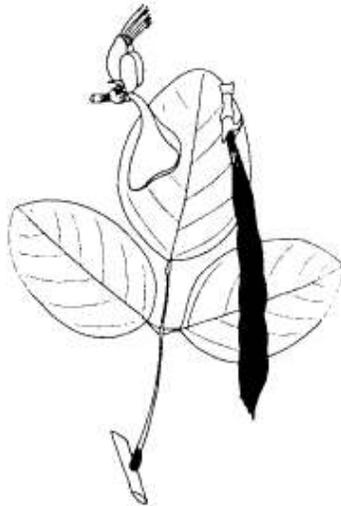


Technical Data Report

for

MULUNGU

Erythrina mulungu
Erythrina cristi-galli



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Mulungu

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Family: Fabaceae

Genus: *Erythrina*

Species: *mulungu*, *crista-galli*

Synonyms: *Erythrina verna*, *Coraliodendron mulungu*

Common Names: Mulungu, corticeira, murungu, muchocho, murungo, totocero, flor-de-coral, árvore-de-coral, amerikadeigo, ceibo, chilichi, chopo, hosoba deiko, pau-imortal, mulungu-coral, capa-homem, suiná-suiná,

Part Used: Bark

Mulungu is a medium-sized, well-branched tree that grows 10–14 m high. It produces a profusion of pretty, reddish-orange flowers that are pollinated by hummingbirds at the ends of the tree's many branches. The tree is sometimes called "coral flower," as the flowers resemble the color of coral. It produces black seed pods containing large, red-and-black seeds, which are sometimes used by indigenous peoples to make necklaces and jewelry. Mulungu is indigenous to Brazil, parts of Peru, and tropical areas in Latin America and, typically, is found in marshes and along riverbanks. The *Erythrina* genus comprises more than 100 species of trees and shrubs (mostly all heavily armed with spines or thorns) in the tropical and subtropical regions of both hemispheres. The mulungu tree (first recorded in 1829) is known by two botanical names, *Erythrina mulungu* and *Erythrina verna*. Another closely-related species, *E. crista-galli*, is used interchangeably in South American herbal medicine systems and is found farther south on the South American continent. The flower of *E. crista-galli* is considered the national flower of Argentina.

Several *Erythrina* tree species are used by indigenous peoples in the Amazon as medicines, insecticides, and fish poisons. Mulungu has long been used in Brazil by indigenous peoples as a natural sedative: it has been used to calm an overexcited nervous system and promote a restful sleep.

In both North and South American herbal medicine systems it is considered to be an excellent sedative to calm agitation and nervous coughs and to treat other nervous system problems including insomnia and anxiety. It also is widely used for asthma, bronchitis, gingivitis, hepatitis, inflammation of the liver and spleen, intermittent fevers, and to clear obstructions in the liver. In both Brazil and Peru mulungu is used for epilepsy. Herbalists and practitioners in the United States use mulungu to quiet hysteria from trauma or shock, as a mild, hypnotic sedative to calm the nervous system, to treat insomnia and promote healthy sleeping patterns (by sedating overactive neurotransmitters), to regulate heart palpitations, and to treat hepatitis and liver disorders. Positive regulatory effects on heart palpitations and decreased blood pressure have been reported; Dr. Donna Schwontkowski, a chiropractor who has used Amazonian plants in her practice, recommends mulungu for hernias, stomachaches, and epilepsy—and to help augment milk flow as well.

The phytochemicals in mulungu have been studied extensively; they have been found to comprise large amounts of novel flavonoids, triterpenes, and alkaloids. Much research has been performed on *Erythrina* alkaloids in the last decade, as they represent a group of very active chemicals with various properties and are almost always present in *Erythrina* species.¹ Thus far, alkaloids have been found in 78 of 107 species in the genus *Erythrina*; mulungu is documented with 20 isoquinoline alkaloids. Many of these have demonstrated piscicidal, anti-inflammatory, cardioactive, narcotic, and hypnotic activities.^{1,2} One novel alkaloid discovered in mulungu is called *cristamidine*. Its positive effect on the liver was demonstrated in a 1995 clinical study with rats.³

Mulungu's hypotensive and heart-regulatory activities were studied and attributed to a group of alkaloids.⁴ Another alkaloid in mulungu (and other *Erythrina* plants), erysodine, has been documented with neuromuscular transition-blocking effects characteristic of curare arrow poisons. Two studies also indicate that it might be useful as an anti-nicotine drug, as it demonstrated actions as a competitive antagonist and to block nicotine receptors.^{5,6} Interestingly, both of these studies were published by major (and competing) pharmaceutical companies!

