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REVIEW

Chemistry, Pharmacological Activities and Analysis of *Ageratina adenophora*

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Ageratina adenophora is an invasive plant and has brought huge harm to the social economy and ecological balance. Recent years, in order to reduce harm of *A. adenophora* and turn waste to treasure, research has been carried out to discover the useful aspect of it. Interestingly, many secondary metabolites from it exhibit important pharmacological effects and make it a potential resource for treating diseases. In present paper, the chemistry, pharmacological activities and component analysis of *A. adenophora* during the period 1981-2013 are reviewed.

Keywords: *Ageratina adenophora*, Natural products, Analysis, Pharmacological activity.

INTRODUCTION

Ageratina adenophora Spreng belongs to the family Compositae. It is a native species of Mexico and Costa Rica and now is a common weed in many parts of the world. Due to the high reproductive ability, the invasive plant spreads rapidly and inhibits the growth of other plants. It caused severe problems in cultured areas and forests. In order to reduce the harm and turn the waste to treasure, scientists have studied on various aspects of it and great progress has been made, especially on the medicinal use of it. As shown in the Chemical Abstract, the number of the research literature related to *A. adenophora* has been increasing year by year.

Study of *A. adenophora* began in the early of 1970s. During the past years, more than 90 ingredients were systematically studied after separation and purification, including monoterpenoids, sesquiterpenoids, triterpenoids, steroids, flavonoids, phenolic derivatives, *etc*. Among them, several new molecular skeleton of sesquiterpenes and phenolic derivatives were discovered. Interestingly, scientists found that many secondary metabolites of *A. adenophora* exhibited excellent pharmacological effects. Compounds isolated from the plant had numerous activities such as antifeedant activity[1], antibacterial or antiviral activity[2], antitumor activity[3], anti-HIV activity, antioxidation activity[4], treatment of insomnia[5]. Herein, it has the potential to be used to treat diseases. The present review mainly focuses on the chemistry, pharmacological activity and analysis of *A. adenophora*.

Chemical constituents from *A. adenophora*

Monoterpenoids: Monoterpenoids were mainly found in volatile oil. Total 9 monoterpenoids (compounds **1-9** in Fig. 1) were separated and characterized. The volatile oil from *A. adenophora* is odorous and stimulating. Ding *et al*.[6] analyzed the oil by gas chromatography tandem mass spectrometry (GC-MS), the main compounds were *p*-cymene (compound **8**) and bornyl acetate (compound **4**). Zhao *et al*.[7] isolated and identified a new monoterpene (compound **9**), the structure of which was established by spectroscopic studies. Compounds **5** and **6** are important oxygenated derivatives of the acyclic monoterpenoids, compounds **7** and **8** are monocyclic monoterpenoids with a parent structure of menthane, compounds **1-4** and **9** are bicyclic monoterpenoids.

Sesquiterpenes: A large number of sesquiterpenes were separated and identified from *A. adenophora* (Fig. 2). Cadinane sesquiterpenoid was found earlier. Bohlmann *et al*.[8] had determined the structure of compound **10**, which is a bicyclic cadinane terpenoid. Along with the intensive investigation of the chemical constituents, more sesquiterpenes were separated and characterized. In 1981, from the aerial parts of *A. adenophora*, five new sesquiterpenes (the cadinene derivatives **11-15**) were reported by Bohlmann and Gupta[9]. The structures of **11-15** were

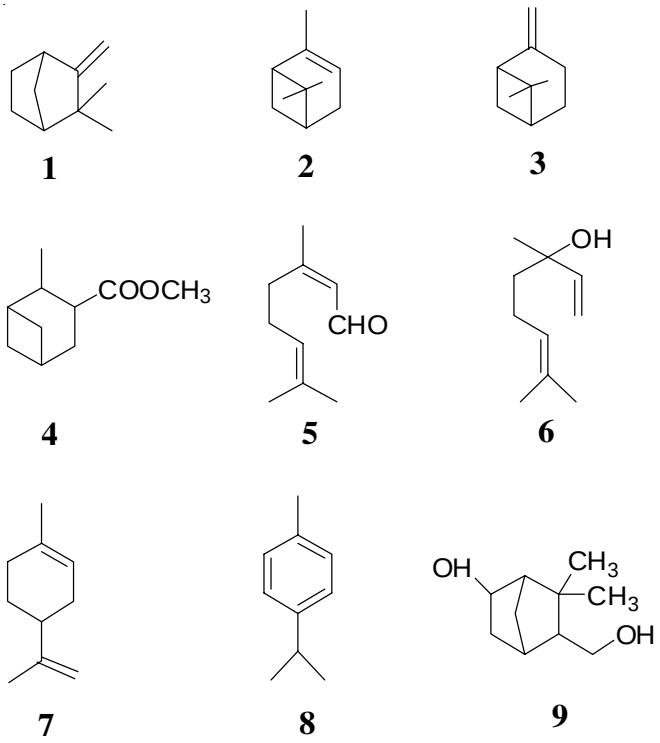


Fig. 1. Chemical structures of monoterpenoids (compounds **1-9**)

