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The Effect of Andrographolide on the Metabolism of Carbamazepine in Rats

Elizabeth Aziz
Cedarville University, eaziz@cedarville.edu

Samuel Franklin
Cedarville University, sfranklin@cedarville.edu

Ankit Pandav
Cedarville University, apandav@cedarville.edu

Abigail Savino
Cedarville University, asavino@cedarville.edu

Caleb Thompson
Cedarville University, calebmthompson@cedarville.edu

See next page for additional authors

Presenters
Elizabeth Aziz, Samuel Franklin, Ankit Pandav, Abigail Savino, Caleb Thompson, Caleb VanDyke, Ruth Choi, and Elisha R. Injeti

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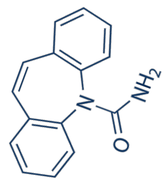
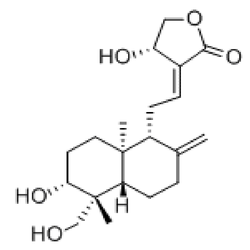


Elizabeth Aziz,[1] Samuel Franklin,[1] Ankit Pandav,[1] Abigail Savino,[1] Caleb Thompson,[1] Caleb VanDyke,[1] Ruth Choi,[1] Dr. Elisha Injeti[2]

Cedarville University School of Pharmacy
1. Student Pharmacists
2. Department of Pharmaceutical Sciences, Vice Chair & Associate Professor



STATEMENT OF THE PROBLEM

Background

Carbamazepine (Tegretol) (CBZ)

- A medication that is most commonly used as an anticonvulsant in patients who experience seizures.[1]
- Metabolized in the liver by the enzyme Cytochrome P450-3A4 (CYP3A4) and Cytochrome P450-2C8 (CYP2C8).[2,3]
  - If drugs affect CYP enzyme activity, in turn influencing how the liver metabolizes drug,; it influences how the drug functions in the body.
- Inhibitors or inducers of CYP3A4 or CYP2C8 would alter CBZ drug therapy.

Andrographis paniculata (AND)

- an inhibitor of CYP according to previous research that found it significantly decreased CYP enzyme activity.[4]
- A medicinal plant excessively used in Asian countries for the treatment of multiple ailments including fungal infections, bacterial infections, inflammatory diseases, hypertension, viral infections, and cancer.[5,6,7,8,9,10]
- AND is a widely used OTC supplement often used without the provision of a prescriber

It is necessary to study possible drug interactions with this herb. While no published studies analyze CBZ and AND coadministration, based on studies of each alone, interactions theoretically exist. This study is about the theoretical herb-drug interaction that can occur through the coadministration of AND and CBZ.

Significance of the Problem

AND and CBZ have very different uses, which might cause an individual with comorbidities to take both at the same time. Since AND is used as an OTC supplement without their prescriber's knowledge there could have drastic consequences for individuals due to possible, unknown drug interactions. As researchers have not yet studied this possibility of an interaction, it is imperative that they analyze interactions between carbamazepine and andrographolide, a goal this study seeks to fulfill.

OBJECTIVE

To determine if andrographolide impacts the pharmacokinetics of carbamazepine

HYPOTHESES

Null Hypothesis: Andrographolide will have no statistically significant impact on the pharmacokinetics of carbamazepine.

Alternative Hypothesis: Andrographolide will have a statistically significant impact on the pharmacokinetics of carbamazepine.

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ACKNOWLEDGEMENTS

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PROPOSED METHODS

Study Design

- **Study design**: Randomized Control Trial
- **Sample size:** 12 Sprague-Daley Rats
  - Control group: 6 rats receive only CBZ
  - Treatment group: 6 rats receive AND and CBZ

Days 1-7

- **Treatment group:** receives AND injection for 7 days

Day 8

- **Treatment group:** receives AND injection and after 30 minutes a CBZ injection
- **Control group:** receives CBZ injection

Sample Collection:

- Blood samples will be collected after the injection of CBZ every 20 minutes for 4 hours
- samples will be labeled and stored for measurement

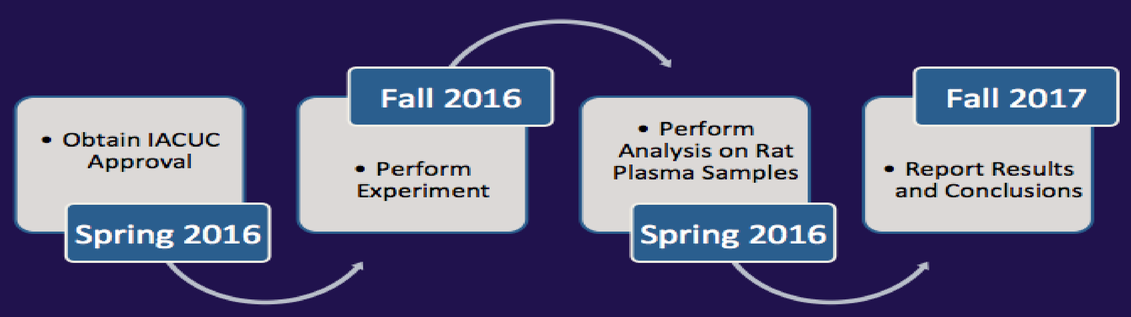
Measurement:

- samples are separated so blood plasma can be drawn out
- samples will be put through the HPLC at 1 ml/min with a wavelength of 220 nm
- mobile phase solution used will be 70:30 water:acetonitrile
- blood plasma concentration levels of CBZ of both the control group and the treatment group will be measured for statistical analysis

PROPOSED ANALYSES

HPLC will yield a time vs. plasma concentration graph that will reveal the rate of elimination (K). The mean K value will be determined for both the control and study group. The mean value of K will be compared and analyzed using SPSS utilizing an unpaired t-test, with a $p<0.05$ deemed statistically significant.

PROJECT TIMELINE



LIMITATIONS

The study has a small sample size which is not generalizable to the entire rat population. The results obtained in rat studies may not translate to human subjects.

FUTURE DIRECTIONS

The goal of this study is to contribute to the literature on andrographolide's drug interactions and to provide more information for future herb-drug interaction studies.