed 43.05% of the adult *Brugia malayi* parasites and sterilized 76% of surviving female worms in the rodent model *Mastomys coucha*. A 34.5% adulticidal activity along with sterilization of 66% of female worms could be demonstrated using the chloroform fraction. In the same study, the extract was also found to be effective against a subcutaneous rodent filariid *Acanthocheilonema viteae* maintained in *M. coucha*, where it exerted strong microfilaricidal (95.04%) and sterilization (60.66%) efficacy with mild macrofilaricidal action. Two compounds, oleanonic acid (8) and oleanolic acid (9), isolated from the hexane and chloroform fractions showed LC100 of 31.25 and 62.5 µg/mL, respectively, against *B. malayi in vitro*.

McGaw & Eloff (2005) assessed the anthelmintic activity of acetone extracts of *L. rugosa* Thunb. leaves against the free-living test nematode *Caenorhabditis elegans*. *L. rugosa* showed notable anti-nematode effects at a concentration of 1 mg/mL. Extracts of *L. camara* L. with organic solvents were found to cause significant mortality *in vitro* of *Meloidogyne javanica* in mungbean, while aqueous and methanolic extracts demonstrated greater inhibition compared to ethyl acetate or hexane extracts, indicating that active principles were polar in nature (Ali et al., 2001).

Anti-protozoal activity (anti-plasmodial, anti-malarial and leishmanicidal activity)

Valadeu et al. (2009) showed that the ethanolic extract from *Lantana* sp. has low activity against *Plasmodium falciparum* (FCR3), a chloroquine-resistant strain, (IC₅₀ 17.5±6.0 µg/mL). In the same study, the extract displayed interesting leishmanicidal activities (IC₅₀ 10±2.1 µg/mL). The experiments were conducted on axenic amastigotes of *Leishmania amazonensis* (strain MHOM/BR/76/LTB-012).

The dichloromethane extract leaf from *L. camara* L. (pink flower) was analyzed in one study and showed very promising activity when tested *in vitro* against cultures of chloroquine-sensitive (3D7) and chloroquine-resistant (W2) strains of *P. falciparum* (IC₅₀ 8.7±1.0 µg/mL and 5.7±1.6 µg/mL, respectively) (Jonville et al., 2008). The dichloromethane extract from *L. camara* L. (orange flower) also showed promising activity (IC₅₀

14.1±8.4 µg/mL and 12.2±2.9 µg/mL, respectively). In the same study, the dichloromethane extract (50 mg/kg) was investigated *in vivo* against *Plasmodium berghei* infected mice, and exhibited only 5% inhibition. Another *in vivo* study reported 8% inhibition of the parasite (Hakizamungu & Weri, 1988). On the other hand, the aqueous extract of at doses of 250 and 500 mg/kg/day were tested *in vivo* in rats infected with *P. berghei*; the extract showed partial anti-malarial activity at the doses tested, reducing parasite load by 25 and 49%, respectively (Carrillo-Rosario & Diaz de Ramirez, 2006).

Katuura et al. (2007) screened extracts of the aerial part of *L. trifolia* L. for *in vitro* antiplasmodial activity against wild-type strains of *P. falciparum* using the nitro-tetrazolium blue-based lactate dehydrogenase assay. The petroleum ether extract of *L. trifolia* showed moderate antiplasmodial activity (13.2 µg/mL). Clarkson et al. (2004) reported that an extract of *L. camara* L. leaves demonstrated *in vitro* anti-plasmodial activity against a chloroquine-sensitive strain (D10) with an IC₅₀ value of 11 µg/mL. The non-polar extract of root-bark also displayed high anti-malarial activity against the multidrug resistant K1 strain (Weenen et al., 1990). An ethanol extract of *L. cujabensis* Schauer showed lower activity when tested against chloroquine-resistant and chloroquine-sensitive strains of *P. falciparum* (IC₅₀ 14.7 µg/mL and 23.3 µg/mL, respectively) (Desjardins, 1979).

Toxicity activity in vitro

One study reported that essential oils from the leaves of *L. camara* L. and *Lantana* sp. were evaluated to toxicity activity using *Artemia salina* larvae. The oils exhibited significant activities with LC₅₀ of 14 µg/mL for *L. camara* and 24 µg/mL for *Lantana* sp. (Costa et al., 2009). In other study, the essential oil of *L. camara* L. leaves showed an LC₅₀ value of 10 µg/mL (Sonibare & Effiong, 2008). The potential toxicity of the acetone extract of *L. rugosa* Thunb. leaves was also investigated and the results showed that *L. rugosa* exhibited toxicity with an LC₅₀ of 0.69 mg/mL (McGaw & Eloff, 2005).

