Tropical Journal of Pharmaceutical Research August 2015; 14 (8): 1525-1536
ISSN: 1596-5996 (print); 1596-9827 (electronic)

Available online at http://www.tjpr.org
http://dx.doi.org/10.4314/tjpr.v14i8.28

Review Article

Phytochemical and Biological Properties of *Ajuga decumbens* (Labiatae): A Review

Boran Ni[1], Xiaoxv Dong[2], Jing Fu[2], Xingbin Yin[2], Longfei Lin[2], Zhenwen Xia[2], Yang Zhao[2], Dan Xue[2], Chunjing Yang[2] and Jian Ni[1]*

[1]School of Basic Medical Sciences, [2]School of Chinese Pharmacy, Beijing University of Chinese Medicine, Beijing, 100102, China

For correspondence: **Email: njtcm@263.net; **Tel:** 010-84738607*

Received: 4 March 2015 *Revised accepted: 23 June 2015*

Abstract

Ajuga decumbens Thunb is a member of Labiatae family and widespread in China, Korea and Japan. This plant possesses diverse pharmacological activities, such as anti-inflammatory, antitumor, antibacterial, antiviral, cytotoxic, as well as insecticidal activities. Several compounds have been isolated from A. decumbens, which display a wide spectrum of biological and pharmacological activities. Hence, it would be useful to review current literature for available pharmacological activities of the plant as well as its active ingredients.

Keywords: *Ajuga decumbens Thunb, Anti-inflammatory, Antitumor, Antibacterial, Antiviral, Cytotoxic, Insecticidal , Diterpenes, Iridoids glycosides*

Tropical Journal of Pharmaceutical Research is indexed by Science Citation Index (SciSearch), Scopus, International Pharmaceutical Abstract, Chemical Abstracts, Embase, Index Copernicus, EBSCO, African Index Medicus, JournalSeek, Journal Citation Reports/Science Edition, Directory of Open Access Journals (DOAJ), African Journal Online, Bioline International, Open-J-Gate and Pharmacy Abstracts

INTRODUCTION

The genus *Ajuga* is widely spread throughout the temperate regions of Europe, Asia, Australia, North America, and Africa [1,2]; this group contains many medicinal plants such as *A. decumbens* Thunb., *A. bracteosa* Wall. ex Benth, *A. forrestii* Diels, *A. nipponensis* Makino, *A. ciliata*, etc. Studies have shown that *Ajuga* spp. are widely used for the treatment of hypertension, hyperglycemia, pneumonia, acute and chronic pharyngitis [3-6]. Additionally, *Ajuga* has been used in Iranian traditional medicine for the treatment of joint pain, gout, and jaundice [7]. All plants of *A. decumbens* have been utilized as a kind of folk medicine for a long time in China and Japan owing to their antibacterial, anti-inflammatory, antitumor and antiviral activities [8-11]. Many compounds whose structures have been characterized were isolated from *A. decumbens*. Diterpenes and iridoid glycosides are the main bioactive compounds for the treatment of chronic pelvic inflammation and hysteromyoma [12,13]. It is urgent to understand the structure-activity relationships between the chemical constituents and biological activities of this plant with regard to its enormous social and economic implications. The primary objective of this review is to comprehensively report the various biological properties of *A. decumbens* as well as its main chemical constituents.

Diterpenes

Previous investigations of *A. decumbens* indicate that its constituents can be classified into four categories, viz, diterpenes, iridoid glycosides, flavonoids and ecdysteroids. Among them, diterpenes and iridoid glycosides are predominant. Neo-clerodane diterpenes mostly

show insecticidal [14,15], antibacterial [16,17], antimalarial [18], and anticancer activities [19]. In 1989, eight compounds, named *Ajugacumbins A, B, C, D* (1 - 4), *Ajugamarins A2, G1, H1 and F4* (5 - 8), were isolated from the ethanol extract of *A. decumbens* [20,21]. After that, two new compounds, *ajugacumbins E, F* (9, 10), were isolated [22]. Similarly, Chen *et al* also obtained a new compound (11) from *A. decumbens* [23]. In late 20th and early 21st century, *Ajugatakasins A* and *B* (12, 13), *Ajugaside A* (14) were isolated from the extracts of *A. decumbens* [24,25]. In 2005, *ajugacumbin H* (15) was obtained from chloroform extracts of *A. decumbens* [26]. With the development of separation and analysis techniques, four new compounds were separated from the whole plants were: *15-epilupulin A* (16), *6-O-deacetylajugamarin* (17), and *ajugadecumbenins A* and *B* (18, 19) [27]. Sun *et al* isolated and characterized compounds 20-30 *Ajugamarin A1 Chlorhydrin* (20) from *A. decumbens* [28].

In addition the same year, they also isolated six new compounds and four well-known analogues, elucidated as (12S)-1α,19-epoxy-6α,18-diacetoxy-4α,12-dihydroxy-neoclerod-13-en-15,16-olide (21), (12s)-6α,19-diacetoxy-18 chloro-4α-hydroxy-12-tigloyloxy-neo-clerod-13-en-15,16-olide (22), (12s,2″s)-6α,19-diacetoxy-18-chloro-4α-hydroxy-12-(2-methylbutanoyloxy)-neo-clerod-13-en-15,16-olide (23), 6α,19-diacetoxy-4α-hydroxy-1β-tigloyloxyneo-clerod-12-en-15-oic acid methyl ester-16-aldehyde (24), (12s)-18,19-diacetoxy-4α,6α,12-trihydroxy-1β-tigloyloxy-neo-clerod-13-en-15,16-olide (25), 4α,6α-dihydroxy-18-(4′-methoxy-4′-oxobutyryl-oxy)-19-tigloyloxy-neo-clerod-13-en-15,16-olide (26), Ajugaciliatin J (27), Ajuganipponin B (28), Ajugamarin A1(29) , Ajugarin I (30) [29-30].

In 2014, Lv *et al* reported a new compound *ajugacumbin J* (31) [31]. Besides, three clerodane diterpenoids and six abietane diterpenoids, including *dihydroclerodin* (32), *clerodinins C* (33), *clerodinins D* (34), *ajuforrestins A, Ajuforrestins B, Ajudecumins A–D* (35 - 38), were obtained from the aerial parts of *A. decumbens* [32]. The structures of these compounds are described in Table 1(a), Table 1(b); Fig 1(a)-1(e).

Iridoid glycosides

Iridoids are a class of secondary metabolites found in a wide variety of plants primarily served as a defense against herbivores or against infection by microorganisms [33]. The iridoids glycosides were firstly found by Takeda *et al* obtained six iridoids glycosides from the MeOH extract of *A. decumbens*, elucidated as *Decumbeside A-D* (39 - 42), *reptoside* (43) and *8-Acetylharpagide* (44) [34]. Similarly, *Harpagide* (45) was isolated from *A. decumbens* [25]. The structures and physical states of these compounds are described in Table 1(b); Fig 1(e), Fig 1(f).

