Review Article

# Investigation of Radix Achyranthis Bidentatae Phytochemistry and Pharmacology

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## Abstract

Radix achyranthis bidentatae (RAB), a member of the *Amaranthaceae* family, has been widely used in Traditional Chinese Medicine for 1000s of years. Increasing interest in RAB-derived medicinal has led to the discovery of additional triterpenoid saponins, phytoecdysones, polysaccharides, and many other compounds, as well as investigations into their pharmacology. A large number of pharmacological studies have shown RAB and its active components possess a range of pharmacological activities, including anti-tumor, anti-fertility, anti-senile, and anti-inflammatory effects. This review is an up-to-date summary and synthesis of the uses of RAB from phytochemical and pharmacological perspectives.

**Keywords:** Pharmacology, phytoecdysones, polysaccharides, radix achyranthis bidentatae, triterpenoid saponins

## Introduction

Radix achyranthis bidentatae (RAB), known as Niuxi in Chinese, is derived from the dried roots of *Achyranthes bidentata* Bl and is a well-known Traditional Chinese Medicine (TCM). This plant is cultivated from different provinces of China, including Henan, Shanxi, Shandong, and Jiangsu, and used in folk medicine. In the Chinese Pharmacopoeia (2015 Edition), RAB is used in the treatment of osteodynia of the lumbar and knees, spasms, and limb flaccidity.

Currently, the traditional uses of RAB have been largely expanded on. Experimental studies indicate RAB possesses a number of pharmacological activities, including anti-tumor,[1] immunostimulant,[2,3] uteri-excitant, anti-fertility,[4,5] anti-bacterial,[6] anti-inflammatory,[7] cognition-enhancing,[8] anti-senile,[9,10] and anti-osteoporosis[11-13] properties. In terms of treatment, RAB has been used to influence carbohydrate metabolism in the blood,[14,15] hasten growth,[16] and improve the dual modulatory function of the immune system.[17,18]

In general, the curative effects of TCMs are due to the synergy of many bioactive compounds.[19,20] Chemically, RAB has been extensively studied, triterpenoid saponins,[21,22] phytoecdysones,[23,24] and polysaccharides have been isolated and identified as the main components of RAB.

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While this plant has been well-studied in China, a significant amount of information on RAB that has been collected by scientists is not available to the international community because many of the scientific articles have only been published in Chinese. Therefore, it is necessary to summarize and present research articles on RAB in English.

This review summarizes the phytochemical composition and pharmacological effects of RAB. It aims to provide a consolidated platform for further study of this plant to better guide clinical applications and sustainable utilization of medicinal resources.

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## Phytochemistry

Several different classes of compounds, primarily triterpenoid saponins, phytoecdysones, and polysaccharides, were previously isolated from RAB.

### Triterpenoid saponins

Triterpenoid saponins are an important class of bioactive substances in *A. bidentata* Blume, and their structures are mainly leanness with 1–4 saccharide groups at C-3 and/or C-28 position, thereby forming disaccharide or monosaccharide chains. To date, a total of 46 triterpenoid saponins, the most abundant compounds in RAB, have been isolated from RAB. 3-*O* ($\alpha$-$_L$-rhamnopyranosyl-[$\beta$-$_D$-glucuro nopyranosyl]) oleanolic acid-28-*O*-$\beta$-$_D$-glucopyranosyl ester (1) and 3-*O*-$\beta$-$_D$-glucosyl-oleanolic acid-28-*O*-$\beta$-$_D$-glucosyl ester (44)[21] were isolated using the ethanol extraction method. Their structures were characterized using chemical and spectral analysis infrared spectroscopy (IR), mass spectrometry (MS), proton magnetic resonance nuclear magnetic resonance ($^1$H-NMR), carbon-13 NMR ($^{13}$C-NMR), and $^1$H,$^{13}$C chemical-shift correlation spectroscopy (C-H COSY). Achyranthoside C dimethyl ester (3), achyranthoside C butyl dimethyl ester (4), achyranthoside D trimethyl ester (6), achyranthoside E trimethyl ester (8), achyranthoside E dimethyl ester (9), achyranthoside E butyl dimethyl ester (10), 18-[$\beta$-$_D$-gluco pyranosyloxy]-28-oxoolean-12-en-3 β-yl 3-*O*-[$\beta$-$_D$-glucop yranosyl]-$\beta$-$_D$-glucopyranosiduronic acid methyl ester (32), achyranthoside A trimethyl ester (34), and hederagenin-2 8-*O*-$\beta$-$_D$-glucopyranosyl ester (40) were isolated from *A. bidentata*.[22] Wei *et al*.[25] used Sephadex LH-20, prep-high performance liquid chromatography (prep-HPLC), and spectroscopic techniques to study the chemical composition of RAB. The compounds isolated from *A. bidentata* and identified in this study, including achyranthoside C (2), chikuserusaponin IV (11), achyranthoside D (5),[26] achyranthoside E (7), and achyranthoside A (33).[27] Subsequently, their structures were determined based on NMR spectroscopy and MS. Chikuserusaponin IVa (12), chikusetsusaponin IVa methyl ester (13), chikusetsusaponin IVa butyl ester (14), 28-deglucose chikusetsusaponin D methyl ester (19), oleanolic acid 3-*O*-$\beta$-$_D$-glucuronopyranoside (20), 28-deglucosyl-chikusetsusaponin IVa butyl ester (23), and momordin IIa (24),[28] were reported from *A. bidentata*.