Fatore et al. (2002) studied the extracts of leaves, twigs, stems and roots of *L. camara* L., which were partitioned and analyzed for activity in the brine-shrimp lethality test. The active fractions yielded lantadene A (1), oleanonic acid (8), and oleanolic acid, which were very toxic to brine shrimp larvae. The three compounds were not lethal to *Spodoptera littoralis* Biosduval (Lepidoptera: Noctuidae), *Clavigralla tomentosicollis* Stal. (Hemiptera: Coreidae) and *Aphis craccivora* Koch (Homoptera: Aphididae) when tested at 5000 µg/mL. Lantadene A, however, suppressed the fecundity of *C. tomentosicollis* at this concentration.

Insecticidal activity

A wide variety of extracts/essential oils of *Lantana* and their constituents possess varying degrees of pest-controlling properties. A recent study investigated the insecticidal activity of essential oil from the leaves of *L. camara* L. against mosquito vectors (Dua et al., 2010). LD50 values of the oil were 0.06, 0.05, 0.05, 0.05 and 0.06 mg/cm² while LD90 values were 0.10, 0.10, 0.09, 0.09 and 0.10 mg/cm² against *Aedes aegypti*, *Culex quinquefasciatus*, *Anopheles culicifacies*, *An. fluviatilis* and *An. Stephensi*, respectively. KDT50 of the oil were 20, 18, 15, 12, and 14 min, and KDT90 values were 35, 28, 25, 18, 23 min against *Ae. aegypti*, *quinquefasciatus*, *An. culicifacies*, *An. fluviatilis* and *An. stephensi*, respectively, on 0.208 mg/cm² impregnated paper. Dharmagadda et al. (2005) showed that 200 ppm oil of *L. camara* L. produced 100% mortality in *C. quinquefasciatus* larvae in 15 min.

The essential oils from leaves of *L. camara* L. and *L. montevidensis* Briq. were tested for larvicidal activity against *A. aegypti* larvae at the third developmental stage (Costa et al., 2010). The results showed that both species have larvicidal potential: *L. camara* with LC50 of 42.3±0.85 µg/mL, and *L. montevidensis* with LC50 of 117±0.5 µg/mL. The essential oil also showed insecticidal activity against adults of *Sitophilus oryzae* L. (LC50 0.22 mg/cm²) and *Tribolium castaneum* (LC50 0.22 mg/cm²), and revealed low fumigant toxicity against *S. oryzae* (LC50 29.47 µL/L) and against *T. castaneum* (LC50 47.68 µL/L) (Mohamed & Abdelgaleil, 2008).

Kumar & Maneemegalai (2008) investigated the methanol and ethanol extracts of leaves and flowers of *L. camara* L. and showed mosquito larvicidal activity against 3rd and 4th instar larvae of the mosquito species *A. aegypti* and *C. quinquefasciatus*. Extracts at 1.0 mg/mL caused maximal mortality in *A. aegypti* exposed for 24 h. In the case of *C. quinquefasciatus*, maximal mortality was seen when the concentration was increased to 3.0 mg/mL. Repellent properties of different fractions obtained from *L. camara* L. flowers have been evaluated against *Aedes* mosquitoes (*Ae. albopictus*, *Ae. vittatus* and *Ae. aegypti*) (Dua et al., 2003). The results showed that one application of the chloroform fraction gave 100% protection for 2 h and up to 75.8% protection at 7 h against *Ae. mosquito* bites.

A methanolic extract of *L. camara* L. was tested on larval weight, pupation and adult emergence of cabbage butterfly (Sharma & Mehta, 2009a). *L. camara* resulted in significantly lower effect on reduction in weight (1.25%). Pupal formation increased significantly (0.0-43.1%) with a decrease in concentration from 5.0 to 1.25%. A similar trend was observed with respect to adult emergence of *Plasmodiophora brassicae* (Sharma & Mehta, 2009b). On the other hand, the methanolic extract of *L. camara* caused a significant reduction in aphid establishment (less than

50%) at 5.0%.

