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# The Utilization of Pasak Bumi Plants (*Eurycoma longifolia Jack.)* as Traditional Medicine and Its Bioactivity

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**A B S T R A C T**

Pasak bumi (*Eurycoma longifolia Jack*.) is a species belonging to Simarobuaceae that has been long used as traditional medicine, which is known very well as an aphrodisiac. The studies have been conducted to reveal the benefits of E. longifolia through ethnobotany, phytochemical, and bio essay approaches, but the review articles on its utilization and bioactivity are limited. This article is based on scientific articles published online or offline, then synthesized so that to be information on the relationship between use and bioactivity. Ethnobotany of E. longifolia has been used as a medicine for fever, malaria, improved stamina, diabetes, cancer, aphrodisiac, and erectile dysfunction. The bioactivity of E. longifolia is antiosteoporotic, antimicrobial, aphrodisiac, anticancer, angiogenesis, and hepatoprotective. Eurycomanone is a secondary metabolite in E, longifolia has activity as an antimalaria, antipyretic, aphrodisiac, and cytotoxic. The quassinoids, coumarin, and glycosides of El have activity increase the production, quality, totality, synthesis, and release of spermatozoa. Eurycoma longifolia is very potential to be developed as an antiosteoporotic and a prosidiac drug, but until now most of it is harvested directly from the forest, so to preserve it, we need to study the cultivation method.

## 1. Introduction

*Eurycoma longifolia* (El) is a plant that has long been used in traditional medicine, especially for people living in Southeast Asia and South Asia, including Indonesia. The vernacular names El among others: stick ali, bitter antidote, bitter powder, stick king, earth petala, earth peg, earth support, cay ba binh, and plaa-lai-pueak. For Indonesians, El is better known as peg Bumi because it has roots that resemble pegs/poles with little or no branching, while for Malaysians it is known as Tongkat ali, which has a connotation similar to male genitalia.

The existence of El has begun to be difficult to find in North Sumatra due to trade or overexploitation, however, the Batak Toba sub-ethnic group in Peadungdung village has started planting it in their yards so that it is easier to access this plant. All parts or organs of El are used as medicine from the roots to the seeds, which has implications for their sustainability. For the Toba Batak ethnic community in North Sumatra, El is also used as a bioindicator, namely as an indication of infertile land so that it is not suitable for use as agricultural land.

The North Sumatra Batak ethnic group has long used El as drugs for malaria, fever, energy booster, drugs for dysentery, fever, malaria, sexual disorders including male infertility for local communities in Malaysia, antimalarials, antidiabetic, anticancer, and aphrodisiac. El can be consumed by combining its extracts in food or in drinks such as tea and coffee for the people of Malaysia and also the Batak ethnic group in Peadundung village is used it as "tea" after activities

in the fields. El root is used to restore energy and vitality, increase blood flow, and is used for postpartum. Although local communities in Indonesia have long used El, their research is mostly carried out by researchers in Malaysia so El is often called "Malaysian ginseng".

The use of plants as medicine is related to their bioactive compounds and most plants produce bioactive compounds that vary from one organ to another. El root contains the main content of eurycomanone, quassinoids, coumarin and glycosinate, phenolic compounds, tannins, eurycomanone, eurycomanol, eurycomalactone, canthine -6-one alcaloid 9-hydroxy canthin-6-one, 14,15β dihydrokxyklaneanone, quassinoids, and triterpenes. El has bioactivity as antiosteoporosis, anticancer, antiproliperasi, antimalarial, antimicrobial, antioxidant, aphrodisiac, anti-inflammatory, antidiabetic, antirheumatic, and antiulcer.