Flavonoids

Flavonoids are another major group of compounds isolated from *A. decumbens*. Jin *et al* isolated *luteolin* (46) from the ethanol extract of *A. decumbens* [35]. In 2005, *5, 7-Dihydroxy-4'-methylflavone* (47) was obtained from the MeOH extract [36]. Other flavonoids, named *Apigenin* (48) and *Acacetin* (49), were isolated [28,32]. The structures and Physical states of these compounds are described in Table 1 (b); Fig 1(f).

Ecdysteroids

Ecdysteroids are a group of chemically related polyhydroxylated steroids present in plants (phytoecdysteroids) and arthropods (zooecdysteroids). The phytoecdysteroids stimulate protein synthesis in plants and activate cell mitosis, and possibly act as plant growth regulators [37]. In 1970, *Ajugalactone* (50) was isolated from *A. decumbens* [38]. Up to 1999, eight ecdysteroids (51 - 58) were obtained from the flowering whole plant [39]. The structures of these compounds are described in Fig 1(f), Fig 1(g).

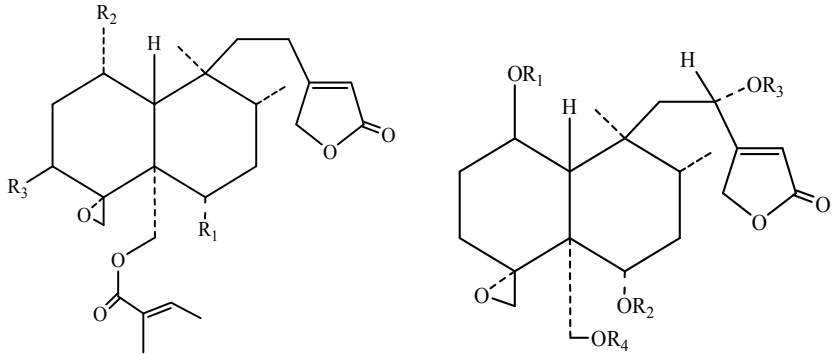
Others compounds

Two known compounds (59 - 60), a new phenethyl alcohol glycoside (61) were isolated from *A. decumbens* [25]. In 1999, two compounds (62 - 63) were obtained and structurally characterized from the flowering whole plant of *A. decumbens* [39].

A few years later, four compounds, *(6R,7E,9R)-9-hydroxy-4,7-megastigmadien-3-one (64),(3S,5R,6S,7E)-5,6-epoxy-3-hydroxy-7-megastigmen-9-one (65), (6E,9S)-9-hydroxy-4,6-megastigmadien-3-one (66), 6-hydroxy-4,7-megastigmadiene-3,9-dione (67)* were identified by comparison of their NMR, optical rotation and MS data with those reported in the literature [32,40,41]. In the same year, five other compounds (68 - 72) were obtained from the methanol extract [28]. The structures of these compounds are stated in Fig 1(g) and Fig 1(h).

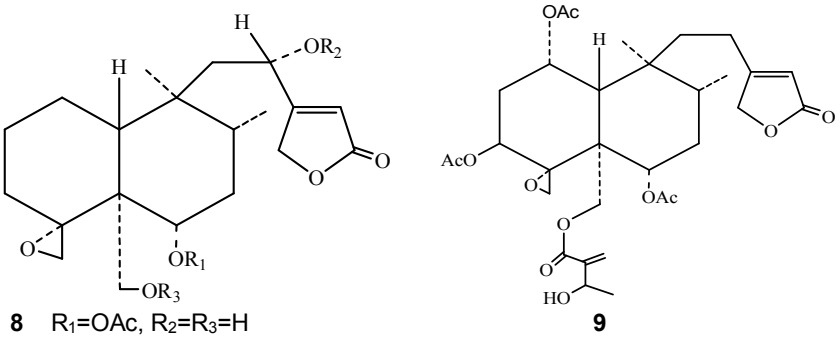
Table 1: Compounds isolated from *A. decumbens Thunb.*

No.	Name	Physical state	Ref
1	*Ajugacumbins A*	Colorless crystal	[20]
2	*Ajugacumbins B*	Colorless crystal	[20]
3	*Ajugacumbins C*	Amorphous powder	[20]
4	*Ajugacumbins D*	Colorless crystals	[20]
5	*Ajugamarins A2*	Amorphous solid	[21]
6	*Ajugamarins G1*	Colorless crystal	[21]
7	*Ajugamarins H1*	Colorless needle	[21]
8	*Ajugamarins F4*	Colorless crystal	[21]
9	*Ajugacumbins E*	Colorless crystal	[22]
10	*Ajugacumbins F*	Colorless crystal	[22]
11	*Ajugacumbins G*	Colorless crystal	[23]
12	*Ajugatakasins A*	Colorless oil	[24]
13	*Ajugatakasins B*	Amorphous solid	[24]
14	Ajugaside A	Colorless crystal	[25]
15	*Ajugacumbins H*	Colorless crystal	[26]
16	*15-epilupulin A*	Colorless needle	[27]
17	*6-O-deacetylajugamarin*	Colorless needle	[27]
18	*Ajugadecumbenins A*	Colorless needle	[27]
19	*Ajugadecumbenins B*	Amorphous powder	[27]
20	*Ajugamarin A1 chlorhydrin*	Amorphous powder	[28]
21	*(12S)-1α,19-epoxy-6α,18-diacetoxy-4α,12-dihydroxy-neo-clerod-13-en-15,16-olide*	Colorless flake	[29]
22	*(12S)-6α,19-diacetoxy-18-chloro-4α-hydroxy-12-tigloyloxy-neo-clerod-13-en-15,16-olide*	Colorless flake	[29]
23	*(12S,2''S)-6α,19-diacetoxy-18-chloro-4α-hydroxy-12-(2-methylbutanoyloxy)-neo-clerod-13-en-15,16-olide*	White powder	[29]
24	*6α,19-diacetoxy-4α-hydroxy-1β-tigloyloxyneo-clerod-12-en-15-oic acid methyl ester-16-aldehyde*	Colorless oil	[30]
25	*(12S)-18,19-diacetoxy-4α,6α,12-trihydroxy-1β-tigloyloxy-neo-clerod-13-en-15,16-olide*	White powder	[30]
26	*4α,6α-dihydroxy-18-(4'-methoxy-4'-oxobutyryloxy)-19-tigloyloxy-neo-clerod-13-en-15,16-olide*	White powder	[30]
27	*Ajugaciliatin J*	White powder	[30]
28	*Ajuganipponin B*	Needle crystal	[29]
29	*Ajugamarin A1*	Colorless crystal	[29]
30	*Ajugarin I*	Colorless crystal	[30]
31	*Ajugacumbin J*	Colorless oil	[31]
32	*Dihydroclerodin*	Amorphous powder	[32]
33	*Clerodinins C*	Amorphous powder	[32]
34	*Clerodinins D*	Amorphous powder	[32]
35	*Ajudecumins A*	Needle crystal	[32]
36	*Ajudecumins B*	Amorphous solid	[32]
37	*Ajudecumins C*	Amorphous solid	[32]
38	*Ajudecumins D*	Orange oil	[32]
39	*Decumbeside A*	Amorphous powder	[34]
40	*Decumbeside B*	Amorphous powder	[34]
41	*Decumbeside C*	Amorphous powder	[34]
42	*Decumbeside D*	Amorphous powder	[34]
43	*Reptoside*	Amorphous powder	[34]
44	*8-acetylharpagide*	Amorphous powder	[34]
45	*Harpagide*	Amorphous powder	[25]
46	Luteolin	Amorphous powder	[35]
47	5, 7-dihydroxy-4'-methylflavone	Needle crystal	[36]
48	Apigenin	Amorphous powder	[28]
49	Acacetin	Amorphous powder	[32]

