Ardisia crenata

Scientific Name

Ardisia crenata Sims (Plate 3).

Synonyms

Ardisia bicolor E. Walker; Ardisia crenata var. bicolor (E. Walker) C. Y. Wu & C. Chen, Ardisia crenulata Lodd. et al., nom. nud., Ardisia crispa (Thunberg ex Murray) A. de Candolle, Ardisia crispa (Thunberg) A. de Candolle var. taquetii H. Léveillé, Ardisia henryii Hemsl., Ardisia konishii Hayata, Ardisia kusukusensis Hayata, Ardisia labordei H. Léveillé, Ardisia lentiginosa Ker Gawler, Ardisia linangensis C. M. Hu, Ardisia miaoliensis S. Y. Lu, Bladhia crenata (Sims) H. Hara, Bladhia crispa Thunberg, Bladhia crispa Thunberg var. taquetii (H. Léveillé) Nakai, Bladhia lentiginosa (Ker Gawler) Nakai var. lanceolata Masamune.

Family

Myrsinaceae also placed in Primulaceae.

Common/English Names

Coral Ardisia, Coral Bush, Coralberry, Coralberry Tree, Hen's-Eyes, Hilo Holly, Japanese Holy, Spear Flower, Spiceberry, Village Ardisia.

Vernacular Names

Afrikaans: Koraalbessieboom; Chinese: Yun Chi Zi Jin Niu, Zhu Sha Gen, Chu Sar Gun: Czech: Klíman Vroubkovaný; Eastonian: Täkiline Ardiisia; French: Baie Corail: German: Gekerbte Spitzblume, Gewürzbeere, Korallenbeere, Spitzenblume; Indonesia: Mata Ayam (Bangka), Popinoh (Lampung); *Khmer*: Ping Chap; Korean: Baek-Ryang-Geum; Malaysia: Mata Ayam, Mata Pelandok; Philippines: Atarolon, Tagpo (Tagalog); **Polish:** Ardizja Drzewiasta; Thai: Chamkhruea, Tinchamkhok, Tappla; Vietnamese: Troun Dua, Com Ngor Raw.

Origin/Distribution

The species' native range stretches from Asia temperate – Japan (Honshu (south), Kyushu, Ryukyu Islands, Shikoku); South Korea; Taiwan, China (Anhui, Fujian, Guangdong, Guangxi, Hainan, Hubei, Hunan, Jiangsu, Jiangxi, SW Xizang, Yunnan, Zhejiang) to Bhutan and Asia tropical, India, Sri Lanka, Myanmar; Thailand; Vietnam, Malaysia and Philippines.

Agroecology

In its native habitat, it is found in the forests, hillsides, valleys, shrubby areas, dark damp places, lowlands forest woods, in low mountains of Central China and S. Japan from 100 to 2,400 m elevation. The plant grows on all soil types from acid to alkaline soils provided they are welldrained. It prefers partial shade but can withstand full sun. The plant performs poorly in cold climate and is killed by hard freeze.

Edible Plant Parts and Uses

Young leaves are used in salads; the small fruits are sweet and edible.

Botany

Evergreen shrub growing to 1.2 m by 2.5 m with glossy, elliptic to lanceolate or oblanceolate leaves, 7–15 cm by 2–4 cm, leathery or papery, prominently punctate with margin sub-revolute, crenate, or undulate, with large vascularized marginal glands, apex acute or acuminate; lateral veins 12–18 on a short, 6–10 mm, glabrous petiole (Plates 1 and 2). Inflorescence sub-umbellulate or corymbose, terminal on terete branchlets, Flowers

small, bisexual, with oblong-ovate, 1–1.5(–2.5) mm sepals, Petals nearly free, ovate, punctate, glandular papillose, 4–6 mm long, white or pinkish, Stamens shorter than petals; filaments nearly obsolete; anthers triangular-lanceolate and yellow, ovary glabrous fruit 6–8 mm across, bright red. Fruit pale green becoming a bright red, globose, 1-seeded drupe, 6–8 mm in diameter produced in clusters (Plates 1 and 2).

Nutritive/Medicinal Properties

The genus *Ardisia* including *A. crenata* is a rich source of novel and biologically potent phytochemical compounds and has the potential as a source of therapeutic agents (Kobayashi and de



Plate 1 Ripe fruits and leaves of spiceberry



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Plate 3 Plant label

Mejía 2005). The roots of *Ardisia crenata* contain saponins, prosaponins, sapogenins and depsipeptide and thus represent a novel source of health-promoting compounds and potential phytopharmaceuticals and therapeutic agents.

