CALIFORNIA STATE SCIENCE FAIR
2014 PROJECT SUMMARY

Name(s)

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Project Number

S0614

Project Title

Separating Mirror Molecules: Computational Evaluation and Novel Framework for HPLC Method Development on CD Columns

Abstract

Objectives/Goals

In this study the ability of beta-cyclodextrins (ß-CD) to enantioselectively complex omeprazole enantiomers was evaluated, and from this information two equilibrium binding constants were hypothesized and used to effectively predict HPLC peak behavior in columns equipped with cyclodextrin-based stationary phases on which omeprazole is not known to have been analyzed previously. A crucial goal of this project was to produce a general framework for future HPLC method development, a process that is often both expensive and time consuming, by allowing researchers to predict optimal temperatures at which to conduct assays beforehand rather than by trial and error as is often the case.

Methods/Materials

Complexation resulted from magnetically stirring a bilayer solution consisting of cyclodextrins in water and the drug omeprazole in a non-polar solvent. The complexed omeprazole extracted from the cyclodextrin cavity was injected into SRI International's HPLC, equipped with a Chiral CD-PH column, at 25 degrees Celsius and wavelength 254.0 in a solvent system consisting of 80% methanol and 50 mM ammonium formate pH 4.

Results

Two relatively large peaks consistently eluted at approximately 10 and 11 minutes respectively. Although omeprazole has been known to degrade significantly in solution in the presence of cyclodextrins, a phenomenon that may have inhibited the use of cyclodextrin columns in the past, degradation was found to be significantly mitigated at higher pH levels approaching 10. The relative amounts of each enantiomer left uncomplexed in solution were obtained via the specific rotation measured by a polarimeter, from which two distinct equilibrium binding constants for each enantiomer were observed and were used to accurately predict differences in elution times between enantiomeric peaks within just 14.33% error. Suitable succinyl-beta cyclodextrin derivates compatible with a CM5 biosensor chip will be processed for the precise validation of determined binding constants.

Conclusions/Discussion

The remarkably accurate predictions of peak behavior that were achieved in this study using novel, low-cost methods have already laid the foundations for an extendable thermodynamic framework for efficient HPLC method development, and an inexpensive method of separation has been validated for omeprazole enantiomers as a potential means of producing relatively enantiopure drugs. Cheaper, safer drugs may soon follow.

Summary Statement

New cyclodextrin-based methods for the analysis and separation of mirror molecules were developed, both of which may significantly lower the production costs of enantiopure drugs.

Help Received

SRI International provided the HPLC; Dr. Mark Stolowitz of Stanford University provided access to a biosensor: Dr. Smriti Koodanjeri advised the project