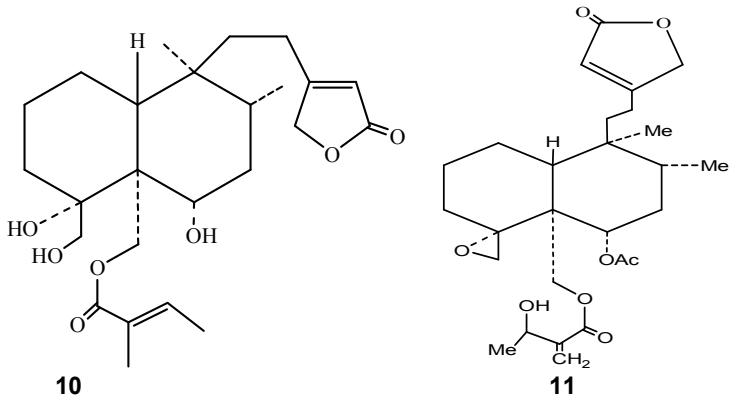


1 R_1=OAc, R_2=R_3=H
2 R_1=OH , R_2= R_3=H
3 R_1= R_2= R_3= OAc
4 R_1=OAc, R_2=H, R_3=OH
5 R_1=Tig, R_2= R_3=R_4=Ac
6 R_1=Tig, R_2=R_4=Ac, R_3=MeBu
7 R_1=MeBu, R_2=R_4=Ac, R_3=Tig

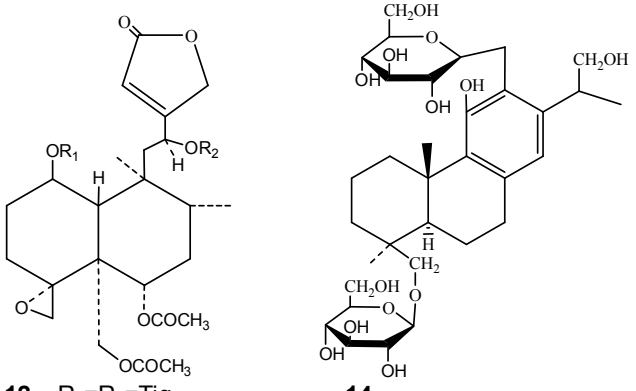
Fig 1(a): Structures of compounds from *A. decumbens Thunb.*



8 R_1=OAc, R_2=R_3=H
9



10
11



12 R_1=R_2=Tig
13 R_1=R_2=MeBu
14

Fig 1(b): Structures of compounds from *A. decumbens Thunb.* (*contd*)

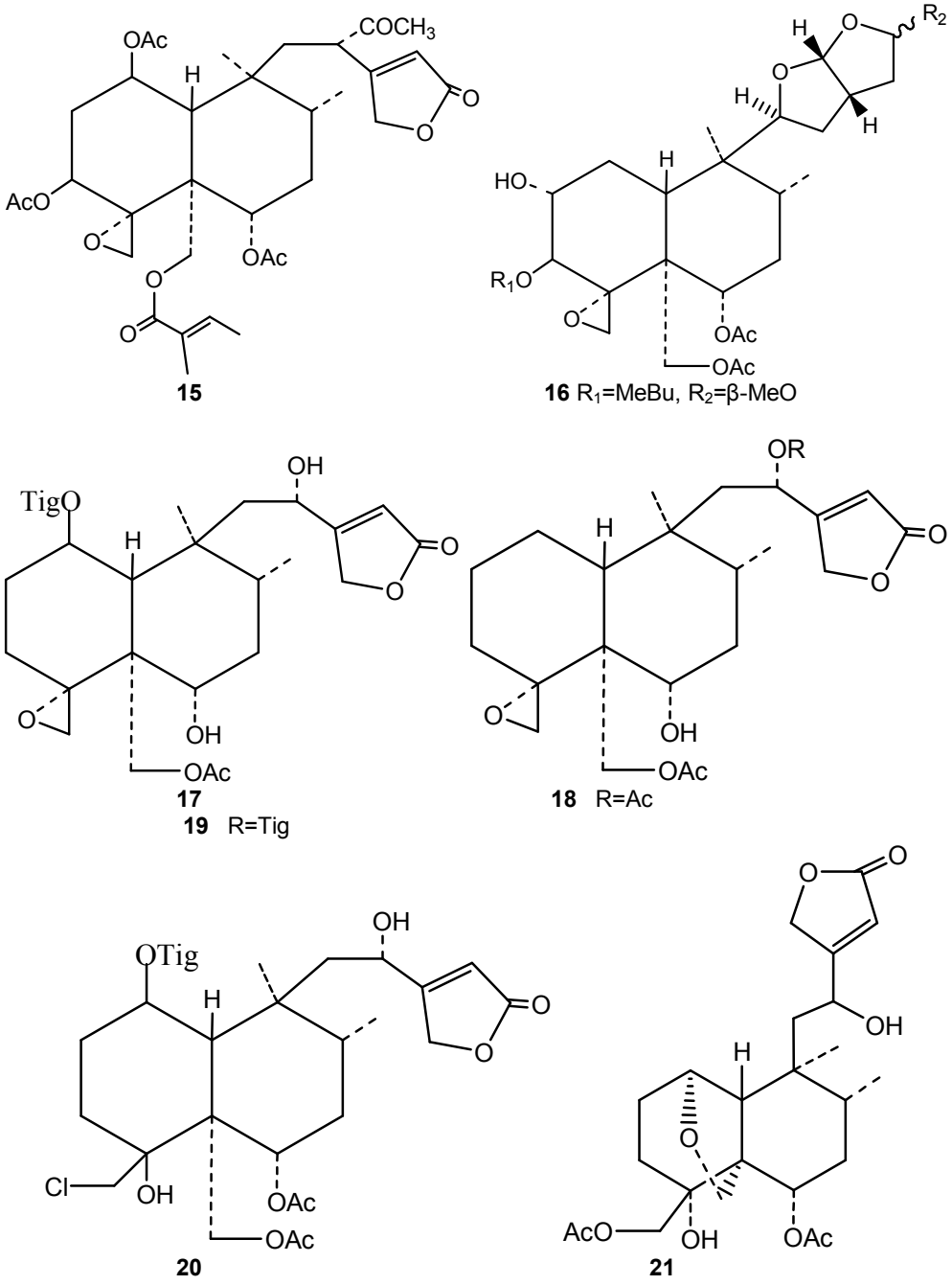
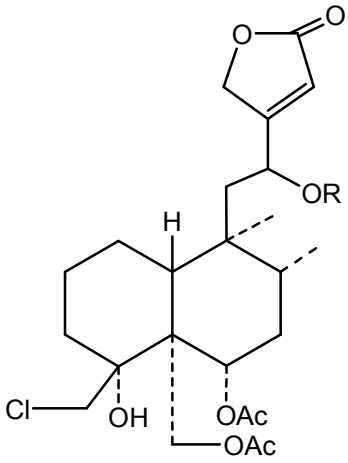
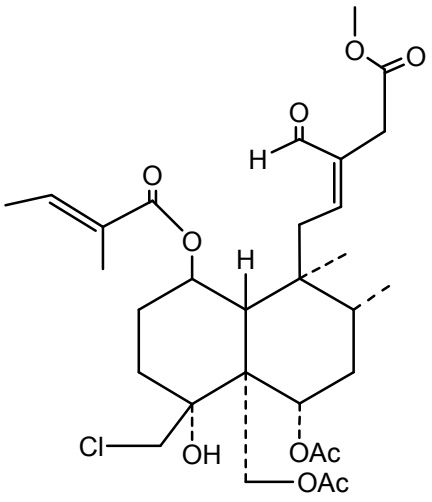


