Meta-Analysis of Exogenous Food Metabolites Contributing to Polymorphic Change in CYP2D6

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Introduction/Background

- CYP2D6 has been identified as the largest polymorphic cytochrome P450 enzyme in the human body. Slightly 55% of each ethnic population subtype is considered a Normal Metabolizer (NM). Star alleles associated with NM are a cytochrome P450 enzyme in the human body. Slightly 55% of most common star (*) alleles resulting in an impaired or non-functioning allele in CYP2D6 are *4, *10, *17, *29, and *41. Intermediate metabolizers (IM) or Poor Metabolizers (PM) will usually carry 1 or 2 of these alleles.

- Human CYP2D6 substrains include many exogenous substances found in fruits, oils, plants, and spices such as: alkaloids, polyphenols, tannins, terpenes, safrrole, and methyleugenol.

- Consumption of certain foods lead to the metabolism of exogenous compounds that may have altered CYP2D6 evolutionary pattern, resulting in many polymorphisms today.

Methods

- Articles were hand selected through PubMed and Web of Science databases.

- MeSH search criteria was utilized, key words such as: advantageous, Asian, African, Caucasian, CYP2D6, CYP2D, CYP450, exogenous, fruits herbs, mutation, negative, positive, spices, selection, safrrole, tannins, terpenes, and selection.

- Minimal research has been conducted on specific plant consumption on early era humans.

Results

- Upon review, 5 articles were chosen where three different compounds were selected: flavonoids, methyleugenol, and safrrole.

- One study found safrrole to have inhibitory effects on CYP2D6, along with CYP1A2, 2E1, 2A6, and 3A4. Inhibitory concentration for 2D6 were detected at 100 µM with a SD of 12 µM.

- Methyleugenol was also found to have inhibitory effects on CYP2D6, having the highest Kcat, but since the Km was found to be at 1.5 mM, low concentrations of methyleugenol would not be able to induce inhibitory effects.

Discussion

- Each compound showed limited to no inhibition as a substrate of CYP2D6, with lack of inhibition, evolution would not be favored into positive selection and not allow genetic conservation.

- Movement and trade of different spices, oils, herbs, and other luxurious foods between civilizations within the last couple of millennia do not suggest that it would be a proponent in influencing selection pressures within CYP2D6.

Conclusion

- No link was found between exogenous compounds found in foods such as flavonoids, methyleugenol, and safrrole in inducing polymorphic change within the CYP2D6 enzyme.

- It may be more of interest and better outcomes to provide more insight on early human eras when agriculture and farming was scarce.

Limitations

- Lack of articles and evidence for possible explanations of certain plants/foods which may have contributed to evolutionary shift.

- More research would need to be done on analyzing diets in earlier human eras.

References


- Darney, K., et al. (2019). Human variability in polymorphic CYP2D6 metabolism: Implications for the risk assessment of chemicals in food and emerging designer drugs. Food and Chemical Toxicology, 125, 112–123.
