Indian Journal of Natural Products and Resources
Vol. 6(2), June 2015 pp. 71-90

Chemistry and biology of genus *Wedelia* Jacq.: A review

Nitin Verma[1]* and R L Khosa[2]

[1]School of Pharmacy and Emerging Science, Baddi University of Emerging Science and Technology, Makhunmajara, Baddi, Distt-Solan, Himachal Pradesh-173205, India.

[2]Department of Pharmacy, Bharat Institute of Technology, Bye-Pass Road, Partapur, Meerut -250 103 Uttar Pradesh, India.

Received 8 July 2014; Accepted 4 February 2015

Over the past few decades genus *Wedelia* Jacq. has gained considerable attention due to the presence of a wide array of chemical constituents having wide spectrum of biological activities. Considering this, an extensive review is presented here comprising of structural and biological properties of chemical constituents from genus *Wedelia*.

Keywords: Biological activity, Phytochemical review, *Wedelia*.

IPC code; Int. cl. (2014.01)−A61K 36/00

Introduction

The genus *Wedelia* (Family Asteraceae, tribe Heliantheae, subtribe Ecliptinae) consists of 60 species distributed in tropical and warm temperate regions, including India, Burma, Ceylon, China, and Japan[1,2]. Among them, *W. biflora*, DC syn. *W. scandens* (C.B.) Clarke and *W. chinensis* (Osbec.) Merr. are found in India[3.] Plate 1 gives worldwide geographical distribution of genus *Wedelia* whereas Plate 2 shows photograph of different species of *Wedelia*.

A number of plants from the genus *Wedelia* are used as traditional herbal medicines throughout the world and they have been reported to possess hepatoprotective, antipyretic-analgesic, bactericidal, molluscicidal, hypoglycaemic and antitumor activities[4] whereas antioxidant[5], wound healing[6], antistress activity[7,8] and hepatoprotective activity on *W. chinensis* (Osbec.) Merr. have been reported by our research group in recent years[9]. Extensive studies of the chemical components of *Wedelia* have led to the identification of numerous compounds (Structure 1–125), including sesquiterpenes, diterpenes, triterpenes, triterpene saponins, flavonoids, etc. In this review article, the phytochemical progress and list of all the compounds isolated from the genus *Wedelia* over the past few decades have been summarized (Table 1). Recent updates with reference to their biological activities are also incorporated in this review.

*Correspondent author:
E-mail: nitin.verma@baddiuniv.ac.in
Phone : 01795-247353
Fax : 01795-247352
Mobile : +91 9736419033

Chemical constituents

Monoterpenes

The monoterpene derivative (1) and the related ketone (2) were isolated from *W. forsteriana* Endl. [10].

Sesquiterpenes

Pseudoguaianolides

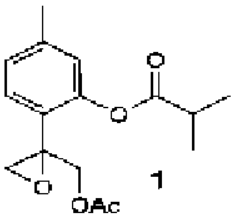
Investigation of the aerial parts of *W. grandiflora* Benth. afforded a complex mixture of minute amounts of sesquiterpene lactones, which could not be completely separated. All the spectroscopic data are, however, in agreement with the proposed structures (3–7) [(Ref. 11)].

Eudesmanolides

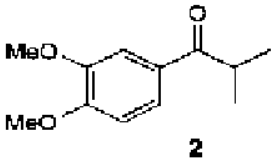
The eudesmanolides (8–38), with a variety of substituents, were isolated from *W. prostrata* Hemsl., *W. trilobata* (L.) Hitchc., *W. hookeriana* Gardner., *W. grandiflora* Benth., *W. pinetorum* (Standl. & Steyerm.) K. M. Becker. and *W. hispida* Kunth. among other species[12-20].

Other sesquiterpenes

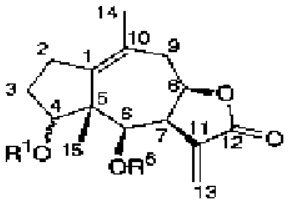
The hydrocarbons isocomnene (39) and 7aH-silphiperfol-5-ene (40) from the roots of *W. hookeriana* Gardner. have been isolated and reported[16]. Caryophyllene, germacrene D and bicyologermacrene were found in several *Wedelia* species[15-18], Caryophyllene 1, 10-epoxide was isolated from *W. regis* H.Rob. [21] and a-humulene was reported from *W. chinensis* (Osbec.) Merr.[15]



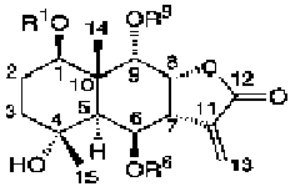
1



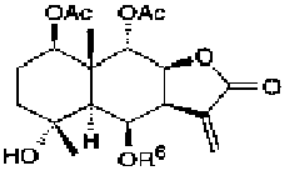
2



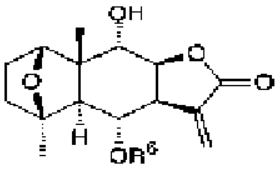
	R^1	R^6
3	H	Mac
4	Ac	Mac
5	Ac	i-Bu
6	Ac	Tig
7	Ac	i-Val



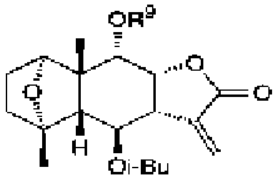
	R^1	R^6	R^9
8	H	i-Bu	Tig
9	H	i-Bu	Ang
10	Ac	i-Bu	Ac
11	Ac	i-Bu	H
12	Ac	Mac	H
13	Ac	Mac	Ac



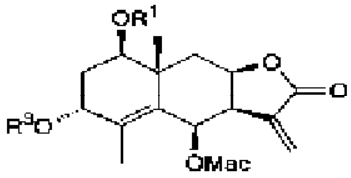
	R^6
14	i-Bu
15	Ang
16	Mac



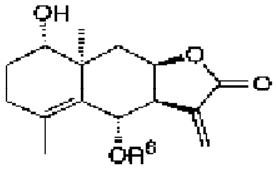
	R^6
17	i-Bu
18	Ang
19	Mac



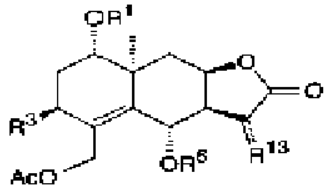
	R^9
20	H
21	Ac



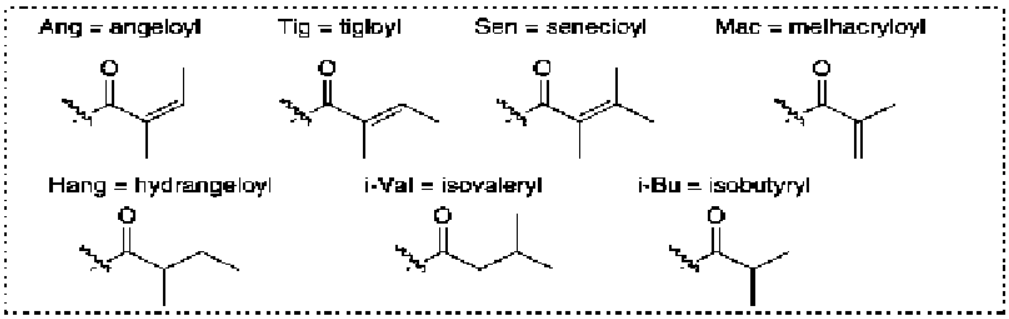
	R^1	R^3
22	H	Ac
23	H	COEt
24	H	i-Bu
25	H	Hang
26	H	i-Val
27	H	Tig
28	H	Sen
29	Ac	Tig

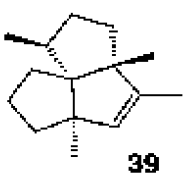


	R^6
30	Tig
31	Ang
32	Mac

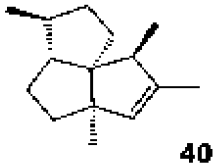


	R^1	R^3	R^6	R^{13}
33	H	H	Tig	α-OH
34	H	H	Ang	α-OH
35	H	OAc	Tig	α-OH
36	Ac	OH	Tig	α-OH
37	H	OAc	Tig	=O
38	H	H	Tig	=O

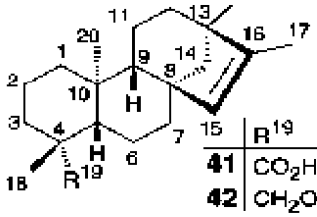




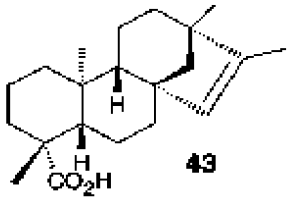
39



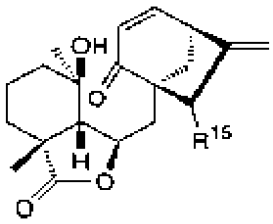
40



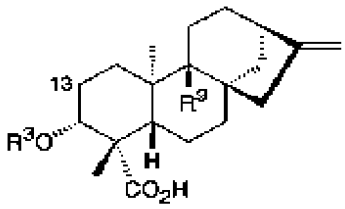
	R^{19}
41	CO_2H
42	CH_2OH



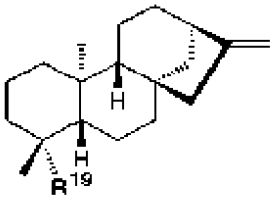
43



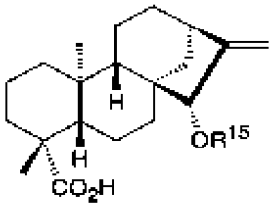
	R^{15}
44	α-OH
45	β-OH
46	β-OAc



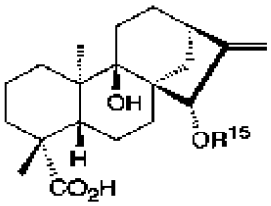
	R^3	R^9
47	Tig	H
48	Sen	H
49	Cin	H
50	Cin	OH
51	Ang	H
52	Ang	OH



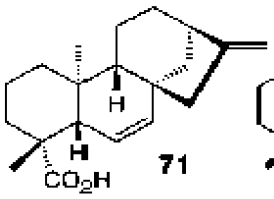
	R^{19}
53	CO_2H
54	CO_2Me
55	CHO
56	CH_2OH



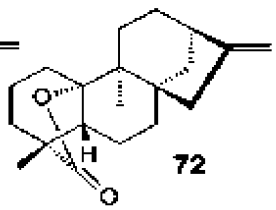
	R^{15}
57	H
58	Ac
59	Cin
60	Ang
61	Sen
62	Tig
63	EpoAng
64	i-Bu
65	i-Val
66	A