Phytochemicals have been found in various parts of the plant:

Fruit: hydroxybenzoquinones 2-hydroxy-5-methoxy-3-pentadecenyl(tridecenyl- and tridecyl-) benzoquinone (Ogawa and Natori 1968).

Leaves: depsipeptide FR900359 (Fujioka et al. 1988; Miyamae et al. 1989).

Roots: saponins, prosaponins, sapogenins and depsipeptide (Kobayashi and de Mejía 2005); emebelin, rapanone (Ogawa and Natori 1968); a triterpene: cyclamiretin A (Guan et al. 1987); bergenin, friedelin, β-sitosterol and rapanone (Ni and Han 1988); bergenin, an isocoumarin and its derivatives; a bergenin derivative, 11-Osyringylbergenin, spinasterol, series of fatty acids, β -sitosterol- β -D-glucoside, norbergenin and sucrose (Han and Ni 1989b); demethylbergenin, 11-O-syrinylbergenin (Han and Ni 1989a); a triterpenoid saponin, ardicrenin elucidated as cyclamiretin A-3-O-[a-L-rhamnopyranosyl- $(1 \rightarrow 4)$ - β -D-glucopyranosyl- $(1 \rightarrow 4)$][β -Dglucopyranosyl- $(1\rightarrow 2)$]- α -L-arabinopyranoside and another partially hydrolyzed saponin was characterized as cyclamiretin A-3-O-β-Dglucopyranosyl- $(1\rightarrow 2)$ - α -L-arabinopyranoside (Wang et al. 1992); two triterpenoid pentasaccharides, ardisicrenosides E and F (Jia et al. 1994a); two triterpenoid saponins, ardisicrenoside A $[3-\beta-O-(\alpha-L-rhamnopyranosyl-(1\rightarrow 2) [\beta$ -D-glucopyranosyl- $(1\rightarrow 4)$ - $[\beta$ -D-glucopyranosyl- $(1\rightarrow 2)$]- α -L-arabinopyranosyl)-13 β ,28epoxy-16a,30-oleananediol]andardisicrenoside B-[3 β -O-(β -D-xylopyranosyl-(1 \rightarrow 2)-[β -D-glucopyranosyl- $(1 \rightarrow 4)$ -[β -D-glucopyranosyl- $(1\rightarrow 2)$]- α -L-arabinopyranosyl)-13 β ,28-epoxy-16 α ,30-oleananediol], ardisiacrispins A and B (Jia et al. 1994c); two triterpenoid saponins, ardisicrenoside C (1) [3 β -O-(α -L-rhamnopyranosyl- $(1\rightarrow 2)$ - β -D-glucopyranosyl- $(1\rightarrow 4)$ - [β -D-glucopyranosyl- $(1\rightarrow 2)$]- α -L-arabinopyranosyl)-16 α, 28-dihydroxy-olean-12-en-30-oic acid 30-O- β -D-glucopyranosyl ester] and ardisicrenoside β -O-(β-D-xylopyranosyl-(1 \rightarrow 2)-D (2) [3 β -D-glucopyranosyl-(1 \rightarrow 4)-[β -D-glucopyranosyl- $(1\rightarrow 2)$]- α -L-arabinopyranosyl)-16 α , 28-dihydroxy-olean-12-en-30-oic acid 30-O- β -D-glucopyranosyl ester] (Jia et al. 1994b); bergenin and bergenins 11-O-galloylbergenin and 11-O-syringylbergenin along with two new bergenin derivatives, 11-O-vanilloyland 11-O-(3',4'-dimethylgalloyl)-bergenins (Jia et al. 1995); ardisicrenoside K and ardisicrenoside L characterised as 3β-O-[α-L-rhamnopyranosyl- $(1\rightarrow 2)$ - β -D-glucopyranosyl- $(1\rightarrow 4)$ - $[\beta$ -D-glucopyranosyl- $(1 \rightarrow 2)$]- α -L-arabinopyranosyl]-13β,28-epoxy-16-oxo-30,30-dimethoxyoleanane 3β-O-[β-D-xylopyranosyland $(1\rightarrow 2)$ - β -D-glucopyranosyl- $(1\rightarrow 4)$ - $[\beta$ -D-g $lucopyranosyl-(1\rightarrow 2)]-\alpha-L-arabinopyranosyl]-$ 13β,28-epoxy-16α, 20-dihydroxyoleanane (Liu et al. 2007); two minor triterpenoidsaponins, ardisicrenosides G and H (Koike et al. 1999); ardisiacrenoside I (Zheng et al. 2008); a new triterpenoidsaponin, 3β -O-{ β -d-glucopyranosyl-(1 \rightarrow 4)- $[\beta$ -d-glucopyranosyl- $(1\rightarrow 2)$]- α -l-arabinopyranosyl}-16 α , 28-dihydroxyolean-12-en-30-oic acid 30-O-\beta-d-glucopyranosyl ester (ardisicrenoside N), together with two known saponins, ardisicrenoside C and D (Liu et al. 2011).

