



The Evidence for the Disturbance of Podophyllotoxin (PPT) Towards Estradiol Homeostasis

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SUMMARY. The toxicity mechanism of podophyllotoxin (PPT) remains to be unclear. The homeostasis of endogenous substances metabolism plays a key role in maintaining the healthy body. The present study aims to evaluate the influence of PPT towards the homeostasis of estradiol through investigation of PPT's inhibition towards the metabolism of estradiol. *In vitro* human liver microsomes (HLMs)-catalyzed estradiol-3-O-glucuronidation reaction was used. The results showed that 100 μ M of PPT inhibited estradiol-3-O-glucuronidation reaction activity by 81.5% at 1 μ M of estradiol. Furthermore, the experiment was performed to investigate whether the inhibition of PPT towards estradiol-3-O-glucuronidation reaction was substrate- and inhibitor-dependent. The results showed that this inhibitory behaviour was dependent on the PPT concentration, but not dependent on the concentration of estradiol. Taken together, *in vitro* evidence of PPT's inhibition towards the metabolism of estradiol was given, strongly indicating potential disturbance of estradiol homeostasis by PPT. The present study provides a new explanation for the toxicity of PPT.

KEY WORDS: Estradiol, Mechanism, Podophyllotoxin, Toxicity.

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