



MEDICINAL USES OF EURYCOMA-LONGIFOLIA: A REVIEW

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ABSTRACT

Eurycoma longifolia Jack (also known as Tongkat Ali or Pasak Bumi) is a flowering plant in the family Simaroubaceae native to Indonesia and Malaysia.. Eurycoma longifolia is a small ever green tree growing to 15 meters (49 feet) tall with spirally arranged pinnate leaves 20-40 meters (8-16 inches)long with 13-41 leaflets.The flowers are diacious with male and female flowers or different trees; they are produced in large panicles each flower with 5-6 very small petals. The fruit is green ripening dark red, 1-2 cm long and 0.5-1 cm broad. The plant's pharmacological activity as such Potential Antimalarial, Aphrodisiac activity, Antitumour promoting and Antiparacytic activity, Antibacterial activity, Anti hyperglycaemic Activity, Anxiolytic Activity, and Plant growth inhibitor is attributed to various quassinoids, squalene derivatives, biphenylneolignans, tirucallane -type triterpenes, canthine-6-1, and beta - carboline alkaloids.

Keywords: Eurycoma londifolia, Antimalrial, Aphrodisiac apoptosis, Quassinoids, Biphenylneolignans. Antitumour, Antibacterial, Anti-hypirglycaermic, Anxiolytic.

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1.0 INTRODUCTION:

It is a popular herb and mainly used as aphrodisiac anti-pyretic and anti-malarial remedy. Not surprisingly village people often use it as anaphrodisiac remedy. This observation agrees with various pharmacological studies in which anti-hyperglycaemic, antimalarial, anti-proliferative, anti-schistosomal, anxiolytic and aphrodisiac activities are found in both *in vivo* and *in vitro* studies^[1] Fractions of Eurycoma longifolia Jack extracts have been shown to induce apoptosis in breast cancer cells^[2] and to be cytotoxic to lung cancer cells^[3] A decoction of the roots, root barks and bark is consumed by mouths to treat numerous conditions including diarrhoea, fever, glandular fever swelling, bleeding, dropsy, persistent cough, hypertension, relief of pain in the bone, and tertian malaria. The bark also has been used topically to treat wounds, ulcers, syphilitic sores, and headache. The plant is primarily known in commerce for its aphrodisiac properties,^[4,5] Long jack (*Eurycoma longifolia*) is believed to stimulate the production of endogenous testosterone and to reduce the levels of bound and metabolically inactive testosterone in the body^[6]. *In vitro*, ethanolic extracts of *Eurycoma longifolia* increase RCG-induced production of testosterone by rat Leydig cells^[7]. The interest in the chemistry of quassinoids has accelerated rapidly with the American National Cancer Institute findings in early 1970, showing that these compounds display marked antileukemic activity (*e.g.* bruceantin)^[8]

SOURCE: *Eurycoma longifolia* Jack (also known as Tongkat Ali or Pasak Bumi) is a flowering

plant in the family Simaroubaceae native to Indonesia and Malaysia. The author abbreviation Jack in the scientific name of the plant refers to the Scottish botanist, William Jack.

Eurycoma longifolia is a small ever green tree growing to 15 meters (49 feet) tall with spirally arranged pinnate leaves 20-40 cm (8-16 inches) long with 13-41 leaflets. The flowers are dioecious with male and female flowers on different trees; they are produced in large panicles each flower with 5-6 very small petals. The fruit is green ripening dark red, 1-2 cm long and 0.5-1 cm broad.

Chemistry

The plant's pharmacological activity is attributed to various quassinoids, squalene derivatives, biphenylneolignans, tirucallane-type triterpenes, canthine-6-1, and beta-carboline alkaloids.^[9,10]

Quassinoids

Including eurycomanol; eurycomanol-2-O-beta-D-glycopyranoside; 13 beta-18-dihydroeurycomanol; 14,15 p-dihydroxyklaineanone; and 6 alpha-hydroxyeurycomalactone have been isolated from the roots^[11,12,13,14,15].