identified by interpreting the ^{1}H NMR data and spin coupling. In 1989, a new sesquiterpene (compound **16**), which was the first representative of a new bicyclic sesquiterpene skeleton, was determined through selective INEPT spectroscopy[10]. In 1997, Weyerstahl *et al.*[11] isolated 8 constituents from the flower essential oil of *A. adenophora*, including two new (compounds **17**, **18**) and three previously isolated (compounds **19**-**21**) sesquiterpenoids. He *et al.*[12] discovered a new sesquiterpenoid (compound **22**) from the chloroform extract of *A. adenophorum*. Wang *et al.*[13] found two norsesquiterpenes (compounds **23** and **24**) for the first time. In 2008, four new cadinane sesquiterpenes (compounds **25-28**) were extracted and separated from the leaves of *A. adenophorum* by He *et al.*[14]. Among them, compound **26** was a dimeric cadinane derivative, while compound **27** was a peroxide cadinane analogue. Zhao *et al.*[7] isolated and identified two new sesquiterpenoids (compounds **29** and **30**), including a peroxide cadinane analogue. The existence of the peroxide derivatives implies that the biosynthesis of sesquiterpene peroxides in *A. adenophora* may not be a coincidence. Cao *et al.*[3] discovered four novel sesquiterpenes (compounds **31-34**) from *A. adenophora*. Compounds **31**, **32**, **33** and **34** had the same plane structure with those of **28**, **27**, **25** and **26**, respectively. In 2012, Shi *et al.*[1] isolated a new defensive sesquiterpenoids (compound **35**) from leaves of *A. adenophora*.

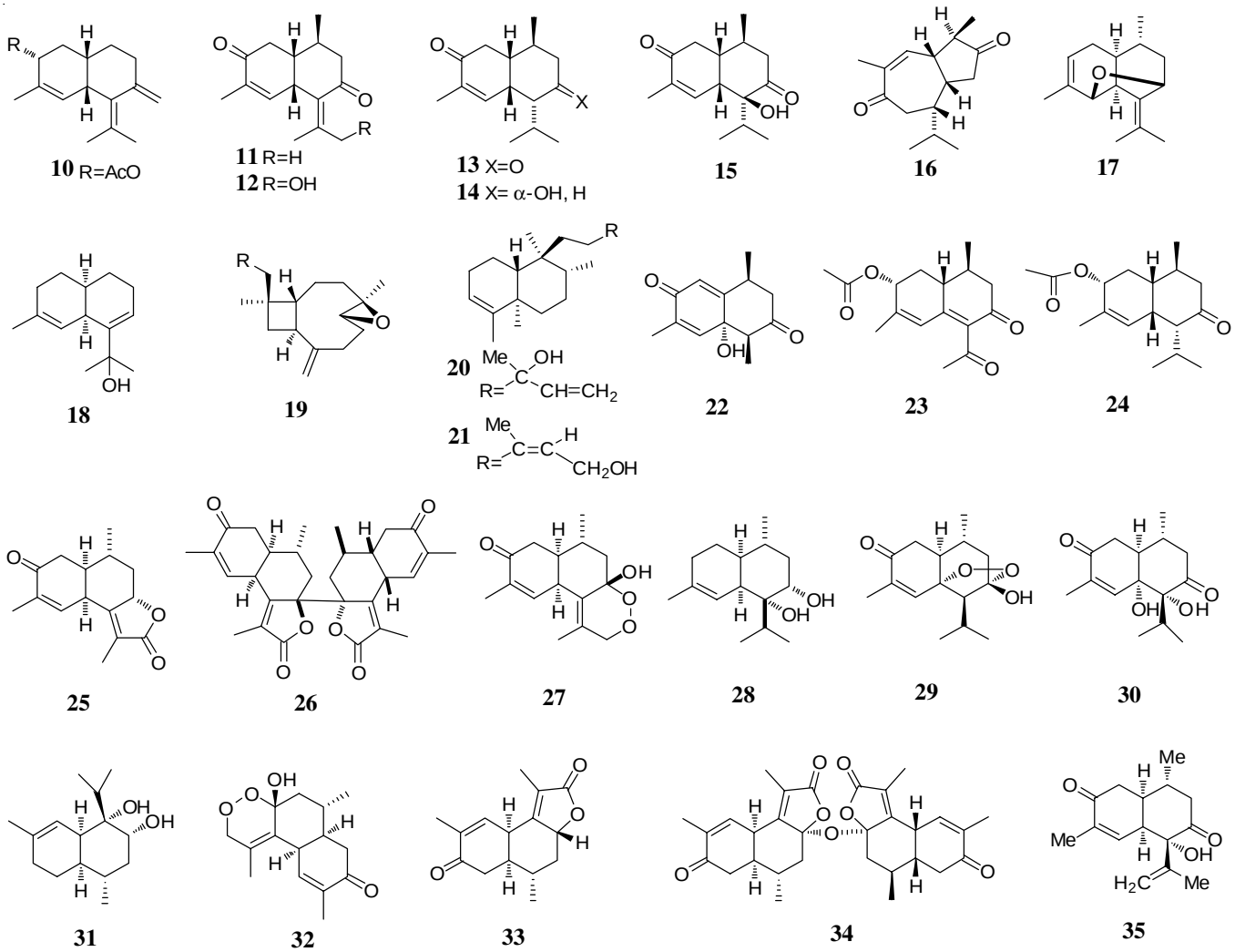
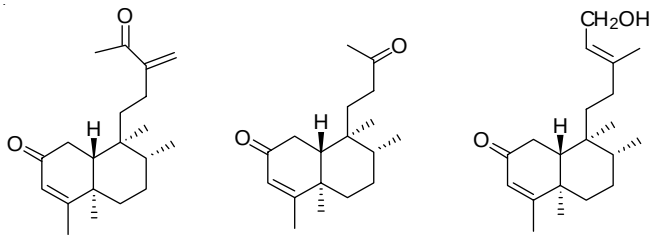


