Technical Data Report

for

MUTAMBA

(Guazuma ulmifolia)

Sage Press

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Mutamba

Preprinted from *Herbal Secrets of the Rainforest,* 2nd edition, by Leslie Taylor

Family: Sterculiaceae

Genus: *Guazuma*

Species: *ulmifolia*

Synonyms: *Bubroma guazuma, Diuroglossum rufescens, Theobroma guazuma, Guazuma coriacea, G. inuira, G. polybotra G. tomentosa, G. utilis*

Common Names: Mutamba, mutambo, embira, embiru, West Indian elm, guazima, guacima, guacimo, guasima de caballo, aquiche, ajya, guasima, cimarrona, guazuma, bolaina, atadijo, ibixuma, cambá-acã, bay cedar, bois d'homme, bois d'orme, bois de hetre, orme d'Amerique

Parts Used: Bark, leaves, root

Mutamba is a medium-sized tree that grows up to 20 m high, with a trunk 30 to 60 cm in diameter. Its oblong leaves are 6 to 12 cm long, and the tree produces small white-to-light-yellow flowers. It produces an edible fruit that is covered with rough barbs and has a strong honey scent. Mutamba is indigenous to tropical America on both continents and found throughout the Amazon rainforest.

Mutamba is called *guasima* or *guacima* in Mexico, where it has a very long history of indigenous use. The Mixe Indians in the lowlands of Mexico use a decoction of dried bark and fruit to treat diarrhea, hemorrhage and uterine pain. The Huastec Mayans of northeastern Mexico employ the fresh bark boiled in water to aid in childbirth, for gastrointestinal pain, asthma, diarrhea and dysentery, wounds, and fevers. Mayan healers in Guatemala boil the bark into a decoction to treat stomach inflammation and regular stomachaches. Mutamba was a magical plant to the ancient Mayans who also used it against "magical illnesses" and evil spells. In the Amazon, indigenous people have long used mutamba for asthma, bronchitis, diarrhea, kidney problems, and syphilis. They use a bark decoction topically for baldness, leprosy, dematosis and other skin conditions.

Mutamba holds a place in herbal medicine systems in many tropical countries; chiefly the bark and leaves are used. In Belizean herbal medicine practices, a small handful of chopped bark is boiled for 10 minutes in 3 cups of water and drunk for dysentery and diarrhea, for prostate problems, and as a uterine stimulant to aid in childbirth. A slightly stronger decoction is used externally for skin sores, infections, and rashes. In Brazilian herbal medicine practices, a bark decoction is considered diaphoretic, depurative, antisyphilitic, and pectoral. There it is used for fevers, coughs, bronchitis, asthma, pneumonia, and liver problems. A bark decoction is also prepared and is used topically to promote hair growth, to combat parasites of the scalp, and to treat various skin conditions. In Peru, the dried bark and/or dried leaves are made into tea (standard infusion) and used for kidney disease, liver disease, and dysentery. There it is also used topically for hair loss. In Guatemala, the dried leaves of the tree are brewed into a tea and drunk for fevers, kidney disease, and skin diseases, as well as used externally for wounds, sores, bruises, dermatitis, skin eruptions and irritations, and erysipelas.

Mutamba's long history of effective uses in herbal medicine propelled researchers to begin studying its properties and activities in the laboratory (beginning in 1968). It has been the subject of numerous studies since. In the first study published, using various animals (rats, rabbits, guinea pigs, cats and insects), mutamba bark extracts demonstrated mild cardiac depressant, cardiotonic, hypotensive, smooth muscle relaxant, and uterine stimulant activities.[1] Two years later, another researcher reconfirmed the uterine stimulant effects in rats, validating its historical uses as a uterine stimulant and childbirth aid.[2] In six different studies from 1987 to 1995, various leaf and bark extracts have clinically demonstrated antibacterial activity *in vitro* against several disease-causing

pathogens, including *Bacillus, Staphylococcus, Streptococcus, E. coli,* and *Neisseria gonorrhea*.[3–8] In a 1995 *in vitro* study, mutamba also demonstrated antiviral activity against *Herpes simplex* type 1.[9] These studies could certainly explain why mutamba has been used so effectively in herbal medicine systems for many types of gastrointestinal problems, such venereal diseases as gonorrhea and syphilis, and upper respiratory conditions (e.g. pneumonia and bronchitis. Subsequent research focusing on particular chemicals found in mutamba documented their ability to interfere with prostaglandin synthetase, a process by which bacteria and pathogens replicate.[10–12] Scientists showed that these phytochemicals interacted with a cholera toxin—preventing chloride secretion and the resultant diarrhea.[11,12]

Traditionally a decoction of mutamba leaves has been used in Mexico for diabetes. It has only been recently (in 1998) that researchers in Mexico validated this indigenous use, publishing a study showing that a leaf extract significantly decreased hyperglycemia in rabbits.[13] Another traditional application of mutamba in herbal medicine has been for the prevention of hair loss and as a natural remedy for alopecia. In 1999, researchers in Japan discovered that a phytochemical named *procyanidin B-2* was a safe topical hair growing agent.[14] From 2000 to 2002, they published three *in vitro* and *in vivo* (in balding men) studies showing that procyanidin B-2 promoted hair cell growth and increased the total number of hairs on a designated scalp area.[15–17] Phytochemical analysis of mutamba bark shows that it is a rich source of this natural chemical compound and it has been documented with other biological activities as well.[12] Of particular note (in 1990), a Brazilian research group demonstrated that a crude extract of mutamba was cytotoxic to cancer cells *in vitro*, exhibiting a 97.3% inhibition rate.[18] It later was shown in independent research that procyanidin B-2 also demonstrated antitumorous and anticancerous effects (even against melanoma) as well as hypotensive and kidney protective properties.[19,20]

Mutamba is a favorite natural remedy among Central and South American health practitioners and the indigenous peoples of the Amazon. Research continues to document the unique properties and actions of this plant while validating its traditional uses.

Documented Properties and Actions: Antibacterial, antidysenteric, antifungal, antihyperglycemic, anti-inflammatory, antimicrobial, antioxidant, antiulcerogenic, astringent, cardiotonic, cytotoxic, depurative, diaphoretic, emollient, febrifuge, hepatoprotective, hypotensive, pectoral, refrigerant, smooth muscle relaxant, stomachic, styptic, sudorific, vulnerary

Main Phytochemicals: Caffeine, caryophyllene, catechins, farnesol, friedelin, kauroic acid, precocene I, procyanidin B-2, procyanidin B-5, procyanidin C-1, sitosterol

Traditional Remedy: One cup of a bark decoction 1–3 times daily before meals or 2–3 ml of a 4:1 tincture twice daily. One to 2 grams of powdered bark daily in tablets or capsules or stirred into water or juice can be substituted if desired.

