

Effect of Food on the Absorption of Orally Administered Drugs

Oljora Rezhdo
Department of Chemical Engineering
Northeastern University
Boston, MA 02115

The oral delivery of lipophilic drugs poses a big challenge for the pharmaceutical industry because of their poor propensity to be absorbed by the gastrointestinal (GI) tract into the systemic circulation. Such a propensity is known by the term bioavailability. It is believed that the dissolution of the drug into the GI fluid is the rate-limiting step to drug absorption. Clinical tests have shown that when these drugs are taken on a fed stomach, their bioavailability increases significantly. An example of this is lapatinib, a chemotherapeutic drug released in the market in 2007. Having an extremely low bioavailability this drug is administered in high dosages in order to produce the desired therapeutic effect. However, it has aggressive side effects as it passes through the GI tract. Although it has been noticed that the drug is absorbed more easily in the presence of food it is impossible to prescribe it on a fed stomach due to the unpredictability of food effects in the drug's bioavailability. Hence, a standard theoretical and experimental model that can predict these food-drug interactions is crucial.

Previous research in our lab has demonstrated that the presence of lipids enhances drug dissolution, and in turn absorption. Moreover, a mathematical model has been developed to predict the effect of lipids on model drug compounds and can quantitatively correlate the dosage required in terms of the amount of lipid intake. A crucial determinant in the enhancement of drug dissolution and in developing the mathematical model is the understanding and quantification of the types of colloidal structures formed during digestion which serve as the drug carrier mechanism while the drug is residing in the GI tract prior to being absorbed. Since our daily diet contains a mixture of lipids, proteins, and carbohydrates it is important to understand how the conglomerate of these components aids drug absorption.

Proteolysis and lipolysis experiments of protein emulsions in the literature have demonstrated the existence of new types of colloidal structures that are not present in purely lipid based systems which could alter the drug dissolution and absorption profile. However, to date no concurrent in-vitro proteolysis and lipolysis experiments have been performed, providing a leeway for neglecting other structural formations that could be relevant to drug dissolution and partitioning modeling. It is therefore crucial to understand the dynamics of the formation of such structures and the potential of new colloidal structures in the presence of additional food components such as proteins and carbohydrates.

This project aims to expand upon the currently available purely lipid based model in order to predict the effect of a mixture of all the aforementioned components in drug absorption with the intention of having a more representative food model that can better compare with the average western diet.