Fig. 2. Chemical structures of sesquiterpenes (compounds **10**-**35**)

Diterpenoids: Diterpenoids were seldom reported from *A. adenophora*. Until now, only 3 diterpenoids had been reported (compounds **36**-**38**, Fig. 3)[15]. Wang *et al*.[15] separated and charaterized three diterpenoids from the flowers of *A. adenophora*. The diterpenoids had a clerodane-type skeleton and the possible biodegradation pathway was proposed:



36 **37** **38**

Fig. 3. Chemical structures of diterpenes (compounds **36**-**38**)

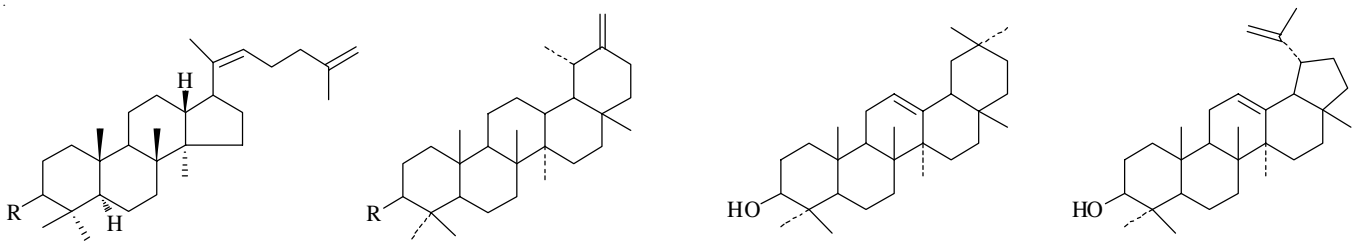
Triterpenoids: Triterpenoids were also found in *A. adenophora* (compounds **39**-**44**, Fig. 4). Yang *et al*.[16] isolated and identified a dammarane-type triterpenoid (compound **39**) from the liposoluble extract of *A. adenophora*. Triterpenoids **40-44** were collected by Yan *et al*.[17].

Steroids: Totally 6 steroids were separated and characterized from the *A. adenophora* (compounds **45**-**50**, Fig. 5). According to the report, steroidal compounds and their derivatives mainly exist in the flower, stem and root of *A. adenophora*. Stigmasterol (**45**), stigmasterol acetate (**46**) and octamethylpicen-3-ol (**47**) were separated from the petroleum extract of *A. adenophora*. Compounds **48**-**50** were reported by Yan *et al*.[17].

Flavonoids: Flavonoids were mainly found from the leaves and the flowers of *A. adenophora*. Until now, there are 8 flavonoids reported, most of the flavonoids were glucosides. Li *et al*.[18] reported the islolation of 5 flavonoids from the aerial part of *A. adenophora*, including quercetagetin 7-β-O-glucoside (**51**), 6-methoxykaempferol 7-methyl ether 3-β-O-glucoside (**52**), quercetagetin 4'-methyl ether 7-β-O-glucoside (**53**), 6-hydroxykaempferol-7-β-O-glucoside (**54**) and 6-methoxygenkwanin (**55**). Ding *et al*.[19] reported the isolation of two flavonoids from the flowers of *A. adenophora*, including 5,4'-dihydroxy-3,6-dimethoxy-7-O-β-D-glucopyranoxyflavonone (**56**), 5,4'-dihydroxy-6,7-dimethoxy-3-O-β-D-glucopyranoxyflavonone (**57**) and 3,5,4'-trihydroxy-6,7-dimethoxyflavonone (**58**).