Squalene

Squalene derivatives including eurylene; 14-deacetylene; longilene peroxide and teurilene.^[16,17]

Biphenylneolignans

including the following: 2 isomeric 2,2-dimethoxy-4-(3-hydroxy-1-propenyl)-4-(1,2,3-trihydroxypropyl) diphenyl esters; and 2



biphenyls, 2-hydroxy-3,2,6-trimethoxy-4-(2,3-epoxy-1-hydroxypropyl)-5-(3-hydroxy-1-propenyl)-bi phenyl and 2-hydroxy -3,2-dimethoxy-4-(2,3- epoxy-1-hydroxy-propyl) -5-(3-hydroxy-1-propenyn)- biphenyl^[18].

including 9,10 – dimethoxy canthin –6- one; 10-hydroxy – 9-methoxy canthin - 6 – one; 11-hydroxy –10- methoxy canthin – 6- one ; 5,9 – dimethoxy canthin –6-one; and 9 – methoxy –3-methyl canthin –5,6- dione.^[19,20]

Alkoids

CHEMICAL CONSTITUENTS FROM EURYCOMA LONGIFOLIA

(A) Eurylactone A **(1)** ^[21]

$C_{19}H_{26}O_8$; (M=382.410);
Needles (MeOH)
(MP 148-150 °C)

(B) Eurylactone B **(2)** ^[22]

$C_{19}H_{22}O_9$; (M=394.377)
Needles (EtoAc)
(MP 210-212 °C)

(C) EvryleneC-1 **(3)** ^[23];

$C_{34}H_{58}O_8$; (M 594.827)
Crystals; (MP 146-148 °C)

(D) EvryleneC-2 **(4)** ^[23];

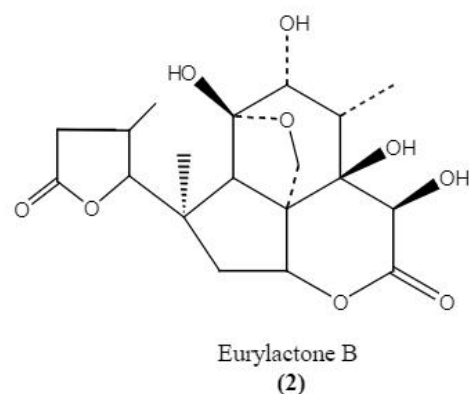
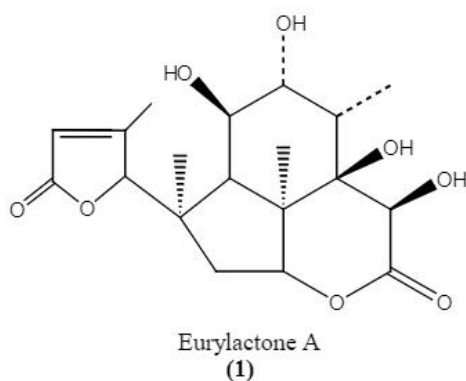
14-deAc ^[24];
 $C_{32}H_{56}O_7$; M 522.790
Needles; MP 142-143 °C.

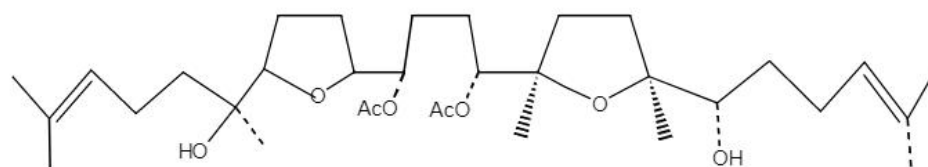
(E) Evrylactone- D **(5)** ^[25]

$C_{39}H_{22}O_9$; M 394.377
Crystal (EtoAc)
(MP 210-212 °C)