L. viburnoides var *kisi* was tested for insecticidal activity against late 3rd or early 4th instar larvae of *Anopheles gambiae* s.s., which were exposed to various concentrations of extracts, fractions, blends and pure compounds (Innocent et al., 2008). The crude extract (LC50 7.70 ppm at 72 h) and fractions exhibited different levels of mosquito larvicidal activity with subtraction of some fractions resulting in activity enhancement. The active fractions contained furanonaphthaquinones regioisomers (LC50 5.48-5.70 ppm at 72 h) and camaric acid (29) (LC50 6.19 ppm at 72 h) as active principles, while betulinic acid (65) (LC50 <10 ppm in 72 h) was obtained from the least active fraction.

Extracts of *L. camara* var. *aculeata* leaves were studied for their termiticidal effects against adult termite workers (Verma & Verma, 2006). Only 5% chloroform extract exhibited excellent termite mortality. With respect to LC50, the effect of 5% chloroform extract against *Microcerotermes beelsoni* termites was the most interesting, compared to 0.5% chlorpyrifos.

Iannacone & Lamas (2003) studied the effects of extracts of *L. camara* L. on eggs, first instar larvae and adults of *Phthorimaea operculella* in bioassays of insecticidal effectiveness. The results showed that hatched eggs were affected by the hexane extract, and that first instar larva mortality was affected by hexane, acetone and water extracts at 10% concentrations.

The petroleum ether and methanol extracts of the aerial part of *L. camara* L. have been reported to be toxic to *Callosobruchus chinensis* (Dixit et al., 1992). The extracts showed 10-43% mortality at 5% concentrations, with fecundity loss at higher doses, and the antioviposition values were 30 mg/100 g for the petroleum ether extract and 40 mg/100 g of seed for the methanol extract.

In other studies, the essential oils of leaves and flowers of *L. camara* L. revealed insecticidal activity against 3rd instar larvae of *Musca domestica*, demonstrating mortality rates of 80 and 100%, respectively (Abdel-Hady et al., 2005), and the oil of leaves was effective against adults of *Sitophilus zeamais* (LC50 0.16% at 24 h) (Bouda et al., 2001). Essential oil of *L. camara* L. leaves also showed insecticidal properties against 3rd instar larvae of *Helicoverpa armigera*, causing 56% inhibition (Kathuria & Kaushik, 2006), and activity against fresh 5th instar nymphs of *Dysdercus similies* (Singh & Upadhyay, 1993).

Anti-viral activity

Garcia et al. (2010) screened the essential oil of *L. grisebachii* var. *grisebachii* L. for cytotoxicity and *in vitro* inhibitory activity against different virus types. The results showed that a better relationship between cytotoxicity and inhibitory activity was observed for the essential oil against dengue virus type 2 (DENV-2) and

herpes simplex virus type 1 (HSV-1) with IC₅₀ values of 21.1 and 26.1 ppm, respectively. Furthermore, this oil was also an effective inhibitor of HSV-2 and acyclovir-resistant variants of herpes virus.

Antioxidant activity

Bhakta & Ganjewala (2009) showed that premature leaves of *L. camara* L. on twigs are very active in the biosynthesis and accumulation of secondary metabolites and, hence, exhibit greater potential antioxidant activity (DPPH scavenging activity, 62%). It was also found that older leaves had less antioxidant activity (55%), indicating loss of secondary metabolites as result of leaf senescence. In another study, *L. camara* L. essential oil showed high antioxidant activity evaluated by the Trolox equivalent antioxidant capacity assay (TEAC) with a level of 29.0 mmol Trolox/kg (Benites et al., 2009).

Antifeedant activity

The chloroform, petroleum ether and methanol extracts of *L. camara* L. showed antifeedant activity against the tea mosquito bug (*Helopeltis theivora* Waterhouse), and among all the extracts, the chloroform extract showed the highest antifeedant effect (Deka et al., 1998). An aqueous extract of leaves was tested for its antifeedant effects on *Plutella xylostella* (Fracknath, 2006). The results showed that cabbage plants sprayed weekly with the extract protected the cabbage from *P. xylostella* to varying degrees. An antifeedant effect of crude lantadene from *L. camara* L. on *P. xylostella* and *Spodoptera litura* larvae has also been reported (Dong et al., 2005).

Phytotoxic activity

Previous evaluations of *L. camara* L. growing in Spain showed that an aqueous extract was not as effective against germination or seedling growth of *Amaranthus hybridus* and *Portulaca oleracea* as its essential oil (Verdeguer et al., 2009). The results suggest that its essential oil could be used as a potential allelopathic substance.