Contraindications: Mutamba bark has been documented to have uterine stimulant activity and it should not be taken during pregnancy. Mutamba leaves have documented *in vivo* hypoglycemic effects (in rabbits). People with hypoglycemia or diabetes should only use this plant with the guidance and advice of a health care practitioner.

Mutamba leaves contain a small amount (0.14%) of naturally-occurring caffeine. Those sensitive to or allergic to caffeine should not use mutamba leaves (mutamba bark has not been documented to contain caffeine).

Drug Interactions: None published; however, mutamba bark has been documented with hypotensive actions and, as such, may potentiate the action of antihypertensive drugs.

WORLDWIDE ETHNOBOTANICAL USES

Country	Uses
Belize	Childbirth, diarrhea, dysentery, infections, prostate, rash, skin, uterine stimulant, sores
Brazil	Alopecia, asthma, blennorrhagia, bronchitis, cough, depurative, diaphoretic, dysentery, fever, liver, parasites (head), pectoral, pneumonia, skin diseases, syphilis, ulcer
Colombia	Uterine stimulant
Cuba	Astringent, bruise, burn, diuretic, emollient, flu, grippe, hemorrhoids, wounds
Dominican Republic	Diaphoretic, dysentery, fertility (veterinary), lung
Guatemala	Bruise, dermatitis, erysipelas, febrifuge, gonorrhea, kidney disease, skin disorders (irritation, eruptions, inflammation, sores, ulcers), sudorific, stomachache, stomach inflammation, wounds
Haiti	Astringent, cough, depurative, diabetes, diarrhea, emollient, fever, flu, fracture, scurvy, skin, stomachic
Jamaica	Diarrhea, elephantiasis, leprosy, malaria
Mexico	Asthma, astringent, chest, childbirth, constipation, diarrhea, dysentery, elephantiasis, emollient, fever, gastrointestinal, hemorrhage, infectious diseases, kidney, leprosy, malaria, rash, skin, syphilis, uterine pain, wounds
Peru	Alopecia, diarrhea, dysentery, asthma, bronchitis, dermatosis, elephantiasis, fever, hepatitis, kidney disease, leprosy, liver disease, malaria, nephritis, pulmonosis, syphilis
Venezuela	Astringent, emollient, refrigerant, sudorific, syphilis
Elsewhere	Asthma, astringent, bronchitis, chest, elephantiasis, hair, hypertension, kidney, liver, medicine, obesity, pectoral, skin, stomach, styptic, sudorific

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Ethnomedical Information on Mutamba (Guazuma ulmifolia)

Plant Part / Location	Documented Ethnic Use	Type Extract / Route	Used For	Ref #
Bark Belize	Used for skin sores, infections and rashes. Used for dysentery and diarrhea, prostate problems and as a uterine stimulant to aid childbirth.	Decoction / External Decoction / Oral	Human Adult Human Adult	ZZ1019 ZZ1019
Bark Brazil	Used as a diaphoretic for fevers. Used for coughs, bronchitis, ulcers, asthma, pneumonia and liver problems.	Hot H2O Ext / Oral	Human Adult	ZZ1013
Bark Brazil	Used to treat alopecia and head parasites. Used to treat skin afflictions. Used as a depurative, antisyphilitic, pectoral, and antiblennorrhagic.	Decoction / External Decoction / External Decoction / Oral	Human Adult Human Adult Human Adult	ZZ1099
Bark Dominican Republic	Used as a diaphoretic and to treat dysentery, fertility (veterinary), and lung problems.	Decoction / Oral	Human / Animal Oral	ZZ1022
Bark Colombia	Used to stimulate uterine contractions.	Hot H2O Ext / Oral	Human (pregnant)	A00709 T15375
Bark Cuba	Used for an astringent, diuretic, and emollient; to treat bruises, burns, flu, grippe, hemorrhoids, wounds	Decoction / Oral & External	Human Adult	AG1022
Bark Guatemala	Used for gonorrhea. Used for stomach inflammation and stomachaches.	Infusion / Oral Decoction / Oral	Human Adult Human Adult	K27236 K28434
Bark Haiti	Used for flu and diarrhea. Used for fractures.	Decoction / Oral Bark / External	Human Adult Human Adult	T13846
Bark Jamaica	Used for leprosy. Used for elephantiasis. Used to treat diarrhea. Used for malaria.	Hot H2O Ext / Oral Hot H2O Ext / Oral Infusion / Oral Hot H2O Ext / Oral	Human Adult Human Adult Human Adult Human Adult	T00701 W01270 K27077 M00695
Bark Panama	Used to treat hypertension.	Infusion / Oral	Human Adult	L12353
Bark Peru	Used for leprosy, alopecia, and dermatosis. Used for liver disease, kidney disease and dysentery.	Decoction / External Decoction / Oral	Human Adult Human Adult	L04137 T15323
Bark Peru	Used for, asthma, bronchitis, diarrhea, dysentery, elephantiasis, fever, hepatitis, malaria, nephritis, pulmonosis, and syphilis.	Decoction / Oral	Human Adult	ZZ1041 L04137

Plant Part / Location	Documented Ethnic Use	Type Extract / Route	Used For	Ref #
Bark Mexico	Used for wounds and rashes. Used for gastrointestinal pain, diarrhea, dysentery, childbirth, asthma, and fever	Decoction / External Decoction/ Oral	Human Adult Human Adult	T09735 T09735
Bark + Fruit Mexico	Used to treat diarrhea, hemorrhage and uterine pain.	Decoction / Oral	Human Adult	K19153
Bark + Leaf Mexico	Used for constipation and kidney disorders.	Decoction / Oral	Human Adult	K16948
Fruit Haiti	Used for diarrhea.	Decoction / Oral	Human Adult	T13846
Fruit Mexico	Used to treat infectious diseases.	Infusion / Oral	Human Adult	J12454
Leaf Guatemala	Used as a febrifuge, sudorific and to treat kidney disease. Used for skin diseases, irritations, eruptions and inflammation, dermatitis, erysipelas, wounds, ulcers, bruises and sores.	Hot H2O Ext / Oral Hot H2O Ext / External	Human Adult Human Adult	T15295 T15445
Leaf Haiti	Used for flu and cough. Used for diabetes.	Decoction / Oral Decoction / Oral	Human Adult Human Adult	T13846 L03570
Leaf Peru	Used for liver disease, kidney disease and dysentery.	Decoction / Oral	Human Adult	T15323
Leaf Mexico	Used for asthma.	H2O Ext / Oral	Human Adult	T09735
Entire Plant Mexico	Used medicinally for "magical" illnesses comprising a variety of physiological illnesses and symptoms. Use is most likely based on magic or superstition.	H2O Ext / Oral	Human Adult	T09735
Root Mexico	Used for childbirth.	H2O Ext / Oral	Human (pregnant)	T09735
Stembark Mexico	Used for diarrhea.	Infusion / Oral	Human Adult	H18875 K23487