The traditional use of mulungu for anxiety and stress has been validated by researchers in a recent (2002) study, where it was shown to alter anxiety-related responses.⁷ An animal model (correlating to human generalized anxiety disorder, as well as panic disorder) was undertaken on a water-alcohol extract of mulungu. The researchers reported that the mulungu extract had an effect similar to the commonly-prescribed anti-anxiety drug diazepam.⁷ It was suggested in this study that the alkaloids in *Erythrina* "may alter GABAergic neurotransmission." GABA (gamma-amino butyric acid) acts as a neurotransmitter in the brain; abnormalities with its function is implicated in diseases including epilepsy, anxiety, and depression.⁸ Further research has validated the traditional use of mulungu as an antimicrobial agent for throat and urinary infections; mulungu has demonstrated antibacterial activity in two studies against *Staphylococcus aureus*, and antimycobacterial activity against *Mycobacterium fortuitum* and *Mycobacterium smegmatis*.^{9,10}

Mulungu is not very widely known or used in North America; mostly appearing as a synergistic ingredient in only a few herbal formulas for anxiety or depression. It is a wonderful rainforest medicinal plant that is deserving of much more attention in herbal medicine systems outside of South America.

Documented Properties and Actions: Analgesic, antianxiety, antibacterial, antimycobacterial, anodyne, anti-inflammatory, hepatotonic, hypnotic, hypotensive, nervine, sedative, soporific

Traditional Remedy: One-half cup of a standard bark decoction or 1–2 ml of a 4:1 tincture once or twice daily.

Main Phytochemicals: Alanine, arginine, aspartic acid, cristacarpin, cristadine, crystamidine, dimethylmedicarpin, erybidine, erycristagallin, erycristanol, erycristin, erydotrine, erysodienone, erysodine, erysonine, erysopine, erysotrine, erysovine, erystagallin A–C, erythrabyssin II, erythralines, erythramine, erythratine, eryvarietyrene, gamma-amino butyric acid, glutamic acid, hypaphorine lectins, n-nor-orientaline, oleanolic acid, oleanonic acid, phaseollidins, proteinases, sandwicensis, ursolic acid, vitexin

Contraindications:

- In large doses the plant is soporific and may cause drowsiness.
- In traditional medicine the plant is used to lower blood pressure. Clinical research with animals has documented hypotensive actions. It is recommended that those on medications to lower blood pressure (and those with low blood pressure) use mulungu with caution and monitor their blood pressure accordingly.

Drug Interactions: None documented; however, mulungu may potentiate some antianxiety drugs (such as diazepam) and antihypertensive drugs.

WORLDWIDE ETHNOBOTANICAL USES

Country	Uses
Argentina	Antiseptic, diarrhea, hemorrhoids, narcotic, piles, respiratory infections, urinary infections
Brazil	Agitation, antimicrobial, anxiety, asthma, astringent, bronchitis, cicatrizant, CNS disorders, convulsions, cough, cuts, epilepsy, fever, gingivitis, hepatitis, hypnotic, hysteria, inflammation, insomnia, liver, menopause, muscle pain, neuralgia, nervous tension, rheumatism, sedative, spleen, stress, throat, whooping cough
Colombia	Diuretic, sedative
Peru	Cystitis, epilepsy, eye irritations, hysteria, insomnia
U.S.	CNS disorders, epilepsy, heart, hepatitis, hernia, high blood pressure, hysteria, insomnia, lactagogue, liver, stomachache
Venezuela	Diuretic, piscicide
Elsewhere	Cardiotonic, diuretic, epilepsy, eye, headaches, heart, hepatitis, hernia, hydropsy, hypertension, hypnotic, hysteria, insomnia, lactagogue, liver, narcotic, palpitations, piscicide, rheumatism, sedative, spasm, stomachache, stomach cancer

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The information contained herein is intended for education, research, and informational purposes only. This information is not intended to be used to diagnose, prescribe or replace proper medical care. The statements contained herein have not been evaluated by the Food and Drug Administration. The plant described herein is not intended to diagnose, treat, cure, mitigate, or prevent any disease.

Ethnomedical Information on Mulungu (*Erythrina mulungu*)

