A review of the Paper Mulberry (Broussonetia papyrifera) (L.) Hert. ex Vent.

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Introduction

We are reviewing a series of Thailand and Far East plants known for their use in traditional medicine and which have also been shown to have excellent application in cosmetic and toiletry applications.

Paper Mulberry (*Broussonetia papyrifera*) (L.) Hert. ex Vent., is the second in this series. See *Pueraria mirifica* [Dweck]



Family: Moraceae (Fig family)

Common names: Wauke, Po'a'aha [Hawai'i]; U'a [Samoa] Chu (whole plant), Chu shi zi (fruit), Gu shi (fruit), Chu tao (fruit) [China]; Paper Mulberry (English). Por-Gra-Saa, Por-Saa or Ton-Saa [Thailand], Lu-a-Shu [Taiwan].

Synonyms: *Papyrius papyrifera* ((L.)Kuntze.), *Morus papyrifera* (L.)

Description: Paper mulberry is a small tree or shrub which grows naturally in Asian and Pacific countries such as Thailand, China, Myanmar, Laos, Japan, Korea, India and the southern USA.

Range: E. Asia - China. Occasionally

naturalized in S.E. Europe

Habitat: Thickets, mountain ravines and forests

Chemical composition (leaves, dried): 17% calcium carbonate.

4',7-Dihydroxyflavan *Plant*:, 4-O-Methyldavidioside *Plant*:, 7-Hydroxy-4'-methoxyflavan *Plant*:; Arsenic *Fruit 0.62 ppm*; Betulinic Acid *Stem*: Broussonins *Plant*: Calcium *Fruit 26,900 ppm*; Copper *Fruit 12 ppm*; Iron *Fruit 560 ppm*; Kazinol *Plant*: Magnesium *Fruit 4,030 ppm*; Manganese *Fruit 81 ppm*; Mercury *Fruit 0.06 ppm*; Potassium *Fruit 7,340 ppm*; Saponins *Fruit 5,000 ppm*; Sodium *Fruit 135 ppm*; Zinc *Fruit 23 ppm* [Duke].

Broussonetia papyrifera was found to contain both calcium oxalate and calcium carbonate. The calcium oxalate crystals were mainly found as druses or prismatic crystals. Druses were located in the crystal cells of both mesophyll and bundle sheath, but prismatic crystals were found only in cells of the bundle sheath. All calcium carbonate cystoliths were located in the epidermal lithocysts, and the types of lithocysts were related to the number of epidermal layers, i.e. hair-like lithocysts in uniseriate epidermis and papillate lithocysts in multiseriate epidermis [Wu et al].

Broussochalcone A [Cheng et al] also {Wang et al}

Papyriflavonol A, a prenylated flavonol (5,7,3',4'-tetrahydroxy-6,5'-di-(gamma,gamma-dimethylallyl)-flavonol) isolated from the root bark [Son *et al*]. Papyriflavonol A (prenylated flavonol) [Kwak *et al*]; Two new compounds, 8-(1,1-dimethylallyl)-5'-(3-methylbut-2-enyl)-3',4',5,7- tetrahydroxyflanvonol (1), 3'-(3-methylbut-2-enyl)-3',4',7- trihydroxyflavane (2) and three known compounds 3,3',4',5,7-pentahydroxyflavone (3), uralenol (4), broussochalcone A (5) were isolated from the roots [Chen *et al*]; Broussoflavonols F and G, broussoflavan A and broussoaurone A [Ko *et al*]. Two new isoprenylated flavonols, named broussoflavonols E and F, squalene, octacosan-1-ol, lignoceric acid, 4'-hydroxy-cis-cinnamic acid octacosyl ester, and (-)-marmesin), and a mixture of 4'-hydroxy-trans-cinnamates, were isolated from the root bark of *B. papyrifera* (collected from Taiwan) [Fang *et al.* 1995].

A new isoprenylated aurone, broussoaurone A, a novel isoprenylated flavan, broussoflavan A, and butyrospermol acetate, erythrinasinate, kazinols A and B, and broussochalcones A and B were isolated from the cortex of *B. papyrifera*, a Formosan medicinal plant collected from Kaohsiung, Taiwan [Fang *et al*, 1994].