Phytochemical investigation of and chemical isolation from the roots of *A. bidentata* yielded chikusetsusaponin IVa ethyl ester (15), oleanolic acid 3-*O*-$\beta$-$_D$-glucuronopyranoside-6-*O*-butyl ester (21), oleanolic acid 3-*O*-$\beta$-$_D$-glucuronopyranoside-6-*O*-methyl ester (22), chikuserusaponin I (41), and oleanolic acid (42),[29] chikusetsusaponin V (16), chikusetsusaponin V butyl ester (18), zingibroside R1 (25), achyranthosid I (26) and achyranthosid II (27) were also isolated from *A. bidentata*,[30] while chikusetsusaponin V methyl ester (17) and bidentatoside II (43) are from the roots.[31] Solvent extraction and column chromatography were used to isolate triterpenoid saponins, while physicochemical constants and spectroscopic analysis were employed for structural elucidation.[32] Ando *et al*.[33] studied the composition of the roots of *A. bidentata* using Sephadex LH-20, prep-HPLC, and spectroscopic techniques. Achyranthoside G (28), achyranthoside G methyl ester (29), achyranthoside H (30) and achyranthoside H methyl ester (31) were identified from *A. bidentata*. The chemical constituents were isolated and purified using macroporous adsorptive resin D101, silica gel, ODS column chromatography, and prep-HPLC. Their structures were elucidated based on one-dimensional and two-dimensional NMR analyses. Achyranthosid IV (35), ginsenoside R0 (39), 28-norolean-17-en-3-ol (45) and $\alpha$-spinasteryl-$\beta$-$_D$-glucoside (46),[34-37] and their structures were elucidated by NMR spectroscopy. Oleanolic acids[38] isolated from the roots and identified them as oleanolic acid 3-*O*-[$\beta$-$_D$-glucuronopyranoside-6-*O*-methyl ester]-28-*O*-$\beta_D$-glucopyranoside (36) oleanolic acid 3-*O*-[$\beta$-$_D$-glucuronopyran-oside-6-*O*-ethylester]-28-*O*-$\beta$-$_D$-glucopyranoside (37), and oleanolic acid 3-*O*-[$\beta$-$_D$-glucuronopyranoside-6-*O*-butylester]-28-*O*-$\beta$-$_D$-glucopyranoside (38). Figure 1 and Table 1 summarize the triterpenoid saponins found.

### Phytoecdysones

Phytoecdysones all possess a tetracyclic pregnane carbon skeleton but differ in the number and nature of the substituents, which are the main drivers of pharmacological activity. 25*S*-inokosterone (1) 25*R*-inokosterone (2) polypodine B (4) podecdysone C (5) stachysterone D (6), rubrosterone (7), achyranthesterone A (8), stachysterone A (19), rhapontisterone B (20), and polypodineB (21),[39-42] were isolated from *A. bidentata*. 25*S*-20,22-*O*-(*R*-ethylidene) inokosterone (11) and 20,22-*O*-(*R*-3-methoxycarbonyl) propylidene-20-hydroxyecdysone (12), together with 25*S*-inokosterone-20,22-acetonide (13), 20,22-*O*-(*R*-ethylidene)-20-hydroxyecdysone (14), and 20-hydroxyecdysone-20,22-monoacetonide (15), were isolated from *A. bidentata*.[43-46] Published literature found on the isolation and structural elucidation of the 29$\alpha$-(3-methoxy-4-hydroxyphenyl)-20,22-*O*-methylidene-20-hydroxyecdysone (16), ecdysteroid serfurosterone A (17),[47-50] from *A. bidentata*. In addition, researchers[51-53] performed a phytochemical study on RAB, and obtained additional RAB-derived compounds, such as ecdysone (3), achyranthesterone B (22), and shidasterone (24), 2 β,3 β,20 β,22$\alpha$,25-pentahydroxy-8,14-diene-cholest-6-one (25), 20*R*,22*R*-2 β,3 β,20,22,26-pentahydroxy-cholestan-7,12-dien-6-one (26) 20-Hydroxyecdysone (27) and from *A. bidentata*. Moreover identified (20*R*,22*R*,24*S*,25*S*)-20-*O*,22-*O*-(5'-hydroxymethyl)-furfurylidene-2 β,3 β,14$\alpha$,26-tetrahydroxycholest-7-en-6-one (18) through interpretation of spectroscopic data, as well as chemical and spectral analysis (IR, MS, $^1$H-NMR, $^{13}$C-NMR, and C-H COSY techniques).[24,53] Another three phytoecdysones, niuxixinsterone A (9), niuxixinsterone C (10), and niuxixinsterone B (23),[54] recently were isolated. Figure 2 and Table 2 summarize the phytoecdysones found.