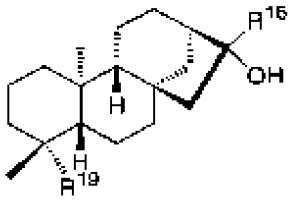
	R^{15}
67	H
68	Ang
69	Sen
70	B



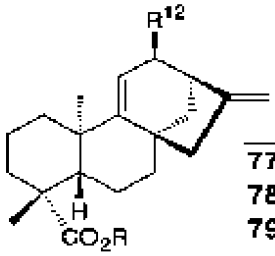
71



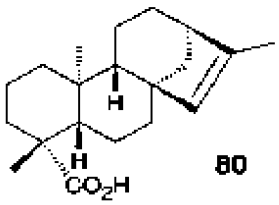
72



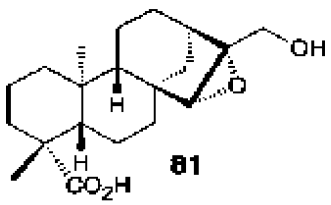
	R^{16}	R^{19}
73	β-Me	CO_2H
74	β-Me	Me
75	β-CH_2OH	CO_2H
76	α-CH_2OH	CO_2H



	R^{15}	R
77	H	H
78	OH	H
79	H	Me



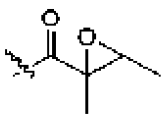
80



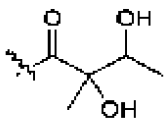
81

Cin = cinnamoyl

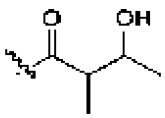
EpoAng = epoxyangeloyl

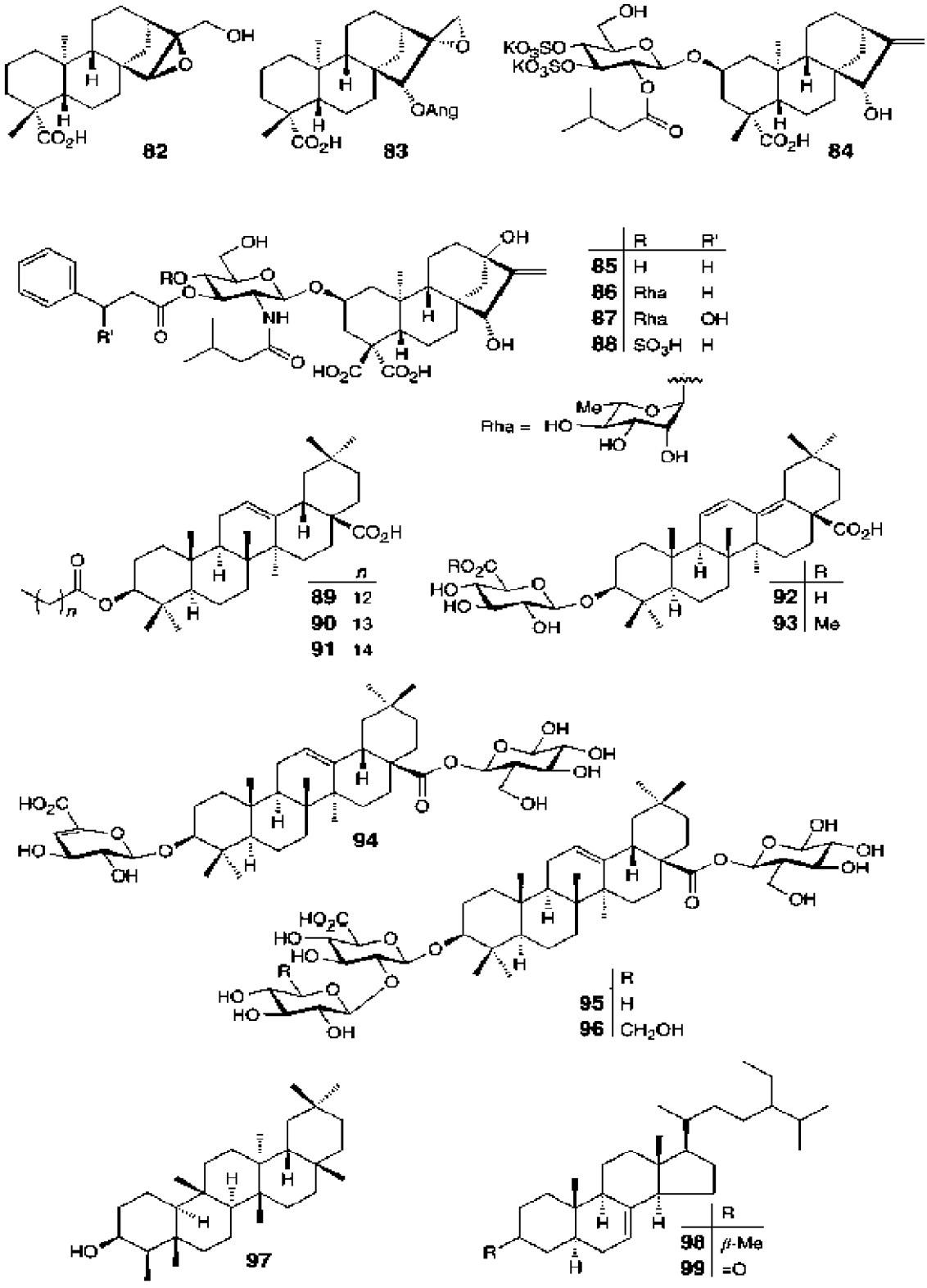


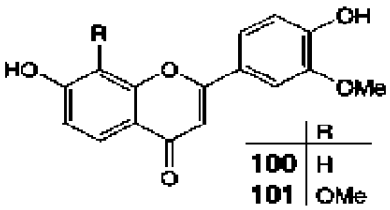
A



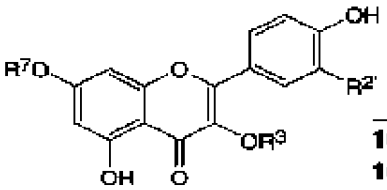
B



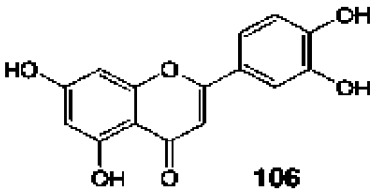

82
83
84
85 R H R' H
86 Rha H
87 Rha OH
88 SO3H H
Rha =
89 n 12
90 13
91 14
92 R H
93 Me
94
95 R H
96 CH2OH
97
98 R β-Me
99 =O



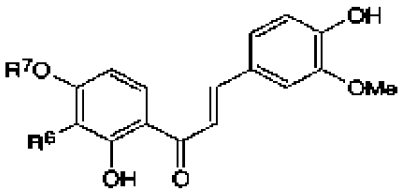
	R
100	H
101	OMe



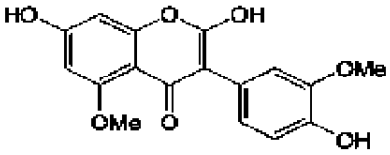
	R^3	R^7	$R^{2'}$
102	β-Glc	H	OH
103	Me	H	OMe
104	H	Me	OMe
105	β-Glc	H	H



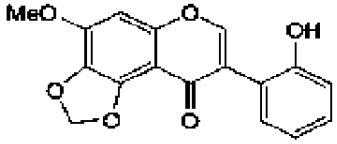
106



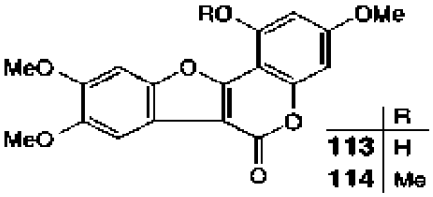
	R^6	R^7
107	OMe	H
108	H	H
109	OMe	β-Glc
110	H	β-Glc