Plant Part / Location	Documented Ethnomedical Use	Type Extract / Route	Used For	Ref #
Bark Amazonia	Used for insomnia, hysteria, heart palpitations, hepatitis and liver dysfunction.	Decoction or Tincture Oral	Not stated	ZZ1016
Bark Amazonia	Used to quiet hysteria from trauma or shock, to balance neurotransmitters and promote peaceful sleep. Used for hepatitis and liver dysfunctions. Considered to help regulate heart palpitations and excess heart yang.	Not stated	Human Adult	ZZ1015
Bark Argentina	Used against diarrhea. Used to treat respiratory tract infections. Used to treat urinary tract infections.	Decoction Oral Decoction Oral Decoction Oral	Human Adult Human Adult Human Adult	K17523 K17523 K17523
Stembark Argentina	Used as a narcotic. Used as an antiseptic.	H2O Ext Oral H2O Ext External	Human Adult Human Adult	K03244 K03244
Leaf Argentina	Used as an antihemorrhoidal agent.	Not stated External	Human Adult	K03244
Bark Brazil	Used in gargles against sore throat. Used to treat cuts. Used for rheumatism and hepatitis.	H2O Ext Gargle H2O Ext External H2O Ext Oral	Human Adult Human Adult Human Adult	ZZ1099
Bark Brazil	Used for fevers.	Decoction Oral	Oral Human Adult	K07977
Bark Brazil	Used to calm an excited nervous system and to combat insomnia. Used for bronchitis, asthma, inflammation of the liver and intermittent fevers. Used gingival abscesses.	Extract External Infusion Oral	Human Adult Human Adult	ZZ1002
Bark Brazil	Used as a hypnotic and sedative to calm the nervous system, combat hysteria and insomnia. Used for rheumatism, liver affections, chronic neuralgia, bronchitis, asthma and whooping cough.	Infusion Oral	Human Adult	ZZ1007
Bark Brazil	Considered an astringent, cicatrizant, deobstruant and hypnotic. Used for hepatitis and chronic rheumatism.	Infusion Oral	Human Adult	ZZ1079
Bark Brazil	Used for anxiety, nervous tension, insomnia, rheumatism, muscle pain and liver affections. Used to calm and relax, for rheumatism and muscular aches and to relieve stress.	Infusion Oral Infusion Bath	Human Adult	ZZ1081

Plant Part / Location	Documented Ethnomedical Use	Type Extract / Route	Used For	Ref #
Leaf + Stem Brazil	Used as an antimicrobial. Used as an astringent in wound healing. Used for throat infections.	Not stated External Not stated External Not stated Oral	Human Adult Human Adult Human Adult	L05437 L05437 L05437
Leaf + Stem Brazil	Used as a sedative to combat insomnia, for convulsions and menopause.	Infusion Oral	Human Adult	ZZ1096
Leaf + Bark Brazil	Used to calm agitation and other disorders of the nervous system such as insomnia.	Decoction or Tincture Oral	Human Adult	AX1004
Bark +Root Brazil	Said to be calming. Used for agitations, nervous coughs and other disturbances of the nervous system. Used for asthma, hepatitis and liver obstruction.	Not stated	Human Adult	ZZ1013
Seed Brazil	The seeds are poisonous.	Not stated	Human Adult	ZZ1002
Seed Brazil	Contain poisonous alkaloids.	Not stated	Human Adult	ZZ1079
Flower Colombia	Used as a sedative and diuretic.	Infusion Oral	Human Adult	ZZ1093
Plant Peru	Used for magic.	Not stated	Not stated	ZZ1093
Leaf Peru	Used for swelling of the legs due to humidity.	Cataplasm External	Human Adult	ZZ1093
Bark Peru	Used for eye irritations. Used for headaches.	Infusion External Infusion Not stated	Human Adult Human Adult	ZZ1093
Seed Peru	Used for the heart, epilepsy, hydropsy. Can cause paralysis of the motor nerves.	Not stated Not stated	Human Adult Not stated	ZZ1093
Seed Peru	Used for cystitis. Used to alleviate irritation of the eye.	Decoction Oral Decoction Ophthalmic	Human Adult Human Adult	ZZ1093
Bark U.S.	Used as a hypnotic and sedative to calm the nervous system, for hysteria and insomnia. Used for epilepsy.	Decoction or Tincture Oral	Human Adult	ZZ1067
Bark U.S.	Used as a mild hypnotic sedative to calm the nervous system, eliminate hysteria, decrease insomnia and promote healthy sleep pattern. Also used for rheumatism, pain in the liver, hepatitis, liver dysfunction, heart palpitations, hypertension, epilepsy, stomach ache and hernia. Considered a lactagogue.	Decoction or Tincture Oral	Human Adult	ZZ1014

Presence of Compounds in Mulungu (*Erythrina mulungu*)

Compound	Chemical type	Plant Part	Plant Origin	Quantity	Ref #
Alanine	Proteid	Seed	Not stated	Not stated	J09666
Arginine	Proteid	Seed	Not stated	Not stated	J09666
Aspartic Acid	Proteid	Seed	Not stated	Not stated	J09666
Butyric acid, gamma-amino-	Proteid	Seed	Not stated	Not stated	J09666
Cristacarpin	Flavonoid	Wood Leaf	Japan Not stated	00.001% Not stated	H20235 N07061
Cristadine	Isoquinoline Alkaloid	Leaf	Japan	Not stated	N00599
Crystamidine	Isoquinoline Alkaloid	Seedling Leaf	Australia Japan	Not stated 00.0006%	K22434 K00691
Erybidine	Isoquinoline Alkaloid	Leaf	Japan	00.036%	K00691
Erycristagallin	Flavonoid	Root	Bolivia	00.00980%	M05541
Erycristanol A	Oxygen Heterocycle	Heartwood	Japan	00.00033%	H14534
Erycristanol B	Benzenoid	Heartwood	Japan	00.0004%	H14534
Erycristanol C	Oxygen Heterocycle	Heartwood	Japan	00.00026%	H14534
Erycristin	Flavonoid	Stembark	Bolivia	00.00954%	H03771
Erydotrine	Isoquinoline Alkaloid	Leaf	Japan	00.0018%	K00691
Erysodienone	Isoquinoline Alkaloid	Entire Plant	Not stated	Not stated	J07704
Erysodine	Isoquinoline Alkaloid	Leaf Seed	Japan Not stated	00.0072% Not stated	K00691 A05062
Erysonine	Isoquinoline Alkaloid	Seed Seed	Not stated Not stated	Not stated Not stated	A05062 A05062
Erysopine	Isoquinoline Alkaloid	Seed	Not stated	Not stated	A05062
Erysotrine	Isoquinoline Alkaloid	Seedling	Australia	Not stated	K22434
Erysovine	Isoquinoline Alkaloid	Seed	Not stated	Not stated	A05062
Erystagallin A	Flavonoid	Wood	Japan	00.000407%	H20235