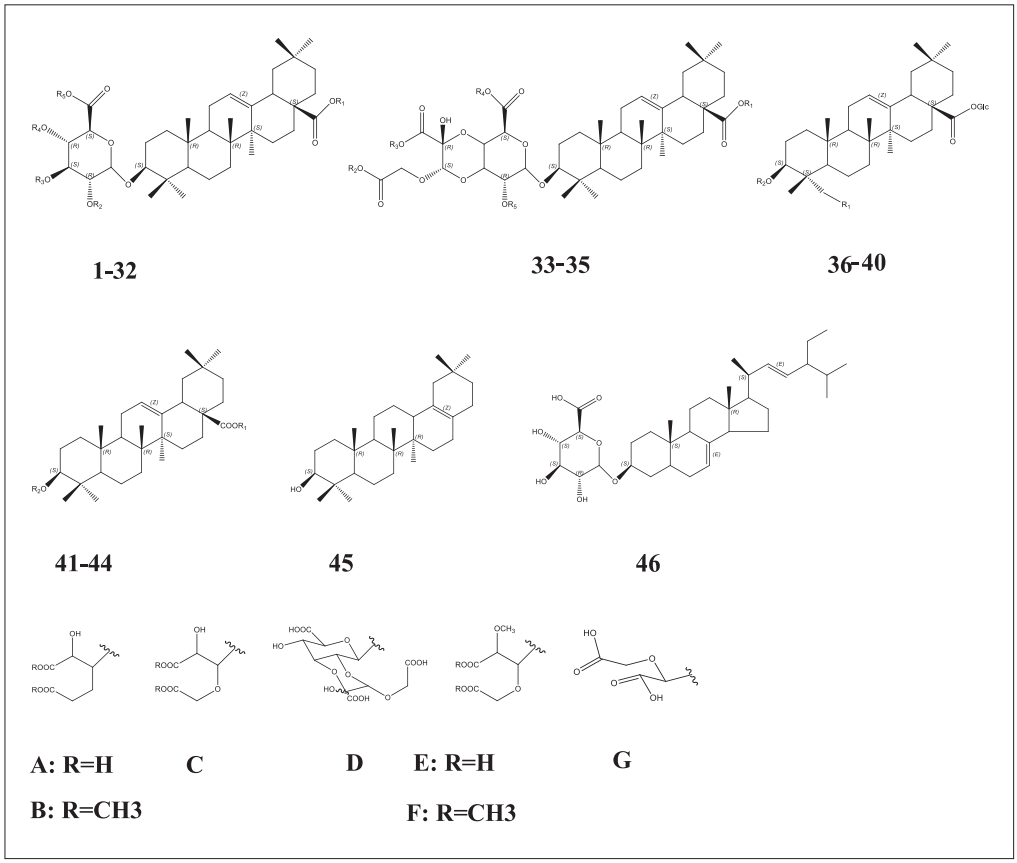


**Figure 1:** Structures of the triterpenoid saponins isolated from radix achyranthis bidentatae. Refer to Table 1 for more details

## Polysaccharides

Polysaccharides are one of the major groups of active components in RAB and have aroused great interest over the last few decades. So far several kinds of *A. bidentata* polysaccharide (ABP) have been isolated from the roots of *A. bidentata*. Hui *et al*.[55] isolated a neutral polysaccharide with a molecular weight of 1440 D composed of fructose and glucose residues at a molar ratio of 8.7:1. Subsequently, a peptide-polysaccharide was isolated, and its structure was determined.[56] A new water-soluble polysaccharide, named ABP70-2, with a molecular weight of 3406 Da was isolated from RAB.[57] Its detailed structure was demonstrated for the first time and laid the foundation for further research, such as a preliminary evaluation of the underlying mechanisms and structural conformation of ABP70-2. The structural study demonstrated ABP70-2 has a backbone composed of (2→6)-linked $\beta$-$_D$-Fruf with (2→1)-linked $\beta$-$_D$-Fruf branched chains and terminates with Glc and Fru residues. ABP70-2 has an irregular shape and appears to be mainly comprised overlapping sheets and strips. Analysis of the constituent monosaccharides, IR, and NMR, combined with the results of heteronuclear multiple bond correlation (HMBC) spectrum studies, allowed prediction of a structure for ABP70-2.(The HMBC spectrum had cross peaks between $^{13}$C spectrum and $^{1}$H spectrum peaks for different residues). The structures are shown in Figure 3.

## Others

*A. bidentata* polypeptides (ABPP) isolated from the aqueous extract of *A. bidentata* are promising bioactive compounds. The twelve different fractions from crude polypeptides by HPLC, which were labeled as ABPPa, b, c, d, e, f, g, h, i, j, k, and l, respectively.[58] Other RAB components, including stigmasterol, stigmasteryl glucoside, $\beta$-sitosteryl glucoside, betaine hydrate, betaine hydrochloride, succinic acid, oxalic acid, $\gamma$-aminobutyric acid, $\alpha$-spinalsterol, $\beta$-sitosterol, chrysophanol, dibutyl phthalate, palmitic acid, and daucosterol were reported from *A. bidentata*.[37,59-61] Two new isoflavonoid glucosides, achyranthosides A and B,[62] were separated from the roots of *A. bidentata*. Their structures were established through extensive analyses using 1H-NMR, 13C-NMR, heteronuclear singular quantum correlation HMBC, and nuclear overhauser effect spectroscopy and high-resolution electrospray ionization mass spectroscopy spectroscopic data. Emodin and physcion[63,64] were isolated from *A. bidentata*. In addition, eugenol, hydroquinone, para-benzoquinone, asarone, $\alpha$-ionone, spathulenol, 5-hydroxymethylfurfural, baicalin, wogonin, berberine, palmatine, coptisine, epiberberine, *N*-butyl-$\beta$-$_D$-fructopyranoside, allantoin, and magnesium phosphate,[35,65,66] were also reported. Cyclo-(-Tyr-Leu), cyclo-(-Leu-IIe), nonanedioic acid, and geniposide[36,67] were discovered in RAB based on HPLC. Glycerol-1,9,12-(*Z, Z*)-octadecadienoic ester, ergosta-7,22-diene-3 β,5$\alpha$,6