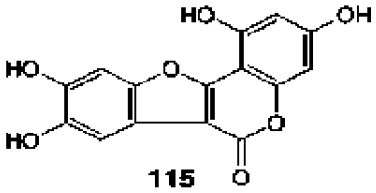
111



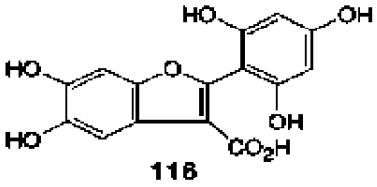
112



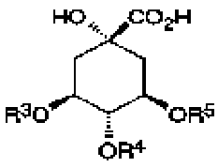
	R
113	H
114	Me



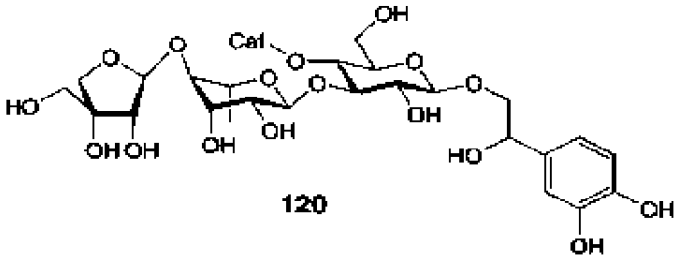
115



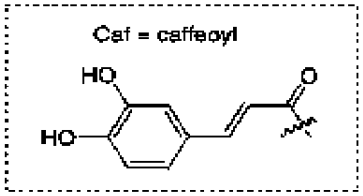
116

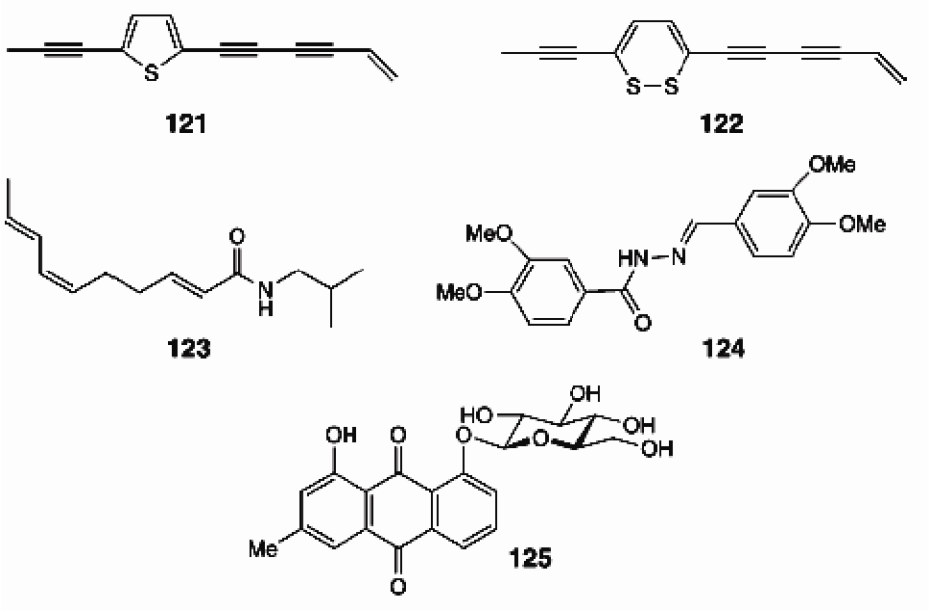


	R^3	R^4	R^5
117	H	Caf	Caf
118	Caf	H	Caf
119	Caf	Caf	H



120





Structure 1-125 – Numerous Compounds isolated from genus *Wedelia*

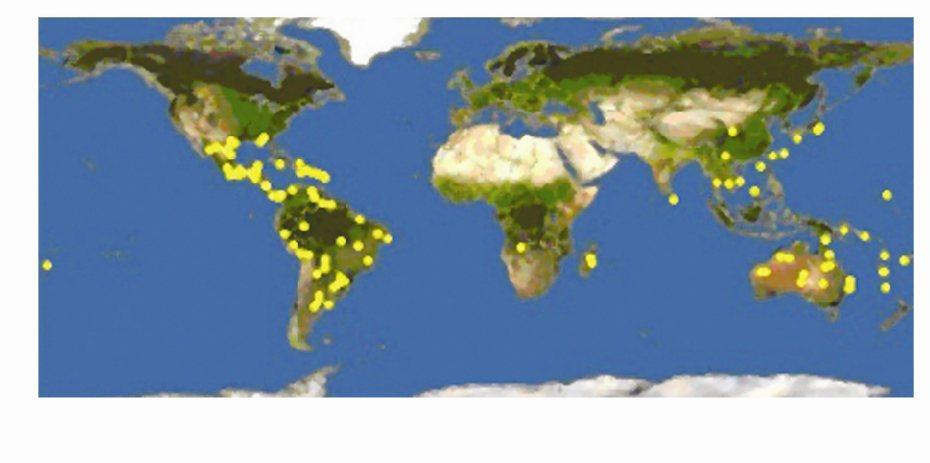


Plate 1— Worldwide geographical distribution of genus *Wedelia*

Diterpenes

Beyerenes

The ent-beyerene derivatives (41) and (42) were isolated from *W. hookeriana* Gardner.[16]. The aerial parts of *W. calycina* Spreng. furnished Beyer-15-en-19-oic acid (43)[(Ref. 19)].

Kaurenes

A dozen species of the large genus *Wedelia* have been investigated phytochemically, and kaurene diterpenoids were found to be major constituents, entkaurane derivatives being found in almost all of them. Their structures were elucidated by spectroscopic methods and by chemical transformation[14-16,19-37].

Triterpenes and triterpene saponins

From *W. asperrima* (Decne) Benth., *β*-amyrin, *β*-amyrin acetate and *β*-amyrone were isolated[36]. Lupeol was obtained from *W. hispida* Kunth.[20] and squalene was found in *W. chinensis* (Osbec.) Merr.[15]. De Carvalho *et al*, isolated acylated triterpenes (89–91) from the flowers of *W. paludosa* DC.[30]. Luo isolated two new saponins (92) and (93) from *W. chinensis* (Osbec.) Merr.[38] and the new saponin (94) was found in the EtOH extract of the leaves of *W. scaberrima* Hook.[39]. Govindachari and Premila reported two bisdesmosidic oleanolic acid saponins (95) and (96) from the fresh leaves of *W. calendulacea* (L.) Less. [40]. The aerial parts of *W. paludosa* DC. furnished Friedelan-3*β*-ol (97)[(Ref. 26)].

Plate 2— Photographs of different species of ***Wedelia***

Table 1—Chemical constituents isolated from genus *Wedelia*

Structure No.	Name	Species	Ref.
1.	10-Acetoxy-8,9-epoxythymol isobutyrate	*W. forsteriana* Endl.	10
2.	3', 4'-Dimethoxyisobutyrophenone	*W. forsteriana* Endl.	10
3.	Wedelifloride 6-*O*-methacrylate	*W. grandiflora* Benth.	11
4.	6-*O*-(Methaacryloyloxy) wedelifloride 4-*O*-acetate	*W. grandiflora* Benth.	11
5.	6-*O*-(Isobutyryloxy) wedelifloride 4-*O*-acetate	*W. grandiflora* Benth.	11
6.	6-*O*-(Tiglinoyloxy) wedelifloride 4-*O*-acetate	*W. grandiflora* Benth.	11
7.	6-*O*-(Isovaleryloxy) wedelifloride 4-*O*-acetate	*W. grandiflora* Benth.	11
8.	1*β*,4*α*-Dihydroxy-6*β*-(isobutyryloxy)-9*α*-(tigloyloxy) prostatoloide	*W. prostrata* Hemsl.	12
		W. trilobata (L.) Hitchc.	13
9.	9*α*-(Angeloyloxy)-1*β*,4*α*-dihydroxy-6*β*-(isobutyryloxy) prostatoloide	*W. prostrata* Hemsl.	12
		W. trilobata (L.) Hitchc.	13
10.	1*β*,9*α*-Diacetoxy-4*α*-hydroxy-6*β*-(isobutyryloxy) prostatoloide	*W. prostrata* Hemsl.	12
		W. trilobata (L.) Hitchc.	13
11.	1*β* -Acetoxy-4*α*,9*α*-dihydroxy-6*β*-(isobutyryloxy) prostatoloide	*W. prostrata* Hemsl.	13,14
12.	1*β* -Acetoxy-4*α*,9*α*-dihydroxy-6*β*-(methacryloxy) prostatoloide	*W. prostrata* Hemsl.	14
13.	1*β*,9*α* -Diacetoxy-4*α*-hydroxy-6*β*-(methacryloxy) prostatoloide	*W. prostrata* Hemsl.	13
		W. trilobata (L.) Hitchc.	14
14.	Trilobolide 6-*O*-isobutyrate	*W. trilobata* (L.) Hitchc.	13,15
15.	Trilobolide 6-*O*-angelate	*W. trilobata* (L.) Hitchc.	15
16.	Trilobolide 6-*O*-methacrylate	*W. trilobata* (L.) Hitchc.	15
17.	Oxidoisotrilobolide 6-*O*-isobutyrate	*W. trilobata* (L.) Hitchc.	15
18.	Oxidoisotrilobolide 6-*O*-angelate	*W. trilobata* (L.) Hitchc.	15
19.	Oxidoisotrilobolide 6-*O*-methacrylate	*W. trilobata* (L.) Hitchc.	15
20.	9*α*-Hydroxy-1*α*,4*α*-epoxy-5*β*H,7*β*H,8*β*H- prostatoloide 6-*O*-isobutyrate	*W. prostrata* Hemsl.	12
21.	9*α*-Acetoxy-1*α*,4*α*-epoxy-5*β*H,7*β*H,8*β*H- prostatoloide 6-*O*-isobutyrate	*W. prostrata* Hemsl.	12
22.	3 *α*-Acetoxy-6*β*-(methacryloyloxy) ivangustin	*W. hookeriana* Gardner.	16
23.	6*β*-(Methacryloyloxy)-3*α*-(propanoyloxy) ivangustin	*W. hookeriana* Gardner.	16
24.	3*α*-(Isobutyryloxy)- 6*β*-(methacryloyloxy) ivangustin	*W. hookeriana* Gardner.	16
25	3*α*-(2-Methylbutyryloxy)- 6*β*-(methacryloyloxy) ivangustin	*W. hookeriana* Gardner.	16
26.	3*α*-(Isovaleryloxy)- 6*β*-(methacryloyloxy) ivangustin	*W. hookeriana* Gardner.	16
27.	6*β*-(Methacryloyloxy)-3*α*-(tigloyloxy) ivangustin	*W. hookeriana* Gardner.	16
28.	6*β*-(Methacryloyloxy)-3*α*-(senecioyloxy) ivangustin	*W. hookeriana* Gardner.	16
29.	6*β*-(Methacryloyloxy)-3*α*-(tigloyloxy) ivangustin acetate	*W. hookeriana* Gardner.	16
30.	1*α*-Hydroxy -6*α*-(tigloyloxy) steiractinolide	*W. grandiflora* Benth.	17
31.	6*α*-(Angeloyloxy)-1*α*-hydroxysteiractinolide	*W. grandiflora* Benth.	17
32.	6*α*-(Methacryloyloxy)- 1*α*-hydroxysteiractinolide	*W. grandiflora* Benth.	17

(*Contd.*)

Table 1—Chemical Constituents from Genus *Wedelia* (*Contd*.)

Structure No.	Name	Species	Ref.
33.	15-Acetoxy-1*α*-hydroxy -10*α*-methyl-6*α*-(tigloyloxy)-7*α*H,8*α*H,11*β*H-eudesm-4-en-8,12-olide	*W. pinetorum* (Standl. & Steyerm.) K. M. Becker	18
34.	15-Acetoxy-6*α*-(angeloyloxy)-1*α*-hydroxy -10*α*-methyl-7*α*H,8*α*H,11*β*H-eudesm-4-en-8,12-olide	*W. pinetorum* (Standl. & Steyerm.) K. M. Becker	18
35.	3*β*, 15-Diacetoxy-1*α*-hydroxy -10*α*-methyl-6*α*-(tigloyloxy)-7*α*H,8*α*H,11*β*H-eudesm-4-en-8,12-olide	*W. hispida* Kunth.	19
36.	1*α*, 15-Diacetoxy-3*β*-hydroxy -10*α*-methyl-6*α*-(tigloyloxy)-7*α*H,8*α*H,11*β*H-eudesm-4-en-8,12-olide	*W. hispida* Kunth.	19
37.	3*β*, 15-Diacetoxy-1*α*-hydroxy -10*α*-methyl-6*α*-(tigloyloxy)-7*α*H,8*α*H, -eudesma-4,11-dien-8,12-olide	*W. hispida* Kunth.	19
38.	15-Acetoxy-1*α*-hydroxy -10*α*-methyl-6*α*-(tigloyloxy)- 7*α*H,8*α*H -eudesma-4,11-dien-8,12-olide	*W. pinetorum* (Standl. & Steyerm.) K. M. Becker	18
39.	Isocomnene	*W. hookeriana* Gardner	12
40.	7*α*H-Silphiperfrol-5-ene	*W. hookeriana* Gardner	12
41.	*ent*-Beyer-15-en-19-oic acid	*W. hookeriana* Gardner	12
42.	*ent*-Beyer-15-en-19-ol	*W. hookeriana* Gardner	12
43.	Beyer-15-en-19-oic acid	*W. calycina* Spreng.	19
44.	15*α*-Hydroxywederegiolide	*W. regis* H. Rob.	20
45.	15*β*-Hydroxywederegiolide	*W. regis* H. Rob.	20
46.	15*β*-Acetoxywederegiolide	*W. regis* H. Rob.	20
47.	3*α*-(Tigloyloxy)-*ent*-kaur-16-en-19-oic acid	*W. prostrata* Hemsl.	14
		W. trilobata (L.) Hitchc.	15
		W. paludosa DC.	21
		W. chinensis (Osbec.) Merr.	22
		W. calendulacea (L.) Less.	23
48.	3*α*-(Senecioyloxy)-*ent*-kaur-16-en-19-oic acid	*W. trilobata* (L.) Hitchc.	24
49.	3*α*-(Cinnamoyloxy)- *ent*-kaur-16-en-19-oic acid	*W. prostrata* Hemsl.	14
		W. trilobata (L.) Hitchc.	15
		W. chinensis (Osbec.) Merr.	22
		W. paludosa DC.	25
50.	3*α*-(Cinnamoyloxy)-9*β*-hydroxy-*ent*-kaur-16-en-19-oic acid	*W. trilobata* (L.) Hitchc.	15
51.	3*α*-(Angeloyloxy)-*ent*-kaur-16-en-19-oic acid	*W. trilobata* (L.) Hitchc.	15
		W. paludosa DC.	21
		W. calendulacea (L.) Less.	23,24,26
52.	3*α*-(Angeloyloxy)-9*β*-hydroxy-*ent*-kaur-16-en-19-oic acid	*W. trilobata* (L.) Hitchc.	15

