

2012-13

RUNNER-UP

Rajnibhai V. Patel

**PharmInnova
Award**

Best M. Pharm Thesis

Runner-Up



Mr. Selim Mondal

Research Guide



Dr. Supratim Ray

Subject:

Quality Assurance

Thesis Title :

Exploring the protective effect of diverse class of antioxidants on docetaxel induced lipid peroxidation: an experimental & theoretical approach

College:

Dr B C Roy College of Pharmacy & Allied Health Sciences, Durgapur, West Bengal.

Evaluation of various antioxidants to minimize side effects of anticancer drugs

Outcome of Research

Many drugs, though highly efficient, are marked by profound and severe toxic effects and hence, are limited in their application. Lipid peroxidation is one of the most important causes of toxicity of the drug produced by changes in the lipid constituents of the membrane barrier of the cell. If this toxicity is reduced, the application and efficacy of the drug can be enhanced. This study evaluated the protective effect of twelve different antioxidants after producing lipid peroxidation by docetaxel (a cytotoxic anticancer drug). Based on the multivariate data analysis, a Structure-Activity Relationship (SAR) model was generated to correlate the protective effect of twelve antioxidant molecules.

Thesis Title: Exploring the Protective effect of Diverse Class of Antioxidant on Docetaxel Induced Lipid Peroxidation :An Experimental And Theoretical Approach

ABSTRACT

The study was designed with an aim to evaluate the protective effects of twelve structurally diverse antioxidants (ascorbic acid, BHT, BHA, hesperidin, dextrose, uric acid, flavone, naringin, caffeic acid, quercetin, morin and rutin) on docetaxel-induced lipid peroxidation. Goat liver was used as lipid source for this in vitro model of study. Goat liver was used due to easy availability and its similarity with human liver in lipid profile. Lipid peroxidation study was performed by measuring the malondialdehyde of tissue homogenates. Interpretation of the result is supported by student "t" test. Analysis of variance (ANOVA) and multiple comparison analysis using least significant different procedure were also performed. The data presented in this work demonstrate the lipid peroxidation induction potential of docetaxel and the antiperoxidative potential of various antioxidants on docetaxel-induced lipid peroxidation. BHT (-21.30%) shows highest potential and Uric acid showing (10.75%) lowest potential among the twelve antioxidants.

The lipid peroxidation inhibition potency of the twelve structurally diverse compounds was used as the response variable for subsequent QSAR analysis. Several types of topological descriptors were used to build the QSAR model. Stepwise regression and PLS were used as chemometric tools. The statistical qualities of the equations were judged by the parameters such as determination coefficient (R^2) and variance ratio (F) at specified degrees of freedom (df). The generated QSAR equations were validated by leave-one-out statistics and the calculated parameters are predicted residual sum of squares (PRESS), cross validation R^2 (Q^2) and standard deviation of error of prediction (SDEP). To better indicate both the internal and external predictive capacities of a QSAR model and to ascertain the proximity in the values of the predicted and observed response data, the rm^2 metrics (average $2()_{moverall}R^2$ and delta $2()_{moverall}R^2$) are calculated. The best equation is obtained from stepwise regression analysis considering both equation statistics and predictive ability ($R^2=0.8321$, $Q^2=0.5464$, Average rm^2 (overall) =0.6967, Delta rm^2 (overall) =0.0814).