Compound	Chemical type	Plant Part	Plant Origin	Quantity	Ref #
Erystagallin B	Flavonoid	Wood	Japan	00.000087%	H20235
Erystagallin C	Flavonoid	Wood	Japan	00.00014%	H20235
Erythrabyssin II	Flavonoid	Stembark	Bolivia	00.05417%	H03771
Erythraline	Isoquinoline Alkaloid	Leaf Seedling Flowers	Japan Australia India	00.053% Not stated 00.11000%	K00691 K22434 H03756
Erythraline, 11-beta-methoxy-n-oxide-	Isoquinoline Alkaloid	Flowers	India	00.05000%	H03756
Erythraline, 11-beta-methoxy-	Isoquinoline Alkaloid	Flowers	India	00.64000%	H03756
Erythraline, 8-oxo:	Isoquinoline Alkaloid	Seedling Leaf	Australia England	Not stated Not stated	K22434 N19334
Erythramine	Isoquinoline Alkaloid	Seed	Not stated	Not stated	A05062
Erythratine	Isoquinoline Alkaloid	Seed	Not stated	Not stated	A05062
Erythratine, 11-methoxy-	Isoquinoline Alkaloid	Flowers	India	00.04000%	H03756
<i>Erythrina christa-galli</i> proteinase	Proteid	Seed	Uruguay	Not stated	M14029
Inhibitor DE-1 <i>Erythrina christa-galli</i> proteinase	Proteid	Seed	Uruguay	Not stated	M14029
Inhibitor DE-2 <i>Erythrina christa-galli</i> proteinase	Proteid	Seed	Uruguay	Not stated	M14029
Inhibitor DE-3 <i>Erythrina christa-galli</i> proteinase	Proteid	Seed	Uruguay	Not stated	M14029
Inhibitor DE-4 <i>Erythrina christa-galli</i> proteinase	Proteid	Seed	Uruguay	Not stated	M14029
Inhibitor DE-5 <i>Erythrina christa-galli</i> proteinase	Proteid	Seed	Uruguay	Not stated	M14029
Inhibitor DE-6 <i>Erythrina christa-galli</i> proteinase	Proteid	Seed	Uruguay	Not stated	M14029
Inhibitor DE-7 <i>Erythrina christa-galli</i> proteinase	Proteid	Seed	Uruguay	Not stated	M14029
Inhibitor DE-8 <i>Erythrina christa-galli</i> proteinase	Proteid	Seed Flowers	Uruguay India	Not stated 01.80000%	M14029 H03756
Erythrinine, 8-oxo-	Isoquinoline Alkaloid	Flowers	India	00.20000%	H03756
Eryvarietyrene	Benzenoid	Heartwood	Japan	00.00033%	H14534
Glutamic Acid	Proteid	Seed	Not stated	Not stated	J09666

Compound	Chemical type	Plant Part	Plant Origin	Quantity	Ref #
Hypaphorine	Indole Alkaloid	Seed Seed	Not stated Not stated	Not stated Not stated	A05062 A05062
Lectin, <i>Erythrina cristagalli</i>		Not stated	Not stated	Not stated	AX1006
Medicarpin, dimethyl-	Flavonoid	Leaf	Not stated	Not stated	N07061
Olean-12-en-28-oic acid, 3-beta-acetoxy-	Triterpene	Leaf	Taiwan	Not stated	L02848
Olean-12-ene-3-beta-28-diol	Triterpene	Leaf	Taiwan	Not stated	L02848
Oleanolic acid	Triterpene	Leaf	Taiwan	Not stated	L02848
Oleanonic Acid	Triterpene	Leaf	Taiwan	Not stated	L02848
Orientaline, n-nor-	Isoquinoline Alkaloid	Leaf	Japan	00.083%	K00691
Ornithine, delta-acetyl-	Proteid	Seed	Not stated	Not stated	J09666
Phaseollidin	Flavonoid	Leaf Wood	Not stated Japan	Not stated 00.000067%	N07061 H20235
Phaseollidin, 6-alpha-hydroxy-2-(gamma-gamma-dimethyl-allyl)	Flavonoid	Wood	Japan	00.000048%	H20235
Sandwicensin	Flavonoid	Stembark	Bolivia	00.01458%	H03771
Urs-11-alpha-12-alpha-epoxy-13-beta-28-olide, 3-beta-hydroxy	Triterpene	Leaf	Taiwan	Not stated	L02848
Ursolic Acid	Triterpene	Leaf	Taiwan	Not stated	L02848
Vitexin	Flavone	Leaf	Taiwan	Not stated	L02848