Zhang et al. (2009) reported the allelopathic effect of aqueous extracts of leaf and reproductive organs (flower and fruit) of *L. camara* L. on seed germination, seedling growth and dry matter production of radish and lettuce. The results showed that fruit extracts were more stimulatory, while flower and leaf extracts had similar stimulatory/inhibitory effects. *L. camara* reproductive organs exerted stronger allelopathic effects compared to vegetative organs. Thus, the allelopathic effect of its reproductive organs makes it more competitive and invasive.

Sousa et al. (2009) investigated for the first time the cytotoxic and genotoxic effects of aqueous extracts of *L. camara* L. leaves on *Lactuca sativa* (lettuce) root tip meristem cells using a cytogenetic approach. The results showed that the highest concentration (30 g/L) of aqueous extracts decreased the mitotic index, seed germination and root development of lettuce. The extracts also induced chromosome aberrations and cell death in root cells of *L. sativa*.

The extracts of *L. camara* L. leaves and their fractions were shown to reduce the biomass of *Eichhornia crassipes* and *Microcystis aeruginosa* within 7 days under laboratory conditions (Kong et al., 2005). Two fractions with highly inhibitory activity were isolated from the extract and subsequently identified as lantadene A (1) and lantadene B (2). Both compounds significantly inhibited *E. crassipes* and *M. aeruginosa* growth, even at a low concentration.

Antibacterial, antifungal activity

Species of *Lantana* have been widely evaluated in various works with respect to antimicrobial activity. One study showed inhibitory activity of an ethanolic extract of *L. montevidensis* Briq. leaves determined by the microdilution test against multiresistant strains of *Escherichia coli* (MIC 16 µg/mL) and *Staphylococcus aureus* (MIC 128 µg/mL) (Sousa et al., 2011a). An investigation of acetone extracts of leaves of *L. camara* L. and *L. rugosa* Thunb. showed growth-inhibitory effects against two Gram-negative (*E. coli* and *Pseudomonas aeruginosa*) and two Gram-positive (*Enterococcus faecalis* and *S. aureus*) bacteria, with MIC values varying from 0.39 mg/mL to 6.3 mg/mL (McGaw & Eloff, 2005).

The antifungal activity of *L. indica* Roxb was found to be greater in the leaf essential oil than leaf extracts (Kumar et al., 2010). The oil inhibited the growth of *Aspergillus flavus* Link completely at 1.5 mg/mL, while ethanolic and chloroform extracts of leaves showed a MIC of 7.5 and 10.0 mg/mL, respectively. The essential oil of aerial parts of *L. achyranthifolia* also displayed antifungal activity against the five fungal strains *A. niger*, *Fusarium nomiliforme*, *F. sporotrithum*, *Trichophyton mentagrophytes*, *Rhizoctonia solani* (IC₅₀ 100-180 µg/mL) (Hernández et al., 2008).

The essential oil of the leaves of *L. camara* L. has been examined for antibacterial activity by the microdilution test (Sousa et al., 2010b). The results showed an inhibitory activity against the multiresistant strains *E. coli* (MIC 512 µg/mL) and *S. aureus* (MIC 256 µg/mL). The essential oils of *L. trifolia* L. and *L. fucata* Sw. leaves were investigated for their activity against *M. tuberculosis*. Both oils exhibited *in vitro* antibacterial activity by the Microplate Alamar Blue assay (MABA)

with a MIC of 80 µg/mL for *L. trifolia* and 100 µg/mL for *L. fucata* (Julião et al., 2009).

A hexane extract from *L. hispida* Kunth aerial parts demonstrated growth inhibition in *M. tuberculosis* H37Rv (MIC 200 µg/mL), as well as in MDR-TB clinical isolates, including isoniazid- and rifampin-resistant variant strains of *M. tuberculosis* H37Rv (Jiménez-Arellanes et al., 2003). The compounds 22β-angeloyloxy-3β-hydroxyolean-12-en-28-oic acid (**5**), 22β-dimethylacryloyloxy-3β-hydroxyolean-12-en-28-oic acid (**6**), and oleanenoic acid (**11**), isolated from *L. hispida* Kunth, have been shown to be active against *M. tuberculosis* H37Rv with a MIC of 50, 50, and 2 µg/mL, respectively. Oleanenoic acid (**11**) showed a MIC of 25 µg/mL against the streptomycin- and isoniazid-resistant strains of *M. tuberculosis* H37Rv and 50 µg/mL against rifampin- and ethambutol-resistant variants. The compounds **5** and **6** were also active at 50 µg/mL against all the drug-resistant variants of *M. tuberculosis* H37Rv tested (Jiménez-Arellanes et al., 2007). The compounds lantanoside (**75**), linaroside (**76**) and isolated from *L. camara* L. were also effective against strains of *M. tuberculosis*, both with a MIC of 6.25 µg/mL (Begum et al., 2000).