Presence of Compounds in Mutamba (Guazuma ulmifolia)

Compound	Chemical Type	Plant Type	Plant Origin	Quantity	Ref #
Caffeine	Alkaloid	Leaf	Brazil	0.14%	W03499
Caryophyllene, beta:	Sesquiterpene	Leaf Essential Oil	Brazil	13.7%	L13823
Catechin, epi: (-):	Flavonoid	Stembark	Mexico	0.0673%	H18875
Catechin, epi:(4-beta-6)-(-)-epi-catechin-(4-beta-d)-(-)-epi- catechin:	Flavonoid	Stembark	Mexico	0.00128%	H18875
Catechin, epi:(4-beta-8)-(-)-epi-catechin-(4-beta-8)-(-)-epi- catechin(4-beta-6)-(-)-epi- catechin:	Flavonoid	Stembark	Mexico	0.0025%	H18875
Catechin, epi:(4-beta-d)-(-)-epi-catechin-(4-beta-8)-(-)-epi-catechin (4-beta-8)-(-)-epi- catechin:	Flavonoid	Stembark	Mexico	0.00471%	H18875
Farnesol, cis-2-trans-8:	Sesquiterpene	Leaf Essential Oil	Brazil	06.6%	L13823
Friedelin-3alpha-acetate	Triterpene	Not Stated	Not Stated	Not Stated	ZZ1092
Friedelin-2beta-ol	Triterpene	Not Stated	Not Stated	Not Stated	ZZ1092
Kaur-16-en-19-oic acid, ent:	Diterpene	Leaf	Brazil	Not Stated	L13883
Precocene I	Oxygen Heterocycle	Leaf Essential Oil	Brazil	56.0%	L13823
Procyanidin B-2	Flavonoid	Stembark	Mexico	0.10769%	H18875
Procyanidin B-5	Flavonoid	Stembark	Mexico	0.00259%	H18875
Procyanidin C-1	Flavonoid	Stembark	Mexico	0.0098%	H18875
Sitosterol, beta	Steroid	Not Stated	Not Stated	Not Stated	ZZ1092

Other Phytochemical Screening:

Alkaloids Absent	Bark	T09735
Flavonoids Absent	Bark	T09735
Saponins Absent	Bark	T09735
Tannins Present	Bark	T09735

Biological Activities for Extracts of Mutamba (Guazuma ulmifolia)

IN VIVO RESEARCH

Plant Part - Origin	Activity Tested For	Type Extract	Test Model	Dosage	Results	Notes/Organism tested	Ref #
Bark Brazil	Uterine Stimulant Effect	ETOH (95%) Ext H20 Ext	Rat Female Rat Female	1:1 1:1	Active Weak Activity	Uterus (non-preg).	W02690
Stembark Brazil	Uterine Stimulant Effect	H2O Ext	Rat Female	Not stated	Active	Uterus (estrog).	A03531
Leaf Mexico	Antihyperglycemic Activity	Decoction	Intragastric Rabbit	4.0 mg/kg	Active	vs. glucose-induced hyperglycemia.	L03570
Leaf Belize	Antispasmodic Activity	Hot H2O Ext	Rat Aorta	300.0 mcl	Inactive	vs. norepinephrine- and carbachol-induced contractions.	L16245
Bark Belize	Antispasmodic Activity	Hot H2O Ext	Rat Aorta	300.0 mcl	Inactive	vs. norepinephrine- and carbachol-induced contractions.	L16245
Bark Brazil	Smooth Muscle Relaxant Activity	ETOH (95%) Ext H2O Ext	Rabbit Rabbit	1:1 1:1	Weak Activity	Duodenum	W02690
Bark Brazil	Smooth Muscle Relaxant Activity	H2O Ext	Guinea Pig	1:1	Equivocal	Ileum	W02690
Bark Brazil	Smooth Muscle Stimulant Activity	ETOH (95%) Ext	Guinea Pig	1:1	Equivocal	Ileum	W02690
Bark Brazil	Cardiac Depressant Activity	ETOH (95%) Ext H2O Ext	Insect (heart) Insect (heart)	1:1 1:1	Inactive Equivocal	Heart - *Thermobia domes*	W02690
Bark Brazil	Cardiotonic Activity	ETOH (95%) Ext	Insect (heart)	1:1	Equivocal	Heart - *Thermobia domes*	W02690
Leaf Guatemala	Diuretic Activity	Decoction	Gastric Rat	1.0 gm/kg	Inactive		T15295
Bark Brazil	Fish Poison	ETOH (95%) Ext H2O Ext	Not stated	1:1 1:1	Inactive Inactive		W02690
Bark Brazil	Hypertensive Activity	ETOH (95%) Ext	IV Cat	Not stated	Inactive		W02690
Bark Brazil	Hypotensive Activity	H2O Ext ETOH (95%) Ext	IV Cat IV Cat	Not stated Not stated	Active Inactive		W02690

GI = Gastric Intubation IG = Intragastric NG = Nasogastric IP = Intraperitoneally IV = Intravenously SC = Subcutaneously IM = Intramuscular

Plant Part - Origin	Activity Tested For	Type Extract	Test Model	Dosage	Results	Notes/Organism tested	Ref #
Stembark Mexico	Antisecretory Effect	ETOH(70%) Ext	Pig (intestine)	400.0 mcg/ml	Inactive	vs. PBE2-induced chloride secretion.	K23487
Stembark Mexico	Antisecretory Effect	ETOH(70%) Ext	Rabbit (intestine)	40.0 mcg/ml	Active	vs. cholera toxin-induced chloride secretion.	K23487
Stembark Mexico	Antisecretory Effect	ETOH (95%) Ext	Rabbit (colon)	Not stated	Active	vs. cholera toxin-induced secretion.	H18875