Phenolic derivatives: Total 25 phenolic derivatives were reported from *A. adenophora*. Weyerstahl *et al*.[11] isolated 4 phenolic constituents from the flower essential oil of *A. adenophora*, including one new compound (compound **59**, Fig. 6) and three previously isolated compounds (**60-62**). Zhang *et al*.[20] isolated 11 phenolic compounds (**63-73**) from the ethanolic extract. Among them, compounds **65-71** and **73** were obtained from *A. adenophora* for the first time. Zhou *et al*.[21] investigated potential allelochems in the roots of the invasive plant *A. adenophora* and isolated seven new phenolic derivatives (compounds **74-80**). A novel qunic acid derivative, compound **81** together with three know ones (compounds **82-84**), were isolated from the aerial parts of *A. adenophora* by Zhang *et al*.[22].

Other compounds: Other compounds, such as fatty alcohols, anhydride and ketones, were also reported. Coumarin-umbelliferone (**85**) and dotriacontanol (**86**) were separated and

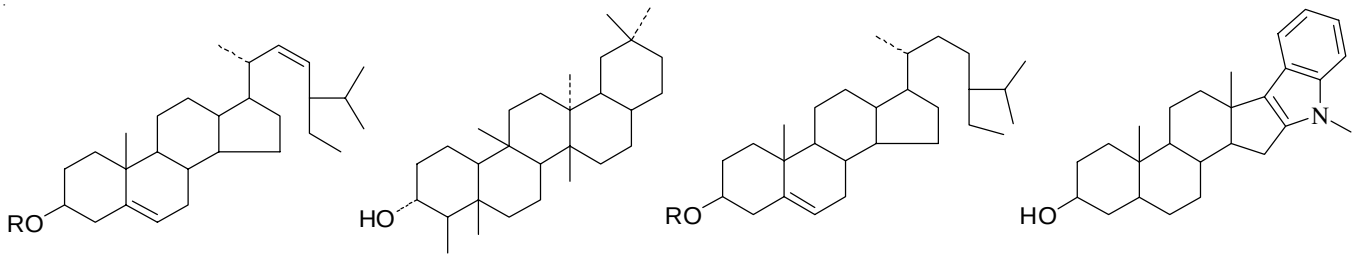


39 R=AcO

40 R=H
41 R=AcO
42 R=$OOCH_2OCH_2(CH_2)_{13}CH_3$

43 **44**

Fig. 4. Chemical structures of triterpenoids (compounds **39**-**44**)



45 R=H
46 R=Ac

47

48 R=H
49 R=glu

50

Fig. 5. Chemical structures of sterols (compounds **45**-**50**)