(*Contd*.)

Table 1—Chemical Constituents from Genus *Wedelia* (*Contd*.)

Structure No.	Name	Species	Ref.
53.	*ent*-kaur-16-en-19-oic acid	*W. hispida* Kunth.	
		W. glauca (Ortega)Hoffm.ex Hicken	23
		W. trilobata (L.) Hitchc.	24
		W. calycina Spreng.	25
		W. chinensis (Osbec.) Merr.	26
		W. paludosa DC.	27
		W. hookeriana Gardner.	28
		W. scaberrima Hook.	29
		W. grandiflora Benth.	30
		W. calendulaceae (L.) Less.	31
		*W. buphthalmiflora (*DC.) Griseb.	32
54.	*ent*-kauren-19-oic acid methyl ester	*W. trilobata* (L.) Hitchc.	24
		W. grandiflora Benth.	24
		W. helianthoides Kunth.	24
55.	*ent*-kauren-19-al	*W. grandiflora* Benth.	24
56.	*ent*-kauren-19-ol	*W. hookeriana* Gardner	16
		W. grandiflora Benth.	24
57.	15*α*-Hydroxy- *ent*-kaur-16-en-19-oic acid (Grandifloric acid)	*W. biflora* (L.) DC.	19
		W. calycina Spreng.	31
58.	15*α*-Acetoxy- *ent*-kaur-16-en-19-oic acid	*W. hookeriana* Gardner	16
59.	15*α*-(Cinnamoyloxy)- *ent*-kaur-16-en-19-oic acid	*W. glauca* (Ortega)Hoffm.ex Hicken	28
		W. trilobata (L.) Hitchc.	24
60.	15*α*-(Angeloyloxy)- *ent*-kaur-16-en-19-oic acid	*W. calycina* Spreng.	16
		W. hookeriana Gardner	18
		W. grandiflora Benth.	19
		W. scaberrima Hook.	24
		W. helianthoides Kunth.	27
		*W. buphthalmiflora (*DC.) Griseb.	27
61.	15*α*-(Senecioyloxy)- *ent*-kaur-16-en-19-oic acid	*W. hookeriana* Gardner	16
		W. grandiflora Benth.	24
62.	15*α*-(Tigloyloxy)- *ent*-kaur-16-en-19-oic acid	*W. hookeriana* Gardner.	16
		W. scaberrima Hook.	24
		W. helianthoides Kunth.	29
		*W. buphthalmiflora (*DC.) Griseb.	27
63.	15*α*-(2,3-Epoxy-2-methybutanoyloxy)- *ent*-kaur-16-en-19-oic acid	*W. calycina* Spreng.	19
		W. grandiflora Benth.	24

(*Contd*.)

Table 1—Chemical Constituents from Genus *Wedelia* (*Contd*.)

Structure No.	Name	Species	Ref.
64.	15*α*-(Isobutyryloxy)- *ent*-kaur-16-en-19-oic acid	*W. buphthalmiflora* (DC.) Griseb.	27
65.	15*α*-(Isovaleryloxy)- *ent*-kaur-16-en-19-oic acid	*W. buphthalmiflora (*DC.) Griseb.	27
66.	15*α*-(2,3-Dihydroxy-2-methybutanoyloxy)- *ent*-kaur-16-en-19-oic acid	*W. calycina* Spreng.	19
67.	9*β*, 15*α*-Dihydroxy- *ent*-kaur-16-en-19-oic acid	*W. calycina* Spreng.	19
68.	15*α*-(Angeloyloxy)- 9*β*-hydroxy- *ent*-kaur-16-en-19-oic acid	*W. trilobata* (L.) Hitchc.	16
		W. hookeriana Gardner	24
		W. grandiflora Benth.	24
		W. helianthoides (L.) Hitchc.	24
69.	9*β*-Hydroxy-15*α*-(senecioyloxy)- *ent*-kaur-16-en-19-oic acid	*W. hookeriana* Gardner	16
70.	9*β*-Hydroxy-15*α*-(3-hydroxy-2- methybutanoyloxy)- *ent*-kaur-16-en-19-oic acid	*W. calycina* Spreng.	19
71.	*ent*-Kaura-6,16-dien-19-oic acid	*W. biflora* (L.) DC.	33
72.	Tetrachyrin	*W. paludosa* DC.	22
73.	16*α*-Hydroxy- *ent*-kauran-19-oic acid	*W. paludosa* DC.	26
74.	*ent*-Kauran-16*α*-ol	*W. paludosa* DC.	24
75.	16*α*, 17-Dihydroxy-*ent*-kauran-19-oic acid	*W. calycina* Spreng.	19
		W. prostrata Hemsl.	34
76.	16*β*, 17-Dihydroxy-*ent*-kauran-19-oic acid	*W. prostrata* Hemsl.	34
77.	*ent*-Kaura-9(11), 16(17)-dien-19-oic acid	*W. hispida* Kunth.	16
		W. calycina Spreng.	19
		W. chinensis (Osbec.) Merr.	25
		W. paludosa DC.	26
		W. hookeriana Gardner.	27
		*W. buphthalmiflora (*DC.) Griseb.	30
78.	12*β*-Hydroxy-*ent*-kaura-9(11), 16-dien-19-oic acid	*W. calycina* Spreng.	16
		W. hookeriana Gardner.	19
79.	*ent*-Kaura-9(11), 16-dien-19-oic acid methyl ester	*W. trilobata* (L.) Hitchc.	24
		W. grandiflora Benth.	24
		W. helianthoides Kunth.	24
80.	*ent*-Kaur-15-en-19-oic acid	*W. biflora* (L.) DC.	33
81.	15*α*,16*α*-Epoxy-17-hydroxy- *ent*-kauran-19-oic acid	*W. calycina* Spreng.	19
82.	15*β*,16*β*-Epoxy-17-hydroxy- *ent*-kauran-19-oic acid	*W. prostrata* Hemsl.	24
83.	16*α*,17*α*-Epoxy-15*α*-angeloyloxy- *ent*-kauran-19-oic acid	*W. penitorum* H.Ro	18
84.	Atractyloside	*W. glauca* (Ortega)Hoffm.ex Hicken	34
		W. asperrima (Decne.) Benth.	34

(*Contd*.)

Table 1—Chemical Constituents from Genus *Wedelia* (*Contd*.)

Structure No.	Name	Species	Ref.
85.	Wedeloside	*W. asperrima* (Decne.) Benth.	35-37
86.	*α*-L-rhamnosyl-(1”→4’)-wedeloside	*W. asperrima* (Decne.) Benth.	37,38
87.	14’-Hydroxy- *α*-L-rhamnosyl-(1”→4’)-wedeloside	*W. asperrima* (Decne.) Benth.	37,38
88.	4’-*O*-Sulphowedeloside	*W. asperrima* (Decne.) Benth.	37
89.	3-*O*-Tetradecanoylolean-12-en-28-oic acid	*W. paludosa* DC.	30
90.	3-*O*-Pentadecanoylolean-12-en-28-oic acid	*W. paludosa* DC.	30
91.	3-*O*-Hexadecanoylolean-12-en-28-oic acid	*W. paludosa* DC.	30
92.	Oleana-11, 13(18)-dienoic acid 3-*O*-*β*-glucuronopyranoside	*W. chinensis* (Osbec.) Merr.	39
93.	Oleana-11, 13(18)-dienoic acid 3-*O*-*β*-(6-*O*-methyl) glucuronopyranoside	*W. chinensis* (Osbec.) Merr.	39
94.	Wedelin	*W. scaberrima* Hook.	40
95.	*β*-D-Glucopyranosyl 3-*O*-[*β*-D-xylopyranosyl-(1→2)-*β*-D-glucuronopyranosyl]oleanolate	*W. calendulacea* (L.) Less.	41
96.	*β*-D-Glucopyranosyl 3-*O*-[*β*-D-glucopyranosyl-(1→2)-*β*-D-glucuronopyranosyl]oleanolate	*W. calendulacea* (L.) Less.	41
97.	Friedelan-3*β*-ol	*W. paludosa* DC.	26
98.	5*α*-Stigm-7-en-3-ol	*W. biflora* (L.) DC.	33
99.	24-Ethylcoprostanone	*W. biflora* (L.) DC.	33
100.	7,4’-Dihydroxy-3’-methoxyflavanone	*W. asperrima* (Decne.) Benth.	37
101.	7,4’-Dihydroxy-8,3’-dimethoxyflavanone	*W. asperrima* (Decne.) Benth.	37
102.	Quercetin 3-*O*-*β*-glucoside	*W. chinensis* (Osbec.) Merr.	42
103.	3,3’-Di-*O*-methylquercetin	*W. biflora* (L.) DC.	43
104.	7,3’-Di-*O*-methylquercetin	*W. biflora* (L.) DC.	43
105.	Kaempferol 3-*O*-*β*-glucoside	*W. chinensis* (Osbec.) Merr.	34
		W. prostrata Hemsl.	42
106.	Luteolin	*W. paludosa* DC.	32,44
107.	4,2’4’-Trihydroxy-3,3’-dimethoxychalcone	*W. asperrima* (Decne.) Benth.	37
108.	4,2’4’-Trihydroxy-3-dimethoxychalcone	*W. asperrima* (Decne.) Benth.	37
109.	4’-*O*-*β*-D-Glupyranosyl-4,2’-dihydroxy-3,3’-dimethoxychalcone	*W. asperrima* (Decne.) Benth.	37
110.	4’-*O*-*β*-D-Glupyranosyl-4,2’-dihydroxy-3-methoxychalcone	*W. asperrima* (Decne.) Benth.	37
111.	2,7,4’-Trihydroxy-5,3’-dimethoxyisoflavone	*W. biflora* (L.) DC.	43
112.	7-Methoxy-2’-hydroxy-5,6-(methylenedioxy)isoflavone	*W. chinensis* (Osbec.) Merr.	39
113.	Wedelolactone	*W. calendulacea* (L.) Less.	45-47
114.	Tri-*O*-methylwedelolactone	*W. calendulacea* (L.) Less.	45
115.	Norwedelolactone	*W. calendulacea* (L.) Less.	45,47
116.	Norwedelic acid	*W. calendulacea* (L.) Less.	45,46
117.	4,5-*O*-Dicaffeoylquinic acid	*W. prostrata* Hemsl.	42,47
		W. chinensis (Osbec.) Merr.	34

(*Contd*.)