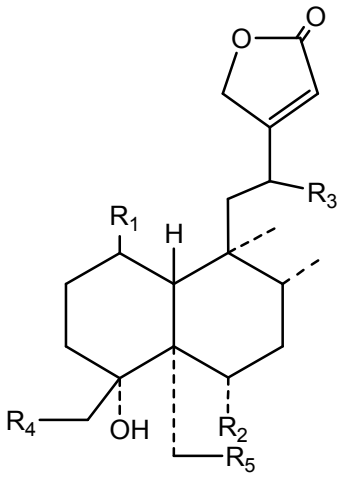
Fig 1(c): Structures of compounds from *A. decumbens Thunb.* (*contd*)

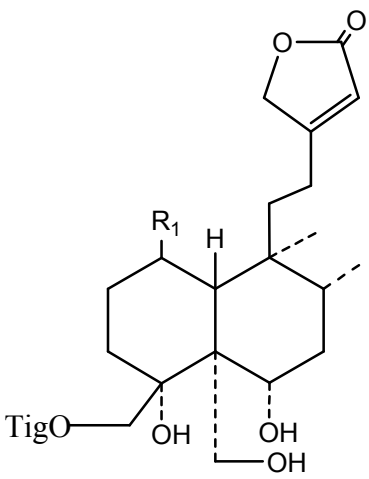


22 R=Tig
23 R=MeBu



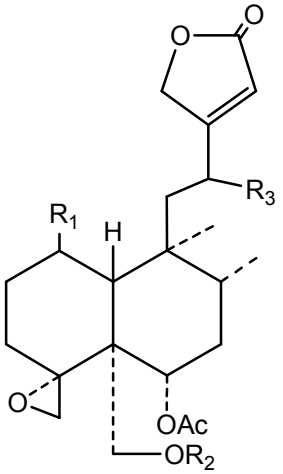
24

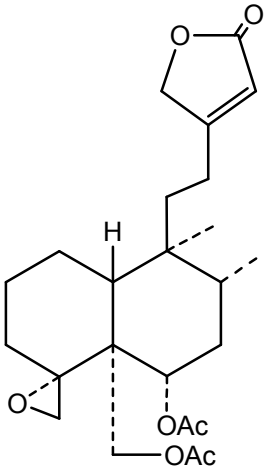




25 R_1=OTig, R_2=R_3=OH, R_4=R_5=OAc
26 R_1=R_3=H, R_2=OH, R_4=OR', R_5=OTig

27





28 R_1=H, R_2=Ac, R_3=OTig
29 R_1=OTig, R_2=Ac, R_3=OH

30

Fig 1(d): Structures of compounds from *A. decumbens Thunb.* (*contd*)

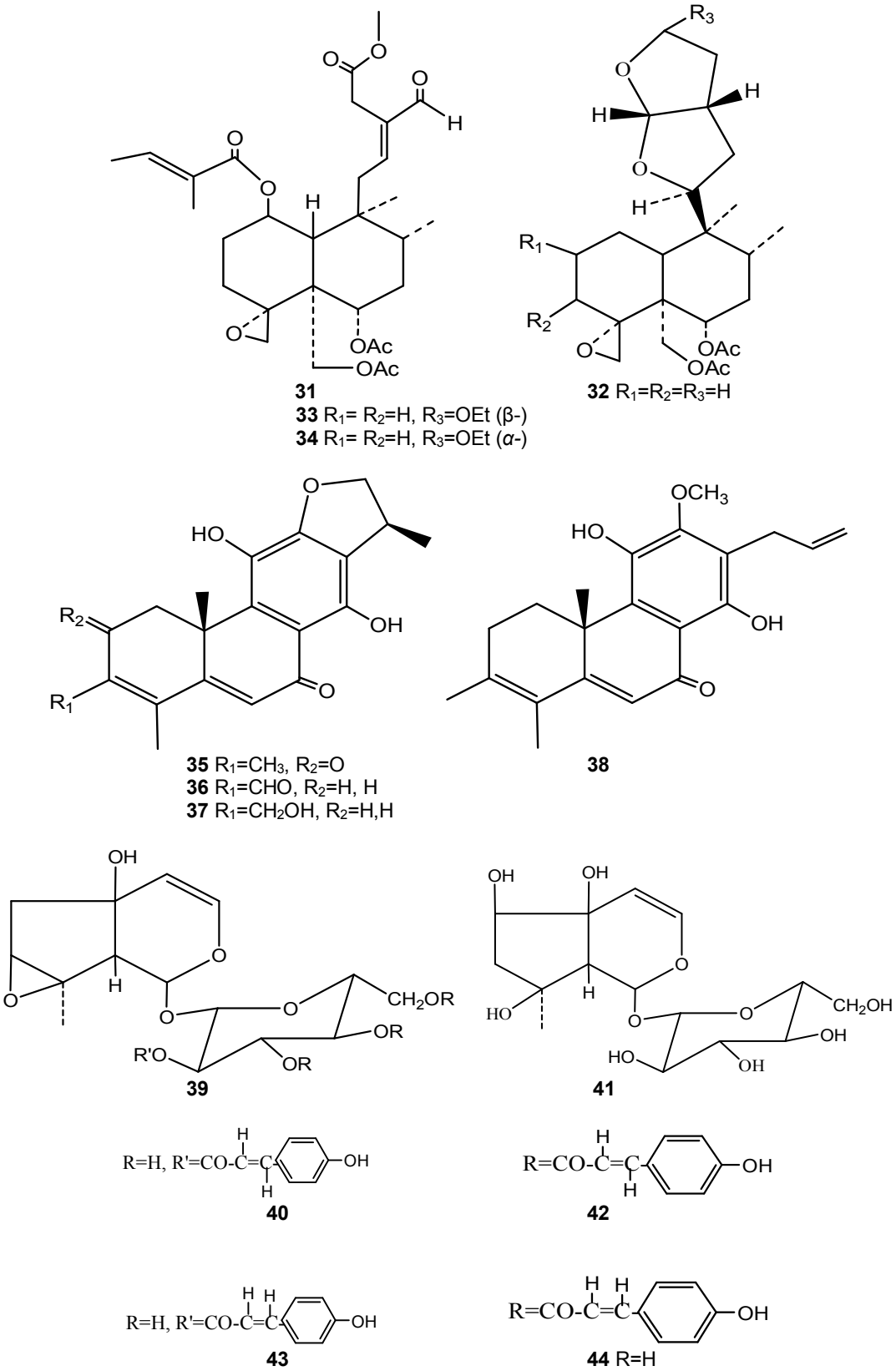


Fig 1(e): Structures of compounds from *A. decumbens Thunb.* (*contd*)