IN VITRO RESEARCH

Plant Part - Origin	Activity Tested For	Type Extract	Test Model	Dosage	Results	Notes/Organism tested	Ref #
Leaf Brazil	Cytotoxic Activity	ETOH (95%) Ext	Cell Culture	Not stated	Strong Activity	Ca-9kb 97.3% inhibition of cell growth.	M25036
Leaf Panama	Cytotoxic Activity	H2O Ext MEOH Ext	Cell Culture	100.0 mcg/ml	Inactive	Cells - vero.	K28424
Root Brazil Stem Brazil	Cytotoxic Activity	ETOH (95%) Ext	Cell Culture	Not stated	Inactive	Ca-9kb (19.9% inhibition of cell growth).	M25036
Leaf Indonesia	Prostaglandin Synthetase Inhibition	ETOH-H2O (1:1) Ext		750.0 mcg/ml	Active	Activity was inhibited 61.8%.	M31096
Bark Mexico	Anti-inflammatory Activity	ETOH (95%) Ext		Not stated	Equivocal	In HET-CAM assay.	L07398
Bark + Fruit Mexico	Antifungal Activity	ETOH (95%) Ext	Agar Plate	10.0 mcg 25.0 mcg	Active Active	*Cladosporium cucumerinum* *Penicillium oxalicum*	K19153
Leaf + Stem India	Antifungal Activity	H2O Ext	Agar Plate	100.0 Mcg	Inactive	*Aspergillus flavus* *Geotrichum candidum*	M19808
Leaf + Stem India	Antiyeast Activity	H2O Ext	Agar Plate	100.0 Mcg	Inactive	*Candida albicans*	M19808
Shade Fruit Mexico	Antiyeast Activity	MEOH Ext	Agar Plate	1.25 Mg/ml	Inactive	*Candida albicans*	J12454
Leaf Panama	Antiviral Activity	H2O Ext MEOH Ext	Agar Plate Agar Plate	100.0 mcg/ml 100.0 mcg/ml	Inactive Weak Activity	Virus-herpes simplex 1	K28424
Bark Brazil	Antibacterial Activity	CH2CL2:MEOH (1:1) Ext	Agar plate	5 mg/plate	Strong Activity	*Staphylococcusa aureus*	BB1006
Bark Brazil	Antibacterial Activity	CH2CL2:MEOH (1:1) Ext	Agar plate	5 mg/plate	Active	*Bacillus cereus*	BB1006
Leaf Guatemala	Antibacterial Activity	ETOH Ext	Agar Plate	10.0 mcl 30.0 mcl 30.0 mcl	Active Active Active	*Bacillus subtilis* *Escherichia coli* *Staphylococcusa aureus*	T15445
Bark + Fruit Mexico	Antibacterial Activity	ETOH (95%) Ext	Agar Plate	10.0 mcg 20.0 mcg 20.0 mcg	Active Active Inactive	*Bacillus subtilis* *Micrococcus luteus* *Escherichia coli*	K19153

GI = Gastric Intubation IG = Intragastric NG = Nasogastric IP = Intraperitoneally IV = Intravenously SC = Subcutaneously IM = Intramuscular

Plant Part / Origin	Activity Tested For	Type Extract	Test Model	Dosage	Results	Notes/Organism tested	Ref #
Bark Guatemala	Antibacterial Activity	ETOH-H2O (1:1) Ext	Agar Plate	50.0 mcl	Active	*Neisseria gonorrhea*	K27236
Bark Guatemala	Antibacterial Activity	ETOH-H2O (50%) Ext	Agar Plate	50.0 mcl	Active Equivocal Inactive Inactive Inactive	*Shigella dysenteriae* *Salmonella typhosa* *Shigella flexneri* *Escherichia coli* *Salmonella enteritidis*	K24899
Leaf Guatemala	Antibacterial Activity	Acetone Ext	Agar Plate	50.0 mg	Weak Activity	*Staphylococcus aureus* *Streptococcus pneumoniae* *Streptococcus pyogenes*	K19264
Leaf Guatemala	Antibacterial Activity	Hexane Ext	Agar Plate	50.0 mg	Weak Activity	*Staphylococcus aureus* *Streptococcus pneumoniae* *Streptococcus pyogenes*	K19264
Leaf Guatemala	Antibacterial Activity	MEOH Ext	Agar Plate	50.0 mg	Weak Activity	*Staphylococcus aureus* *Streptococcus pneumoniae* *Streptococcus pyogenes*	K19264
Leaf Guatemala	Antibacterial Activity	MEOH Ext	Agar Plate	Not stated	Equivocal	*Escherichia coli* *Salmonella typhimurium* *Shigella flexneri*	K11657
Leaf Guatemala	Antibacterial Activity	ETOH Ext	Agar Plate	0.1 ml	Inactive	*Proteus vulgaris* *Pseudomonas aeruginosa* *Salmonella typhi* *Shigella flexneri* *Streptococcus pyogenes*	T15445
Shade Fruit Mexico	Antibacterial Activity	MEOH Ext	Agar Plate	10.0 mg/ml	Inactive	*Staphylococcus aureus* *Escherichia coli* *Pseudomonas aeruginosa*	J12454
Leaf + Stem India	Antibacterial Activity	H2O Ext	Agar Plate	100.0 mcg	Inactive	*Bacillus megaterium* *Bacillus subtilis* *Escherichia coli* *Pseudomonas sp* *Staphylococcus aureus* *Streptococcus sobrinus* *Xanthomonas rryzae*	M19808

Plant Part / Origin	Activity Tested For	Type Extract	Test Model	Dosage	Results	Notes/Organism tested	Ref #
Bark Mexico	Transcription Inhibition	ETOH (95%) Ext	Cell Culture	100.0 mcg/ml	Inactive	Ca-HeLa vs. inhibited NF-kappa B activation.	L07398
Bark Panama	Radioligand-Receptor-Binding Inhibition Activity	Acetone Ext	Cell Culture (hamster ovary cells)	10.0 mcg/ml	Active	Inhibited binding to Angiotensin II receptor cells by more than 50%.	L12353
Bark Panama	Radioligand-Receptor-Binding Inhibition Activity	CHCL3 Ext ETOAC Ext H2O Ext Hexane Ext MEOH-CH2CL2 (1:1) Ext		10.0 mcg/ml	Inactive	AT-1 Receptor Inhibition	L18181
Bark Panama	Radioligand-Receptor-Binding Inhibition Activity	H2O Ext		1000 mcg/ml	Weak Activity	AT-1 Receptor Inhibition	L18181
Bark Panama	Radioligand-Receptor-Binding Inhibition Activity	ETOH (80%) Ext		100.0 mcg/ml	Inactive	ET-A Receptor Inhibition	L18181
Bark Panama	Radioligand-Receptor-Binding Inhibition Activity	CHCL2 Ext ETOAC Ext H2O Ext MEOH-CH2Cl2 (1:1) Ext		10.0 mcg/ml	Inactive	Y-1 Receptor Inhibition	L18181
Bark Panama	Radioligand-Receptor-Binding Inhibition Activity	Hexane Ext		10.0 mcg/ml	Weak Activity	Y-1 Receptor Inhibition	L18181
Bark + Fruit Mexico	Antiamebic Activity	ETOH (95%) Ext		MIC > 250 mcg/ml	Inactive	*Entamoeba histolytica*	K19153
Fresh Fruit + Leaf India	Antifilarial Activity	Not stated		Not stated	Inactive	*Setaria gigitata* (worm)	M25236
Trunkbark Brazil	Molluscicidal Activity	ETOH (95%) Ext H2O Ext		1000 ppm	Weak Activity	*Biomphalaria glabrata* *Biomphalaria straminea*	W02949
Bark Not stated	Plant Germination Inhibition	MEOH Ext	Plant	50.0 ppm	Active	Tested on bean plants.	T09735