Table 1—Chemical Constituents from Genus *Wedelia*

Structure No.	Name	Species	Ref.
118.	3,5-*O*-Dicaffeoylquinic acid	*W. prostrata* Hemsl.	34
		W. chinensis (Osbec.) Merr.	42,47
119.	3,4-*O*-Dicaffeoylquinic acid	*W. prostrata* Hemsl.	34
		W. chinensis (Osbec.) Merr.	42,47
120.	Wedelosin	*W. chinensis* (Osbec.) Merr.	42
121.	Thiophene acetylene	*W. trilobata* (L.) Hitchc.	16
		W. grandiflora Benth.	24
		W. hookeriana Gardner.	24
122.	Dithiophene acetylene	*W. hookeriana* Gardner.	16
123.	Affinin	*W. parviceps* Blake.	48
124.	Veratrylidenehydrazide	*W. biflora* (L.) DC.	43
125.	Chrysophenol 8-*O*-*β*-D-glucopyranoside	*W. chinensis* (Osbec.) Merr.	39

Steroids

Many species of the genus *Wedelia* furnished stigmasterol, stigmasteryl glucoside, sitosterol, and sitosteryl glucoside[15,16,20,26,28-32]. An extract of the stem of *W. biflora* (L.) DC. from Thailand afforded the antifungal compounds (98) and (99) [(Ref. 32)].

Flavonoids

A new flavanone (101), related chalcone (107) and its glucopyranosyl congener (109) as well as a number of known compounds (100, 108 and 110) were isolated from the aerial parts of *W. asperrima* (Decne) Benth.[36]. *W. chinensis* (Osbec.) Merr. furnished two known flavonoid glycosides (102 and 105)[(Ref. 41)]. Miles *et al*, isolated flavonoids (103 and 104) and isoflavonoid (111) from the leaves of *W. biflora* (L.) DC.[42]. In 2005, a new isoflavone (112) was reported from *W. chinensis* (Osbec.) Merr.[38].

Coumarins

Compound (116) was isolated from *W. calendulacea* (L.) Less. for the first time, together with the constituents (113–115)[(Ref. 43)].

Cyclitols

Several caffeic acid derivatives, compounds (117–119) were isolated from *W. chinensis* (Osbec.) Merr.and *W. prostrata* Hemsl.[41,44].

Organic acids

Some organic acids were also found in the genus *Wedelia*. Herz and Kulanthaivel isolated stearic acid, linoleic acid, linolenic acid, and methyl linolenate from the aerial parts of *W. hispida* Kunth.[20]. Further, (10E, 15E)-9, 12, 13- trihydroxyoctadeca-10, 15-dienoic acid and (10E)-9, 12, 13-trihydroxyoctadec-10-enoic acid were isolated from *W. pinetorum* (Standl. & Steyerm.) K. M. Becker[19]. The AcOEt extract of *W. chinensis* (Osbec.) Merr. afforded lignoceric acid (n-$C_{23}H_{47}CO_2H$) and melissic acid (n-$C_{29}H_{59}CO_2H$)[31]. *W. rugosa* Greenm. furnished oleate and palmitate esters[45]. A new compound, (9E, 11Z, 13E)-8, 15- dioxooxadeca-9, 11, 13-trienoic acid was isolated from *W. chinensis* (Osbec.) Merr.[38].

Other compounds

W. chinensis (Osbec.) Merr. afforded wedelosin (120)[(Ref. 41)]. *W. hookeriana* Gardner. furnished (121) as well as the corresponding dithio derivative (122) [(Ref. 16,36)]. An unsaturated aliphatic isobutyl amide, affinin (123), was isolated from the flowers of *W. parviceps* Blake.[46]. The curious hydrazine derivative (124) was isolated from *W. biflora* (L.) DC.[42]. Recently, the anthraquinone (125) was obtained from *W. chinensis* (Osbec.) Merr.[38]. In addition, essential oils containing menthene, limonene, *α*-pinene, *α*-phellandrene, *β*-phellandrene, *γ*-perpinene, *γ*-muurolene, *para*-cymene, spathulenol, and sabinene were also isolated from several *Wedelia* species[15,16,47].

Biological activities

Hepatoprotective Effects

Coumestans from the leaves of *W. calendulacea* (L.) Less. were reported to exhibit significant

protection upon paracetamol-induced hepatocellular injury[48]. Sharma *et al*, reported that the alcoholic extract of the whole plant of *W. calendulacea* (L.) Less. exhibit protective activity against carbon tetrachloride (CCl_4)-induced liver injury *in vivo*. The extract was also found to increase the bile flow in rats, suggesting a stimulation of liver-secretory capacity[49]. In simultaneous studies on potentially antihepatotoxic plant principles, Yang and co-workers found that the MeOH extract of the herbs of *W. chinensis* (Osbec.) Merr. show a strong antihepatotoxic action in CCl_4-induced cytotoxicity using primary cultured rat hepatocytes. *ent* Kaur-16-en-19-oic acid and a mixture of three other kaurenoids, exhibited strong activity against liver damage induced by paracetamol or CCl_4. Lignoceric acid at 1 mg/mL in the culture medium, also showed significant protective activity against CCl_4-induced liver damage, although it was found inactive in a GalN-induced cytotoxicity model system[31.] The coumestans wedelolactone (113) and norwedelolactone (115) isolated by Wagner & co-workers from *W. calendulacea* (L.) Less. as the main active principles were both active in CCl_4-, GalN-, and phalloidin-cytotoxicity models in rat hepatocytes[50]. The same authors also demonstrated a significant stimulatory effect on liver-cell regeneration. Meotti *et al*, reported that the crude extract from *W. paludosa* DC. protects against paracetamol induced hepatotoxicity in mice[51]. Recently our research group showed the hepatoprotective activity of the aqueous and alcoholic extract of *W. chinensis* (Osbec.) Merr. in CCl_4 induced hepatotoxicity in Wister albino rats. The extracts registered a significant fall in the levels of serum liver marker enzymes (biochemical evidence) and liver inflammation supported by histopathological studies on liver[9].

Antipyretic-analgesic effects

Block *et al*, described the antinociceptive effects of compounds obtained from *W. paludosa* DC. The different fractions, as well as (53) and luteolin (106) exhibited marked antinociceptive action in mice upon acetic acid induced writhing. These compounds and fractions were more active than some well-known analgesic drugs such as acetyl salicylic acid, acetaminophen, dipyrone or indomethacin[52].

Molluscicidal effects

The flowers of *W. parviceps* Blake. contain affinin (123), which showed strong molluscicidal activity against *Physa occidentalis* and the cercariae of the fluke was reported[32,46]. Batista *et al*, reported the trypanosomicidal activity of ent-kaura-9(11),16(17)-dien-19-oic acid (77) and 3α- (angeloyloxy)-ent-kaur-16-en-19-oic acid (51), up to a lowest dose of 0.68 mg/mL, in an *in vitro* assay against trypomastigotes of *Trypanosoma cruzi*, the causative agent of Chagas' disease[26]. Miles *et al*, tested the extracts from the stems and leaves of *W. biflora* (L.) DC., and showed that 2,7,4'-trihydroxy-5,3'-dimethoxyisoflavone (111), 24-ethylcoprostanone (99) and ent-kaura-6,16-dien-19-oic acid (71) exhibit antifungal and boll-weevil antifeedant activities. 7, 3'-Di-O-methylquercetin (104), entkaur- 15-en-19-oic acid (80) and grandifloric acid (57) also showed antifungal activities[32,42].

Antibacterial effects

The cytotoxic and antibacterial activities of the petroleum ether, $CHCl_3$ and MeOH extracts of *W. calendulacea* (L.) Less. were also reported. The diterpenes isolated from the plant were also evaluated for *in vitro* antibacterial activities. The LC_{50} values for the crude extracts against brine shrimp nauplii were found to be 4.59, 7.99, and 14.88 mg/mL, respectively. Among the crude extracts and pure compounds tested, compound (53) isolated from the $CHCl_3$ extract and showed the highest inhibitory activity against most of the bacterial strains[22].

Taddei *et al*, reported the activities of crude extracts from *W. trilobata* (L.) Hitchc. against Gram-positive and negative bacteria, yeasts and fungi. The hexane extract showed antibacterial activity against *Bacillus subtilis, Mycobacterium smegmatis, Staphylococcus aureus* and *Staphylococcus epidermidis* (Gram-positive bacteria), along with *Proteus vulgaris, Pseudomonas aeruginosa, Salmonella group C, Salmonella paratyphi,* and *Shigella sonnei* (Gram-negative bacteria). The AcOEt extract was active only against *Salmonella group C* and the aqueous extract was inactive against the tested bacteria, also, none of the extracts tested were active against yeast or fungi[53].

Sartori *et al*, reported that several fractions, as well as the pure compounds (53) and (106) isolated from the flowers of *W. paludosa* DC. showed antifungal activities. The hexane, CH_2Cl_2 and BuOH soluble fractions inhibited the growth of *Epidermophyton floccosum, Trichophyton rubrum* and *T. mentagrophytes*, with minimal-inhibitory-concentration values of 250 and 1000 µg/mL[54].