OTHER PHYTOCHEMICAL SCREENING:

Alkaloids Present	Leaf	K03244
	Leaf	K03244
Coumarins Present	Seed	T00485

Biological Activities for Extracts of Mulungu (*Erythrina mulungu*)

Plant Part – Origin	Activity Tested For	Type Extract	Test Model	Dosage	Result	Notes/Organism Tested	Ref #
Flowers Not Stated	Antimutagenic Activity	MEOH Ext MEOH Ext	Agar Plate Agar Plate	50.0 mcl/Disc 50.0 mcl/Disc	Inactive Inactive	<i>Bacillus subtilis</i> . NIG-1125 HIS MET <i>Escherichia coli</i> . B/R-WP2-TRP	T08867 T08867
Inflorescence Brazil	Antianxiety Activity	H2O-ETOH Ext	Oral Rat	100 mg/kg 200 mg/kg 400 mg/kg	Active	In the T-maze, an animal model that correlates to human generalized anxiety disorder and panic, avoidance latencies were impaired, without altering escape. Activity similar to drug diazepam.	AX1002
Inflorescence Brazil	Antianxiety Activity	H2O-ETOH Ext	Oral Rat	100 mg/kg 200 mg/kg 400 mg/kg	Active	Number of transitions was increased (light/dark transition model). Activity similar to drug diazepam.	AX1002
Inflorescence Brazil	Antianxiety Activity	H2O-ETOH Ext	Oral Rat	100 mg/kg 200 mg/kg 400 mg/kg	Inactive	Behavioral responses in the cat odor test were resistant to all forms of treatment.	AX1002
Stem + Bark Brazil	Antianxiety Activity	H2O-ETOH Ext	Not stated Mice	Not stated	Active	Increased the number and entries and time spent by mice in the open arms of the elevated plus-maze model of anxiety.	AX1003
Leaf + Stem Brazil	Cytotoxic Activity	MEOH (75%) Ext	Cell Culture	IC50 = 1000 mcg/ml	Inactive	Vero cells.	L05437
Not stated Argentina	Antitumor Activity	Not stated	Cell Culture	Not stated	Active	Inhibited the growth of crown gall tumors.	AX1001
Bark Argentina	Antibacterial Activity	Decoction H2O Ext Hot H2O Ext Hot H2O Ext	Agar Plate Agar Plate Agar Plate Agar Plate	Not Stated 1.0 mg/ml 62.5 mg/ml 62.5 mg/ml	Inactive Inactive Inactive Inactive	<i>Pseudomonas aeruginosa</i> . <i>Salmonella typhi</i> . <i>Escherichia coli</i> . <i>Staphylococcus aureus</i> .	K17523 J11153 K14683 K14683
Root Bolivia	Antibacterial Activity	ETOH (95%) Ext	Agar Plate	Not Stated	Active	<i>Staphylococcus aureus</i> .	M05541
Leaf Egypt	Antibacterial Activity	ETOH (70%) Ext ETOH (70%) Ext ETOH (70%) Ext ETOH (70%) Ext	Agar Plate Agar Plate Agar Plate Agar Plate	Not Stated Not Stated Not Stated Not Stated	Active Active Active Inactive	<i>Bacillus cereus</i> . <i>Bacillus megaterium</i> . <i>Staphylococcus albus</i> . <i>Staphylococcus aureus</i> .	T06729 T06729 T06729 T06729
Stembark Bolivia	Antibacterial Activity	ETOH (95%) Ext	Agar Plate	1.0 mg/ml	Weak Activity	<i>Staphylococcus aureus</i> .	H03771
Stembark Bolivia	Antimycobacterial Activity	ETOH (95%) Ext	Agar Plate	100.0 mcg/ml	Active	<i>Mycobacterium fortuitum</i> .	H03771