**Table 1: Triterpenoid saponins isolated from radix achyranthis bidentatae**

| *n* | Compound name | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_5$ | Reference |
|---|---|---|---|---|---|---|---|
| 1 | 3-*O*[*α*-*L*-rhamnopyranosyl-(*β*-*D*-glucuronopyranosyl)]oleanolic acid-28-*O*-*β*-*D*-glucopyranosyl ester | -Glc | -H | -Rha | -H | -H | [21] |
| 2 | Achyranthoside C | -Glc | -H | A | -H | -H | [25] |
| 3 | Achyranthoside C dimethyl ester | -Glc | -H | B | -H | -H | [22] |
| 4 | Achyranthoside C butyl dimethyl ester | -Glc | -H | B | -H | -Bu | [22] |
| 5 | Achyranthoside D | -Glc | -Glc | A | -H | -H | [26] |
| 6 | Achyranthoside D trimethyl ester | -Glc | -Glc | B | -H | $-CH_3$ | [22] |
| 7 | Achyranthoside E | -Glc | -H | C | -H | -H | [27] |
| 8 | Achyranthoside E trimethyl ester | -Glc | -H | B | -H | $-CH_3$ | [22] |
| 9 | Achyranthoside E dimethyl ester | -Glc | -H | B | -H | -H | [22] |
| 10 | Achyranthoside E butyl dimethyl ester | -Glc | -H | B | -H | -Bu | [22] |
| 11 | Chikuserusaponin IV | -Glc | -H | -H | -Ara | -H | [24] |
| 12 | Chikuserusaponin IVa | -Glc | -H | -H | -H | -H | [28] |
| 13 | Chikusetsusaponin IV a methyl ester | -Glc | -H | -H | -H | $-CH_3$ | [28] |
| 14 | Chikusetsusaponin IVa butyl ester | -Glc | -H | -H | -H | -Bu | [28] |
| 15 | Chikusetsusaponin IVa ethyl ester | -Glc | -H | -H | -H | -Et | [29] |
| 16 | Chikusetsusaponin V | -Glc | -Glc | -H | -H | -H | [30] |
| 17 | Chikusetsusaponin V methyl ester | -Glc | -Glc | -H | -H | $-CH_3$ | [31] |
| 18 | Chikusetsusaponin V butyl ester | -Glc | -Glc | -H | -H | -Bu | [30] |
| 19 | 28- deglucose chikusetsusaponin D methyl ester | -H | -Glc | B | -H | $-CH_3$ | [28] |
| 20 | Oleanolic acid 3-*O*-*β*-*D*-glucuronopyranoside | -H | -H | -H | -H | -H | [28] |
| 21 | Oleanolic acid 3-*O*-*β*-*D*- glucuronopyranoside-6-*O*-butyl ester | -H | -H | -H | -H | -Bu | [29] |
| 22 | Oleanolic acid 3-*O*-*β*-*D*- glucuronopyranoside-6-*O*-methyl ester | -H | -H | -H | -H | $-CH_3$ | [29] |
| 23 | 28-deglucosyl chikusetsusaponin Iva butyl ester | -Glc | -H | -H | -H | -H | [28] |
| 24 | Momordin IIa | -Glc | -H | -Rha | -H | $-CH_3$ | [28] |
| 25 | Zingibroside R1 | -H | -Glc | -H | -H | -H | [30] |
| 26 | Achyranthoside I | -Glc | -Glc | A | -H | -H | [32] |
| 27 | Achyranthoside II | -H | -H | A | -H | -H | [32] |
| 28 | Achyranthoside G | -H | -Glc | A | -H | -H | [33] |
| 29 | Achyranthoside G methyl ester | $-CH_3$ | -Glc | B | -H | $-CH_3$ | [33] |
| 30 | Achyranthoside H | -Glc | -H | E | -H | -H | [33] |
| 31 | Achyranthoside H methyl ester | -Glc | -H | F | -H | $-CH_3$ | [33] |
| 32 | 18-[*β*-*D*-Oxyglucose)-28-oxo-12-oleanolic-3*β*-3-*O*-(*β*-*D*-glucosel)-*β*-*D*-glucuronic | -Glc | -H | -Glc | -H | $-CH_3$ | [22] |
| 33 | Achyranthoside A (achyranthosid III) | -Glc | -H | -H | -H | -H | [27] |
| 34 | Achyranthoside A trimethyl ester | -Glc | -H | $-CH_3$ | $-CH_3$ | $-CH_3$ | [22] |
| 35 | Achyranthoside IV | -H | -H | -H | -H | -H | [34] |
| 36 | Oleanolic acid 3-*O*-[*β*-*D*-glucuronopyranoside-6-*O*-methyl ester]-28-*O*-*β*-*D*-glucopyranoside | -H | -Me-6-O-GlcUA | | | | [38] |
| 37 | Oleanolic acid 3-*O*-[*β*-*D*-glucuronopyran-oside-6-*O*-ethyl ester]-28-*O*-*β*-*D*-glucopyranoside | -H | -Et-6-O-GlcUA | | | | [38] |
| 38 | Oleanolic acid 3-*O*-[*β*-*D*-glucuronopyranoside -6-*O*-butyl ester]-28-*O*-*β*-*D*-glucopyranoside | -H | -Bu-6-O-GlcUA | | | | [38] |
| 39 | Ginsenoside R0 | -H | -Glc (1-2) GlcUA | | | | [35] |
| 40 | Hederagenin-28-*O*-β-*D*-glucopyranosyl ester | -OH | -H | | | | [22] |
| 41 | Chikuserusaponin I | -Glc | -H | | | | [29] |
| 42 | Oleanolic acid | -H | -H | | | | [29] |
| 43 | Bidentatoside II | -Glc | G | | | | [31] |
| 44 | 3-*O*-*β*-*D*-glucosyl-oleanolic acid-28-*O*-*β*-*D*-glucosyl ester | -Glc | -Glc | | | | [21] |