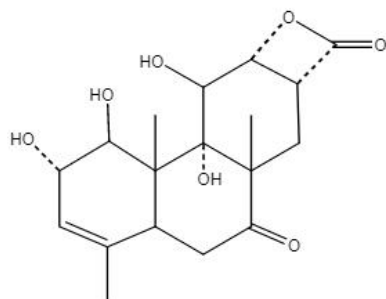
(F) Evrylactone- E **(6)** ^[25]

$C_{39}H_{26}O_7$; M 394.377
Crystal (EtoAc)
(MP 206-212 °C)

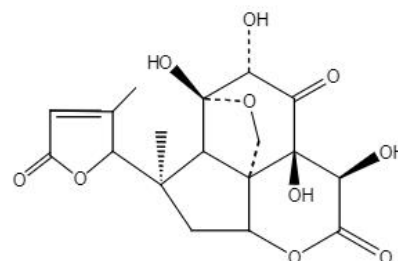




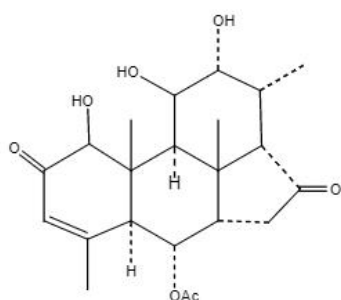
Eurylactone C-1
(3)



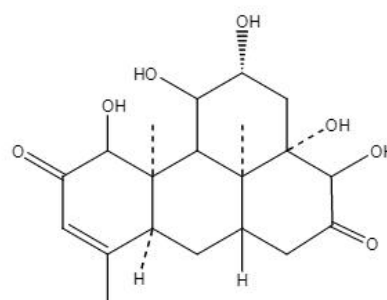
Eurycolactone C-2
(5)



Eurylactone D
(4)



Eurycolactone E
(6)



14,15-dihydroxyklaineaneone
(7)

A new C_{19} -skeleton quassinoid, named longilacton and three new quassinoid viz. 13,21- dihydroxyeurycomenone and 14,15 beta-dihydroxyklaineaneone were isolated from the roots of *Eurycoma longifolia*^[26]. 14,15 beta-dihydroxyklaineaneone (7).

TRADITIONAL USES

Established effects:

Potential Antimalarial

Several Quassinoid, eurycomanone was identified as the most potent and toxic

inhibitor or chloroquine- resistant Gombak A isolates of *Plasmodium falciparum*. Several diacylated derivatives of eurycomanone: 1,15-di-O-(3,3- di methyl acetyl) – eurycomanone 1,15-di-O-benzoyl eurycomanone and 1,15- di – O-isovaleryl eurycomanone were synthesized. These diacylated eury comanones exhibited lower anti plasmodial activity against the Gombak A isolate and lower toxicity in the brine shrimp assay when compared to eury comanone. In contrast, the monoacylated derivative displayed comparable



antiplasmodicidal potency to eurycomanone.^[27]

Aphrodisiac activity:

It increase male virility and sexual prowess during sexual activity .As such the effect of 200,400 and 800mg /kg of butanol , methanol and water and chloroform fractions of *Eurycoma longifolia* Jack were studied on the laevator animuscle in both uncastrated and testosterone –stimulated castrated intact male rats after dosing them for 12 consequitive weeks.Result showed that 800 mg/kg of butanol , methanol ,water and chloroform fraction of *Eurycoma longifolia* Comanone; 1 isovaleryl eurycomanone were synthesized.

These diacylated eurycomanones exhibited lower antiplasmodial activity against Gombak the monoacylated derivative displayed comparable antiplasmodicidal potency to eurycomanon.