Biological Activities for Compounds found in Mutamba (Guazuma ulmifolia)

Compound	Activity Tested For	Test Model	Dosage	Results	Notes/Organism tested	Ref #
Procyanidin B-2	Antitumor Activity	Cell Culture	Not stated	Active	Inhibited 12-O-tetradecanoylphorbol-13-acetate-induced activation of epstein-barr virus early antigen in Raji cells.	AG1009
Procyanidin B-2	Antitumor Activity	Cell Culture	ED50=1-4 mcg/ml	Active	PRMI-7951 melanoma cells.	AG1021
Procyanidin B-2	Antitumor Activity	Cell Culture	ED50=1-4 mcg/ml	Inactive	Lung carcinoma (A-549). Ileocecal adenocarcinoma (HCT-8). Epidermoid carcinoma of nasopharnyx (KB). Medulloblastoma (TE-671) .	AG1021
Procyanidin B-2	Mutagenic Effect	Cell Culture	Not stated	Inactive	Bacteria	AG1015
Procyanidin B-2	Toxic Effect	CHL cells	Not stated	Inactive	Caused no structural aberrations	AG1015
Procyanidin B-2	Toxic Effect	Mice	Not stated	Inactive	Micronucleus test.	AG1015
Procyanidin B-2	Toxic Effect	SC Rat	LD >2gm/kg	Inactive		AG1015
Procyanidin B-2	Toxic Effect	Guinea Pig	Not stated	Inactive	No sensitization.	AG1015
Procyanidin B-2	Toxic Effect	Rabbits	Not stated	Weakly Active	Slight irritation of conjunctiva, thought to be caused by ethanol.	AG1015
Procyanidin B-2	Toxic Effect	Rabbits	Not stated	Inactive	No primary irritation.	AG1015
Procyanidin B-2	Hair Growth Promoter Effect	Cell Culture	Not stated	Active	Down regulates protein kinase C (PKC) isozymes (-alpha, -betaI, -betaII, -eta) in hair cells, promoting hair cell growth. Inhibition of PKC isozyme translocation to the particulate fraction of hair epithelial cells.	AG1010
Procyanidin B-2	Hair Growth Promoter Effect	Human Adult (male)	1% External	Active	No adverse effects. 78.9% had increase in hair diameter (30% in placebo) and an increase in number of total hairs.	AG1011
Procyanidin B-2	Neuroprotective Effect	Cell Culture	100-300 mM	Active	Protected against glutamate-induced neuronal death in cultured cerebellar granule cells by inhibition of calcium influx.	AG1012

GI = Gastric Intubation IG = Intragastric NG = Nasogastric IP = Intraperitoneally IV = Intravenously SC = Subcutaneously IM = Intramuscular

Compound	Activity Tested For	Test Model	Dosage	Results	Notes/Organism tested	Ref #
Procyanidin B-2	Hair growth promoter Effect	Human Adult (male)	1% External	Active	Increase in number of total hairs and terminal hairs (hairs more than 60 mm in diameter).	AG1013
Procyanidin B-2	Protein Kinase C Inhibitory Activity	Not stated	Not stated	Active		AG1014
Procyanidin B-2	Hair growth promoter Effect	in vitro in vivo	Not stated Not stated	Active Active	Promote hair epithelial cell proliferation and stimulate anagen induction.	AG1014
Procyanidin B-2	Hair growth promoter Effect	Mouse	Not stated	Active	Growth-promoting activity 300% (controls 100%).	AG1016
Procyanidin B-2	Antihypertensive Effect	IV Rat	Not stated	Active	Lowered blood pressure through decrease of sympathetic tone and direct vasodilatation.	AG1017
Procyanidin C-1	Hair growth promoter Effect	Mouse	Not stated	Active	Growth-promoting activity 220%.	AG1016
Procyanidin C-1	Anticoagulant Activity	In vitro	Not stated	Active	Inhibited platelet aggregation. Comparable with aspirin.	AG1019
Procyanidin C-1	Antiviral Activity	Cell Culture	Not stated	Active	*Herpes simplex* virus type 1.	AG1020
Procyanidin C-1	Protein Kinase C Inhibitory Activity	Not stated	Not stated	Active		AG1014
Procyanidin C-1	Hair growth promoter Effect	In vitro In vivo	Not stated Not stated	Active Active	Promote hair epithelial cell proliferation Stimulate anagen induction.	AG1014
Procyanidin C-1	Antioxidant Activity		Not stated	Active	Lipid peroxidation and hydroxyl radical scavenging assay.	AG1020

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J12454	ANTIMICROBIAL EVALUATION OF SOME PLANTS USED IN MEXICAN TRADITIONAL MEDICINE FOR THE TREATMENT OF INFECTIOUS DISEASES.NAVARRO,V: VILLARREAL,ML: ROJAS,G: LOZOYA,X:J ETHNOPHARMACOL 53 3: 143-147 (1996)(CENTRO INVEST BIOMED SUR INST MEXICAN DEGURO SOCIAL MORELOS MEXICO)
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K28424	INHIBITORY EFFECTS OF VARIOUS AYURVEDIC AND PANAMANIAN MEDICINAL PLANTS ON THE INFECTION OF HERPES SIMPLEX VIRUS-1 IN VITRO AND IN VIVO.HATTORI,M: NAKABAYASHI,T: LIM,YA: MIYASHIRO,H: KUROKAWA,M: SHIRAKI,K: GUPTA,MP: CORREA,M: PILAPITIYA,U:PHYTOTHER RES 9 4: 270-276 (1995)(RES INST ORIENTAL MED TOYAMA MED & PHARM UNIV TOYAMA 930-01 JAPAN)
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L13823	VOLATILE CONSTITUENTS FROM LEAVES OF GUAZUMA ULMIFOLIA LAM. ARRIAGA,AMC: MACHADO,MIL: CRAVEIRO,AA: POULIQUEN,YBM: MESQUITA,AG:J ESSENT OIL RES 9 6: 705-706 (1997) (DEPT QUIM ORG & INORG UNIV FED DO CEARA FORTALEZA CEARA 60,000 BRAZIL)
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T15323	VEGETALES EMPLEADOS EN MEDICINA TRADICIONAL NORPERUANA. RAMIREZ,VR: MOSTACERO,LJ: GARCIA,AE: MEJIA,CF: PELAEZ,PF: MEDINA,CD: MIRANDA,CH: BANCO AGRARIO DEL PERU & NACL UNIV TRUJILLO, TRUJILLO, PERU, JUNE, 1988 : 54PP- (1988)(UNIV TRUJILLO TRUJILLO PERU)
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W02949	MOLLUSCICIDAL ACTIVITY OF PLANTS FROM NORTHEAST BRAZIL.PINHEIRO DE SOUSA,M: ROUQUAYROL,MZ: REV BRASIL PESQ MED BIOL 7 4: 389-394 (1974) (DEPT FARMACOL EXP CENT CIENC SAUDE UNIV FED CEARA CEARA BRAZIL)