Darah *et al*, recently reported the antibacterial activity of the methanol extract of *W. chinensis* (Osbec.) Merr. leaves against three pathogenic Gram-positive bacteria (*Bacillus cereus, B. subtilis* and . *aureus*) and three pathogenic Gram-negative bacteria (*Escherichia coli, Proteus rettgeri* and *P. aeruginosa*) by the disk diffusion assay and broth dilution methods. The extract exhibited favourable antibacterial activity against the bacterial cells but was more potent against Gram-positive bacteria with the minimum inhibition concentration of 3.12 to 6.25 mg/mL compared to the Gram-negative bacteria which had minimum inhibition concentration values of 25 mg/mL. The time-kill study suggested that the extract possessed bactericidal properties at higher concentrations and eradicated the growth of bacterial cells. The major abnormalities was observed in the bacterial cells after exposure to the extract were complete alterations in their morphology and cell collapse beyond repair. The methanol extract of *W. chinensis* (Osbec.) Merr. may be an effective antibacterial agent to treat bacterial infections[55].

Biswas *et al*, evaluated the antimicrobial activity of the ethanol extract of leaves of *W. biflora* (Linn.) DC. In *in vitro* assays the extract was subjected to antimicrobial activity by agar well-diffusion method and minimum inhibitory concentration method in different microbial strains, which established the antimicrobial efficacy[56].

Pratap *et al*, reported antimicrobial efficacy of *W. chinensis* (Osbec.) Merr. on three pathogenic microorganisms in the oral cavity (*Streptococcus mutans, Lactobacillus casei,* and *S. aureus*). Aqueous extract concentrations (5, 10, 25, and 50 %) were prepared from leaves of *W. chinensis*. The antimicrobial efficacy was tested using agar well diffusion method and the size of the inhibition zone was measured in mm. The results showed that the extract was effective against dental caries causing bacteria[57].

Hypoglycemic effects

Novaes *et al*, evaluated the extract of *W. paludosa* DC. for its hypoglycaemic effect, and it was found that the crude extract decreases the blood sugar level in mice with alloxan-induced diabetes[58]. Kaurenoic acids isolated from *W. paludosa* DC. exhibit hypoglycemic effects[59].

Anti-osteoporotic effects

Annie *et al*, reported that the EtOH extract of *W. calendulacea* (L.) Less. is effective in an ovariectomized-rat model of osteoporosis[60].

Antitumor effects

Oelrichs *et al*, isolated the toxin wedeloside (85) from *W. asperrima* (Decne) Benth., which in preliminary experiments, was found to inhibit tumors produced by aflatoxin B1 in rats[35].

The methanolic extract of *W. calendulacea* (L.) Less. (MEWC) was evaluated for their anticancer activity against Ehrlich Ascites Carcinoma (EAC) in Swiss albino mice. MEWC increased the life span of EAC treated mice and restored the hematological parameters as compared with the EAC bearing mice. Wedelolactones present in *W. calendulacea* (L.) Less. were found to have 5-lipooxygenase and caspase inhibiting activities[50,61]. The anticancer activity may be due to the LOX inhibition or due to induction of detoxifying system[62].

Exposure of prostate cancer cells to *W. chinensis* (Osbec.) Merr. extract induced apoptosis selectively in androgen receptor positive prostate cancer cells and shifted the proportion in each phase of cell cycle toward G(2)-M phase in AR-negative prostate cancer cells. Oral herbal extract (4 or 40 mg/kg/d for 24-28 days) attenuated the growth of prostate tumors in nude mice implanted at both subcutaneous (31 and 44 %, respectively) and orthotopic (49 and 49 %, respectively) sites. The tumor suppression effects were associated with increased apoptosis and lower proliferation in tumor cells as well as reduced tumor angiogenesis. The antitumor effect was correlated with accumulation of the principle active compounds wedelolactone, luteolin and apigenin *in vivo*[63].

Thu *et al*, isolated six new phenolic glycosides and one new ceramide from the flowers of *W. biflora* (Linn.) DC. The cytotoxic activities against HeLa, MCF-7 and NCI-H460 were evaluated on some purified compounds at the concentration of 100 µg/mL. All Compounds showed significant cytotoxic activities against three surveyed cancer cell lines[64].

Halder *et al*, reported the chemopreventive effect of MEWC against 20-methylcholanthrene (20-MC) induced carcinogenesis in Swiss albino mice. MEWC treatment significantly ($p<0.001$) modulated the liver biochemical parameters as compared to 20-MC control. *W. calendulacea* (L.) Less. showed remarkable chemopreventive efficacy in Swiss mice[65].

Wound healing effect

In 2008, our research group evaluated the wound healing efficacy of the ethanolic extract of *W. chinensis* (Osbec.) Merr. leaves. The parameters studied included rate of wound contraction, period of

complete epithelialization, tensile strength of incision wound and granulation tissue dry weight. The extract was found to possess significant wound healing activity as evidenced by decrease in the period of epithelialization, increase in the rate of wound contraction, skin breaking strength, granulation tissue dry weight and its breaking strength[6].

Biswas *et al*, evaluated the wound healing activity of ethanol extract of leaves of *W. biflora* (Linn.) D.C. Wound healing was studied by excision and incision wound model in Wistar albino rats. In excision wound model, 97.90 % wound healing was recorded in 10 % w/w extract treated group on 16th day postsurgery, whereas only 58.50 % healing was observed in control group. In incision model, higher breaking strength, high hydroxyl proline content and histopathological study in extract treated groups revealed higher collagen redeposition than the control group. These observations supported the traditional claim and therapeutic activity of *W. biflora* (Linn.) DC., which may be a potent wound healing candidate in future[56].

Balekar *et al*, reported the wound healing activity of ent-kaura-9(11),16-dien-19-oic acid isolated from *W. trilobata* (L.) Hitchc. leaves. The study provided scientific evidence for the traditional use of *W. trilobata* (L.) Hitchc. in wound healing due to a combination of antimicrobial, stimulation of fibroblast growth and protection of the cells from hydrogen peroxide-induced injury, all of which could affect tissue repair[66,67].

Antioxidant effect

Our research group reported the antioxidant activity of defatted ethanolic extract of *W. chinensis* (Osbec.) Merr. leaves in different *in vitro* models as 1, 1-Diphenyl-2-picryl hydrazyl (DPPH), nitric oxide, superoxide, hydroxyl radical and lipid peroxide radical model. The extract showed significant dose-dependent free radical scavenging property in all the models. IC_{50} values were found to be 9.16, 13.21, 25.27 and 17.33 µg/mL, respectively in DPPH, nitric oxide, superoxide and lipid peroxidation inhibition assays. Measurement of total phenolic compounds by Folin-Ciocalteu's phenol reagent indicated that 1 mg of the extract contained 200.56 µg/g equivalent of gallic acid. The results of the present investigation revealed that the antioxidant property of the extract may be due to the high content of phenolic compounds[5].

Manjamalai *et al*, evaluated the effects of essential oils of *W. chinensis* (Osbec.) Merr. on free radicals and *in vivo* antioxidant properties. The essential oil exhibited significant inhibition in DPPH free radical formation. Whereas reducing power and hydroxyl radical scavenging activity are dose dependent. When compared with the standard, it was found that the essential oil has more or less equal activity in scavenging free radicals produced. In animal studies, the level of antioxidant enzymes catalase, superoxide dismutase and glutathione peroxidase as well as glutathione were found to be increased in treated groups whereas lipid peroxidation and nitric oxide were reduced. From the results, the essential oil may be recommended for treating disease related to free radicals and to prevent cancer development[68].

Antistress effect

Our research group reported the antistress activity of ethanolic extract of the *W. chinensis* (Osbec.) Merr., studied on cold immobilization induced lipid peroxidation in albino rats. Extract administered at a dose of 500 mg/kg bw significantly inhibited cold immobilization stress induced increase in lipid peroxidation in the liver and brain of the albino rat. The results suggested the potential use of the plant for decreasing anxiety and stress in many emotional and physical disorders[7].

The extract was further evaluated for stress induced changes in brain neurotransmitters and enzyme monoamine oxidase levels in albino rats. The extracts were found to possess normalizing activity against cold immobilization stress induced changes in norepinephrine, dopamine, 5-hydroxy tryptamine, 5-hydroxy indole acetic acid and enzyme monoamine oxidase. The results provided biochemical evidence for antistress activity of the tested extracts[8].

Neuroprotective activity

An ethyl acetate extract of *W. chinensis* (Osbec.) Merr. (EAW) was prepared and analyzed by HPLC. The neuroprotective potential was assessed by tert-butylhydroperoxide (t-BHP)-induced damage in PC12 cells and D-galactose-induced damage in mouse cortex. EAW exhibited potent radical scavenging property and contained high amount of luteolin and wedelolactone. EAW decreased t-BHP-induced reactive oxygen species accumulation, cytotoxicity and apoptosis in PC12 cells. EAW and its major constituents blocked t-BHP-induced cytochrome

C release and Bcl-2 family protein ratio change. They also increased the endogenous antioxidant capacity evaluated by the binding activity assay of nuclear factor E2-related factor 2 (Nrf2) to antioxidant response element and nuclear translocation of Nrf2 respectively in PC12 cells. Finally, EAW inhibited D-galactose-induced lipid peroxidation, apoptosis and neuron loss in the cerebral cortex of mice through blocking oxidative stress-induced damage and that luteolin and wedelolactone contribute to the protective action[69].

Prakash *et al*, evaluated the neuroprotective activity of *W. calendulacea* (L.) Less. against cerebral ischemia/reperfusion induced oxidative stress in the rats. The ischemic changes were preceded by increase in concentration of MDA, hydrogen peroxide and followed by decreased GPx, GR and GST activity. Treatment with *W. calendulacea* (L.) Less. significantly attenuated ischemia-induced oxidative stress. *W. calendulacea* (L.) Less. administration markedly reversed and restored to near normal level in the groups pre-treated with methanolic extract (250 and 500 mg/kg, given orally in single and double dose/day for 10 days) in dose-dependent way. Similarly, *W. calendulacea* (L.) Less. reversed the brain water content in the ischemia reperfusion animals. The neurodegenaration also confirmed by the histopathological changes in the cerebral-ischemic animals. The study revealed that *W. calendulacea* (L.) Less. protects neurons from global cerebral-ischemic injury in rat by attenuating oxidative stress[70,71].