Verbascoside (**113**) isolated from *L. lilacina* Desf. showed antibacterial activity with MIC and MBC values against *Aspergillus hydrophila*, *Bacillus subtilis*, *P. aeruginosa* and *S. aureus* of 0.12, 1.00, 1.00 and 0.25 mg/mL, respectively (Pereira et al., 2008). In an agar dilution assay, *Proteus mirabilis* and *S. aureus* were growth inhibited by verbascoside at 0.128 mg/mL (Didry et al., 1999).

The antibacterial activity of lantic acid (**57**) isolated from *L. camara* leaves was studied in Gram-positive and Gram-negative bacteria using bioautography assays (Saleh et al., 1999). Lantic acid was found to possess strong antibacterial activity against *E. coli* and *Bacillus cereus*, in which 0.08 and 0.1 µg were the minimum inhibitory doses, respectively, compared to 0.05 and 0.005 µg for chloramphenicol, respectively.

Camarinic acid (**55**) isolated from *L. camara* L. leaves was found to be active (30 mg/disk) against *S. aureus* and *Salmonella typhi* with an average antibacterial index of 0.95 and 0.55, respectively. By comparison, chloramphenicol against *S. aureus* and tetracycline against *S. typhi* had an index of respectively 1.6 and 0.8 at the same concentration (Barre et al., 1997). Rwangabo et al. (1988) reported that umuhengerin (**90**) isolated from *L. trifolia* L. leaves exhibited antimicrobial activity against *Salmonella typhimurium*, *S. aureus*, *Candida tropicalis*, *Aspergillus niger*, *A. fumigatus*, *Trichophyton mentagrophytes* and *Microsporium canis*.

Modulatory activity

Modulatory activity has been studied and demonstrated in species of *Lantana*. In one study, a synergistic effect of gentamicin and amikacin against *S. aureus* was observed in the presence of the essential oil constituents of *L. montevidensis* Briq., by the gaseous contact method. Enhancement of the antibacterial activity of amikacin and gentamicin was found against *P. aeruginosa*, where the essential oil increased amikacin activity by 102% (Sousa et al., 2011b).

The synergistic effects of the ethanolic extracts of leaves and roots of *L. montevidensis* Briq. on aminoglycoside activity were demonstrated by the microdilution test. The maximum effects were obtained with the root extract on gentamicin activity against multiresistant strains of *E. coli* with a reduction in MIC from 312 to 2 µg/mL (Sousa et al., 2011a). On the other hand, the ethanolic extract of *L. montevidensis* Briq. root combined with amikacin against *P. vulgaris*, also reduced the MIC (625 to 20 µg/mL) (Sousa et al., 2011c). Synergism between the essential oil of the leaves of *L. camara* L. and aminoglycosides was demonstrated with a significant reduction in MIC (1250 to 5 µg/mL) against *E. coli*.

The modulatory evaluation of a mixture of the compounds 22β-dimethylacryloyloxy-3β-hydroxyolean-12-en-28-oic acid (**6**) and oleanenoic acid (**11**) of *L. hispida* Kunth against *M. tuberculosis* H37Rv and drug-resistant variants of H37Rv strains showed MIC values ranging from 50 to 100 µg/mL, suggesting that a synergistic effect did not occur (Jiménez-Arellanes et al., 2007).

Antiinflammatory, analgesic, sedative and antipyretic activity

The sedative properties of *L. trifolia* L. extracts were demonstrated using the open field method, and one hour after their administration, the ethanolic and ethyl acetate extracts produced an intense sedative effect in all animals, expressed as a reduction in walked squares, with similar pattern and intensity at 1 and 10 mg/kg (Julião et al., 2010).

Ghosh et al. (2010) investigated the antiinflammatory activity of oleanonic acid (**8**) isolated from *L. camara* L. using the carrageenan-induced rat paw edema model. Oleanonic acid caused a reduction in edema, which validated its *in vivo* antiinflammatory effect. Another study reported that *L. camara* essential oil showed a relatively low antiinflammatory activity due to its weak ability to inhibit lipooxygenase (IC₅₀ 81.5 mg/mL) (Benites et al., 2009). On the other hand, *in vitro* assays showed that the alcoholic extract and fucatoside C (**121**) isolated from *L. fucata* Lindl. had significant antiinflammatory effects, inhibiting NO release in the LPS-induced J774. A1 murine macrophage cell line (Julião et al., 2009).

