APHRODISIAC PROPERTY AND ANTI TUMOR AGENT OF EURYCOMA LONGIFOLIA JACK (TONGKAT ALI)

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Eurycoma longifolia Jack, identified by its local name as Tongkat Ali is commonly found along the hilly jungle slopes of Malaysia. It has gained notoriety as a male aphrodisiac among malaysian since it is reputed to increase male sexual. In this present study, sexual attractiveness test showed that *E. longifolia* increased the sexual behaviour with regard to the lesser time taken for the male to copulate the estrus female. It was showed that *E. longifolia* aqueous extract increased the sexual activities in a dose and time dependent manner. The aqueous extract of *E. longifolia* also increased sexual responsiveness of female rats by decreased the time taken for the female rats to copulate towards the male rats. This study provides evidence that the aqueous extract of *E. longifolia* acts specifically on sex hormones, neurotransmitter nitric oxide (NO) in penile erection and also phosphodiesterase enzymes (PDEs). The extract increased the levels of testosterone in congruence with DHT in male rats. The highest level of testosterone was observed when the extract at 90mg/kg was used. At the highest concentration used in this experiment (150mg/kg) testosterone levels 'slogged off'. In treated female rats, aqueous extract of *E. longifolia* also regulated the testosterone and DHT levels including estrogen and progesterone. *E. longifolia* was also found to maintain penile erection. This extract acts via NO and PDEs. It was increased nitric oxide synthase (NOS) expression to form NO and inhibited PDE3, PDE4 and PDE5. The antiproliferation assay showed the extract inhibited cell proliferation towards human malignant melanoma cell (HM3KO), human cervical cancer cell (Hela), human liver cancer cell (HepG2) and human ovarian carcinoma cell ($CaOV_3$). The extracts did not inhibit the cell proliferation for both normal cell lines used, human normal skin cell (CCD11114sk), and human normal liver cells, Chang's liver. Eurycomanone is a compound found in *E. longifolia*. Eurycomanone significantly increased apoptosis in HepG2 cells (3.8±0.12 μg/ml) and showed less toxicity towards both normal liver cells, Chang's liver (17±0.15 μg/ml) and WLR-68 (20±0.22 μg/ml) as compared to tamoxifen (1.4±0.31 μg/ml) and vinblastine sulfate (4.2±0.37 μg/ml). The characteristics of apoptosis including chromatin condensation, DNA fragmentation and apoptotic bodies were found following eurycomanone treatment. The apoptotic process triggered by eurycomanone involved the up-regulation of p53 tumor suppressor protein. The up-regulation of p53 was followed by the increasing of pro-apoptotic Bax and decreasing of anti-apoptotic Bcl-2. The increased of cytochrome C levels in cytosol also resulted in induction of apoptosis.

Key words: *E. longifolia*, eurycomanone, aphrodisiac, nitric oxide, phosphodiesterase, anticancer