β-triol, and *N*-trans-feruloyltyramine[68] were reported in the isolation, from a 70% ethanol extract. Linoleic acid, *Z*-8,11,12,-trihydroxy-9-octadecenoic acid, *Z*-8,11,12,-trihydroxy-9-octadecenoic acid methyl ester, *N*-cis-feruloyltyramine, and *N*-cis-feruloy-3-methoxytyramine were isolated from *A. bidentata*.[52] *N*-trans-feruloyl-3-meth oxytyramine-4-*O*-*β*-$_D$-glucopyranoside,[38] *N*-trans-feruloyl -3-methoxytyramine-4′-*O*-*β*-$_D$-glucopyranoside,[33] recently were isolated from *A. bidentata*. In addition to the compounds listed above previously, other compounds, including rutinum, astragalin, caffeic acid, kaempferol-3-*O*-glucoside, and isoquercitrin[69,70] were also reported from *A. bidentata*.

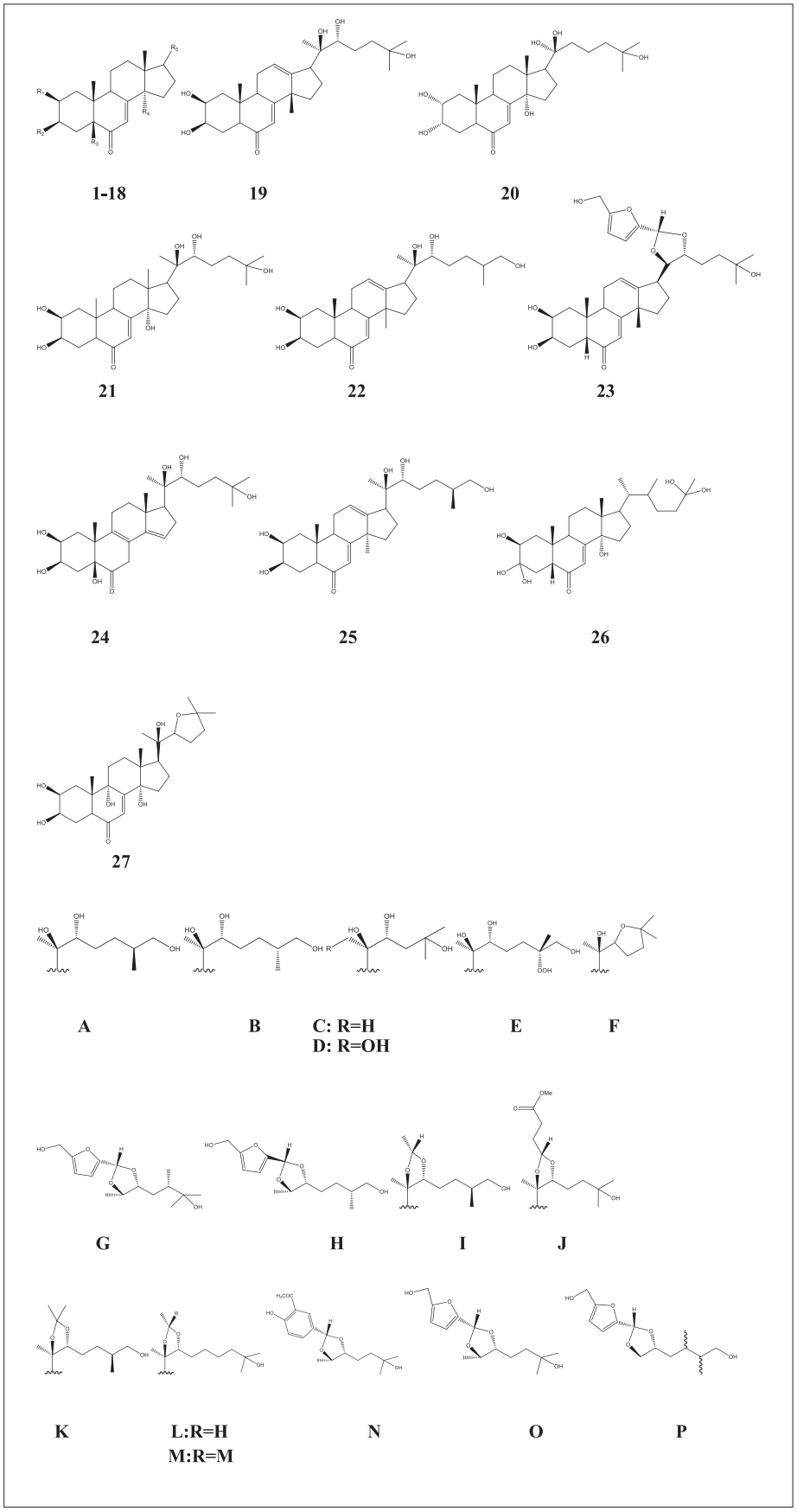


**Figure 2:** Structures of the phytoecdysones isolated from radix achyranthis bidentatae. Refer to Table 2 for more details

**Table 2: Phytoecdysones isolated from radix achyranthis bidentatae**

| *n* | Compound name | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_5$ | Reference |
|---|---|---|---|---|---|---|---|
| 1 | 25*S*-inokosterone | -OH | -OH | -H | -OH | A | [39] |
| 2 | 25*R*-inokosterone | -OH | -OH | -H | -OH | B | [39] |
| 3 | Ecdysterone | -OH | -OH | -H | -OH | C | [49] |
| 4 | Polypodine B | -OH | -OH | -OH | -OH | C | [40] |
| 5 | Podecdysone C | -OH | -OH | -H | -OH | E | [42] |
| 6 | Stachysterone D | -OH | -OH | -H | -OH | F | [40] |
| 7 | Rubrosterone | -OH | -OH | -H | -OH | =O | [41] |
| 8 | Achyranthesterone A | -OH | -OH | -OH | -OH | D | [40] |
| 9 | Niuxixinsterone A | -OH | -OH | -H | -OH | G | [24] |