Plant Part – Origin	Activity Tested For	Type Extract	Test Model	Dosage	Result	Notes/Organism Tested	Ref #
Root Bolivia	Antimycobacterial Activity	ETOH (95%) Ext	Agar Plate	Not Stated	Active	<i>Mycobacterium smegmatis</i> .	M05541
Leaf Egypt	Antifungal Activity	ETOH (70%) Ext	Agar Plate	Not Stated	Inactive	Several fungi.	T06729
Leaf + Stem Brazil	Antiviral Activity	MEOH (75%) Ext MEOH (75%) Ext MEOH (75%) Ext MEOH (75%) Ext	Cell Culture Cell Culture Cell Culture Cell Culture	Not Stated ED50 = 400.0 mcg/ml ED50 = 400.0 mcg/ml ED50 = 666.0 mcg/ml	Inactive Inactive Inactive Inactive	Adenovirus (unspec.) in vero cells. <i>Herpes simplex</i> 1 virus in vero cells. <i>Herpes simplex</i> 2 virus in vero cells. Vesicular stomatitis virus in vero cells.	L05437 L05437 L05437 L05437
Bark Argentina	Antifungal Activity	Hot H2O Ext	Agar Plate	62.5 mg/ml	Inactive	<i>Aspergillus niger</i> .	K14683
Fresh Fruit + Leaf + Stem Greece	Antiphage Activity	H2O Ext H2O Ext H2O Ext H2O Ext H2O Ext H2O Ext	Agar Plate Agar Plate Agar Plate Agar Plate Agar Plate Agar Plate	0.1 g/Plate 0.1 g/Plate 0.1 g/Plate 0.1 g/Plate 0.1 g/Plate 0.1 g/Plate	Inactive Inactive Inactive Inactive Inactive Inactive	Bacteriophage MS2. Bacteriophage Phi-Chi-174. Bacteriophage T-7. Bacteriophage T2. Bacteriophage T4. Bacteriophage 0PS7.	L15988 L15988 L15988 L15988 L15988 L15988
Leaf + Stem Germany	Repellent Activity (Animal)	Leaves	Not Stated	Variable	Active	<i>Helix pomatia</i> .	T07907
Seed Uruguay	Chymotrypsin Inhibition	Chromatographic Fraction Saline Ext	Not Stated Not Stated	4040 Units Per mg Protein 890 Units Per mg Protein	Active Active		M14029 M14029
Seed Uruguay	Trypsin Inhibition	Chromatographic Fraction Saline Ext	Not Stated Not Stated	3740 Units Per mg Protein 940 Units Per mg Protein	Active Weak Activity		M14029 M14029

Biological Activities for Compounds of Mulungu (*Erythrina mulungu*)

Compound	Activity Tested For	Test Model	Dosage	Result	Notes/Organism tested	Ref #
Erysodine	Neuronal Nicotinic Receptor Inhibition	IV Rat	0.3-10 mg/kg 0.32-32 mg/kg	Active Active	Blocked nicotine receptors; competitive antagonist. Reduced nicotine self-administration and lowered break points.	AX1007
Erysodine	Neuronal Nicotinic Acetylcholine Receptor Inhibition	Not stated	Not stated	Active	Inhibited cytosine binding at neuronal nicotinic acetylcholine receptors. A competitive reversible antagonist of nicotine-induced dopamine release from striatal slices and nicotine-induced 86Rb+ efflux from IMR-32 cells.	AX1008
Erysodine	Neuronal Nicotinic Acetylcholine Receptor Inhibition	Oral Mice	Not stated	Active	Attenuated nicotine's hypothermic effects and its anxiolytic-like effects in the elevated plus-maze test. Prevented early developing decrease and the late-developing increase in locomotor activity produced by nicotine. Crosses the blood brain barrier.	AX1008
Erycristagallin	Antibacterial Activity	Agar Plate	MIC=3.13-6.25 mcg/ml	Active	Staphylococcus aureus, methicillin-resistant.	AX1005
Lectin	Neurotransmitter Inhibition	Bound to clostridial neurotoxin Cell Culture	Not stated	Active	Selective for nociceptive afferents.	AX1006
Lectin	Neurotransmitter Inhibition	Bound to clostridial neurotoxin. In vivo	Not stated	Active	Attenuated sensory transmission form nociceptive afferents through the spinal cord.	AX1006
Lectin	Agglutination Activity	in vitro	Not stated	Active	Agglutination of sperm.	AX1016
Oleanolic acid	Antitumor Activity	Cell Culture	IC50=60 micromol/L	Active	Human colon carcinoma cell line HCT15.	AX1009
Oleanolic acid	Hepatoprotective Activity	Mice	Not stated	Active	Pre-treatment protected against CCl(4)-induced hepatotoxicity.	AX1013
Oleanolic acid	Anti-ulcer Activity	Oral Rat Oral Mice	50 mg/kg 100 mg/kg 200 mg/kg 200 mg/kg	Active Active Active Active	Inhibited gastric lesions induced by ethanol, aspirin and pylorus ligation; comparable to ranitidine (50 mg) and omeprazole (100 & 200 mg). Inhibited HCl-ethanol-induced ulcers.	AX1011