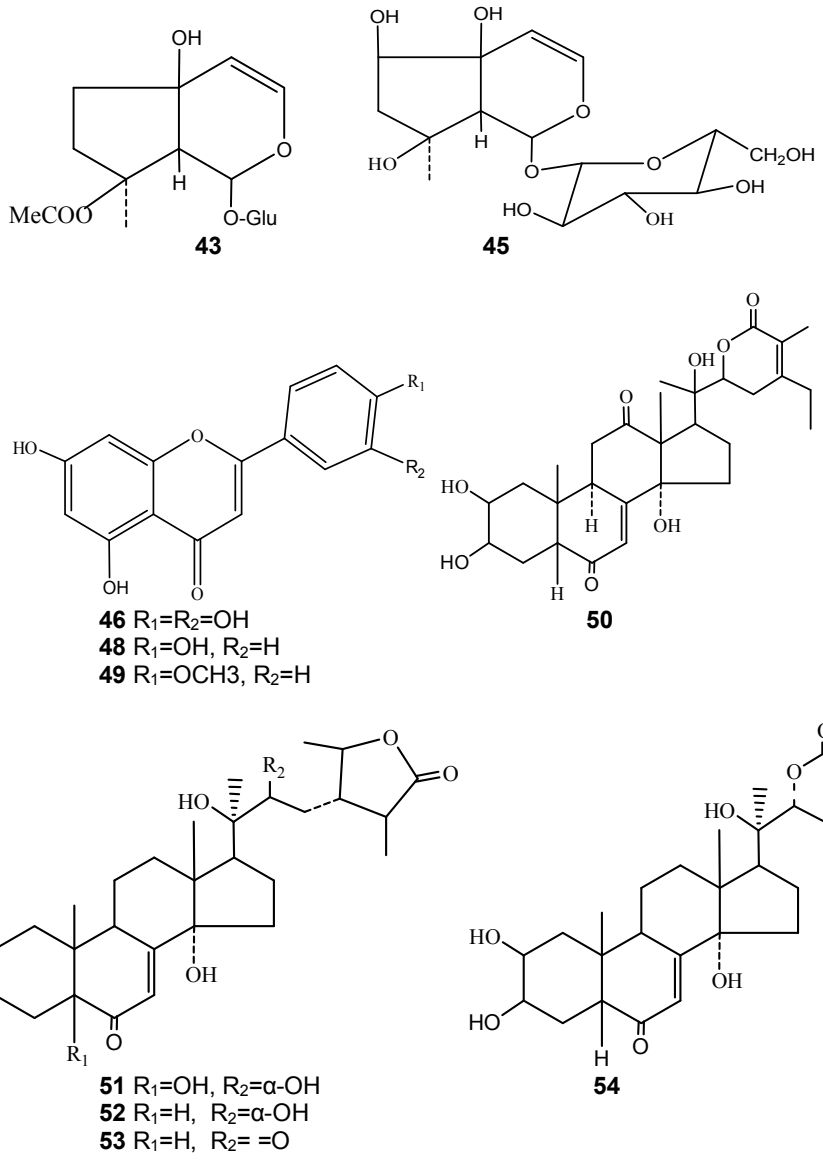


Fig 1(f): Structures of compounds from *A. decumbens Thunb.* (*contd*)

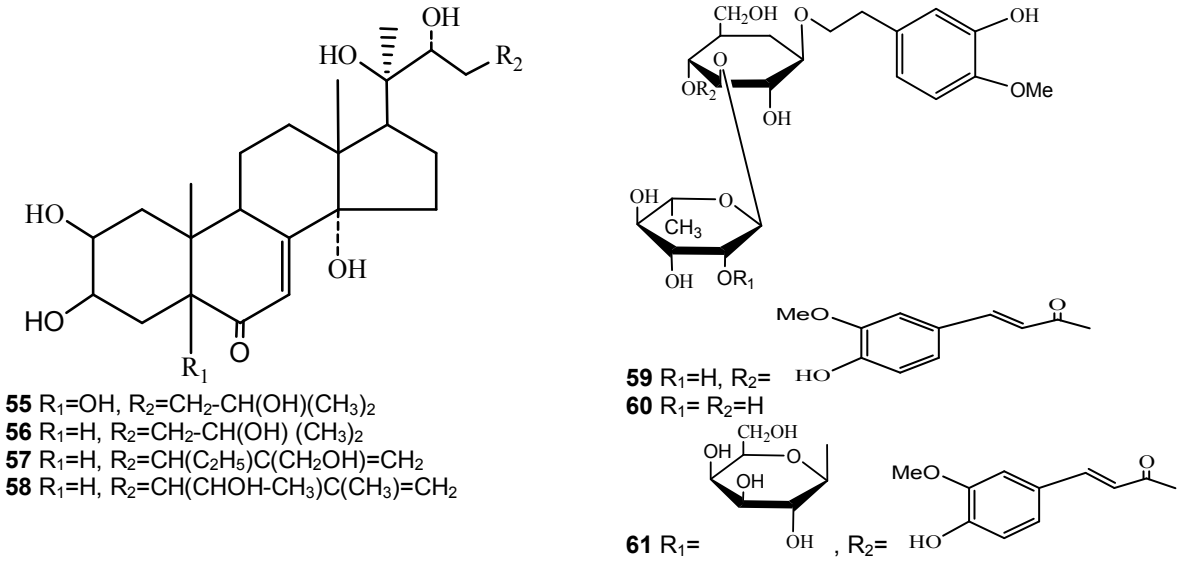


Fig 1(g): Structures of compounds from *A. decumbens Thunb.* (*contd*)