| 10 | Niuxixinsterone C | -OH | -OH | -OH | -OH | H | [24] |
| 11 | 25*S*-20,22-*O*-(*R*-ethylidene) inokosterone | -OH | -OH | -H | -OH | I | [43] |
| 12 | 20,22-*O*-(*R*-3-methoxycarbonyl) propylidene-20-hydroxyecdysone | -OH | -OH | -H | -OH | J | [43] |
| 13 | 25*S*-inokosterone-20,22-acetonide | -OH | -OH | -H | -OH | K | [44] |
| 14 | 20,22-*O*-(*R*-ethylidene)-20-hydroxyecdysone | -OH | -OH | -H | -OH | L | [45] |
| 15 | 20-hydroxyecdysone-20,22-monoacetonide | -OH | -OH | -H | -OH | M | [46] |
| 16 | 29$\alpha$-(3-methoxy-4-hydroxyphenyl)-20,22-*O*-methylidene-20-hydroxyecdysone | -OH | -OH | -H | -OH | N | [49] |
| 17 | Serfurosterone A | -OH | -OH | -H | -OH | O | [50] |
| 18 | (20*R*,22*R*,24*S*,25*S*)-20-*O*,22-*O*-(5'-hydroxymethyl)-furfurylidene-2$\beta$,3$\beta$,14$\alpha$,26-tetrahydroxycholest-7-en-6-one | -OH | -OH | -H | -OH | P | [53] |

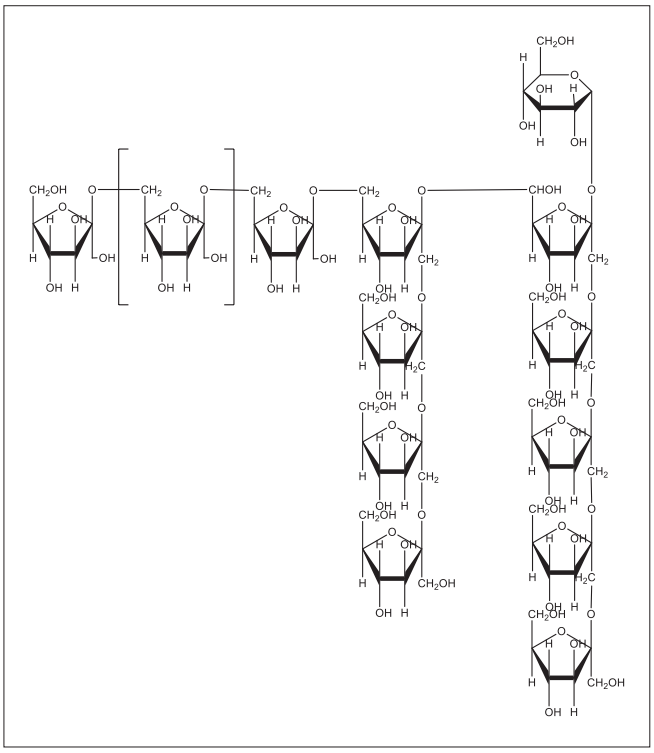

**Figure 3:** Structures of the ABP70-2 isolated from radix achyranthis bidentatae

## Pharmacology

TCM states that RAB is bitter and sour, and has many physiological functions, including dissipating blood stasis, nourishing the liver and kidney, and strengthening the bones and muscles. TCM also holds RAB can be used for the treatment of osteodynia of the lumbar and knees, as well as spasms and flaccidity of limbs. Pharmacological and clinical investigations carried out during the last few years have shown that root extracts have specific biological effects, including immune system regulating, anti-fertility, anti-tumor, analgetic, anti-inflammatory, old-age-resisting, cardiovascular, and nervous system activity, and can treat osteoporosis.

