## Chemical Modification of Acetaminophen to Decrease Liver Toxicity

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Each week, over 60 million individuals consume acetaminophen in the U.S. alone. Despite global reliance for its analgesic & antipyretic (pain & fever relief) properties in medications, acetaminophen toxicity causes liver damage. In fact, its toxicity is a leading cause of liver transplantation worldwide. Acetaminophen is oxidized by cytochrome p450 (CYP2EI) to toxic NAPQi. NAPQi, an electrophile, depletes glutathione and eventually attacks liver proteins, which are nucleophilic by nature. The first approach to modification that decreases toxicity without sacrificing drug efficacy, this research aims to chemically modify acetaminophen by sequential transition-metal catalysis for precise C–H silylation of acetaminophen and subsequent nucleophilic addition of an alkyne to the silicon center. Modifications were first computationally designed by quantum chemical calculations. An original reaction scheme, monitored by TLC and NMR Spectroscopy, was completed and optimized to synthesize a less toxic acetaminophen compound. The target compound, 2-phenylalkylsilyl acetaminophen, is less toxic but maintains efficacy. This is supported by the LUMO energy of this compound and because the alkyne in the compound can potentially inactivate CYP2EI to block acetaminophen's oxidation to toxic NAPQi. The research also discovered a previously unknown mechanism of transition metal-catalysts: Their chemoselectivity is consistent with the Hard/Soft Acid Base Theory. This was deduced after finding the relatively hard acid Rh preferred the hard base O (O, O acetal) whilst the relatively soft base N preferred the soft acid lir (N, O acetal) in modification. Overall, the novel compound represents a promising approach in mitigating acetaminophen toxicity.

## Awards Won:

Third Award of \$1,000 American Chemical Society: Second Award of \$3,000 The University of Texas at Dallas: Scholarship awards of \$5,000 per year, renewable for up to four years Patent and Trademark Office Society: A flag that was flown over the U.S. Capitol will be given to the top winner of this Special Award. Patent and Trademark Office Society: Top Award of \$1,000, and an American flag and a framed copy of the first patent granted in the USA

YM American Academy: Third Award of \$500.00