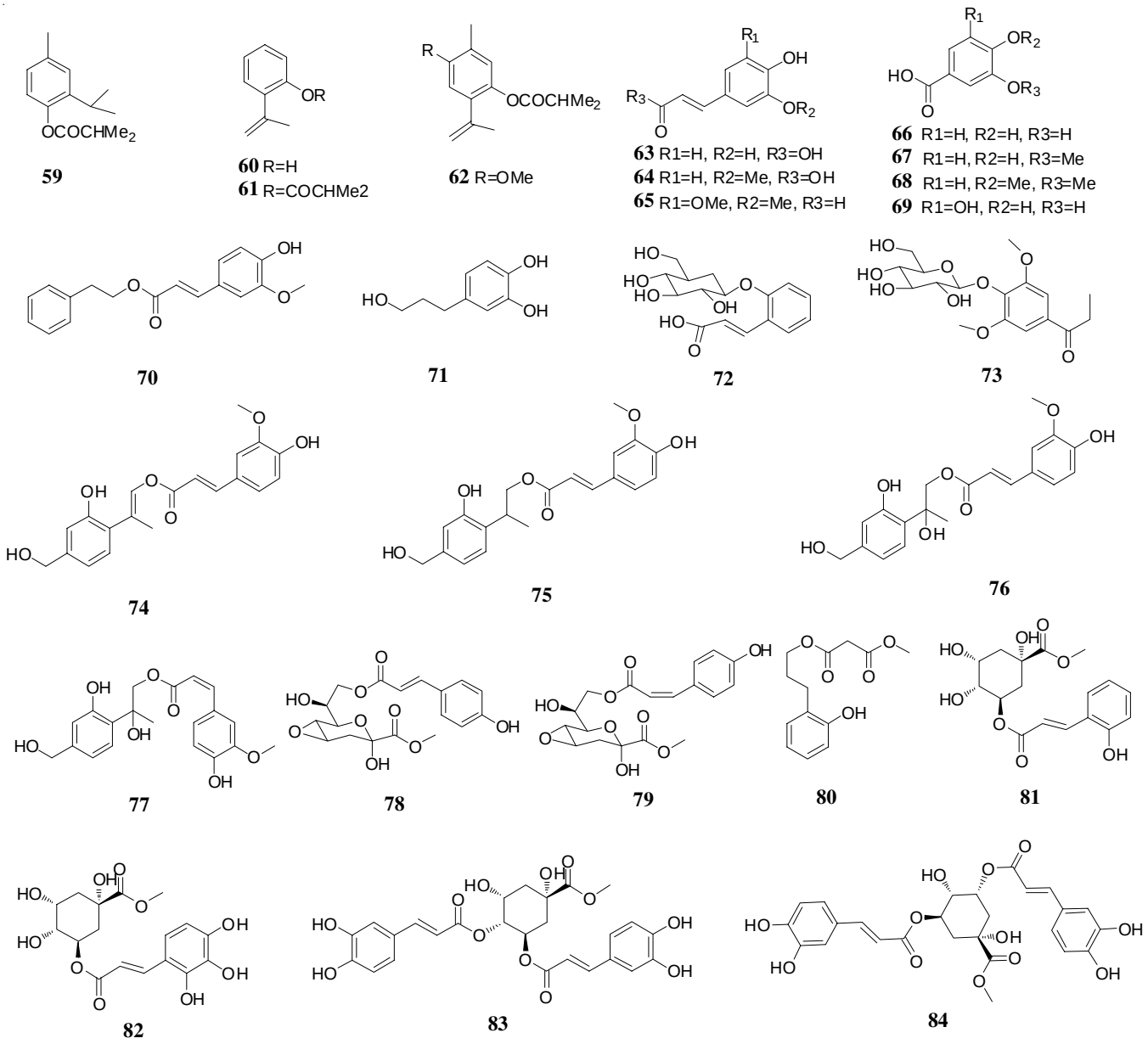


Fig. 6. Chemical structures of sterols (compounds **59**-**84**)

characterized from the aerial part of *A. adenophora* by Li *et al.*[18]. Tritriacontan-17-one (**87**) and nonatetracontan-25-one (**88**) were isolated and identified from the liposoluble parts of *A. adenophora*[16]. Succinic anhydride (**89**) was reported from the flowers of *A. adenophora*[19].

Pharmacological activity

Antibacterial activity: Recent studies[20,21] indicated that the chemical constituent from *A. adenophora* has the antibacterial activity. The polysaccharide from *A. adenophora* has inhibitory activity against *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli*, *etc.*[2]. Bioactive quinic acid derivatives from *A. adenophora* showed *in vitro* antibacterial activity toward five assayed bacterial strains, especially *macranthoin F* and *macranthoin G*. 5-O-*trans*-*o*-coumaroylquinic acid methyl ester (compound **81**), which showed *in vitro* antibacterial activity against *Salmonella enterica*, was further found to display *in vitro* antifungal activity against spore germination of *Magnaporthe grisea*[22]. The essential oil of *A. adenophora* has the antibacterial activity against *Arthrobacter protophormiae*, *Escherichia coli*, *Micrococcus luteus*, *Rhodococcus rhodochrous* and *Staphylococcus aureus*. The antibacterial mechanism may involve in affecting cell membrane integrity, protein and nucleic acid synthesis[23]. Subba and Kandel[24] reported that the essential oil of *A. adenophora* had significant antibacterial activity against both Gram-positive (*Klebsiella pneumoniae* and *Staphylococcus aureus*) and Gram-negative (*Escherichia coli* and *Proteus vulgaris*) bacteria.

Antifungal activity: The experiment for pathogen inhibition by Tian *et al.*[25] showed that volatile oil from *A. adenophora* had certain effect against four fungal, including *Fusarium oxysporum*, *Botrytis cinerea*, *Cercospora personata* and *Gibberlla saubinetii*. The inhibitory effect against *Botrytis cinerea* was the highest[25]. The bioactive constituents of *A. adenophora* were also investigated for antifungal activity. A structure-antifungal activity relationship of cadinene

sesquiterpenes was predicted by evaluating individual derivatives. Antifungal evaluation of these compounds against *pathogenic fungi* was found to be selective. The cadinan-3-ene-2,7-dione was highly inhibitory towards *S. rolfsii* and *R. solani*. Availability of the plant material and significant antifungal activity make the plant a potential source of antifungal agent and it can be exploited for the development of a natural fungicide[26].