cAMP Phosphodiesterase Inhibition Activity

Two triterpenoid saponins, ardisicrenoside C and ardisicrenoside D along with their prosapogenins

and sapogenins showed inhibitory activity on cAMP phosphodiesterase (Jia et al. 1994b). Two triterpenoid pentasaccharides, ardisicrenosides E and F, isolated from the roots of *Ardisia crenata* also exhibited moderate inhibitory activity on cAMP phosphodiesterase (Jia et al. 1994a).

Abortifacient Activity

Two of the Ardisia saponins, ardisiacrispins A and B were found to be utero-contracting (Jansakul et al. 1987). At a concentration of $8 \mu g/$ ml both saponins gave contractive responses of the isolated rat uterus corresponding to 84% of the contraction caused by a standard dose of acetylcholine (0.2 µg/ml). In-situ intra-uterine injections of ardisiacrispin B isolated from A. crenata root, caused dose-dependent contraction of uterine smooth muscle in a manner similar to that of prostaglandin E, derivatives with no changes in mean arterial blood pressure (Jansakul 1995). Intra-uterine injection of ardisiacrispin B or prostaglandin E₂ did not cause softening of the cervix as observed with intra-uterine injection of saline, suggesting that ardisiacrispin B may exert a prostaglandin E₂ effect which may act at the prostaglandin E receptor but not by stimulation or enhancement of prostaglandin E₂ synthesis. The results suggested ardisiacrispin B may have potential to be used as alternative abortifacient drug to oxytocin or prostaglandin E₂ to terminate pregnancy

Antiplatelet Aggregation and Hypotensive Activities

A bioactive cyclic depsipeptide FR900359, was isolated from leaves of *Ardisia crenata*, (Fujioka et al. 1988; Miyamae et al. 1989). The cyclic depsipeptide was found to inhibit platelet aggregation in rabbits, decreased blood pressure and induced hypotension in anesthetized, normotensive rats. Their studies revealed that the biological activity of FR900359 may be due to the vulnerability of the *N*-methyldehydro-l-alanine residue to nucleophilic attack. Methylene chloride and methanol extracts

of *Ardisia crenata* demonstrated >80% antithrombin activity using a chromogenic bioassay (Chistokhodova et al. 2002). A benzoquinonoid compound, 2-methoxy-6-tridecyl-1,4-benzoquinone was characterized as the potent PAF (plateletactivating factor) receptor-binding antagonist with nonspecific antiplatelet effects on platelet aggregation induced by various agonists including PAF, ADP, thrombin and collagen (Kang et al. 2001).

Anticancer/Antimetastatic Activity

An antimetastatic and cytostatic substance, termed AC7-1, was isolated from Ardisia crispa and identified as a benzoquinonoid compound, 2-methoxy-6-tridecyl-1,4-benzoquinone (Kang et al. 2001). The antimetastatic activities of AC7-1 were confirmed using various in-vitro and in vivo metastasis assays. AC7-1 strongly blocked B16-F10 melanoma cell adhesion to extracellular matrix (ECM) and B16-F10 melanoma cell invasion. AC7-1 also remarkably inhibited pulmonary metastasis and tumour growth in vivo. AC7-1 inhibited B16-F10 melanoma cell adhesion to only specific synthetic peptides including RGDS. These findings suggested that antimetastatic activities of AC7-1 could be caused by blocking integrin-mediated adherence indicating AC7-1 to be a potential candidate for the development of a new antimetastatic drug. Ardisia crenata plant extract was found to have in-vitro photo-cytotoxic activity using a human leukaemia cell line HL-60 (Ong et al. 2009). It was able to able to reduce the in-vitro cell viability by more than 50% when exposed to 9.6 J/cm(2) of a broad spectrum light when tested at a concentration of 20 µg/ml.