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AG1004	LOCAL ANAESTHETIC ACTIVITY OF BETA-CARYOPHYLLENE. GHELARDINI,C: GALEOTTI,N: DI CESARE MANNELLI,L: MAZZANTI,G: BARTOLINI,A: FARMACO. 56 5-7: 387-9 (2001) (DEPT PHARMACOL, UNIVERSITY OF FLORENCE, ITALY)
AG1005	GASTRIC CYTOPROTECTION OF THE NON-STEROIDAL AND ANTI-INFLAMMATORY SESQUITERPENE, BETA-CARYOPHYLLENE. TAMBE,Y: TSUJIUCHI,H: HONDA,G: IKESHIRO,Y: TANAKA,S: PLANTA MED 62 5: 469-70 (1996
AG1006	CYTOTOXIC AND ANTIOXIDATIVE SESQUITERPENOIDS FROM HETEROTHECA INULOIDES. KUBO,I: CHAUDHURI,SK: KUBO,Y: SANCHEZ,Y: OGURA,T: SAITO,T: ISHIKAWA,H: HARAGUCHI,H: PLANT MED 62 5: 427-30 (1996) (DEPT ENVIR SCI, POLICY AND MANAGEMENT, UNI CALIFORNIA, BERKELEY, USA)
AG1007	ANTI-INFLAMMATORY ACTIVITY OF THE ESSENTIAL OIL OF BUPLEURUM FRUTICESCENS. MARTIN,S: PADILLA,E: OCETE,MA: GALVEZ,J: JIMENEZ,J: ZARZUELO,A: PLANTA MED 59 6: 533-6 (1993) (DEPT DE FARMACOLOGICA, FACULTAD DE FARMACIA, UNIVERSIDAD DE GRANADA, SPAIN)
AG1008	SESQUITERPENES FROM CLOVE (EUGENIA CARYOPHYLLATA) AS POTENTIAL ANTICARCINOGENIC AGENTS. ZHENG,GQ: KENNEY,PM: LAM,LK: J NAT PROD 55 7: 999-1003 (1992) (LKT LAB INC. MINNEAPOLIS, MINNESOTA, USA)
AG1009	ANTITUMOR ACTIVITY OF COMPOUNDS ISOLATED FROM LEAVES OF ERIOBOTRYA JAPONICA. ITO,H: KOBAYASHI,E: LI,SH: HATANO,T: SUGITA,D: KUBO,N: SHIMURA,S: ITOH,Y: TOKUDA,H: NISHINO,H: YOSHIDA,T: J AGRIC FOOD CHEM 50 8: 2400-3 (2002) (FAC OF PHARMACEUTICAL SCIENCES, OKAYAMA UNI, TSUSHIMA, OKAYAMA, JAPAN)
AG1010	PROCYANIDIN B-2, EXTRACTED FROM APPLES, PROMOTES HAIR GROWTH: A LABORATORY STUDY. KAMIMURA,A: TAKAHASHI,T: BR J DERMATOL 146 1: 41-51 (2002) (TSUKUBA RESEARCH LAB, KYOWA HAKKO KOGYO CO, TSUKUBA, IBARAKI,K JAPAN)
AG1011	THE FIRST CLINICAL TRIAL OF TOPICAL APPLICATION OF PROCYANIDIN B-2 TO INVESTIGATE ITS POTENTIAL AS A HAIR GROWING AGENT. TAKAHASHI,T: KAMIMURA,A: YOKOO,Y: HONDA,S: WATANABE,Y: PHYTOTHER RES 15 4: 331-6 (2001) (TSUKUBA RES LAB, KYOWA HAKKO KOGYO CO, TSUKUBA, IBARAKI, JAPAN)
AG1012	PROTECTIVE EFFECT OF PHENOLIC COMPOUNDS ISOLATED FROM THE HOOKS AND STEMS OF UNCARIA SINENSIS OF GLUTAMATE-INDUCED NEURONAL DEATH. SHIMADA,Y: GOTO,H: KOGURE,T: SHIBAHARA,N: SAKAKIBARA,I: SASAKI,H: TERASAWA,K: AM J CHIN MED 29 1: 173-80 (2001) (DEPT JAPANESE ORIENTAL MED, FAC OF MEDICINE, TOYAMA MEDICAL AND PHARMACEUTICAL UNI)
AG1013	INVESTIGATION OF TOPICAL APPLICATION OF PROCYANIDIN B-2 FROM APPLE TO IDENTIFY ITS POTENTIAL USE AS A HAIR GROWING AGENT. KAMIMURA,A: TAKAHASHI,T: WATANABE,Y: PHYTOMEDICINE 7 6: 529-36 (2000) (TSUKUBA RES LAB, KYOWA HAKKO KOGYO CO, IBARAKI, JAPAN)
AG1014	SEVERAL SELECTIVE PROTEIN KINASE C INHIBITORS INCLUDING PROCYANIDINS PROMOTE HAIR GROWTH. TAKAHASHI,T: KAMIMURA,A: SHIRAI,A: YOKOO,Y: SKIN PHARMACOL APPL SKIN PHYSIOL 13 3-4: 133-42 (2000) (TSUKUBA RES LAB, KYOWA HAKKO KOGYO CO, TSUKUBA, IBARAKI, JAPAN)