Empirically, it can be seen that there are still many people who are confused about the efficacy and effectiveness of traditional medicines. This is related to the assumption that the efficacy of traditional medicinal plants is only based on empirical evidence without being supported by scientific evidence, even though scientific research is also being carried out to develop traditional medicinal plants. This article will discuss the relationship between the use of EL and its bioactivity so that it becomes information for the development and use of EL in traditional medicine as well as modern medicine.[1-6]

**Botanical *Eurycoma longifolia***

Eurycoma longifolia is one of the species used as a medicine that comes from the Simaroubaceae family. Eurycoma distribution is limited in Southeast Asia, however, some researchers claim it is also found in South Asia. E. longifolia and E. apiculata are two species that are widely used in medicine, with relatively the same distribution. However, El is found up to an altitude of 1000 m above sea level while E. apiculata is found up to an altitude of 1200 m above sea level. This plant is actually easily found in primary and secondary forests on the island of Sumatra, including North Sumatra. The local Toba Batak ethnic community in Peadundung, El is used as a bio-indicator to show acidic soils with good drainage. Physta is an exclusive product containing freeze-dried water extract from El, which is traditionally used as an energy booster and apropos in Malaysia. Aphrodisiacs are compounds used to increase libido.[7-9]

The Batak ethnic group knows El as bulung besan (Karo), tongkat ali (Phakpak), horis kotala (Simalungun), tengku ali (Toba), and ampahan gunjo (Angkola-Mandailing). El is distributed in parts of South Burma (Myanmar), Indo-China (Cambodia, Laos and Vietnam), Thailand, Peninsular Malaysia, Sumatra, Kalimantan, and the Philippines.

El can grow to be up to 10 m tall with very few branches. The leaves are up to 100 cm long and green in color. The leaves are pinnate (paired) and lanceolatus to obovate-lanceolatus with a size of 5-20 cm x 1.5-6 cm. Petal lanceolatus to ovate or obovate (Figure 1). Diocese flowers with ovoid-shaped fruit turn dark brown when the fruit ripens.

For the people of Malaysia, El is one of the most important among many medicinal plants and has been developed into a variety of easy-to-use medicines. Although, El is one that has been bought and sold in Malaysia and is declared an aprosidic drug. The study reported that herbal medicinal products (HBP) which were stated to contain El extract, turned out that 27% of the 37% of HBP studied were fake. Furthermore, Abubakar et al. (2018) stated that DNA bar-coding with ITS2 barcodes can be used as the first screening step for HBP testing containing El.[6-9]

**Benefits and bioactivity**

*Eurycoma longifolia* has long been used as traditional medicine, therefore herbal medicinal products (HMP) containing El are easily found in the market in the form of raw crude root powder (root powder) or capsules, tablets, or a mixture of tea with coffee in Malaysia and markets in North Sumatra. Ethnobotanical, El is used as a medicine for malaria, fever, aprodisiac, anti-diabetic Mellitus, anticancer,

overcome erectile dysfunction, improve sexual function and increase spermatogenesis. Based on the results of research in the El laboratory, it has bioactivity as antiosteoporosis, anticancer, hepaprotective, antimicrobial, antiaging, and aprosidiac.[10-13]

**Antiosteoporosis**

Osteoporosis is a serious health problem associated with aging which is characterized by a decrease in bone density or density. Steroid sex hormones are thought to play an important role in the development and maintenance of the bone system in humans and animals, so hormone reduction is directly or indirectly related to osteoporosis in humans. A decrease in estrogen in women leads to a rapid reduction in bone density, while a decrease in the hormone estrogen in men induces osteopenia.[9-12]

Hypogonadism or reduced androgen levels is associated with lower bone mineral density and an increased risk of fracture. The main causes of osteoporosis in men are divided into primary causes (age-related and idiopathic osteoporosis) and secondary causes (alcohol abuse, excess glucocorticoids, and hypogonadism). Various drugs used in the treatment of osteoporosis, especially estrogen replacement therapy with bisphosphonates, selective estrogen receptor modulators, and calcitonin, however, have side effects, such as breast cancer, hypercalcemia, and hypertension.[13,14]

Eurycoma longifolia can be used as an alternative treatment to prevent and treat male osteoporosis without causing side effects associated with testosterone. Improving bone regeneration on the one hand and suppressing osteoclast differentiation on the other hand may have great therapeutic value in treating osteoporosis and other erosive bone diseases such as rheumatoid arthritis and metastases associated with bone loss. El extract supplementation increases testosterone levels which may contribute to reducing bone damage. El bioactive compounds that inhibit El include eurypeptides, glycosaponins, and eurycomanone. Based on the histomorphometric index, the standardized extract of quassinoid El has the same effect as testosterone in reducing degenerative changes in the osteoporosis model of bone caused by androgen deficiency, through inhibition differentiation, maturation, and osteocast function.[15-17]