Silva et al. (2005) studied the antiinflammatory and analgesic activities of *L. trifolia* L. leaves. ethanol, dichloromethane, ethyl acetate, butanol and aqueous extracts (at 30 mg/kg) inhibited carrageenan- and histamine-induced rat paw edema. The most powerful reduction in paw edema was obtained with the ethanol (80%) and butanol (70%) extracts. Although the extracts did not show any effect on acetic acid-induced writhings, they all produced a significant increase in the tail flick antinociceptive index (doses varying between 1 and 30 mg/kg), indicating a spinal antinociceptive effect.

The methanolic extract of aerial parts of *L. trifolia* L. was evaluated for antiinflammatory, analgesic and antipyretic properties (Uzcátegui et al., 2004). The extract produced an inhibition of edema induced by carrageenan in the rat paw at doses of 10-300 mg/kg. The extract also produced a small but significant increase in the response latency of rats submitted to the hot plate test, a test for thermal pain, which detects analgesia by high efficacy agents. The extract did not show antipyretic activity.

Whole plant and ethanolic extracts of fresh leaves of *L. camara* L. were investigated for their antiinflammatory properties using the cotton pellet antiinflammatory bioassay technique (Oyedapo et al., 1999). The treatments of the inflamed rats with the extracts resulted in the inactivation of phosphatase and transaminase activities and the stimulation of adenosine triphosphatase activity in plasma and exudates.

Antiproliferative (antitumor and anticancer) and cytotoxic activity

In a study by Shikha et al. (2010), oleanolic acid (**9**), isolated from the roots of *L. camara* L., was converted into six semi-synthetic ester and seven amide derivatives. The ester derivatives showed 3-6 times more selective activity than did oleanolic acid against the human ovarian cancer cell line IGR-OV-1, while amide derivatives showed 16-53 times more selective activity against the human lung cancer cell line HOP-62.

A crude extract of *L. camara* L. leaves had a cytotoxic effect on HeLa cells at 36 h (at 100 µg/mL) to 72 h (at 25 µg/mL), by employing the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) cell viability assay (Srivastava et al., 2010). The results showed that an increase in the concentration or duration of the extract treatment was effective in killing cancer cells.

The compounds raduloside (**119**) and radulignan (**174**), isolated from *L. radula* Sw. roots, were tested for cytotoxicity against several cell lines (HL-60, K562, U937, CEM, KG-1, Jurkat, U266, and NCI-H929) and were found to have no effect on cell viability at 10 µM (Sena Filho et al., 2009). Lantadenes A (**1**), B (**2**), C (**3**)

and 22β-dimethylacryloyloxy-24-hydroxy-3-oxo-olean-12-en-28-oic acid (**17**), isolated from leaves of *L. camara* L., displayed weak to moderate cytotoxic activities against four cancer cell lines: human oral epidermoid carcinoma (KB), human colon cancer (HCT-116), human breast cancer (MCF-7), and mouse lymphocytic leukemia (L1210) (IC50 values of 4.7-44.7 µM) (Litaudon et al., 2009).

Litaudon et al. (2009) evaluated the compounds icterogenin (**16**) and 22β-dimethylacryloyloxy-24-hydroxy-3-oxo-olean-12-en-28-oic acid (**17**), isolated from leaves of *L. camara* L., for their interaction with the antiapoptotic protein Bcl-xL/Bak association. The two compounds exhibited binding activity with *K_i* values between 7.6 and 5.3 µM, indicating that they both act as antagonists of the Bcl-xL/Bak association.

Sharma et al. (2008) studied methyl ester derivatives of lantadene obtained from the lantadene fraction of leaves of *L. camara* L. and showed cytotoxicity against four human cancer cell lines (HL-60, HeLa, colon 502713, and lung A-549). Cytotoxicity increased as the length of the side chain increased from acetoxy to propoxy. There was a significant decrease in cytotoxicity with branching of the side chain. The C-17 methyl esters were all more cytotoxic, with 22 showing the best activity (IC50 19.3-22.4 µg/mL). In the same study, lantadene A (**1**) and four methyl ester derivatives of lantadene exhibited tumor inhibitory activity on two-stage squamous cell carcinogenesis in Swiss albino mice, induced by DMBA and promoted by TPA. Lantadene A showed an 18.1% incidence of tumors and a delay of three weeks, while animals in the group treated with a derivate compound showed a significant decrease in the incidence of cancer (17.2% vs 100%) at the end of twenty weeks.