Broussonin A (2-3-(4-hydroxyphenyl)propyl)-5-methoxy-phenol) which was formerly reported as a phytoalexin [Iida *et al*]

5,7,2',4'-tetrahydroxy-3-geranylflavone, isogemichalcone C, 3'-[gamma-hydroxymethyl-(E)-gamma-methylallyl]-2,4,2',4'-tetrahydroxychalcone 11'-O-coumarate, demethylmoracin I, and (2S)-2',4'-dihydroxy-2"-(1-hydroxy-1-methylethyl)dihydrofuro[2,3-h]flavanone. Isolicoflavonol, (2S)-abyssinone II, 5,7,3',4'-tetrahydroxy-6-geranylflavonol, 5,7,3',4'-tetrahydroxy-3-methoxy-6-geranylflavone, (2S)-7,4'-dihydroxy-3'-prenylflavan, 1-(2,4-dihydroxyphenyl)-3-(4-hydroxyphenyl)propane, and 1-(4-hydroxy-2-methoxyphenyl)-3-(4-hydroxy-3-prenylphenyl)propane [Lee *et al*]

Edible Uses: Paper mulberry can be used as a food for both human and animal consumption. The flower and young leaf of the variety *Broussonetia kurzii* has a protein content of 16-21%, together with nutrient minerals such as P, K, Ca and Mg and is suitable for human consumption.

The raw fruit. The fruit comprises a ball about 1.5cm in diameter with numerous small edible fruits protruding - there is not much edible flesh but it has been reported to have a lovely flavour. Prolonged ingestion is said to weaken the bones.



The cooked leaves [Tanaka]. The dried leaf contains 1% calcium carbonate [Reid]. The leaves of *Broussonetia kurzii* are suitable for animal consumption and have 14 - 22 % protein content.

Flowers. No more details.

Medicinal Uses: Astringent; Diaphoretic; Diuretic; Galactogogue; Haemostatic; Laxative; Ophthalmic; Skin; Stimulant; Stomachic; Tonic; Vulnerary.

It is said to be astringent, diuretic, tonic, vulnerary [Stuart]. The leaf juice is diaphoretic and laxative - it is also used in the treatment of dysentery [Duke & Ayensu] and is also poulticed onto various skin disorders, bites etc. The authors also report that the stem bark is haemostatic and that the fruit is diuretic, ophthalmic, stimulant, stomachic and tonic. The root is cooked with other foods as a galactogogue.

The bark is decocted for ascites and is used to reduce swelling or oedema and used for abdominal distension. The juice is used in anuria.



Medicinally in Hawaii, the slimy sap of paper mulberry is a mild laxative. Thrush, a mouth disease, is said to be improved when the ash from the burned beaten sheet made from the bark is applied to the mouth.

Other uses include using the latex, which is said to be useful externally for neurodermatitis, tinea infection, eczema, bee sting, insect bites, and is also used as a vulnerary.

The leaves are employed for blood in sputum, vomiting blood, uterine bleeding, excess menstrual bleeding, bleeding wounds in Chinese medicine and for a bleeding stomach in Hawaii. The

leaves are also said to be astringent in "fluxes" and gonorrhoea and are also used for dysentery, and enteritis. The sap is reported to remove pus in Chinese medicine. Leaves infused for stomach and abdominal pain according to Samoan folklore. The stems are used for skin eruptions in China.

Western Functions: Antidiarrheal, hemostatic.

Energetic Functions: According to traditional Chinese medicine, paper mulberry tonifies the liver and kidneys, clears heat and cools the blood, drains dampness, clears damp heat in the middle and lower burners. It is also used to stop diarrhoea..

Chinese Uses: Tonifies the liver and kidneys. Clears the vision, nourishes the eyes. It is used for debility of the loins and knees, blood deficiency, vertigo and impotence as well as weakness of joints and muscles.