Antitumor activity: Some of the chemical constituents from *A. adenophora* exhibited antitumor activity. Cao *et al*.[3] reported that Eupatorium adenophorum H (compound **31**), which is a sesquiterpene from *A. adenophora*, exhibited good inhibiting effect on human colon cancer cell line HCT-8, human liver cancer cell line Bel-7402 and human ovary cancer cell line A2780. The results indicated that Eupatorium adenophorum H has the potential to be used for developing new anticancer drugs.

Anti-HIV activity: By applying principal component analysis on the trace element of *A. adenophora*, Liu *et al*.[27] singled out three equations and found the effect of trace elements on main components. The results showed that *A. adenophora* had the activity of anti-HIV.

Antioxidant activity: The chemical constituents from *A. adenophora* were evaluated for the antioxidant activity. The result showed that polysaccharides from *A. adenophora* had the effect of antioxidant, especially in marked inhibition of the production of lipid peroxides in normal liver homogenate of mice[4]. The antioxidant activities of the oil and cadinenes were also evaluated using 2,2-diphenyl-1-picrylhydrazyl and the ferric reducing ability assay, together with 3 antioxidant standards (ascorbic acid, *tert*-butyl-4-hydroxy toluene and gallic acid). The essential oil and the cadinene sesquiterpene-rich extract of *A. adenophora* had exhibited potential antioxidant activities[28]. In the mean time, Vasanthi *et al*.[29] also reported that the oil form *A. adenophora* showed good antioxidant acitivity by ferrous reducing antioxidant power assay.

Treatment of insomnia: Zhu and Wang[5] discovered that the extract of *A. adenophora* had tranquilizing and hypnotic effects and could be used for the treatment of neurasthenia and insomnia.

Hepatotoxicity: Some chemical constituents from *A. adenophora* showed hepatotoxicity. Isolation of a compound 9-oxo-10,11-dehydroagerophorone from *A. adenophora* caused hepatotoxicity in mice and chronic pulmonary disease in horses[30]. Kaushal *et al*.[31] reported that hepatotoxicity in rat induced by partially purified toxins from *A. adenophora* leaf powder and the methanolic extract. Histopathology of the livers from these animals revealed dilated bile ducts and proliferative changes. Hepatocytes around the bile ducts showed necrotic changes. On the other hand, Fu and Fu[32] reported that the combination of *A. adenophora* and other Chinese medicine could treat chronic active hepatits and early cirrhosis. The above studies indicated that we should pay attention to the hepatotoxicity of the plant. We'd better remove the toxins before we use it to treat diseases.

Insecticial activity: Wang *et al*.[33] separated and purified an active aphid-killing substance (Eupation A, compound **51**) from the chloroform extract of *A. adenophora*. Its mechanism might be that it inhibited the activity of AChE of the cotton aphids *in vitro* and *in vivo*. Eupatorin A was also found to be able to inhibit the activity of Na-K-ATPase of cotton aphids both *in vitro* and *in vivo*[34]. The zelan C (compound **22**) can prevent and kill *Helicoverpa armigera* and *Spodoptera exigua* and can inhibit *Cercospora arachidicola*, *Botrytis cinerea* and *Fusarium*[35]. The study by Wu *et al*.[36] found that the homicidal poisoning effect of crude extract of *A. adenophora* on *Myzus persicae* was significant.

Insect antifeedant activity: *A. adenophora* had been phytochemically investigated for the defensive chemical substances in its leaves. The active sesquiterpenoids were isolated and identified and they exhibited the antifeedant activities against two generalist plant-feeding insects, including *Helicoverpa armigera* and *Spodoptera exigua*[1]. Eupatorium adenophorum lactone, which is bitter and has special herbal odor, had a stimulative effect on the animal and insect gastic mucosa. Tannins had a stimulating effect on the stomach. These findings suggested a defensive role of sesquiterpenoids in *A. adenophora* against herbivores. Clavulanic alcohol had antifeedant effect on pierisrapae larvae[34]. At the same time, sesquiterpenes had anthelmintic, insecticidal effect, α-pinene and β-pinene from the oil of *A. adenophora* had killing effect on body lice and scabies mite[17].

Qualitative and quantitative analysis of *A. adenophora*

Analysis of the root and stems of *A. adenophora:* The chemical components of the extract from roots and stems of *A. adenophora* were studied by the system preliminary experiments. The research showed that the chemical components probably included sugar, polysaccharide, anthraquinone, flavonoids, coumarin, lactones, but no alkaloids, saponins, protein or cardiac glycosides[37]. Using the component analysis method, 10 components in the stem of *A. adenophora* were determined. The study showed that the contents of stem included 10.00-11.60 % moisture content, 3.54 % ash content, 28.25 % cold water extractive, 32.40 % warm water extractive, 12.50 % benzene-alcohol extractive, 52.40 % NaOH extractive, 17.80 % acid-insoluble lignin, 13.14 % pentosan, 51.81 % holocellulose and 26.45 % cellulose. The stem of *A. adenophora* shared similar chemical component constitution with pine tree and maize stem[38].