The neuropharmacological activities of the methanolic and aqueous extract of *W. calendulacea* (L.) Less. stem were screened in rats and mice. The extracts effect on pentobarbital-induced sleeping time, pentylenetetrazole- and styrychnine-induced seizure, spontaneous motor activity (SMA), exploratory behaviour and rota-rod performance (motor coordination) were evaluated. The methanolic extract (20 and 50 mg/kg, i p) and aqueous extract (200 and 500 mg/kg, i p) produced a significant ($p<0.001$) prolongation of pentobarbital-induced sleeping time and reduced the SMA as well as exploratory behaviour. The extract prolonged onset of the phases of seizure activity but did not protect mice against lethality induced by pentylenetetrazole and strychnine. It also failed to affect the motor coordination test. The results suggested that the extract contained an agent with neuropharmacological activity that may be sedative in nature. In addition, from the crude methanolic extract of *W. calendulacea* (L.) Less. stem a HPLC fingerprint profile and liquid chromatography/ sequential mass spectrometry were performed[72].

Menstrual problems

Recent study by Flores *et al*, revealed the use of *W. trilobata* (L.) Hitchc. used by Dominica women to treat dysmenorrheal, delayed menses and menorrhagia. The ethnobotanical treatments reflect their perceived ethnophysiological efficacy and the plants may contain bioactive compounds appropriate for the menstrual conditions for which Dominicans employ the plants[73].

Anti-inflammatory effect

Yuan *et al*, reported the anti-inflammatory effects and mechanism of Wedelolactone, a major coumestan ingredient in *W. chinensis* (Osbec.) Merr. with a cellular model of lipopolysaccharide (LPS)-induced RAW 264.7 cells. Nuclear factor-kappaB (NF-κB) transcription activity was detected by luciferase reporter assay. The important pro-inflammatory transcription factors, NF-κB p65 and inhibitory kappaB alpha (IκB-α); and mitogen-activated protein kinases (MAPKs), including extracellular signal-regulated kinase (ERK), c-Jun N-terminal kinase (JNK) and p38 MAPK (p38) were analyzed by Western blotting. The study showed that Wedelolactone (0.1, 1, 10 μM) significantly inhibited the protein expression levels of iNOS and COX-2 in LPS-stimulated cells, as well as the downstream products, including NO, PGE2 and TNF-α. Moreover, Wedelolactone also inhibited LPS-induced NF-κB p65 activation via the degradation and phosphorylation of IκB-α and subsequent translocation of the NF-κB p65 subunit to the nucleus. The results indicated that Wedelolactone has a potential to be a novel anti-inflammatory agent targeting the NF-κB signaling pathway[74].

In colitis

Huang *et al*, reported that dietary uptake of *W. chinensis* (Osbec.) Merr. extract attenuates dextran sulfate sodium-induced colitis in mice**.** C57BL/6 mice were administrated hot water extract of fresh *W. chinensis* (Osbec.) Merr. (WCHF) orally for one week followed by drinking water containing 2 % DSS for nine days. WCHF significantly attenuated the symptoms of colitis including diarrhoea, rectal bleeding and loss of body weight; it also reduced the shortening of colon length and histopathological

damage caused by colonic inflammation. Among four *W. chinensis* (Osbec.) Merr. extracts prepared by different extraction techniques, WCHF showed the highest anti-colitis efficacy. Analyses of specific T-cell regulatory cytokines (TNF-α, IL-4, IFN-γ, IL-17, TGF-β, IL-12) revealed that WCHF treatment can suppress the Th1 and Th17, but not Th2, responses in colon tissues and dendritic cells of DSS-induced colitis mice. A 28-day subacute toxicity study showed that daily oral administration of WCHF (100, 500, 1000 mg/kg bw) was not toxic to mice[75].

Conclusion

Plants of the genus *Wedelia* Jacq. have complex constituents, many of which have been used in traditional folk medicine throughout the world. Phytochemical investigations of various *Wedelia* species have revealed that many components from this genus express significant biological and pharmacological activities. Nevertheless, there are still many *Wedelia* species that have received very little or no attention. Further phytochemical and biological studies should be done now on these plants. *(Note: Figure in the parenthesis indicates the structure No.)*

References

1 Li X, Dong M, Liu Y, Shi Q and Kiyota H, Structures and biological properties of the chemical constituents from genus *Wedelia*, *Chem Biodiv*, 2007, **4**, 823-836.

2 Anonymous, Editorial committee of the administration bureau of Chinese plant medicine, Chinese flora Science press Beijing, 1979, 201-232.

3 Anonymous, The Wealth of India-A Dictionary of Indian raw materials & industrial products, Vol. X (Sp-W), Publication and information directorate, CSIR, New Delhi, 2005.

4 Jiangsu, New Medical College, NA *Comprehensive dictionary of traditional Chinese materia medica*, Shanghai Peoples Press, Shanghai, 1977.

5 Verma N and Khosa R L, Antioxidant potential of some Indian medicinal plants, *Naresuan Phayao J* 2008, **1**, 99-101.

6 Verma N, Khosa R L and Garg V K, Wound healing activity of *Wedelia chinensis* leaves, *Pharmacologyonline*, 2008, **2**, 139-145.

7 Verma N and Khosa R L, Effect of alcoholic extract of *Wedelia chinensis* on cold immobilization stress induced tissue lipid peroxidation, *Pharmacologyonline,* 2009, **1**, 493-497.

8 Verma N and Khosa R L, Effect of *Costus speciosus and Wedelia chinensis* on brain neurotransmitters and enzyme monoamine oxidase following cold immobilization stress, *J Pharm Sci Res,* 2009, **1**, 22-27.

9 Verma N, Mishra G, Sinha R, Khosa R L, Garg V K and Singh P, Hepatoprotective activity of alcoholic and aqueous extracts of *Wedelia chinensis, Pharmacologyonline,* 2009, **1**, 345-356.

10 Bohlmann F and Zdero C, Naturally occurring terpene derivatives, LV, A new constituent from *Wedelia forsteriana. Endl Chem Ber,* 1976, **109,** 791-92.

11 Bohlmann F, Rosenberg E, Robinson H and King R M, Naturally occurring terpene derivatives: Pseudoguaianolides from *Wedelia grandiflora*, *Phytochem,* 1980, **19**, 2047-2048.

12 Farag S F, El-Emary N A and Niwa M, Trilobolide-6-*O*-isobutyrate, a eudesmanolide from *Wedelia trilobata*, *Chem Pharm Bull*, 1996, **44**, 661-664.

13 Zhang Y H, Liu M F, Ling T J and Wei X Y, New eudesmanolide of *yaredai zhiwu xuebao Redai, Yaredai Zhiwu Xuebao*, 2004, **12**, 533-537.

14 Ragasa C Y and Padolina W G, New eudesmanolide sesquiterpenes from a philippines collection of *Wedelia prostata*, *J Nat Prod*, 1993, **56**, 386-393.

15 Bohlmann F, Ziesche J, King R M and Robinson H, Naturally occurring terpene derivatives : Eudesmanolides and diterpenes from *Wedelia trilobata* and an ent-kaurenic acid derivative from *Aspilia parvifolia*, *Phytochem,* 1982, **20**, 751-756.

16 Bohlmann F, Zdero C, King R M and Robinson H, Naturally occurring terpene derivatives: Eudesmanolides and kaurene derivatives from *Wedelia hookeriana*, *Phytochem,* 1982, **21**, 2329-2333.

17 Bohlmann F, Ang W, King R M and Robinson H, A further steiractinolide from *Wedelia grandiflora, Phytochem,* 1984, **23**, 2069-2070.

18 Bohlmann F and Van N L, Naturally occurring terpene derivatives: New kaurenic acid derivatives from *Wedelia* species, *Phytochem,* 1977, **16**, 579-581.

19 Herz W and Sosa V E, 10α-methyl-eudesman-8αH, 12-olides and other constituents from *Wedelia pinetorum*, *Phytochem,* 1986, **25**, 1481-1483.

20 Herz W and Kulanthaivel P, *En*t-kauranes and 10α-methyl-eudesman-8αh, 12-olides from *Wedelia calycina* and *Wedelia hispida*, *Phytochem,* 1984, **23**, 2271-2275.

21 Bohlmann F, Gerke T, Jakupovic J, Borthakur N, King R M and Robinson H, Diterpene lactones and other constituents from *Wedelia* and *Aspilia* species, *Phytochem,* 1984, **23**, 1673-1676.

22 Mottakin A K M, Chowdhury R, Haider M S, Rahman K M, Hasan C M and Rashid M A, Cytotoxicity and antibacterial activity of extractives from *Wedelia calendulacea*, *Fitoterapia,* 2004, **75**, 355-359.

23 Vieira H S, Takahashi J A, Boaventura M A, Constituents from aerial parts of *Wedelia paludosa*, *Fitoterapia,* 2001, **72**, 854-856.

24 Haider M A, Chowdhury R, Mottakin A K M, Sohrab M H, Hasan C, Mahbubar- Rahman A H M and Rashid M A, Kauren diterpenes from *Wedelia calendulacea*, *Biochem Syst Ecol*, 2003, **31**, 539-540.

25 Huang Y, Pieters L, Cimanga K, De Bruyne T, Claeys M, Lemiere G, Vanden Berghe D and Vlietinck A J, Terpenoids from *Wedelia chinensis*, *Pharm Pharmacol Lett,* 1997, **7**, 175-177.

26 Batista R, Chiari E and Oliveira A B, Trypanosomicidal kaurane diterpenes from *Wedelia paludosa*, *Planta Med,* 1999, **65**, 283-284.

27 Schteingart C D and Pomilio A B, Terpenoids from *Wedelia buphthalmiflora*, *Phytochem,* 1981, **20**, 2589-2590.

28 Oberti J C, Pomilio A B and Gros E G, Diterpenes sterols from *Wedelia glauca*, *Phytochem,* 1980, **19**, 2051-2052.

29 Tomassini T C B and Matos M E O, On the natural occurrence of 15α-tiglinoyloxy-kaur-16-en-19-oic acid, *Phytochem,* 1979, **18**, 663-664.

30 De Carvalho G J A, De Carvalho M G, Ferreira D T, Faria T J and Braz-Filho R, Diterpenes, triterpenes and steroids from flowers *of Wedelia paludosa*, *Quim Nova,* 2001, **24**, 24-26.

31 Yang L L, Yen K Y, Konno C, Oshima Y, Kiso Y and Hikino H, Antihepatotoxic principles of *Wedelia chinensis* herbs, *Planta Med,* 1986, **52**, 499-500.

32 Miles D H, Chittawong V, Payne A M, Hedin P A and Kokpol U, Cotton boll-weevil antifeedant activity and antifungal activity *(Rhizoctonia lani* and *Pythium ultimum*) of extracts of the stems of *Wedelia biflora*, *J Agric Food Chem,* 1990, **38**, 1591-1594.