Clears damp heat in the middle and lower burners. Stops diarrhea Clears heat and cools the blood Drains dampness



Other Uses: A fibre from the bark is used in making paper, cloth, rope etc. The fibre is produced by beating strips of bark on a flat surface with a wooden mallet. A very fine cloth can be made in this way, and the greater the beating of the bark the finer the cloth. Larger sizes of cloth are made by overlapping two sections of the bark and then beating them together. It is reported that a leather substitute can also be made from the bark. It has been known for almost 1,500 years as a plant whose bark can be used to make paper of various grades up to the highest quality. It is used in the production of flowers, umbrellas, fans, lanterns as well as lamps, dolls and toys, cloth and others.

The tree also produces a natural dye that is green to yellow-green in colour, but the chemical responsible does not seem to have been determined.

Potential Cosmetic uses: It appears to be a potent antioxidant [Cheng *et al*] said to be as potent as butylated hydroxytoluene (BHT), a common antioxidant used for food preservation.

It may also be considered to have anti-fungal activity [Iida *et al*] because of the compound identified as broussonin A (2-3-(4-hydroxyphenyl)propyl)-5-methoxy-phenol) which was formerly reported as a phytoalexin. There are other compounds that have been identified as having antibacterial properties, although none of these appear to have been commercially exploited.

Skin depigmentation

The depigmenting activity of paper mulberry has been measured using three colorimetric instruments [Ha *et al*]. They examined the effects of a tyrosinase inhibitor extracted from *Broussonetia kazinoki* x *B. papyrifera* and identified as Kazinol F with the same structure as shown in Fig.1. They reported that this material had the same level of tyrosinase

inhibition activity at a lower concentration when compared with kojic acid, ascorbic acid and hydroquinone. They also reported that Kazinol F had a good free-radical scavenging activity compared to tocopherol.

Skin depigmentation has been described by one author [D'Amelio] using the root bark of paper mulberry. The active ingredient was described as 5-(3'-(2,4-dihydroxyphenyl) propyl)-3,4-bis(3-methyl-2-butenyl)-1,2-benzenediol.

The authors said that an extract of Paper Mulberry containing 5.0% of this active compound would be sufficient to show a fairly potent lightening effect when used at a concentration as low as 0.1-1.0% in the final product.

Fig.1 Kazinol F

They suggested a final blend of materials of Bearberry (*Arctostaphylos uva-ursi*), a debridement enzyme and other co-factors and stabilisers. This skin depigmentation activity was considered appropriate and applicable to conditions such as freckles and age spots particularly prevalent in Caucasian skin types. It will also be useful in skin discoloration associated with pregnancy.

Tyrosinase inhibition values

Active ingredients	IC50 (μg/mL.)
Kazinol F	0.396
Kojic acid	10.0
Ascorbic acid	70.0
Hydroquinone	5.5

Other related molecules are mentioned in a data sheet [SNP] and are referred to as Kazinol A (Fig. 2) and Kazinol E (Fig.3). It is not known whether these molecules contribute to the skin depigmenting effects.

Fig. 2 Kazinol A

Fig. 3 Kazinol E

Hazards: None known. It has been reported that prolonged ingestion of the fruit will weaken the skeletal structure. Paper Mulberry compound was effective in an *in vivo* guinea pig depigmentation test and the material showed no primary irritation and no sensitising potential on human skin and in rabbit eye (irritation test) [Jang *et al*].

Dosage: Use 9-15 grams.

In skin care for skin depigmentation: 3-5% of the liquid extract

References

D'Amelio, Frank. Sr, and Mirhom, Youssef.: Paper Mulberry and its preparations as Tyrosinase Inhibitors and Skin Lightening Agents. Cosmetic & Toiletries Manufacture Worldwide 31-34 (2000).

Chen RongMin; Hu LiHong; An TianYing; Li Jia; Shen Qiang: Natural PTP1B inhibitors from *Broussonetia papyrifera*.

Cheng Z, Lin C, Hwang T, Teng C.: Broussochalcone A, a potent antioxidant and effective suppressor of inducible nitric oxide synthase in lipopolysaccharide-activated macrophages. Biochem Pharmacol. 2001 Apr 15;61(8):939-46.

