Eurycomanone, the major quassinoid in Eurycoma longifolia root extract increases spermatogenesis by inhibiting the activity of phosphodiesterase and aromatase in steroidogenesis.

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Abstract

ETHNOPHARMACOLOGICAL RELEVANCE: Eurycoma longifolia Jack (Simaroubaceae family), known locally as ‘Tongkat Ali’ by the ethnic population, is popularly taken as a traditional remedy to improve the male libido, sexual prowess and fertility. Presently, many tea, coffee and carbonated beverages, pre-mixed with the root extract are available commercially for the improvement of general health and labido. Eurycomanone, the highest concentrated quassinoid in the root extract of E. longifolia improved fertility by increasing testosterone and spermatogenesis of rats through the hypothalamus-pituitary-gonadal axis, but the mechanisms underlying the effects are not totally clear.

AIM OF THE STUDY: To provide evidences on the plant ethnopharmacological use and the involvement of eurycomanone, the major indigenous plant quassinoid in testosterone steroidogenesis and spermatogenesis increase.

MATERIAL AND METHODS: The rat testicular Leydig cell-rich interstitial cells were isolated and incubated in the culture medium M199. The viability of the cells was determined with trypan blue staining and the concentration of the viable cells was counted with a haemocytometer. The 3β-hydroxysteroid dehydrogenase (HSD) staining method was used to measure the abundance of Leydig cells in the preparation. Eurycomanone and the standard steroidogenesis inhibitors were incubated with 1.0 × 10(5) cells, and after 2h, the testosterone and the oestrogen concentrations were determined by the ELISA method. Computational molecular docking was performed to determine the binding affinity of the compound at the respective steroidogenesis enzymes.

RESULTS: Eurycomanone (EN) significantly increased testosterone production dose-dependently at 0.1, 1.0 and 10.0 μM (P<0.05), but the two lower doses when combined with 3-isobutyl-1-methylxanthine (IBMX), the phosphodiesterase inhibitor were not significantly higher than EN or IBMX alone, except at a higher concentration. The molecular docking studies indicated EN and IBMX were binding at different sites of the enzyme. EN has no reversal of inhibition by aminoglutethimide, ketoconazole or nifedipine at the respective steroidogenesis enzyme. The quassinoid was also non-responsive to the inhibition of oestrogen receptor by tamoxifen, but displayed improved formestane inhibition of aromatase in reducing oestrogen production. The molecular docking studies further supported that EN and formestane bound to aromatase with similar orientations and free energy binding values.
CONCLUSION: Eurycomanone enhanced testosterone steroidogenesis at the Leydig cells by inhibiting aromatase conversion of testosterone to oestrogen, and at a high concentration may also involve phosphodiesterase inhibition. The quassinoid may be worthy for further development as a phytomedicine to treat testosterone-deficient idiopathic male infertility and sterility.

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