Dichloromethane extracts of leaves from *L. camara* L. (colors of flowers: pink and orange) were tested for *in vitro* cytotoxicity against human WI-38 fibroblasts. The dichloromethane extracts showed IC50 values of 69.5±12.1 and 97.2±2.4 µg/mL for *L. camara* with pink and orange flowers, respectively (Jonville et al., 2008).

The flavonoid fraction from the leaves of *L. montevidensis* Briq. showed antiproliferative activity against human gastric adenocarcinoma (MK-1, GI50 12 µg/mL), human uterine carcinoma (HeLa, 5 µg/mL), and murine melanoma (B16F10, 5 µg/mL) cells *in vitro* (Nagão et al., 2002). In the same study, flavones isolated from the flavonoid fraction of this plant, 5,3',4'-trihydroxy-6,7,5'-trimethoxyflavone (**95**), apigenin (**90**), cirsilinol (**98**) and eupafolin (**99**), showed higher activity against the three tumor cell lines followed by eupatorin (**92**), 5,6-dihydroxy-7,3',4'-trimethoxyflavone (**80**), 5,6,4'-trihydroxy-7,3',5'-trimethoxyflavone (**96**) and 5,6,3'-trihydroxy-7,4'-dimethoxyflavone (**81**). cirsilinol (**91**) and 5,4'-dihydroxy-6,7,3',5'-tetramethoxyflavone (**94**) were the least active, although cirsilinol showed high selective activity against MK-1 cells. In addition, the methanolic

extracts of *L. camara* L. and *L. montevidensis* Briq. leaves were very effective in inhibiting tumor cell growth, where 50% growth inhibition (GI₅₀) was seen at concentrations of 8 µg/mL in MK-1, 3 µg/mL, in HeLa and 4 µg/mL in B16F10 for *L. montevidensis* extract, which was more potent than the *L. camara* extract (12.5 µg/mL in MK-1 and 25 µg/mL in HeLa and B16F10). The inhibitory activity was found to be localized in the nonglycoside fraction that contains several flavonoids.

Another study found that the leaf extract of *L. camara* L., administered at dose of 400 mg/kg, showed a chemopreventive effect against DMBA-induced squamous cell carcinogenesis in Swiss albino mice (Sharma et al., 2007a). It was also found that lantadene A (**1**) induces apoptosis in human leukemia HL-60 cells by activating the caspase-3 pathway and through down- and upregulation of Bcl-2 and Bax expression, respectively (IC₅₀ value of 19.8±0.10 µg/mL following 48 h incubation) (Sharma et al., 2007b).

Verbascoside (**113**) isolated from *L. camara* was shown to be an inhibitor of protein kinase C (PKC) from rat brain (Herbert et al., 1991). The study reported that half-maximal inhibition of the kinase occurs at 25 µM. Verbascoside interacts with the catalytic domain of PKC and is a competitive inhibitor with respect to ATP (*K_i* 22 µM) and a non-competitive inhibitor with respect to the phosphate acceptor (histone H₃). The antitumor activity of verbascoside measured *in vitro* may be due at least in part to the inhibition of PKC.

Antiulcerogenic activity

Sathisha et al. (2011) studied the antiulcerogenic effect of a methanolic extract of *L. camara* L. in aspirin-induced gastric ulcerogenesis in pylorus-ligated rats and ethanol-induced gastric ulcer, and cysteamine-induced duodenal ulcer models. The extract was administered orally at two different doses, 250 and 500 mg/kg. The results showed that the extract significantly reduced the ulcer index and total acidity and significantly increased gastric pH of aspirin- and pylorus ligation-induced ulcerogenesis and ethanol-induced intestinal ulcer model. The extract also significantly reduced the ulcer index of cysteamine-induced duodenal ulcer.

Anti-motility activity

L. camara L. var. *aculeata* leaf powder, methanolic extract, lantadene A (**1**), neostigmine and neostigmine but with methanolic extract were evaluated for anti-motility activity in the intestine of treated mice (Sagar et al., 2005). Neostigmine was used as a promotility agent and the intestinal motility was assessed by the charcoal meal test. In this evaluation, the percent intestinal transit significantly increased with neostigmine, but significantly

decreased by all concentrations of methanolic extract and lantadene A. In the same study, an anti-diarrheal effect of the methanolic extract was studied in the castor oil-induced diarrhea model in mice. When the plant extract at 125 and 250 mg/kg doses was administered intraperitoneally, there was a significant reduction in fecal output compared with castor oil-treated mice. At higher doses (500 and 1000 mg/kg), fecal output was almost completely stopped.