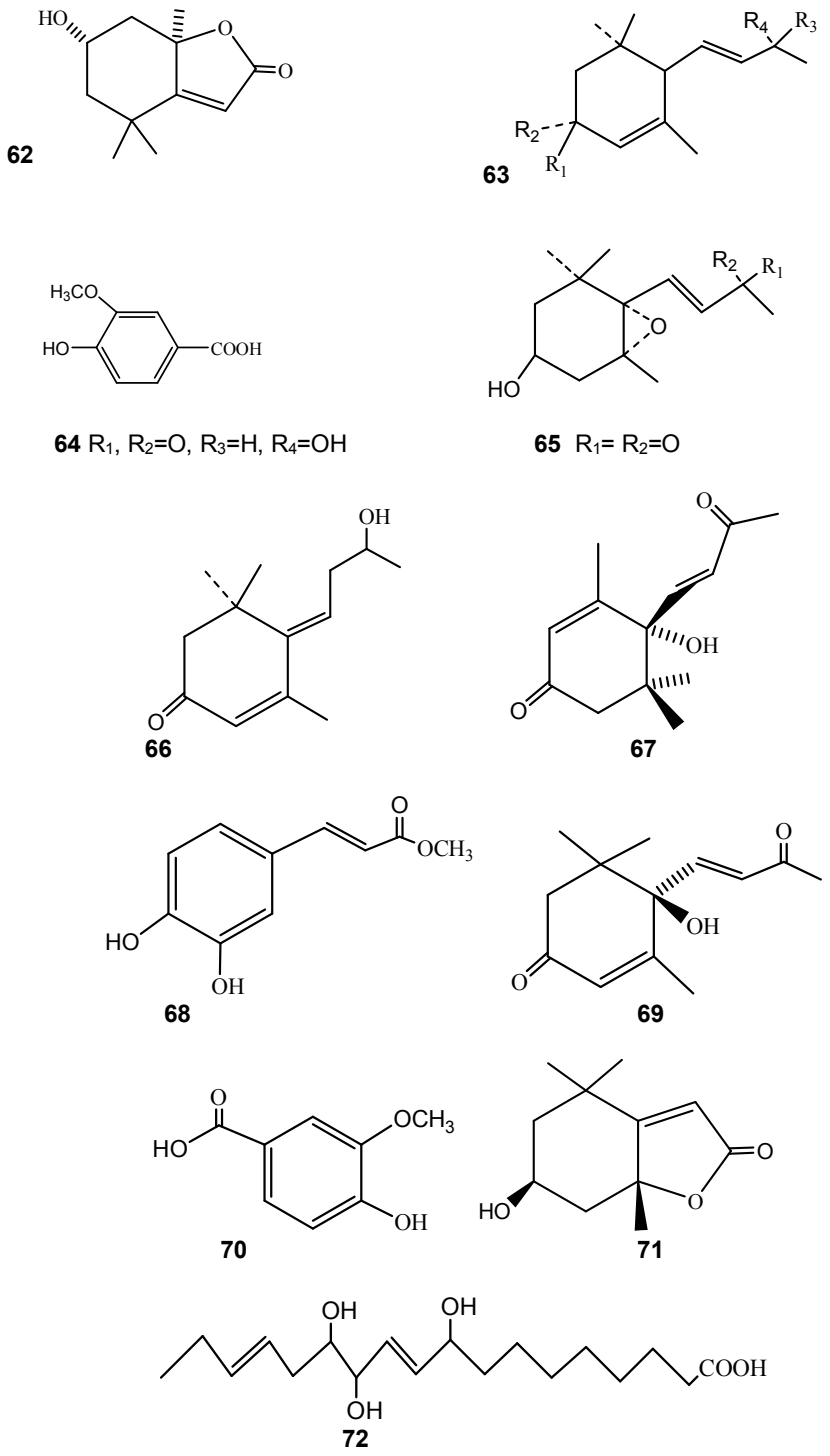


Fig 1(h): Structures of compounds from *A. decumbens Thunb.* (*contd*)

BIOLOGICAL PROPERTIES

Various extracts or purified compounds from *A. decumbens* exhibit diverse biological characteristics, which are anti-inflammatory, antitumor, antibacterial, antivirus, cytotoxic, as well as insecticidal activities. Herein, we describe the biological activities as well as its active extracts or compounds.

Anti-inflammatory activities

Several studies investigated that the whole plant of *A. decumbens* possessed the anti-inflammatory effects described in the famous pharmacy book of China, Dictionary of Chinese Materia Medica [42-43]. The inhibitory activities on LPS - induced NO production of diterpenes were evaluated, compounds (22-26, 28) showed inhibitory effects, indicating these substances

were expected to be useful as effective potential anti-inflammatory agents [29,30]. Similarly, *Ajugacumbin J* (31) and *ajugacumbin D* (4) exhibited the inhibitory activities of LPS-induced NO production in RAW 264.7 macrophages with an IC_{50} value of 46.2 and 35.9 mM, respectively [31]. The ethanol extracts of *A. decumbens* extracts (KE) improved the balance of bone resorption and bone formation, showing anti-inflammatory effects. The results exhibited that KE were beneficial for sufferers of bone and joint disease [44]. Total flavonoids of *A. decumbens* (TFA) had a therapeutic effect on chronic serum sickness glomerulonephritis (CSS-GN) rats by increasing SOD activity, lowering MDA and inhibiting lipid peroxidation [45].

Antitumor activities

The inhibitory effects of these compounds (14, 43-45, 59-61) on EBV activation induced by TPA were examined via a primary screening for anti-tumor activity, and the results showed that *8-Acetylharpagide* (44).

exhibited the strongest inhibitory effect on EBV activation [25]. In addition, compound 44 exhibited an anti-proliferative effect on mouse hepatic tumor using N-nitrosodiethylamine (DEN) as an initiator and phenobarbital (PB) as a promoter [46]. Takasaki et al also found that compounds 44 and 52 had potent antitumor-promoting activities on mouse skin *in vivo* two-stage carcinogenesis procedure. Furthermore, compound 44 also exhibited potent chemopreventive activity in a mouse pulmonary tumor model [39]. Compounds 35 - 37 exhibited moderate inhibitory activity on the proliferation of human breast cancer MCF-7 cells [32]. *A. decumbens* extracts showed anticancer and antimetastatic effects towards breast cancer through regulating the expression of MMPs and TIMPs [47]. Additionally, *A. decumbens* extracts exhibited an anti-proliferative effect on lung cancer A-549, liver cancer SMMC-7721 and Sarcoma S18 [48,49]. What is more, water extracts of *A. decumbens* significantly inhibited the proliferation of HepG2 cells in a dose-dependent manner [50].

Antibacterial activities

A. decumbens extracts exhibited significantly antibacterial effect by inhibiting the growth of *S. aureus, S. epidermidis, K. pneumonia, E. coli* and *P. aeruginosa* [51]. Besides, through the analysis of antibacterial activity *in vivo* and *in vitro*, water extracts of *A. decumbens* also possessed antibacterial activities against *Streptococci* [52].

Antivirus activities

Ma *et al* found that the whole plant of *A. decumbens* showed potent antiviral activities against respiratory syncytial virus (RSV) with an IC_{50} value of 131.6 μg/ml [53]. In addition, *A. decumbens* water extracts could inhibit infectious bronchitis virus (IBV) *in vitro* with the concentration of 750 - 1500 mg/ml [54].

Cytotoxicity

Myrotheciumone A isolated from *A. decumbens* was found to exert cytotoxicity via induction of apoptosis in cancer cell lines [55].