Oleanonic acid	Anti-inflammatory Activity	Mice Cell Culture (rat leukocytes)	Not stated IC50=17 microM	Active Active Active Active	Vs 12-deoxyphorbol-13-phenylacetate induced ear edema. Vs. TPA-induced dermatitis. Vs. bradykinin and phospholipase A2-induced paw edema. Inhibited the production of leukotriene B4.	AX1012
Oleanolic acid	Nuclear factor-kappa B Activation	Cell Culture	Not stated	Active	Activated the protein/DNA binding of NF-kappaB resulting in increased production of nitric oxide and TNF-alpha.	AX1014
Oleanolic acid	Antitrypanocidal Activity	in vitro	MC100=250 mcg/ml	Active	<i>Trypanosoma cruzi</i> .	AX1015
Oleanolic acid	Urease Inhibition	Not stated	Not stated	Inactive		AX1010
Oleanolic acid	Beta-lactamase Inhibition	Not stated	Not stated	Inactive		AX1010
Oleanolic acid	Acetyl cholinesterase Inhibition	Not stated	Not stated	Inactive		AX1010
Oleanolic acid	Alpha-glucosidase	Not stated	Not stated	Active		AX1010

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AX1012	OLEANONIC ACID, A 3-OXOTRITERPENE FROM PISTACIA, INHIBITS LEUKOTRIENE SYNTHESIS AND HAS ANTI-INFLAMMATORY ACTIVITY. GINER-LARZA, EM: MANEZ, S: RECIO, MC: GINER, RM: PRIETO, JM: CERDA-NICOLAS, M: RIOS, JL: EUR J PHARMACOL 428 1: 137-43 (2001) (DEPT DE FARMACOLOGIA, FACULTAT DE FARMACIA, UNIVERSITAT DE VALENCIA, BURJASSOT, SPAIN)
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AX1015	URSOLIC ACID AS A TRYPANOCIDAL CONSTITUENT IN ROSEMARY. ABE, F: YAMAUCHI, T: NAGAO, T: KINJO, J: OKABE, H: HIGO, H: AKAHANE, H: BIOL PHARM BULL 25 11: 1485-7 (2002) (FACULTY OF PHARMACEUTICAL SCIENCES, FUKUOKA UNIVERSITY, FUKUOKA, JAPAN)
AX1016	METHOD OF USING LECTINS FOR CONTRACEPTION AND PROPHYLAXIS AGAINST DISEASES TRANSMITTABLE BY SEXUAL CONTACT AND CONDOM CONTAINING LECTINS. OLDHAM, MJ: ROSE, BF: KRIVAN, HC: LEGERE PHARMACEUTICALS, LTD. US PATENT #6,074,671 (2000)

Clinical Research

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Effect of acute treatment with a water-alcohol extract of *Erythrina mulungu* on anxiety-related responses in rats.

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We investigated the effect of acute oral treatment with a water-alcohol extract of the inflorescence of *Erythrina mulungu* (EM, Leguminosae-Papilionaceae) (100, 200 and 400 mg/kg) on rats submitted to different anxiety models: the elevated T-maze (for inhibitory avoidance and escape measurements), the light/dark transition, and the cat odor test. These models were selected for their presumed capacity to demonstrate specific subtypes of anxiety disorders as recognized in clinical practice. Treatment with 200 mg/kg EM impaired avoidance latencies (avoidance 1 - 200 mg/kg EM: 18 +/- 7 s, control group: 40 +/- 9 s; avoidance 2 - 200 mg/kg EM: 15 +/- 4 s, control group: 110.33 +/- 38 s) in a way similar to the reference drug diazepam (avoidance 1: 3 +/- 0.79 s; avoidance 2: 3 +/- 0.76 s), without altering escape. Additionally, the same treatments increased the number of transitions (200 mg/kg EM: 6.33 +/- 0.90, diazepam: 10 +/- 1.54, control group: 2.78 +/- 0.60) between the two compartments and the time spent in the lighted compartment in the light/dark transition model (200 mg/kg EM: 39 +/- 7 s; diazepam: 61 +/- 9 s; control group: 14 +/- 4 s). The dose of 400 mg/kg EM also increased this last measurement (38 +/- 8 s). These results were not due to motor alterations since no significant effects were detected in the number of crossings or rearings in the arena. Furthermore, neither EM nor diazepam altered the behavioral responses of rats to a cloth impregnated with cat odor. These observations suggest that EM exerts anxiolytic-like effects on a specific subset of defensive behaviors, particularly those that have been shown to be sensitive to low doses of benzodiazepines.

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Cytotoxic and DNA interaction activities of extracts from medicinal plants used in Argentina.

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Eight crude extracts from seven Argentine plants with cancer-related ethnobotanical uses have been subjected to a bioscreening study to detect cytotoxic activity. The plants studied were: *Aristolochia triangularis*, *Baccharis grisebachii*, *Bolax gummifera*, *Eupatorium hecatanthum*, ***Erythrina crista-galli***, *Pterocaulon polystachium* and *Salpichroa organifolia*. Crown gall tumour inhibition, DNA interaction and cytotoxicity towards KB cells were assayed using the potato disc, the DNA-methyl green (DNA-MG) and the KB cells cytotoxicity bioassays respectively. The results obtained indicate that *A. triangularis* (ED₅₀=47 microg/ml), *B. gummifera* (ED₅₀=32 microg/ml) and *E. hecatanthum* (ED₅₀=35 microg/ml) contained cytotoxic compounds against KB cells. All of the plants studied inhibited the growth of crown gall tumours, showing correlation between the experimental data and the uses reported for these plants. Moreover, the results obtained for the extracts of *E. hecatanthum* and *P. polystachium* indicate the presence of compounds that interact with DNA (48 and 22% of absorbance decrease, respectively). The results obtained suggest that cytotoxicity could play an important role in the activities claimed for the plants under study.