UNDER INVESTIGATION:-

Antitumour promoting and Antiparacytic activity:-

Some quassinoids isolated from the leaves of *Eurycoma longifolia* Jack were subjected to *in vitro* test on antitumour promoting , and antischistosomal activities the most active compounds for induced Epstein-Barr virus activation (antitumour Promotion) was 14,15 beta-dihydroxyklaineanvne . Longilactone gave significant antischistosomal effect at a concetration of 200 microg/ml.^[29]

Jack significantly increased the laevator animuscle to 58.56+/-1.22,58.23+/-0.31,60.21+/-0.86 and 62.35+/-0.98mg/100gm body weight, respectively when compared with the control (untreated in the uncastrated intact male rats and 49.23+/-0.82,52.23+/-0.36,50.21+/-0.66and 52.35+/-0.58 mg/100gm body weight respectively, when compared to control untreated) in the testosterone –stimulated castrated intact male rats .Hence ,the proandrogenic effect as shown by this study further supported the traditional use of this plant as an aphrodisiac^[28].

Antibacterial activity:-

The Study took place in the Laboratory of Molecular Biology of Biotechnology Engineering Department, Malaysia between Jan 2005 and June 2006. The alcoholic and acetone extract of the leaves and stem extracts were active on both Gram – positive and Gram – negative bacteria (*Escharicha coli* and *Salmonella typhi*). The root extract had no antibacterial activity against Gram-positive and Gram –negative bacteria tested. Aqueous leave's extract showed antibacterial activity against *Staphylococcus aureus* and *Serratia marscesens*.^[30]

Anti hyperglycaemic Activity-

Screening of aqueous extract of *Eurycoma longifolia* (TA-a and TA-b) to determine their blood glucose lowering effects were conducted in normoglycaemic and streptagocin-induced hyper glycaemic rats. In the administration of TA-a and TA-b



positive results were obtained when 150mg/kg Body weight of the aqueous extract was used.^[31]

Anxiolytic Activity-

The anxiolytic activity of *Eurycoma longifolia* Jack in mice was examined. Fractions of *Eurycoma longifolia* Jack extract produced a significant increase in the numbers of square crossed [control = 118.2±10.2 square], but significantly decreased both the immobility [control= 39.4±4.0 sec] and fecal pellets (control =12.3±2.1 fecal pellets) when compared with control mice in open field test. In addition, these results were found to be consistent with anxiolytic effects produced by the diazepam. Hence; this study supports the medicinal use of this plant for anxiety therapy.^[32]

Plant growth inhibitor

Seven quassinoids including a new 12- epi – 11- dehydroklaineaneone were isolated from the leaves of *Eurycoma longifolia* as plant growth inhibitor. The strongest activity was found in 14, 15 beta- dihydroxyklaineaneone.

Induction of apoptosis-

The present study investigated the effects of roots extracts and their chromatographic fraction from the root of *Eurycoma longifolia* on the growth of a human breast cancer cell line MCF-7. Data indicated that *Eurycoma longifolia* extracts and fraction exert a direct antiproliferative activity on MCF-7.

*Genetic diversity of *eury coma longifolia* inferred from single nucleotide polymorphism

Widespread harvesting of wild grown trees has led to rapid thinning of natural population, causing a potential decrease in genetic diversity among *Eurycomalongifolia*. Suitable genetic marks would be very useful for propagation and breeding programmes to support conservation of this species although no such marker currently exist. To meet the need, a genome complexity reduction strategy to identify a series of single nucleotide polymorphism (SNPs) within the genomes of several *Eurycoma longifolia* access has been applied. Occurance of these SNPs reflects the geographic origin of individual plants and can distinguish different natural population.^{[33], [34]}

CONCLUSION-

The alcoholic and acetone extracts from leaves and stem of *Eurycoma longifolia* containing potent antibacterial agent (s). This plant can serve as a potential source of anti bacterial compound. The plant is actually native to Malaysia and is widely used as an aphrodisiac than anti malarial, although both of these activities, viz-aphrodisiac and anti malarial have been established. Some other activities as described above have some ground of small or occasional researches on which they stand. Some more activities like antipyretic, glandular swelling, bleeding dropsy and



persistent cough are yet to be explored further more deeply. These activities are available on bases of weather accidental use or something else and needs a solid base of research, both *in vivo* and *in vitro*, studies.

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