Analysis of the leaves of *A. adenophora:* Zhang *et al*.[39] analyzed the volatile compounds from the leaves of *A. adenophora* by GC-MS. The component identified included α-phellandrene, camphene, *p*-cymene, 2-carene, α-pinene, limonene, *etc*. Kundu *et al*.[28] analyzed the essential oil obtained from the leaves of *A. adenophora* using GC-MS. Twenty six essential oil constituents comprising sesquiterpenes and monoterpenes were identified. γ-Cadinene was the most abundant followed by germacrene-D and γ-elemene. Ji *et al*.[40] reported the result of GC-MS of the essential oils from the invasive plants. Total 78 compounds were identified, monoterpenes and sesquiterpenes were found to be the major components.

Analysis of the flower and fruit of *A. adenophora:* The flower essential oils of *A. adenophora* from North Indian origin were analyzed. The results indicated that it consists of 66 % of monoterpenes and 28 % of sesquiterpenes. Sixty-four consti-

tuents were identified by GC-MS. Amorphene derivatives (10 %), which were significant for *A. adenophora*, were main constituents of the sesquiterpenes part[11]. Vasanthi *et al.*[30] analyzed the essential oil from flowers of *A. adenophora* using gas chromatography. Twenty five compounds, which accounted for 91.3 % of the oils, were identified. The essential oil was dominated by sesquiterpenoids (81.90 %) represented by sesquiterpene hydrocarbons (36.50 %) and oxygenated sesquiterpenoids (45.4 %). The major compounds are copaen (19.72 %), α-bisabolol (9.8 %), *etc*. The chemical constituents of essential oil in fruits of *A. adenophora* were investigated by GC-MS with capillary column. Sixty eight contents were identified, the major chemical constituents of essential oil in fruits of *A. adenophora* were terpenes[41].

Conclusion

In the face of serious harm of *A. adenophora*, the artificial excavation, chemical control is not enough, we must take comprehensive prevention and control measures. In recent years, over a hundred kinds of chemical constituents of *A. adenophora* have been discovered by scientists through continued efforts and the medicinal value of *A. adenophora* has been gradually found. The medical use and new drug development from *A. adenophora* will gradually become a hot research field in the future for period of time. Through the study of all aspects of the *A. adenophora*, we can make full use of it and find the value where it exist.