Chinese National Center for Drug Screening, Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai 200031, China. EMsimmhulh@mail.shcnc.ac.cn . Bioorganic & Medicinal Chemistry Letters. 2002, **12**, 23. p.3387-3390. SN-0960-894X

Duke, James: Dr. Duke's Phytochemical and Ethnobotanical Databases Chemicals and their Biological Activities in: *Broussonetia papyrifera* (L.) VENT (Moraceae) -- Paper Mulberry. Agricultural Research Services.

Duke. J. A. and Ayensu. E. S.: *Medicinal Plants of China* Reference Publications, Inc. 1985. ISBN 0-917256-20-4

Dweck, A.C.: The Pueraria family with special interest in *Pueraria mirifica*. Personal Care Magazine **4**, 1, p. 7-8. 2002.

Fang, SC; Shieh, BJ; Lin, CN. Phenolic constituents of Formosan *Broussonetia papyrifera*. Phytochemistry (1994) 37(3): 851-853. [En, 13 ref.] [Graduate Institute of Chemistry, Chung Yuan Christian University, Chung Li 320, Taiwan.]

Fang, SC; Shieh, BJ; Wu, RR; Lin, CN. Isoprenylated flavonols of Formosan *Broussonetia papyrifera*. Phytochemistry (1995) 38(2): 535-537.

Ha J.H, Jo N.S, Lee H.K, Kim J.I, Lee B.G, Park W.J,: The depigmentation effect of a new material extracted from paper mulberry and its comparison by three colorimetric instruments. Proceedings of the IFSCC Congress October 1996, Sydney, Australia.

Iida Y, Yonemura H, Oh KB, Saito M, Matsuoka H.: [Sensitive screening of antifungal compounds from acetone extracts of medicinal plants with a Bio-Cell Tracer]. Yakugaku Zasshi. 1999 Dec;119(12):964-71.

Jang, D,I., Lee, B.G., Jeon, C.O., Jo, N.S., Park, J.H., Cho, S.Y., LKee, H., Ko, J.S.: Cosmetics & Toiletries **112**, 80, (1997)

Ko HorngHuey, Yu SheuMeei, Ko FengNien, Teng CheMing, Lin ChunNan. Bioactive constituents of Morus australis and *Broussonetia papyrifera*. Journal of Natural Products 1997 60 10 1008-1011.

Kwak WieJong; Moon TaeChurl; Lin ChangXiu; Rhyn HyeunGee; Jung Hyejin; Lee Eunkyung; Kwon DongYeul; Son KunHo; Kim HyunPyo; Kang SamSik; Murakami, M.; Kudo, I.; Chang HyeunWook: Papyriflavonol A from *Broussonetia papyrifera* inhibits the passive cutaneous anaphylaxis reaction and has a secretory phospholipase A2-inhibitory activity. Biological & Pharmaceutical Bulletin, **3**, 26, 2003. p.299-302

Reid. B. E. Famine Foods of the Chiu-Huang Pen-ts'ao. Taipei. Southern Materials Centre 1977

Lee D, Bhat KP, Fong HH, Farnsworth NR, Pezzuto JM, Kinghorn AD.: Aromatase inhibitors from Broussonetia papyrifera. J Nat Prod. 2001 Oct;64(10):1286-93.

Son KH, Kwon SJ, Chang HW, Kim HP, Kang SS.: Papyriflavonol A, a prenylated flavonol. Fitoterapia. 2001 May;72(4):456-8.

Speciality Natural Products (SNP) – private communication November 2003.

Stuart. Rev. G. A. Chinese Materia Medica. Taipei. Southern Materials Centre

Tanaka. T. Tanaka's Cyclopaedia of Edible Plants of the World. Keigaku Publishing 1976

Wang JP, Tsao LT, Raung SL, Lin CN.: Investigation of the inhibitory effect of broussochalcone A on respiratory burst in neutrophils. Eur J Pharmacol. 1997 Feb 12;320(2-3):201-8.

Wu, Chi-Chih and Kuo-Huang, Ling-Long: Calcium crystals in the leaves of some species of Moraceae. Bot. Bull. Acad. Sin. (1997) 38: 97-104