**Anticancer**

Cancer is the uncontrolled growth of cells and is one of the main causes of human death. Various compounds are extracted directly from plants and some of them have been commercialized such as taxol, vinblastine, and vincristine. Even so, the exploration of plants that have the potential to act as anticancer continues, including El. The basic principle of anticancer compounds is compounds that can inhibit cell division. Eurycomanone is the main compound in EL affecting the expression of various cellular proteins and many of these proteins have multiple functions in cell proliferation and survival and are associated with cancer development and metastasis. Eurycomanone induces apostosis and decreases antiapoptotic protein. Based on the bioessay study stated that El extract has activity as an anticancer compound, especially in lung cancer with multi-target activity in inhibiting the proliferation of lung cancer cells. El root extract induces apoptosis in a dose and time-dependent manner. Euryco- manone inhibits the proliferation of lung cancer A549 cells ranging from 5 to 20 µg / ml. The concentration that inhibits 50% cell growth (GI50) is 5.1µg / ml, however, the antiproliferative effect was not completely reversible following the removal of eurycomanone.[18-19]

Flow cytometry was used to measure apoptosis and cell cycle resistance. The El root extract showed various levels of growth inhibition with IC50 values of 19.55 and 62 mg/ml, respectively. Root extracts hold the cell cycle in the G1 and S phases. Administration of El extract intraperitoneally (50 mg/kg) resulted in significant growth inhibition of subcutaneous tumors compared to control mice. The El root extract showed strong anti-proliferative activity in in vitro and in vivo models of the K-562 leukemia cell line.[16-18]

**Hepatoprotective**

Various chemicals cause liver damage and to protect the structure and function of the liver, a hepatoprotective compound is needed. In laboratory experiments, carbon tetrachloride (CCl4) was used to induce acute hepatotoxicity in rats. El is not hepatoxic and has heterotactic activity against CCl4-induced hepatotoxicity and does not result in side effects such as anorexia, hypoplasia, or weight loss. In mice given El at low (300 mg/kg) and moderate (750 mg/kg) doses, CCl4 was found to induce moderate inflammation, fatty acid changes, and transient hepatic necrosis at high doses (1500 mg/kg), CCl4 induces severe inflammation, fatty acid changes, and hepatocyte necrosis. The increase in serum total bilirubin (moment) caused by CCl4 was not significantly reduced by all El doses. Animals treated with CCl4 alone and in groups treated with CCl4 and dose El had decreased bodyweight, diet, and water intake. In the El 750 mg/kg treatment group, there was no reduction in body weight, dietary, and water intake. EL administered alone does not cause liver toxic effects but, in combination with CCl4, appears to synergize the CCl4-induced hepatotoxicity which increases as the El dose is increased.[18-20]

**Antimicrobial**

Various types of diseases and food damage are caused by bacteria, fungi, and protozoa. Antimicrobial compounds are compounds that inhibit microbial growth, through the destruction of cell walls and inhibit protein synthesis. Various types of plants have long been used as an antimicrobial including El. Methanol extract, acetone, ethyl acetate, chloroform, and petroleum ether extract from the stem and roots of El have antimicrobial activity. El extract at a concentration of12.5-200 µg/µl with the disc diffusion method inhibited the growth of gram-positive bacteria, gram-negative bacteria, and fungi. The antibacterial activity of root and stem extracts El depends on the dose, but in general, the highest antibacterial activity against Gram-positive bacteria. The difference in antibacterial activity in bioactive compounds is influenced by the structure of the bacterial cell wall. Gram-negative bacteria have lipopolysaccharides in the outer membrane which acts as a permeability barrier and limits the diffusion of active compounds. Gram-positive bacteria allow direct contact of the extract constituents with the phospholipid bilayer of the cell membrane, causing either increased ion permeability, leakage of vital intracellular constituents, or damage to the bacterial enzyme system. The ability of El extracts to inhibit microbial growth depends on the concentration, organs, and materials used in the extraction. El stem extract was stronger than root extract against Bacillus cereus and Staphylococcus aureus. Ethyl acetate extract from the stem showed moderate activity against gram-negative bacteria, Pseudomonas aeruginosa, and high activity against the fungus, Aspergillus niger. El root extract has activity against Toxoplasma gondii. Toxoplasma gondii given El extract showed cell wall changes with invagination followed by wall damage and decreased cytoplasmic volume, structural disorganization of the cell cytoplasm, and destruction of organelles 12 hours after administration of the extract.[17-21]