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REFERENCES

1. W. Shi, S.H. Luo and S.H. Li, *Chin. J. Chem.*, **30**, 1331 (2012).
2. P. Gao, W.T. Su, N.N. Pi and D. Su, Chinese Patent CN 101422481 A, (2009).
3. A.C. Cao, L. He, J. Hou, Q. Wang and M. Guo, Chinese Patent CN 101481299 A (2009).
4. W.T. Su, N.N. Pi, D.H. Su, Y. Xie, D. Ji and P. Gao, *Ziran Kexueban*, **46**, 814 (2009).
5. Z.Y. Zhu and J.K. Wang, Chinese Patent CN 1569059 A (2005).
6. J.K. Ding, Z. Yu, P. Wang, X.-J. Yu, Y.-F Yi and Z.-H. Ding, *Acta Botan. Yunnan*., **13**, 441 (1991).
7. X. Zhao, G.W. Zheng, X.M. Niu, W.-Q. Li, F.-S. Wang and S.-H. Li, *J. Agric. Food Chem.*, **57**, 478 (2009).
8. F. Bohlmann, J. Jakupovic and M. Lonitz, *Chem. Ber.*, **110**, 301 (1977).
9. F. Bohlmann and R.K. Gupta, *Phytochemistry*, **20**, 1432 (1981).
10. S. Ananvoranich, K. Likhitwitayawuid, N. Ruangrungsi, G. Blasko and G.A. Cordell, *J. Org. Chem.*, **54**, 2253 (1989).
11. P. Weyerstahl, H. Marschall, I. Seelmann and V.K. Kaul, *Flav. Fragr. J.*, **12**, 387 (1997).
12. L. He, J. Yang, A.C. Cao, Y.-M. Liu, Y. An and J.-G. Shi, *Chin. J. Chem.*, **24**, 1375 (2006).
13. M.Z. Wang, Y.Y. Zhang, S.L. Li, X.-H. Cai and X.-D. Luo, *Helv. Chim. Acta*, **89**, 3104 (2006).
14. L. He, J. Hou, M.L. Gan, J. Shi, S. Chantrapromma, H.-K. Fun, I.D. Williams and H.H.-Y. Sung, *J. Nat. Prod.*, **71**, 1485 (2008).
15. M.Z. Wang, X.H. Cai, G.H. Du, G.S. Du and X.D. Luo, *Z. Naturforsch. B*, **62**, 577 (2007).
16. J. Yang, A.C. Cao, D.X. Zhou, D. Zhang and L. He, *Zhongcaoyao*, **37**, 30 (2006).
17. Q.S. Yan, J. Yang, H.M. Li, A. Cao, Q. Chen, Y.Q. Wen and L. He, *J. Beijing Normal Univ. (Nat. Sci. Ed.)*, **42**, 70 (2006).
18. R.T. Li, Z.H. Ding and J.K. Ding, *Acta Botan. Yunnan*., **19**, 196 (1997).
19. Z.H. Ding, Y.S. Guo and J.K. Ding, *Acta Botan. Yunnan*., **21**, 505 (1999).
20. M. Zhang, Z.Y. Zhou, H. Ren, J.W. Tan and F.H. Wan, *Redai Yaredai Zhiwu Xuebao*, **21**, 63 (2013).
21. Z.Y. Zhou, W.X. Liu, G. Pei, H. Ren, J. Wang, Q.-L. Xu, H.-H. Xie, F.-H. Wan and J.-W. Tan, *J. Agric. Food Chem.*, **61**, 11792 (2013).
22. M. Zhang, W.X. Liu, M.F. Zheng, Q.-L. Xu, F.-H. Wan, J. Wang, T. Lei, Z.-Y. Zhou and J.-W. Tan, *Molecules*, **18**, 14096 (2013).
23. S.X. Liu, H.P. Wei, J. Cheng and J.Q. Yang, *Zhongguo Yiyuan Yaoxue Zazhi*, **32**, 1742 (2012).
24. B. Subba and R.C. Kandel, *J. Nepal Chem. Soc.*, **30**, 78 (2012).
25. Y. Tian, J. Hou, J.P. Wu, L. He and A. Cao, *Nongyaoxue Xuebao*, **9**, 137 (2007).
26. A. Kundu, S. Saha, S. Walia, N.A. Shakil, J. Kumar and K. Annapurna, *J. Environ. Sci. Health B*, **48**, 516 (2013).
27. Y.H. Liu, C.X. Yin, L. Peng, X. Zhang, H.M. Zhao, Y.T. Pu and Y. Zhao, *Weiliang Yuansu Yu Jiankang Yanjiu*, **29**, 28 (2012).
28. A. Kundu, S. Saha, S. Walia, V. Ahluwalia and C. Kaur, *Toxicol. Environ. Chem.*, **95**, 127 (2013).
29. S. Vasanthi and V.K. Gopalakrishnan, *Res. J. Pharm. Biol. Chem. Sci.*, **4**, 1419 (2013).
30. P.B. Oelrichs, C.A. Calanasan, J.K. MacLeod, A.A. Seawright and J.C. Ng, *Nat. Toxins*, **3**, 350 (1995).
31. V. Kaushal, R.K. Dawra, O.P. Sharma and N.P. Kurade, *Toxicon*, **39**, 615 (2001).
32. L.J. Fu and J.J. Fu, Chinese Patent CN101099850A (2008).
33. Y.D. Wang, P. Gao, Q.H. Zhang, Y. Zheng, K. Liu and S. Liu, *Gaojishu Tongxun*, **12**, 21 (2002).
34. Y.D. Wang, P. Gao and Y. Zheng, *Zhiwu Baohu Xuebao*, **29**, 337 (2002).
35. L. He, A.C. Cao, M.X. Guo, CN 1948256 A, (2007).
36. D. Wu, L.R. Zhao and Y.W. Zhang, *Anhui Nongye Kexue*, **40**, 5931 (2012).
37. Y. Zhang, X.F. Li, L. Yang, L. Yang, K. Zhou and H.J. Zhang, *Beifang Yuanyi*, **23**, 23 (2012).
38. Y.F. Yang, J.X. Li and L.L. Jia, *J. West China Forestry Sci.*, **34**, 91 (2005).
39. F.J. Zhang, J.Y. Guo, F.X. Chen, W. Liu and F. Wan, *Weed Sci.*, **60**, 205 (2012).
40. M. Ji, S.Z. Ze and M. Sun, *Xibu Linye Kexue*, **41**, 84 (2012).
41. A. Fang, C.L. Sun, X. Du, Y.M. Bi and J. Tian, *Shizhen Guoyi Guoyao*, **18**, 1831 (2007).