Ardisiacrenoside I, a new triterpenoid pentasaccharide with an unusual glycosyl glycerol side chain, was isolated from *Ardisia crenata* together with five closely related triterpenoid saponins (Zheng et al. 2008). Their cytotoxic activities were determined against several different human tumour cell lines by the 3-[4,5-dimethylthiazol-2yl]-2,5-diphenyl tetrazolium bromide (MTT) method. Ardipusilioside was found to have antitumour activity (Zheng et al. 2008). Ardisiacrispin (A+B), a mixture of ardisiacrispins A and B, with a fixed proportion (2:1) inhibited proliferation of several human cancer cell lines with IC_{50} values in the range of 0.9-6.5 µg/ml by sulphorhodamine B-based colorimetric assay, in which human hepatoma Bel-7402 was the most sensitive cell line (Li et al. 2008). Ardisiacrispin (A+B) induced dosedependent apoptosis in human hepatoma Bel-7402 cells at doses of 1-10 µg/ml and resulted in the changes of the mitochondrial membrane depolarization, membrane permeability enhancement, and nuclear condensation in a dose-dependent manner and could disassemble microtubule in human hepatoma Bel-7402 cells. The findings suggested that ardisiacrispin (A+B) could inhibit the proliferation of Bel-7402 cells by inducing apoptosis and disassembling microtubule.

Of six Ardisia species, Ardisia compressa showed the highest topoisomerase II catalytic inhibition against liver cancer HepG2 cells followed by A. crenata (Newell et al. 2010). Total polyphenols ranged from 21 to 72 mg equivalents of gallic acid (GA)/g solid extract (SE). The following chemicals were found gallic acid, quercetin derivatives, ardisenone, ardisiaquinone, ardisianone, bergenin, norbergenin, and embelin. However, neither total polyphenol concentration nor antioxidant capacity correlated with anticancer capacity. Significant HepG2 cytotoxicity was also achieved by bergenin (IC₅₀ = 18 μ M) and embelin (IC₅₀=120 μ M). AC, bergenin, embelin, and quercetin showed a tendency to accumulate cells in the G1 phase and reduced G2/M leading to apoptosis. A. crenata was one of four Ardisia species with the greatest anticancer potential against liver cancer cells in-vitro. The saponin ardisicrenoside N showed cytotoxicity against MCI-7 and NCI-H460 cancer cell lines at 11.0 and 22.1 µmol/L in-vitro (Liu et al. 2011).

Antibacterial Activity

The ethanol extract of A. crenata exerted the significant anti-bacteria activity against α -*Streptococcus hemolyticus*, β -*Streptococcus hemolyticus* and *Staphylococcus aureus* in-vitro (Tian et al. 1998).

Antiinflammatory Activity

Intraperitoneal administration of the ethanol extract of *A. crenata* inhibited capillary permeability in mice and plantar swelling in rats induced by acetic acid and albumen respectively (Tian et al. 1998).

Antiplasmodial Activity

Studies of Malaysian medicinal plants by Noor Rain et al. (2007), found that *Ardisia crispa* (leaf extract) had antiplasmodial activity. The leaf extract demonstrated antiplasmodial activity against *Plasmodium falciparum* D10 strain (sensitive strain) with an IC₅₀ at 5.90 μ g/ml.

Miscellaneous Pharmacological Activities

Bergenin an isocoumarin found in various plant species including *A. crenata* had been reported to exhibit a wide range of biological activities including hepatoprotective (Lim et al. 2000), antifungal (Prithivirai et al. 1997), anti-HIV (Piacente et al. 1996), antiarrhythmic (Pu et al. 2002) and hypolipidemic (Jahromi et al. 1992).

Ma et al. (2009) isolated ardicrenin from the roots of *A. crenata* and developed an effective and economical method to extract ardicrenin which was found suitable for industrial production. The final product was a white powder and its purity and yield were 98% and 1.65 respectively.

Traditional Medicinal Uses

The genus *Ardisia* is widely used as the traditional medicine to cure diseases, e.g. pulmonary tuberculosis, hepatitis, chronic bronchitis and irregular menstruation (Kobayashi and de Mejía 2005). *Ardisia crenata* root is anodyne, depurative, febrifuge, antidotal and diuretic. Its roots have been used in traditional Chinese medicine for the treatment of several kinds of diseases including tonsillitis, tooth- ache, trauma, arthralgia, respiratory tract infections, and menstrual disorders and also to stimulate blood circulation. The root also has anti-fertility effects. An infusion is pectoral. The leaves are crushed and applied to scurf; it is also applied to the ears in the treatment of earache. The juice is used internally against fever, cough, and diarrhoea and also used to treat infections of the respiratory tract and menstrual disorders. In Thailand, the roots are used in combination with other medicinal plants to wash-out dirty blood in women who suffer from menstrual pain.

Other Uses

Ardisia crenata is a popular ornamental garden and potted plant.

Comments

In some countries like USA, *Ardisia crenata* is deemed an invasive weed.

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