Insecticidal activities

Min *et al* reported that these compounds (1-4, 9-10) from the ethanol extract of *A. decumbens* displayed growth-inhibitory properties against insects [20,22]. Similarly, compound 11 also exhibited significant insecticidal activities [23].

The active extracts/compounds of *A. decumbens* and their mechanisms of action are provided in Table 2.

Table 2: The active extracts or compounds together with their bioactivities

Biological property	Mechanism of action	Extract/Compound no.
Anti-inflammatory effect	iNOS	22, 23, 24, 25, 26, 28, 31
	Lipid peroxidation	Total flavonoids
Antitumor effect	EBV	14, 43, 44, 45, 59, 60, 61
	human breast cancer	35, 36, 37
	lung cancer, liver cancer HepG2 cells	Water extract
Antibacterial effect	Bacterium	Water extract
Antivirus effect	RSV	Water extract
	IBV	
Cytotoxicity	Tumor cell lines	*Myrotheciumone A*
Insecticidal effect	insect antifeedant	1, 2, 3, 4, 9, 10, 11

CONCLUSION

The chemical composition of *A. decumbens* (Labiatae) includes diterpenes, iridoids glycosides, flavonoids, ecdysteroids, and phenethyl alcohol glycoside. A variety of biological properties recorded for *A. decumbens* extracts and chemical compounds indicate that they are of medicinal value. Limited efforts have, however, been made to determine the pharmacokinetics and mechanisms of action of the individual compounds of the plant. The therapeutic potentials of the new chemical compounds from the plant needs to be explored in detail.

ACKNOWLEDGEMENT

This work is partly supported by the National Natural Science Foundation of China (no. 81173563), and Compound Chinese Pharmaceutical Innovation Team of Beijing University of Chinese Medicine (no. 2011-CXTD-13).

REFERENCES

1. *Cai ZY, Yi GQ, Li YY, Liang XL, Gan L, He GX. Nuclear magnetic resonance characteristics of neo-clerodane diterpene in Genus Ajuga. Cent South Pharm 2014; 12: 1108-1112.*
2. *Israili ZH, Lyoussi B. Ethnopharmacology of the plants of genus Ajuga. Pak J Pharma Sci 2009; 22: 425–462*
3. *Liu B, Shi RB, Ge XX, Zhou Y, Zhou J. Chemical constituents and Pharmacological activities of Ajuga. World Phytomedicine 2001; 16: 96-101.*
4. *Nawaz HR, Malik A, Khan PM, Ahmed S. Ajugin E and F: Two withanolides from Ajuga parviflora. Phytochem 1999; 52: 1357–1360.*
5. *Akbay P, Calis I, Heimann J, Sticher O. Ionon, iridoid and phenylethanoid glycosides from Ajuga salicifolia. Z Naturforsch 2003; 58c: 177–180.*
6. *Hilaly JE, Israili ZH, Lyoussi B. Acute and chronic toxicological studies of Ajuga iva in experimental animals. J Ethnophar 2004; 91: 43–50.*
7. *Naghibi F, Mosaddegh M, Mohammadi Motamed S, Ghorbani A. Labiatae family in folk medicine in Iran: from ethnobotany to pharmacology. Iran J Pharm Res 2005; 2: 63–79.*
8. *Ono Y, Fukaya Y, Imai S, Yamakuni T. Beneficial effects of Ajuga decumbens on osteoporosis and arthritis. Biol Pharm Bull 2008; 31: 1199-1204.*
9. *Jiangsu New Medical College. Dictionary of Chinese Materia Medica. Shanghai: People's Publishing House; 1986; p 751.*
10. *Konoshima, M, Shibata, S, Shimomura, T, Azuma, T. Tokyo: Yakuyo Shokubutu Daijiten Hirokawa Publishing Co; 1963. 111p.*
11. *Zhang LQ, Feng L, Jia Q, Xu JW, Wang R, Wang ZT, Wu YC, Li YM. Effects of β-glucosidase hydrolyzed products of harpagide and harpagoside on cyclooxygenase-2(COX-2) in vitro. Bioo Med Chem 2011; 19: 4882–4886.*
12. *Wang L, Lu W, Shen Q, Wang SJ, Zhou H, Yu LS, Wang S, Jiang HD, He LC, Zeng S. Simultaneous determination of imperatorin and its 2 metabolites in dog plasma by using liquid chromatography–tandem mass spectrometry. J Pharmaceut Biomed 2012; 70: 640-646.*
13. *Takasaki M, Tokuda H, Nishino H, Konoshima T. Cancer chemopreventive agents (antitumor-promoters) from Ajuga decumbens. J Nat Prod 1999; 62: 972–975.*
14. *Jannet HB, Harzallah-Skhiri F, Mighri Z, Simmonds MSJ and Blaney WM. Responses of Spodoptera littoralis larvae to Tunisian plant extracts and to neoclerodane diterpenoids isolated from Ajuga pseudoiva leaves. Fitoterapia 2000; 71: 105-112.*
15. *Bondì ML, Al-Hillo MRY, Lamara K, Ladjel S, BrunoM, Piozzi F, Simmonds MSJ. Occurrence of the antifeedant 14, 15-dihydroajugapitin in the aerial parts of Ajuga iva from Algeria. Biochem Syst Ecol 2000; 2: 1023-1025.*
16. *Jannet HB, Chaari A, Mighri Z, Martin MT, Loukaci A. Neo-clerodane diterpenoids from Ajuga pseudoiva leaves. Phytochem 1999; 52: 1541-1545.*
17. *Chen H, Tan RX, Liu ZL, Zhao CY, Sun J. A clerodane diterpene with antibacterial activity from Ajuga lupulina. Acta Cryst C 1997; 53: 814-816.*
18. *Kuria KAM, Chepkwony H, Govaerts C, Roets E, Busson R, de Witte P, Zupko I, Hoornaert G, Quirynen L, Maes L, et al. The antiplasmodial activity of isolates from Ajuga remota. J Nat Prod 2002; 65: 789-793.*
19. *Takasaki M, Tokuda H, Nishino H, Konoshima T. Cancer chemopreventive agents (antitumor-promoters) from Ajuga decumbens. J Nat Prod 1999; 62: 972-975.*
20. *Min ZD, Wang SQ, Zheng QT, Wu B, Tanaka T, Iinuma M. Four new insect antifeedant neo-clerodane diterpenoids, ajugacumbins A, B, C and D, from Ajuga decumbens. Chem Pharma Bull 1989; 37: 2505-2508.*
21. *Shimomura H, Sashida Y, Ogawa K. neo-Clerodane diterpenes from Ajuga decumbens. Chem Pharma Bull 1989; 37: 996-998.*
22. *Min ZD, Mizuno M, Wang SQ, Linuma M, Tanaka T. Two new neo-clerodane diterpenes in Ajuga decumbens. Chem Pharma Bull 1990; 38: 3167-3168.*
23. *Chen HM, Min ZD, Iinuma M, Tanaka T. Clerodane diterpenoids from Ajuga decumbens. Chem Pharma Bull 1995; 43: 2253-2255.*
24. *Amano T, Nishida R, Kuwahara Y. Ajugatakasins A and B, new diterpenoids from Ajuga decumbens, and feeding stimulative activity of related neoclerodane analogs toward the turnip sawfly. Biosci Biotech Bioch 1997; 61: 1518-1522.*