### Immunomodulatory effect

It is well-known that macrophages play a key role in host defense, and many plant extracts activate immune responses primarily by the activation of macrophages, although direct activation of B cells and other immune cells have also been implicated. During the last decades, *ABP* has been shown to have immunostimulatory properties that affect lymphocyte proliferation and serum antibody levels.[18,71] Meanwhile, ABP can potentiate the humoral immune response. Activated macrophages release many inflammatory cytokines to exert their biological effects, including nitric oxide (NO), tumor necrosis factor-$\alpha$ (TNF-$\alpha$), and TNF-$\beta$, which play critical roles in the immune defense. ABP also generates potent humoral and cellular immune responses against cancer cells and induces production of immune responses.[18,72]

Sun[73] evaluated the hemolytic activity of *A. bidentata* saponins (ABS) and their potential as adjuvants for cellular and humoral immune responses in the Institute of Cancer Research mice against ovalbumin (OVA), and found ABS significantly increases the activation potential of T and B cells in OVA-immunized mice. In addition, ABS has a slight hemolytic effect and significantly enhances a specific antibody and cellular response against OVA in mice.

### Anti-fertility effect

The researchers evaluated the anti-fertility effect of ABS in rats and mice and found ABS could effectively prevent

pregnancy.[74,75] Guo *et al*.[76] studied the effects of ABS on isolated uteri from rats and rabbits *in situ* and found ABS caused a concentration-dependent excitation in the uterine preparations. When ABS was introduced, it clearly excited both virgin and pregnant rabbit uteri *in situ*. Subsequently, the anti-fertility effect of ABS has received growing attention. ABS was studied anti-fertility effect and found ABS causes a dose-dependent stimulation of rat uteri that is enhanced by 5-hydroxytryptamine (5-HT). ABS and 5-HT induce $Ca^{2+}$(0)-and $Ca^{2+}$(1)-dependent contractions of the uterus. Therefore, they concluded ABS has an important anti-fertility effect.[77]

## Analgetic, anti-inflammatory, and antimicrobial activity

An analgetic effect of different products from processed *A. bidentata* was observed in mice using the hot plate and acetic acid-induced writhing test. Specifically, water extract of *A. bidentata* and its processed products inhibited pain. The analgetic effect of these products is the most powerful and lasting when processed with wine.[78,79]

Different doses of the total saponins of achyranthes markedly lighten inflammatory reactivity in rats and mice, ease the pain of mice on a hot plate, and improve the hemorheology of rats. Obvious anti-inflammatory, analgetic, and hemorheological effects have been noted for the total saponins of achyranthes.[80] Tang *et al*.[62] evaluated their anti-inflammatory activity against lipopolysaccharide-induced NO production in RAW 264.7 (Mouse Leukaemic Monocyte-Macrophage Cell Line) murine macrophage cells, and found these compounds significantly inhibited this NO production.

Therefore, RAB extracts have analgetic, anti-inflammatory, and antimicrobial activity.

## Old-age-resistant function

Ma[81,82] studied the effect of continuous administration of water extracts of *A. bidentata* to mice for 7 days, and found these extracts effectively improve the acquisition of memory of and enhance the endurance of mice. These results indicate the decoction of RAB has memory- and endurance-enhancing activity. When mice were given the decoction of RAB for 30 days, there was an increase in superoxide dismutase vigor in the senile model mice and a reduction in plasma lipid peroxide.

## Cardiovascular and nervous systems

Using a model of atherosclerosis induced by high lipid feed, Researchers discovered *Achyranthes* has an anti-atherosclerosis effect, as well as reduces blood fat and lipid peroxidation.[83]

Wang *et al*.[84] assessed the effects of saponins *A. bidentata* on blood pressure, changes in nerve state, death rate, brain index, and pathologic changes in the hippocampal neurons of spontaneously hypertensive rats. It was concluded that saponins from *A. bidentata* are beneficial as therapeutics when treating strokes in this model.

