

Inhibitory effect of mitragynine on human cytochrome P450 enzyme activities

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ABSTRACT

Context To date, many findings reveal that most of the modern drugs have the ability to interact with herbal drugs. **Aims** This study was conducted to determine the inhibitory effects of mitragynine on cytochrome P450 2C9, 2D6 and 3A4 activities. **Methods and Material** The in vitro study was conducted using a high-throughput luminescence assay. **Statistical Analysis** Statistical analysis was conducted using one-way ANOVA and Dunnett's test with $P < 0.05$ vs. control. The IC₅₀ values were calculated using the GraphPad Prism 5 (Version 5.01, GraphPad Software, Inc., USA). **Results** Assessment using recombinant enzymes showed that mitragynine gave the strongest inhibitory effect on CYP2D6 with an IC₅₀ value of 0.45 ± 0.33 mM, followed by CYP2C9 and CYP3A4 with IC₅₀ values of 9.70 ± 4.80 and 41.32 ± 6.74 mM respectively. Positive inhibitors appropriate for CYP2C9, CYP2D6, and CYP3A4 which are sulfaphenazole, quinidine and ketoconazole were used respectively. V_{max} values of CYP2C9, CYP2D6 and CYP3A4 were 0.0005, 0.01155 and 0.0137 mM luciferin formed/pmol/min respectively. K_m values of CYP2C9, CYP2D6, and CYP3A4 were 32.65, 56.01, and 103.30 mM respectively. Mitragynine noncompetitively inhibits CYP2C9 and CYP2D6 activities with the K_i values of 61.48 and 12.86 mM respectively. On the other hand, mitragynine inhibits CYP3A4 competitively with a K_i value of 379.18 mM. **Conclusions** The findings of this study reveal that mitragynine might inhibit cytochrome P450 enzyme activities, specifically CYP2D6. Therefore, administration of mitragynine together with herbal or modern drugs which follow the same metabolic pathway may contribute to herb-drug interactions.

KEYWORDS

Cytochrome P450 . herb-drug interactions . luminescence . mitragynine

REFERENCES