

Distribution of *CYP2C9* variant genes in the healthy Thai population associated with medical cannabis metabolic pathway

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ABSTRACT:

Background: Medical cannabis consists of two main cannabinoids, tetrahydrocannabinol (THC) and cannabidiol (CBD). THC is associated with numerous serious adverse events upon consumption such as respiratory, gastrointestinal, and nervous system disorders. *CYP2C9* is a major metabolizer of THC and the frequency of *CYP2C9* genotypes vary between populations worldwide. The occurrence of adverse effects (AE) can be explained in terms of *CYP2C9* gene variants in pharmacogenetics.

Purpose of study: This study aims to investigate the impact of the frequency of *CYP2C9* variants related to THC metabolic pathways in the healthy Thai population.

Method: In our research, we have recruited a set of unrelated healthy Thai subjects (n=160). Genotyping for *CYP2C9* (*2 and *3) were subsequently carried out via real-time PCR.

Results and Discussion: From this research study, we found that *CYP2C9**1 alleles is the most common form of the *CYP2C9* gene among the Thai population, comprising a percentage frequency of approximately 95.94%. *CYP2C9**3 alleles were found to occur at only 4.06%, which is significantly lower than *CYP2C9**1. However, no *CYP2C9**2 alleles were found among the Thai subjects. Furthermore, in the aspect of phenotypes and genotypes, we found that the phenotype of extensive metabolizers (EM) (*CYP2C9**1/*1, wild-type) genes have the highest frequency. Intermediate metabolizers (IM) (*1/*3) and poor metabolizers (*3/*3) were also found from the samples, respectively 6.88% and 0.62%. On the other hand, *CYP2C9* (*1/*2, *2/*2, and *2/*3) genotypes were not present. Compared to the Chinese population, the frequency of *CYP2C9**1 allele in Thais is very similar. However, the Mexican population is found to have just 82.4%. Likewise to Thais, the Chinese's *CYP2C9**2 frequency was less than 0.001 whereas Mexicans have 0.07. Our results for *CYP2C9**1/*3 and *3/*3 frequency is also similar to previous studies in Asian populations. The allelic variants *CYP2C9**2 and *CYP2C9**3 have been presented to experience decreased enzymatic activity in the THC metabolism pathway.

Conclusion: In conclusion, the distribution of *CYP2C9**3 in Thai populations might be associated with THC-induced serious adverse effects through metabolic pathways.

KEYWORDS: *CYP2C9* gene, Thai population, THC, Cannabis