AG1015	TOXICOLOGICAL STUDIES ON PROCYANIDIN B-2 FOR EXTERNAL APPLICATION AS A HAIR GROWING AGENT. TAKAHASHI,T: YOKOO,Y: INOUE,T: ISHII,A: FOOD CHEM TOXICOL 37 5: 545-52 (1999)(TSUKUBA RES LAB, KYOWA HAKKO KOGYO CO, IBARAKI, JAPAN)
AG1016	PROCYANIDIN OLIGOMERS SELECTIVELY AND INTENSIVELY PROMOTE PROLIFERATION OF MOUSE HAIR EPITHELIAL CELLS IN VITRO AND ACTIVATE HAIR FOLLICLE GROWTH IN VIVO. TAKAHASHI,T: KAMIYA,T: HASEGAWA,A: YOKOO,Y: J INVEST DERMATOL 112 3: 310-6 (1999) (TSUKUBA RES LAB, KYOWA HAKKO KOGYO, IBARAKI, JAPAN)
AG1017	ANTIHYPERTENSIVE PRINCIPLES FROM THE LEAVES OF MELASTOMA CANDIDUM. CHENG,JT: HSU,FL: CHEN,HF: PLANTA MED 59 5: 405-7 (1993) (DEPT PHARMACOL, COLLEGE OF MEDICINE, NATIONAL CHENG KUNG UNI, TAINAN CITY, TAIWAN, REPUBLIC CHINA)
AG1018	EFFECTS OF RHUBARB TANNINS ON RENAL FUNCTION IN RATS WITH RENAL FAILURE. YOKOZAWA, T: FUJIOKA,K: OURA,H: NONAKA,G: NISHIOKA,I: NIPPON JINZO GAKKAI SHI 35 1: 13-8 (1993) (RES INSTITUTE FOR WAKAN-YAKU, TOYAMA MED AND PHARMACEUTICAL UNI, JAPAN)
AG1019	INHIBITION OF PLATELET AGGREGATION AND ARACHIDONATE METABOLISM IN PLATELETS BY PROCYANIDINS. CHANG,WC: HSU,FL: PROSTAGLANDINS LEUKOT ESSENT FATTY ACIDS 38 3: 181-8 (1989) (DEPT PHARM, COLLEGE OF MEDICINE, NATIONAL CHENG KUNG UNI, TAIWAN)
AG1020	ANTIVIRAL AND ANTIOXIDANT ACTIVITY OF FLAVONOIDS AND PROANTHOCYANIDINS FROM CRATAEGUS SINAICA. SHAHAT,AA: COS,P: DE BRUYNE,T: APERS,S: HAMMOUDA,FM: ISMAIL,SI: AZZAM,S: CLAEYS,M: GOOVAERTS,E: PIETERS,L: VANDEN BERGHE,D: VLIETINCK,AJ: 68 6: 539-41 (2002)
AG1021	ANTITUMOR AGENTS, 129. TANNINS AND RELATED COMPOUNDS AS SELECTIVE CYTOTOXIC AGENTS. KASHIWADA,Y: NONAKA,G: NISHIOKA,I: CHANG,JJ: LEE,KH: J NAT PROD 55 8: 1033-43 (1992) (NAT PRODUCTS LAB, SCHOOL OF PHARMACY, UNI OF NORTH CAROLINA, CHAPEL HILL)
BB1006	BIOLOGICAL SCREENING OF BRAZILIAN MEDICINAL PLANTS. DE ALMEIDA ALVES, TM., ET AL. MEM INST OSWALDO CRUZ. 95(3): 367-373 MAY/JUN. 2000 (BELO HORIZONTE, MG BRAZIL)
ZZ1019	RAINFOREST REMEDIES, ONE HUNDRED HEALING HERBS OF BELIZE. ARVIGO, ROSITA AND MICHAEL BALICK. (BOOK 1993) (TWIN LAKES, WI: LOTUS PRESS, INC.)
ZZ1091	MEDICINAL PLANTS OF BRAZIL. MORS, W.B., RIZZINI, C. T., PEREIRA, N. A.,. (BOOK. 2000) (ALGONAC, MICHIGAN, REFERENCE PUBLICATIONS, INC.)
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Clinical Abstracts

Phytomedicine 2001 Jan;8(1):59-70
Biological screening of selected medicinal Panamanian plants by radioligand-binding techniques.
Caballero-George, C., et al.
Nineteen plants from the Republic of Panama were selected by their traditionaluses in the treatment of hypertension, cardiovascular, mental and feeding disorders and 149 extracts were screened using radioligand-receptor-binding assays. The methanol:dicloromethane extracts of the bark and leaves of Anacardium occidentale L., the leaves of Begonia urophylla Hook., the roots of Bocconia frutescens L., the stems and leaves of Cecropia cf.obtusifolia Bertol., the branches of Clusia coclensis Standl., the bark of Cochlospermum vitifolium (Willd.)Spreng., the roots of Dimerocostus strobilaceus Kuntze, the bark of Guazuma ulmifolia Lam., the leaves of Persea americana Mill. and the branches of Witheringia solanaceae L'Her. inhibited the [3H]-AT II binding (angiotensin II AT1 receptor) more than 50%. Only extracts of the roots of Dimerocostus strobilaceus Kuntze and the stems of Psychotria elata (Sw.) Hammel were potent inhibitors of the [3H] NPY binding (neuropeptide Y Y1 receptor) more than 50% and the ethanolic extracts of the leaves of Cecropia cf. obtusifolia Bertol., the leaves of Hedyosmum bonplandianum H.B.K., the roots of Bocconia frutescens L., the stem of Cecropia cf. obtusifolia Bertol. and the branches of Psychotria elata (Sw.) Hammel showed high inhibition of the [3H] BQ-123 binding (endothelin-1 ET(A) receptor) in a preliminary screening. These results promote the further investigation of these plants using the same assays.

J Ethnopharmacol 1998 Jun;61(2):101-10
Study of the anti-hyperglycemic effect of plants used as antidiabetics.
Alarcon-Aguilara, F. J., et al.
The purpose of this research was to study the anti-hyperglycemic effect of 28 medicinal plants used in the treatment of diabetes mellitus. Each plant was processed in the traditional way and intragastrically administered to temporarily hyperglycemic rabbits. The results showed that eight out of the 28 studied plants significantly decrease the hyperglycemic peak and/or the area under the glucose tolerance curve. These plants were: Guazuma ulmifolia, Tournefortia hirsutissima, Lepechinia caulescens, Rhizophora mangle, Musa sapientum, Trigonella foenum graceum, Turnera diffusa, and Euphorbia prostrata. The results suggest the validity of their clinical use in diabetes mellitus control, after their toxicological investigation.