**Aphrodisiac**

The use of El as aphrodisiacs is more prominent than other uses. The people of Southeast Asia have long used El to overcome sexual dysfunction and infertility and South Asia. El root extract has been recognized for its aphrodisiac and anabolic properties. The decrease in testosterone concentration usually occurs in adult men aged 40 years and over. The glycopeptides in the aqueous extract of El are responsible for the aphrodisiac and fertility-enhancing effects. Mice given the El extract (8 mg/kg - 500 µg / kg BW) intramuscular showed significantly higher sperm count and sperm motility when compared to the control group.

Twenty-four adult male albino rats with Wistar strain were divided into 3 groups; control, group A, and group B. Group A received 5 mg/kg twice daily from pure El root extract, while group B received 10 mg/kg twice daily from the same extract for 6 weeks.

The serum testosterone level was significantly higher in group B than in control and group A, while group A did not show any statistically significant difference compared to control. El root extract can significantly reduce serum leptin levels due to an increase in serum test levels. Consumption of EL also causes a significant reduction in total body weight which points to a possible reduction in body fat content.[17-21]

Standardized and water-soluble extracts of El root increased male fertility associated with higher semen volume, sperm concentration, percentage of normal sperm morphology, and mate sperm motility of sub-fertile male partners with idiopathic infertility. A total of 350 patients were given 200 mg of El extract and analyzed for daily semen and follow-up was done every 3 months for 9 months. Of these 350 patients, 75 patients completed a full 3-month cycle. Follow-up semen analysis in this patient showed significant improvement in all semen parameters. El's extract significantly improved sperm quality in these patients, allowing 11 (14.7%) spontaneous pregnancies. EL is known as an aphrodisiac and drug to increase male libido. In the 12-week study, 109 men between the ages of 30 and 55 were given 300 mg of an aqueous extract of El root. The group given El showed higher scores in overall erectile function, sexual libido (14% at week 12), SFA with 44.4% sperm motility, and 18.2% semen volume at the end of treatment.[21,22]

**Angiogenesis**

Apoptosis is a programmed cell death process and one of the biological mechanisms involved in the aging process and cell degeneration. Caspase3 is an enzyme that plays a role in activity in cellular apoptosis. Angiogenesis is an excellent strategy to combat angiogenesis-dependent pathophysiologies such as cancer, rheumatism, obesity, systemic lupus erythematosus, psoriasis, proliferative retinopathy, and atherosclerosis. El root can be used as an alternative medicine to prevent and treat angiogenesis-related diseases.

The quassinoid-rich El extract caused significant suppression in the budding of small blood vessels in the rat aorta with IC50 (11.5 µg / ml). The quassinoid-rich El extract (50 µg / ml) showed remarkable inhibition (63.13%) of neo-vascularization in the allantoic chorion of the chicken embryo membrane. In vitro, quassinoid-rich El extracts significantly inhibited major angiogenesis steps such as proliferation, migration, and differentiation of human umbilical vein endothelial cells (HUVEC). Elangiogenic activity may be due to its inhibitory effects on endothelial cell proliferation, differentiation, and migration that can be attributed to quassinoids.[21-23]

Figure 1. The shoot (shoot) of *Eurycoma longifolia Jack* with compound leaves.

## 2. Conclusion

*Eurycoma longifolia* produces various secondary metabolites, eurycomanone, coumarin, and quassinoids. Eurycomanone has activity as an anti-malarial drug, antipyretic, aphrodisiac, and cytotoxic activity, while quassinoids and coumarin, and glycosides can increase the production and quality of spermatozoa in the form of morphology and motility and also increase the synthesis and release of testosterone in male cells. To overcome infertility El can be consumed orally. The bioactivity of El has been tested as antiosteoporotic- sis, antimicrobial, afrosi-deac, anti-cancer, angiogenesis, and hepatoprojective.

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