25. Takasaki M, Yamauchi I, Haruna M, Konoshima T. New glycosides from Ajuga decumbens. J Nat Prod 1998; 61: 1105-1109.
26. Sang JS, Huang ZH, Min ZD. A New neo-Clerodane Diterpene Isolated from Ajuga decumbens. Chin J Nat Med 2005; 3: 284-286.
27. Huang XC, Qin S, Guo YW, Krohn K. Four New Neoclerodane Diterpenoids from Ajuga decumbens. Helvetica Chimica Acta 2008; 91: 628-634.
28. Sun ZP, Gui LP, Guo YQ, Xu J, Li YS. Isolation and identification of chemical constituents from the whole plants of Ajuga decumbens. J Shenyang Pharm Univy 2012; 29: 758-760.
29. Sun ZP, Li YS, Jin DQ, Guo P, Song HB, Xu J, Guo YQ, Zhang L. neo-Clerodane diterpenes from Ajuga decumbens and their inhibitory activities on LPS-induced NO production. Fitoterapia 2012; 83: 1409-1414.
30. Sun ZP, Li Y, Jin DQ, Guo P, Xu J, Guo YQ, Zhang L. Structure Elucidation and Inhibitory Effects on NO Production of Clerodane Diterpenes from Ajuga decumbens. Planta Med 2012; 78: 1579-1593.
31. Lv H, Luo J, Kong L. A new neo-clerodane diterpene from Ajuga decumbens. Nat Pro Res2014; 28: 196-200.32
32. Wang B, Wang X N, Shen T, Wang SQ, Guo DX, Lou HX. Rearranged abietane diterpenoid hydroquinones from aerial parts of Ajuga decumbens Thunb. Phytochem Letts, 2012; 5: 271-275.
33. Israili Z H, Lyoussi B. Ethnopharmacology of the plants of genus Ajuga. Pak J Pharm Sci 2009; 22: 425-462.
34. Takeda Y, Tsuchida S, Fujita T. Four new iridoid glucoside p-coumaroyl esters from Ajuga decumbens. Phytochem 1987; 26: 2303-2306.
35. Jin JS, Dou SH. Study on the flavonoids of Ajuga decumbens. Anhui Med J 1994; 15: 51.
36. Guo XD, Huang ZS, Bao YD, An DK, Ma L, Gu LQ. Chemical constituents of Ajuga decumbens. Chinese Tradit Herbal Drugs 2005; 36: 645-648.
37. Ramazanov NSh. Phytoecdysteroids and other biologically active compounds from plants of the genus Ajuga. Chem Nat Compd 2005; 41: 361-369.
38. Koreeda M, Nakanishi K, Goto M. Ajugalactone, an insect moulting inhibitor as tested by the Chilo dipping method. J Amer Chem Soc 1970, 92:7512-7513.
39. Takasaki M, Tokuda H, Nishino H, Konoshima T. Cancer Chemopreventive Agents (Antitumor-promoters) from Ajuga decumbens. J Nat Prod 1999; 62: 972-975.
40. D'Abrosca B, DellaGreca M, Fiorentino A, Monaco P, Oriano P, Temussi F. Structure elucidation and phytotoxicity of C13 nor-isoprenoids from Cestrum parqui. Phytochem 2004; 65: 497-505.
41. Metuno R, Ngandeu F, Tchinda AT, Ngamenni B, Kapche GDWF, Djemgou PC, Ngadjui BT, Bezabih M, Abegaz BM. Chemical constituents of Treculia acuminata and Treculia africana (Moraceae). Biochem Syst Ecol 2008; 36: 148-152.
42. Edita. Dictionary of Chinese Materia Medica. Shanghai: Shanghai Science and Technology Publishing House; 2006; p 1035.
43. Chinese Pharmacopoeia Commission. Chinese pharmacopoeia. Beijing: The Medicine Science and Technology Press of China; 2010; p 325.
44. Ono Y, Fukaya Y, Imai S, Yamakuni T. Beneficial effects of Ajuga decumbens on osteoporosis and arthritis. Biol Pharm Bull 2008; 31: 1199-1204.
45. Nan LH, Peng WH, Zheng SL, Fang TH, Wu FH, Xu ZT. Experimental Effects Study of Total Flavonoids of Ajuga on Free Radical Damage in Chronic Serum Sickness Glomerulonephritis Rats. Chinese J Interg Tradit West Nephrol CHTWN 2009; 10: 967-969.
46. Konoshima T, Takasaki M, Tokuda H, Nishno H. Cancer chemopreventive activity of an iridoid glycoside, 8-acetylharpagide, from Ajuga decumbens. Cancer Lett 2000; 57: 87-92.
47. Peng B, He R, Xu QH, Gao J, Lu YL, Li JR. Correlation between antimetastatic action of Ajuga decumbens and expression of MMPs and TIMPs. China J Chinese Materia Medica 2011; 36: 3511-3513.
48. Li D, Jiang M. Anticancer Research of water extracts from Ajuga decumbens in vitro. Jilin Journal of TCM 2009; 29: 434-435.
49. Zeng FM, Jia R, Wu FW. Experiment of Tumor Inhibition of Ciliate Bugle Herb in S180 Sarcom Mice. J Fujian Coll Tradit Chinese Med 2003; 13: 30-32.
50. Zhang XX, Wu J, Li D, Zou X. Effects of Ajuga Decumbens Thunb on Liver Carcinoma Cells in vitro and in vivo. J Liaoning Univ Tradit Chinese MedM. 2013; 15: 58-61.
51. Zhang B, Zeng FJ, Zhang XY. Study on anti-infection effect of Ajuga decumbens. Chin J Nosocomiol 2014; 24: 2937-3939.
52. Li M, Peng WH. Chemical constituents and pharmacological research progress of Ajuga decumbens. J pr tradit Chinese mede 2012; 28: 322-323.
53. Ma SC, Du J, But PPH, Deng XL, Zhang YW, Ooi VEC, Xu HX, Lee SHS, Lee SF. Antiviral Chinese medicinal herbs against respiratory syncytial virus. J Ethnopharmacol 2002; 79: 205-211.
54. Luo MC, Zheng XF, Fan XP. In vitro Inhibition of Infectious Bronchitis Virus by Ciliate Bugle Herb (Jin Gu Cao). J Longyan Univ 2009; 27: 77-79.
55. Lin T, Wang G, Shan W, Zeng D, Ding R, Jiang X, Zhu D, Liu XX, Yang SY, Chen HF. Myrotheciumones: Bicyclic cytotoxic lactones isolated from an endophytic fungus of Ajuga decumbens. Bioorg Med Chem Lett 2014; 24: 2504-2507.