Planta Med 1995 Jun;61(3):208-12
Inhibition of intestinal chloride secretion by proanthocyanidins from Guazuma ulmifolia.
Hor, M., et al.
The antisecretory activity of Guazuma ulmifolia bark was examined in rabbit distal colon mounted in an Ussing chamber. Chloride secretion was stimulated by cholera toxin and prostaglandin E2 (PGE2). Guazuma ulmifolia extract (GUE) completely inhibited cholera toxin-induced secretion if the extract was added to the mucosal bath prior to the toxin. Adding the extract after administration of the toxin had no effect on secretion. GUE did not inhibit PGE2-induced chloride secretion. These results indicate an indirect antisecretory mechanism. SDS-PAGE analysis of cholera toxin treated with GUE confirmed this presumption. GUE specifically interacted with the A subunit of the toxin. Preliminary phytochemical examinations showed that the most active fraction contains procyanidins with a degree of polymerisation higher than 8.

J Ethnopharmacol 1990 Aug;30(1):55-73
Plants used in Guatemala for the treatment of gastrointestinal disorders. 1. Screening of 84 plants against enterobacteria.
Caceres, A., et al.
Gastrointestinal disorders are important causes of morbidity in developing countries. Natural healing is the traditional way of treating these
diseases in Guatemala. Ethnobotanical surveys and literature reviews showed that 385 plants from 95 families are used in Guatemala for the treatment of gastrointestinal disorders. The activity of 84 of the most commonly used plants was screened in vitro against five enterobacteria pathogenic to man (enteropathogenic Escherichia coli, Salmonella enteritidis, Salmonella typhi, Shigella dysenteriae and Shigella flexneri). Results indicate that 34 (40.48%) plants inhibit one or more of the enterobacteria tested. The most commonly inhibited bacterium was S. typhi (33.73%) and the most resistant was E. coli (7.35%). The plants of American origin which exhibited the best antibacterial activity were: Byrsonima crassifolia, Diphysa robinioides, Gnaphalium stramineum, Guazuma ulmifolia, Psidium guajava, Sambucus mexicana, Simarouba glauca, Smilax lundelii, Spondias purpurea and Tagetes lucida. These results indicate a scientific basis for use of these medicinal plants for attacking enterobacterial infections in man.

J Nat Prod 1992 Aug;55(8):1033-43

Antitumor agents, 129. Tannins and related compounds as selective cytotoxic agents.

Kashiwada, Y., et al.

Fifty-seven tannins and related compounds, including gallotannins, ellagitannins, and condensed and complex tannins, were evaluated for their cytotoxicities against human tumor cell lines, including malignant melanoma, lung carcinoma, ileocecal adenocarcinoma, epidermoid carcinoma, malignant melanoma, and medulloblastoma cell lines. Among them, chebulagic acid [1], geraniin [2], sanguiin H-11 [3], 4,5-di-O-galloylquinic acid [12], 1,3,4,5-tetra-O-galloylquinic acid [15], 1(beta)-O-galloylpedunculagin [24], furosin [29], castalagin [38], sanguiin H-2 [34], vescalagin [39], grandinin [40], phyllyraeoidin A [42], (-)-epicatechin 3-O-gallate [50], cinnamtannin B2 [55], and acutissimin A [56] exhibited moderate selective cytotoxicity against PRMI-7951 melanoma cells with ED50 values in the range of 0.1-0.8 microgram/ml. Selective cytotoxicities against the melanoma cells were also observed for strictinin [22], pedunculagin [23], eugeniin [25], elaeocarpusin [28], punicacortein C [37], casuarinin [41], sanguiin H-6 [43], **procyanidin B-2** [51], **procyanidin C-1** [52], and cinnamtannin B1 [54] with ED50 values of 1-4 micrograms/ml.

Skin Pharmacol Appl Skin Physiol 2000 May-Aug;13(3-4):133-42

Several selective protein kinase C inhibitors including procyanidins promote hair growth.

Takahashi, T., et al.

We have previously reported that procyanidin oligomers selectively promote growth of murine hair epithelial cells in vitro and stimulate anagen induction in vivo. We report here the possible relationship between the protein kinase C-inhibiting activity of procyanidins and their hair-growing activity. Of the procyanidins, **procyanidin B-2** and **procyanidin C-1**, which selectively inhibit protein kinase C, intensively promote hair epithelial cell proliferation in vitro and stimulate anagen induction in vivo. On the other hand, procyanidins, which inhibit both protein kinase C and A, showed relatively low activity in in vitro and in vivo evaluations. We also found that calphostin C, which is a selective inhibitor of protein kinase C, possesses hair epithelial cell growth- pro-moting activity in vitro and anagen phase-inducing hair-growing activity in vivo. Other selective protein kinase C inhibitors, such as hexadecyl-phosphocholine, palmitoyl-DL-carnitine chloride, and polymyxin B sulfate, also show marked anagen phase-inducing hair- growing activity in vivo. Nonselective protein kinase inhibitors, such as staurosporine and K252a, inhibit the growth of hair epithelial cells. 1,2-Dioctanoyl-sn-glycerol, a protein kinase C activator, dose-depend-ently decreases the growth of hair epithelial cells. Forskolin, an adenylate cyclase activator, promotes hair epithelial cell growth and boosts the growth-promoting effect of procyanidin B-2. It is speculated that the hair-growing activity of procyanidins is related to their protein kinase C-inhibiting activity.

J Invest Dermatol 1999 Mar;112(3):310-6

Procyanidin oligomers selectively and intensively promote proliferation of mouse hair epithelial cells in vitro and activate hair follicle growth in vivo.

Takahashi T, et al.

We have previously reported that proanthocyanidins extracted from grape seeds possess growth-promoting activity toward murine hair epithelial cells in vitro and stimulate anagen induction in hair cycle progression in vivo. This report constitutes a comparison of the growth-promoting activity of procyanidin oligomers and the target cells of procyanidins in the skin. Results show that procyanidin dimer and trimer exhibit higher growth-promoting activity than the monomer. The maximum growth-promoting activity for hair epithelial cells with **procyanidin B-2**, an epicatechin dimer, reached about 300% (30 microM) relative to controls (= 100%) in a 5 d culture. Optimum concentration of procyanidin C-1, an epicatechin trimer, was lower than that of procyanidin B-2; the maximum growth-promoting activity of procyanidin C-1 was about 220% (3 microM). No other flavonoid compounds examined exhibit higher proliferative activities than the procyanidins. In skin constituent cells, only epithelial cells such as hair keratinocytes or epidermal keratinocytes respond to procyanidin oligomers. Topical application of 1% procyanidin oligomers on shaven C3H mice in the telogen phase led to significant hair regeneration [procyanidin B-2, 69.6% +/- 21.8% (mean +/- SD); procyanidin B-3, 80.9% +/- 13.0%; procyanidin C-1, 78.3% +/- 7.6%] on the basis of the shaven area; application of vehicle only led to regeneration of 41.7% (SD = 16.3%). In this paper, we demonstrate the hair-growing activity of procyanidin oligomers both in vitro and in vivo, and their potential for use as agents to induce hair growth.