Jiang *et al*.[85] found that nerve growth factor (NGF) deficiency is the main cause of certain types of degenerative neuron diseases, such as Alzheimer's disease, and administration of NFC can prevent decay of neuronal function and promote nerve regeneration. NGF actions are mediated by their corresponding receptors. The NGF receptor binding assay was used as a model when screening for components from 14 Chinese medicinal herbs active against NGF receptors, and a component from the roots of ABPP was found to possess such inhibitory activity. Subsequently, scholars investigated the effects of polypeptides isolated from ABPP on rat sciatic crush injury and tested the possible involvement of neurotrophic factors. Based on walking track, electrophysiological, and histological evaluations, it was found the repair outcomes of ABPP treatment were similar to those of NGF treatment, but an improvement over treatment with saline alone. Therefore, ABPP may protect peripheral nerves against crush injury by stimulating the release of neurotrophic factors and other cytokines.[86]

Scholars[87,88] showed *A. bidentata* extract protects hippocampal neurons against glutamate neurotoxicity by interfering with increases in intracellular calcium ion concentrations and reversing the down regulation of B-cell lymphoma-2 (Bcl-2). Because glutamate-evoked cell injury in hippocampal neurons is implicated in many central nervous system (CNS) disorders, the protective effects of *A. bidentata* extract raise the possibility of using medicinal herb-based drugs as potential alternatives or supplements to therapeutic strategies for these CNS diseases. Furthermore, ABPP can enhance the function of NR2A-containing N-methyl-D-aspartate receptors.

Previous research found[89] that ABPP fraction k (ABPPk) could effectively inhibit neuronal apoptosis induced by glucose deprivation *in vitro* and exert neuron protection on a rat transient middle cerebral artery occlusion model by improving neurologic deficit, decreasing infarction volume and inhibiting neuronal apoptosis in penumbra area. Indicated that the ABPPk could be considered as a new strategy for developing a novel small molecular active peptide to remedy transient brain ischemia because of its neuron protective effects.

Peng *et al*.[90] found that ABPP might play a beneficial role against Parkinson's disease (PD) by protecting dopaminergic neurons from apoptosis. Cells and primary rat dopaminergic neurons were pretreated with ABPPk, a purified fraction of ABPP, and then the cells were exposed to 1-methyl-4-phenylpyridinium iodide (MPP+) to induce apoptosis. In an *in vivo* PD model induced by 1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), ABPPk was intranasally delivered to mice. Behavioral tests, Nissl staining, immunostaining, immunohistochemistry, and Western blot were used to evaluate the potential effects of ABPPk on PD in mice. In an *in vivo* MPTP-induced PD model, ABPPk significantly improved behavioral performances and prevented tyrosine hydroxylase loss in the substantia nigra pars compacta and striatum. Scholars proposed that ABPPk protects dopaminergic neurons from apoptosis, suggesting that ABPPk might be an effective intervention for treating the neuron loss associated with disorders such as PD.

In conclusion, ABPP has potent activity in the cardiovascular and nervous systems.

### Osteoporosis

Gan *et al*.[91,92] studied the effect of daucosterol in RAB on the proliferation of osteosarcoma cell (UMR 106 cells) and quickly screened daucosterol by cultivating it with OB-like cells *in vitro*. Meanwhile, Gao *et al*. studied the effects of RAB extracts on OB-like UMR 106 cells and found RAB may contain compounds that stimulate OBs.

The study found the effects of *A. bidentata* root extract (ABRE) on postmenopausal osteoporosis. After 16 weeks of ABRE treatment, an improvement in the biomechanical quality of bone through modifications of bone mineral density and trabecular microarchitecture without hyperplastic effects on the uterus were observed. Therefore, ABRE may be a potential alternative medicine for the treatment of postmenopausal osteoporosis.[93]

A study by Yu *et al*.[94] found characterized the effects of ABS on osteoclast differentiation and elucidated its potential anti-osteoporosis mechanism. They found ABS inhibits osteoclast formation, indicating that it could be used as a bone resorption inhibitor to treat osteoporosis.

Zhang *et al*.[49] showed that a novel *A. bidentata* polysaccharide (ABPB-3) significantly increased the relative fluorescence intensity of the skull bone mass in a concentration-dependent manner, indicating that it stimulated bone formation activity. Subsequently, Wang *et al*.[50] indicated that a novel oligosaccharide (ABW90-1) from *A. bidentata* that ABW90-1 exhibited favorable effects on the proliferation and differentiation of primary OBs.

### Others

The major effective compounds in RAB, also affect the regulation of glucose metabolism,[15,53] have an anti-arthritic effect,[95-97] protect endothelial cells,[98-101] regulate gene expression,[102-107] anticoagulant and antithrombotic activities,[10,108,109] and hypoglycemic activity.[110]

## Toxicity

According to the available knowledge, the toxicity of *A. bidentata* is low and safe enough for medical uses. The cytotoxic composition of *A. bidentata* extract was studied. The high-molecular fraction from the water-macerating extract of RAB root was found to have remarkable cytotoxicity against P388 leukemia cells *in vitro*. In addition, polysaccharide derived from *A. bidentata* root may be cytotoxic.[111]

## Conclusion

Overall, RAB is a traditional plant medicine possessing multiple pharmacological properties, with considerable potential clinical value, as demonstrated by a large number of pharmacological and phytochemical studies carried out over the past few years. Specifically, these studies have shown RAB has notable immunomodulatory, anti-fertility, anti-tumor, analgetic, anti-inflammatory, and anti-oxidant activity, bioactivity toward the cardiovascular and nervous system, and potential as an osteoporosis treatment. Because of this outstanding biological activity of RAB, an increased number of chemical and toxicity studies should be performed assessing RAB. Therefore, RAB is the plant of choice for future research and will surely attract the attention of research scholars in the fields of pharmacology, drug discovery, and phytochemistry.

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### Conflicts of interest

There are no conflicts of interest.

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