33 Schteingart C D and Pomilio A B, Atractyloside, toxic compound from *Wedelia glauca*, *J Nat Prod,* 1984, **47**, 1046-1047.

34 Eichholzer J V, Lewis I A S and Macleod J K, The toxic extractives from *Wedelia asperrima* : The structure and synthesis of the unusual glycosidic portion of wedeloside, *Tetrahedron,* 1981, **37**, 1881-1891.

35 Oelrichs P B, Vallely P J, Macleod J K and Lewis I A S, Isolation of a new potential antitumor compound from *Wedelia asperrima*, *J Nat Prod,* 1980, **43**, 414-416.

36 Caleanasan C A and Macleod J K, A diterpenoid sulphate and flavonoids from *wedelia asperrima*, *Phytochem,* 1998, **47**, 1093-1099.

37 Macleod J K, Lewis I A S, Moeller P D R and Oelrichs P B, The toxic extractives from *Wedelia asperrima*, III: Structures of two naturally occurring rhamnosyl analogues of Wedeloside, *J Nat Prod,* 1990, **53**, 1256-1261.

38 Luo X R, Master Thesis, The Academy of Military Medical Sciences, Beijing, China, 2005.

39 Matos M E O and Tomassini TCB, Wedelin, a saponin from *Wedelia scaberrima*, *J Nat Prod,* 1991, **46**, 836-840.

40 Gobindachari T R and Premila MS, Triterpenoids saponins from *Wedelia calendulaceae* Less, *Indian J Chem, Sect B,* 1991, **30**, 466-468.

41 Apers S, Huang Y, Van Miert S, Dommisse R, Vanden - Berghe D, Pieters L and Vlietinck A, Characterisation of new oligoglycosidic compounds in two Chinese medicinal herbs, *Phytochem Anal,* 2002, **13**, 202-206.

42 Miles D H, Chittawong V, Hedin P A and Kokpol U, Potential agrochemicals from leaves of *Wedelia biflora*, *Phytochem,* 1993, **32**, 1427-1429.

43 Govindachari T R and Premila M S, The benzofuran norwedelic acid from *Wedelia calendulaceae*, *Phytochem,* 1985, **24**, 3068-3069.

44 Farag S F, Hassanean H A, Makboul A M, El-Emary N A and Niwa M, Ent kaurane diterpenes and further constituents from *Wedelia trilobata, Bull Pharm Sci Assiut Univ,* 1998, **21**, 81-84.

45 Aleman E, Rosado A, Rodriguez M and Bertran J F, Componentes de la *Wedelia rugosa* G, *Rev Cubana Farm,* 1977, **11**, 47-54.

46 Johns T, Graham K and Towers G H N, Molluscicidal activity of affinin and other isobutylamides from the Asteraceae, *Phytochem,* 1982, **21**, 273727-38.

47 Craveiro A A, Matos F J A, Alencar J W, Machado M I L, Krush A, and Silva M G V, Volatile constituents of two *Wedelia* species, *J Essent Oil Res,* 1993, **5**, 439-441.

48 Emmanuel S, Amalraj T and Ignacimuthu S, Hepatoprotective effect of coumestans isolated from the leaves of *Wedelia calendulacea* Less. in paracetamol induced liver damage, *Indian J Exp Biol,* 2001, **39**, 1305-1307.

49 Sharma A K, Anand K K, Pushpangadan P, Chandan B K, Chopra C L, Prabhakar Y S and Damodaran N P, Hepatoprotective effects of *Wedelia calendulacea*, *J Ethnopharmacol,* 1989, **25**, 93-102.

50 Wagner H, Geyer B, Kiso Y, Hikino H and Rao G S, Coumestans as the main active principles of the liver drugs *Eclipta alba* and *Wedelia calendulacea*, *Planta Med,* 1986, **52**, 370-374.

51 Meotti F C, Rosa J M, Brocardo P S, Balz D, Waltrick A P, Bagio A, Goulart E C, Dafre A L, Rodrigues A L S and Santos A R S, Protective effect of crude extract from *Wedelia paludosa* (Asteraceae) on the hepatotoxicity induced by paracetamol in mice, *J Pharm Pharmacol,* 2006, **58**, 137-142.

52 Block L C, Santos A R S, Marcia de Souza M, Scheidt C, Yunes R A, Santos M A, Monache F D and Filho V C, Chemical and pharmacological examination of antinociceptive constituents of *Wedelia paludosa, J Ethnopharmacol,* 1998, **61**, 85-89.

53 Taddei A and Rosas-Romero A J, Antimicrobial activity of *Wedelia trilobata* crude extracts, *Phytomedicine,* 1999, **6**, 133-134.

54 Sartori M R K, Pretto J B, Bresciani L F V, Yunes R A, Sortino M, Zacchino S A and Cechinel Filho V, Antifungal activity of fractions and two pure compounds of flowers from *Wedelia paludosa* (*Acmela brasiliensis*) (Asteraceae), *Pharmazie,* 2003, **58**, 567-569.

55 Darah I, Lim S H and Nithianantham K, Effects of methanol extract of *Wedelia chinensis* Osbeck (Asteraceae) leaves against pathogenic bacteria with emphasis on *Bacillus cereus*, *Indian J Pharm Sci,* 2013, **75**, 533-539.

56 Biswas D, Yoganandam G P, Dey A and Deb L, Evaluation of antimicrobial and wound healing potentials of ethanol extract of *Wedelia biflora* Linn D.C. leaves, *Indian J Pharm Sci,* 2013, **75**, 156-161.

57 Pratap G M J S, Manoj K M G, Sai S A J, Sujatha B and Sreedevi E, Evaluation of three medicinal plants for anti-microbial activity, *Ayurveda*, 2012, **33**, 423-428.

58 Novaes A P, Rossi C, Poffo C, Pretti Junior E, Oliveira A E, Schlemper V, Niero R, Cechinel-Filho V and Biirger C, Preliminary evaluation of the hypoglycemic effect of some Brazilian medicinal plants, *Therapie,* 2001, **56**, 427-430.

59 Bresciani L F V, Yunes R A, Biirger C, De Oliveira L E, Bo´ f KL, Cechinel-Filho V, Seasonal variation of kaurenoic acid, a hypoglycemic diterpene present in *Wedelia paludosa (Acmela brasiliensis)* (Asteraceae), *Z Naturforsch* C, 2004, **59**, 229-232.

60 Annie S, Prabhu R G and Malini S, Activity of *Wedelia calendulacea* Less. in post-menopausal osteoporosis, *Phytomed*, 2006, **13**, 43-48.

61 Kobori M, Yang Z, Gong D, Heissmeyer V, Zhu H, Jung Y K, Gakidis M A, Rao A, Sekine T, Ikegami F, Yuan C and Yuan J, Wedelolactone suppresses LPS induced caspase-11 expression by directly inhibiting the IKK complex, *Cell death differ*, 2004, **11**,123-130.

62 Gupta M, Mazumder U K, Haldar P K, Kandar C C, Manikandan L and Senthil G P, Anticancer activity of *Indigofera aspalathoides* and *Wedelia calendulaceae* in Swiss albino mice, *Iranian J Pharmaceutical Res*, 2007, **6**, 141-145.

63 Tsai C H, Lin F M, Yang Y C, Lee M T, Cha T L, Wu G J, Hsich S C and Hsiao P W, Herbal extract of *Wedelia chinensis* attenuates androgen receptor activity and orthotopic growth of prostate cancer in nude mice, *Clin Cancer Res*, 2009, **14**, 5435-5444.

64 Thu N T, Ha le T, Nga V T, Tuyen P N, Quang T T, Daniellee F R, Lawrence P and Phung N K, Six new phenolic glycosides and a new ceramide from the flowers of *Wedelia biflora* and their cytotoxicity against some cancer cell lines, *Nat Prod Commun*, 2013 , **8**, 367-372.

65 Haldar P K, Bhattacharya S, Dewanjee S and Mazumder U K, Chemopreventive efficacy of *Wedelia calendulaceae* against 20-methylcholanthrene-induced carcinogenesis in mice. *Environ Toxicol Pharmacol*, 2011, **31**, 10-17.

66 Balekar N, Nakpheng T, Katkam N G and Srichana T, Wound healing activity of ent-kaura-9(11), 16-dien-19-oic acid isolated from *Wedelia trilobata* (L.) leaves. *Phytomedicine*, 2012, **19**, 1178-1184.

67 Balekar N, Katkam N G, Nakpheng T, Jehtae K and Srichana T, Evaluation of the wound healing potential of *Wedelia trilobata* (L.) leaves, *J Ethnopharmacol*, 2012, **141**, 817-824.

68 Manjamalai A and Berlin Grace V M, Antioxidant activity of essential oils from *Wedelia chinensis* (Osbeck) *in vitro* and *in vivo* lung cancer bearing C57BL/6 mice, *Asian Pac J Cancer Prev*, 2012, **13**, 3065-3071.

69 Lin W L, Wang S M, Ho Y J, Kuo H C, Lee Y J and Tseng T H, Ethyl acetate extract of *Wedelia chinensis* inhibits tert-butyl hydroperoxide-induced damage in PC12 cells and D-galactose-induced neuronal cell loss in mice, *BMC Complement Altern Med*, 2014, Dec, **14**, 491-495.

70 Prakash T, Kotresha D and Nedendla R R, Neuroprotective activity of *Wedelia calendulacea* on cerebral ischemia/reperfusion induced oxidative stress in rats, *Indian J Pharmacol*, 2011, **43**, 676-682.

71 Prakash T, Kotresha D and Rama Rao N, Cerebroprotective activity of *Wedelia calendulacea* on global cerebral ischemia in rats, *Acta Biol Hung*, 2011, **62**, 361-375.

72 Prakash T, Rao N R and Swamy A H, Neuropharmacological studies on *Wedelia calendulacea* Less stem extract, *Phytomedicine*, 2008, **15**, 959-70.

73 Flores K E and Quinlan M B, Ethnomedicine of menstruation in rural Dominica, West Indies, *J Ethnopharmacol*, 2014, **153,** 624-634.

74 Yuan F, Chen J, Sun P P, Guan S and Xu J, Wedelolactone inhibits LPS-induced pro-inflammation via NF-kappaB pathway in RAW 264.7 cells, *J Biomed Sci*, 2013, **31**, 20-28.

75 Huang Y T, Wen C C, Chen Y H, Huang W C, Huang L T, Lin W C, Arulselvan P, Liao J W, Lin S H, Hsiao P W, Kuo S C and Yang N S, Dietary uptake of *Wedelia chinensis* extract attenuates dextran sulfate sodium-induced colitis in mice, PLoS One, 2013, **8**, 6-13.