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Biosynthesis of *Erythrina* alkaloids in *Erythrina crista-galli*.

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A precursor application system was developed to allow the study of *Erythrina* alkaloid formation in *Erythrina crista-galli*. Fruit wall tissue of this species was recognized as the major site of alkaloid biosynthesis. The application of radioactively and ¹³C-labelled potential precursors showed that the hitherto assumed precursor (S)-norprotosinomenine was not incorporated into the *Erythrina* alkaloids. In contrast,

(S)-coclaurine as well as (S)-norreticuline were metabolized to erythraline and erythrine, respectively, suggesting that a coclaurine-norreticuline pathway is operative in Erythrina alkaloid formation. Feeding of [1-¹³C]-labelled (S)-norreticuline with subsequent NMR spectroscopy demonstrated that the resulting erythraline was exclusively labelled at position C-10. Therefore, the participation of a symmetrical intermediate of the diphenoquinone type in Erythrina alkaloid biosynthesis can be excluded.

Psychopharmacology (Berl) 2000 Feb;148(3):234-42

Effects of the competitive nicotinic antagonist erysodine on behavior occasioned or maintained by nicotine: comparison with mecamlamine.

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RATIONALE: The cellular effects of nicotine underlying its addictive liability are thought to be mediated by neuronal nicotinic receptors (nAChRs) in the central nervous system. It is believed that densely expressed beta2-containing nAChRs in the central nervous system are responsible for these actions, but few data are available that can directly assess subtype mediation of nicotine's acute subjective and reinforcing effects. **OBJECTIVE:** The present study compared the effects of the competitive nAChR antagonist erysodine and the noncompetitive antagonist mecamlamine in rats trained to discriminate or self-administer nicotine. **METHODS:** Adult male rats were trained to discriminate 0.4-mg/kg injections of nicotine from vehicle in a two-lever procedure of food-maintained behavior, or to self-administer 0.03-mg/kg injections of nicotine under fixed-ratio 5 or progressive-ratio schedules of reinforcement. Additional rats were trained under a food-maintained procedure of lever pressing. **RESULTS:** Erysodine (0.3-10 mg/kg) and mecamlamine (0.1-1.0 mg/kg) blocked nicotine discrimination, although only erysodine produced the rightward shift that would be predicted of a competitive antagonist. Erysodine (0.32-32 mg/kg) and mecamlamine (0.32-3.2 mg/kg) also selectively reduced nicotine self-administration on a fixed-ratio schedule and lowered break points on a progressive-ratio schedule. **CONCLUSIONS:** Based on the known affinity of erysodine for alpha4beta2 nAChRs and its selectivity relative to alpha7 and alpha1beta1gammadelta receptors, the present data support a critical role of beta2-containing nAChR constructs in the discriminative and reinforcing actions of nicotine.

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Erysodine, a competitive antagonist at neuronal nicotinic acetylcholine receptors.

Decker MW, Anderson DJ, Brioni JD, Donnelly-Roberts DL, Kang CH, O'Neill AB, Piattoni-Kaplan M, Swanson S, Sullivan JP.

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Erysodine, an erythrina alkaloid related to dihydro-beta-erythroidine, was found to be a more potent inhibitor of [³H]cytisine binding at neuronal nicotinic acetylcholine receptors but a less potent inhibitor of [¹²⁵I]alpha-bungarotoxin binding at muscle-type nicotinic acetylcholine receptors than dihydro-beta-erythroidine. Erysodine was a competitive, reversible antagonist of (-)-nicotine-induced dopamine release from striatal slices and inhibited (-)-nicotine-induced 86Rb⁺ efflux from IMR-32 cells. Erysodine was equipotent with dihydro-beta-erythroidine in the dopamine release assay but 10-fold more potent in the 86Rb⁺ efflux assay, suggesting differential subtype selectivity for these two antagonists. Erysodine, systemically administered to mice, entered the brain and significantly attenuated nicotine's hypothermic effects and its anxiolytic-like effects in the elevated plus-maze test. There was greater separation between antagonist and toxic doses for erysodine than for dihydro-beta-erythroidine, perhaps because of erysodine's greater selectivity for neuronal receptors. In rats, erysodine prevented both the early developing decrease and the late-developing increase in locomotor activity produced by (-)-nicotine. The potent and competitive nature of erysodine's antagonism together with its ability to enter the brain after systemic administration suggest that erysodine may be a useful tool in characterizing neuronal nicotinic acetylcholine receptors.