Anti-fertility activity

Mello et al. (2005) investigated the effects of the hydroalcoholic extract of the leaves of *L. camara* var. *aculeata* on reproduction. Three doses were tested in pregnant rats, 1, 3 and 7 g equivalent of plant material/kg body weight. The extract decreased the frequency of fetal skeleton anomalies in females and induced embryotoxicity as indicated by post-implantation loss, without any signs of maternal toxicity. In another study, the hydroalcoholic extract of *L. camara* L. leaves on fertility did not interfere with overall weight or internal organ weights of male rats, but interfered with sperm count, daily sperm production and sperm morphology in a dose-dependent manner (Melo et al., 2003).

Anticoagulant activity

Methanolic extracts prepared from the leaves of *L. camara* L. were found to inhibit human R-thrombin (O'Neill et al., 1998). The activity was shown to be associated with the euphane lactone triterpenes (**70-74**). The mechanism of the inhibition of the blood-clotting cascade was shown to involve acylation of the active-site Ser 195 residue of thrombin. This acylating activity is generic towards other serine proteases. Weir et al. (1998) showed that the inhibitors bind to the active site of human R-thrombin and R-chymotrypsin. Tight-binding reversible competitive inhibition was shown by euphane lactone B (**70-71**). Protease inhibition involves the opening of the lactone ring and acylation of the active-site serine 195. The IC₅₀ with α -thrombin, α -chymotrypsin and trypsin was respectively 0.004, 0.07 and 0.07 for euphane lactone B (**70**) and 0.004, 0.01, 0.12 mM for euphane lactone C (**72**).

Toxicity activity in vivo

Tokarnia et al. (1999) diagnosed an outbreak of poisoning by *L. camara* var. *aculeata* in cattle in Quatis County, state of Rio de Janeiro. The results showed that the plant caused lethal poisoning when given as a single dose of 40 g/kg; 20 g/kg caused severe poisoning, 10 g/kg slight or no poisoning and 5 g/kg failed to provoke symptoms. Another study showed that ingestion of 340-453 g of leaves of the *L. camara* L. causes liver and kidney damage,

photosensitization, intestinal hemorrhage, paralysis of the gall bladder, and death in 1-4 days in horses, cattle and sheep (not goats) (Motion, 1994).

Lantadene C (**3**) isolated from *L. camara* var. *aculeata* leaves was shown to elicit a strong hepatotoxic response in guinea pigs associated with decrease in fecal output, feed intake, hepatomegaly, hepatic injury at the cellular and subcellular level, and increase in plasma bilirubin and acid phosphatase activity (Sharma et al., 1992).

Sharma et al. (1989) had also reported that the oral administration (125 mg/kg) of a toxin fraction obtained from *L. camara* L. leaves, whose main constituents were lantadene A (**1**) and lantadene B (**2**), in male and female guinea pigs, caused icterus and photosensitization within 48 h. A single dose of the lantadene A at 1-3 mg/kg injected intravenously in sheep was found to cause mild hepatocellular injury characterized by transient rises in serum enzymes, with or without hyperbilirubinemia, where higher doses resulted in hepatic necrosis (Pass et al., 1979).

In other studies, a partially purified fraction obtained from *L. camara* L. leaves containing seven chemicals was investigated. Lantadene A and lantadene B were the major compounds and nontoxic to guinea pigs (Sharma et al., 1987). 22 β -hydroxyoleanonic acid (**7**) was isolated from the lantadene fraction of *L. camara* and was studied for hepatotoxicity using lantadene A (**1**) as standard and found to be nontoxic (Sharma & Sharma, 2006).

Antimutagenic activity

A study of the compounds lantanilic acid (**27**) and camarinic acid (**55**), which were isolated from *L. camara* L., showed high antimutagenic activity in the mouse; at 6.75 mg/kg, they reduced the number of micronucleated polychromatic erythrocytes induced by mitomycin C by 76.7% and 60%, respectively (Barre et al., 1997).

Concluding remarks

In the present review, we compiled ethnopharmacological, phytochemical, pharmacological and toxicological information on the genus *Lantana*. The studies reported in the literature revealed the presence of terpenoids, flavonoids, phenylethanoid glycosides, furanonaphthoquinones, iridoid glycosides and steroids, demonstrating thus that the genus *Lantana* includes species that are a rich source of a variety of organic compounds with varying structural patterns.

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