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Review Article

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Chemical Kinetics-A Study Determining the Transformation of a Good Food Gone Bad

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ABSTRACT

Chemical kinetics as the title suggests holds most significance in determining the efficacy of various biologically important components especially the interactions and the release of the drugs. The study holds its prominence in various fields most importantly being the formulations of new drugs. In this mini review we focus on the comparative study on drugs functioning with their kinetics known and hence to relate its significance with its reaction rates. The review is an effort to understand the reaction rates of various drugs and how this influences its release into the body.

Keywords: Pharmacokinetics; Type 2 diabetes mellitus; Raman spectroscopy; Interface-depletion sequential adsorption model; Real-time HD exchange kinetics of proteins; High performance affinity chromatography; Tandem mass spectrometry

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INTRODUCTION

Pharmacokinetics is the study which deals with the compatibility of the drug with the host. It also describes the varied routes such as absorption, metabolism, which the body undergoes when it is administered with the specific drug. The action of the drug usually takes place in the tissues or the target sites in which it is subjected to. When administered, the drug first channelizes itself into the blood (absorption) and then is transported to the particular tissue. The drug now gets an idea as to how to be metabolized by the body. After which the body catalyzes the final step called as elimination. In order to investigate the characteristics of the drug, chemical kinetics is exploited to observe the mechanisms as this depends on various factors such as genotype, response to the stimulus (the drug), phenotype etc. [1]. Recently novel approaches are developed to study the mechanism of different drugs on various syndromes. One of which is an explosion seen in the global epidemic of type 2 diabetes mellitus which comes with conditions such as vascular endothelial dysfunction. The condition comes with the dysfunction of endothelium followed by the manifestation of symptoms related to neurons. Development of drugs in the form of therapeutics for diabetic renal diseases is studied extensively to discover its kinetics [2]. This science emerges to establish vital diagnostic tools which are sensitive to develop treatment ideologies and also to diminish side effects. The need to study the kinetics of these drugs is very important as it defines the parameters in which a prescribed reaction contributing to the formation and development of the drug entering the body should possess [3]. Another most important aspect in this field is the invigilation of specific drug-target kinetics and characterization. In this case, the magnitude and the receptivity of the drug become at most important as it is the criteria to analyze the pharmacological activity. *In vitro* methods are employed to study interactions of the receptor-drug mediated equilibrium affinities [4]. Recently, studies on digestive enzymes regarding its kinetic attributes are intensively seen. This involves the determination of the kinetic processes which are required to analyze the complete digestion profile

along with the quantity of starch which is primarily involved in every process. As of now, kinetics of 4 types of amylases have been discovered namely RS1, 2, 3 and 4. These enzymes investigate the vital kinetic parameters such as determination of the rate of the reaction and the substrate-enzyme binding action [5]. Raman Spectroscopy is also an extensively used technique which is used to monitor the enzymatic assays. The results obtained through this principle prove the successful study of the kinetics of enzyme-catalyzed oxygen isotope exchange in the phosphate-water system [6]. Adsorption kinetics of different proteins on hydrophobic surfaces can be detected. Experimental evidences have been derived using serum albumin on a hexadecanethiolated gold surface. In order to elucidate sequential adsorption kinetics, new interface-depletion sequential adsorption model is developed. Interpretation of the data shows that the results can be explained on the grounds of depleting interfacial region where the flow of proteins is limited. Alongside this various other molecular dynamic studies prove the kinetics of proteins using this approach. These studies prove that the interconnection between the reduced diffusion and the adsorption rate leads to the depletion of the protein molecules in the interfacial region in which the protein concentration is found to be much lesser than the actual. This now justifies that the slow rate of the proteins [7]. Chemical kinetics is therefore a topic of broad importance as it contributes to a lot of understanding in terms of drug designing, synthesis of chemicals etc., The rate of these reactions determine an enormous range of parameters under which a reaction can function. Examples include factors which lead to food spoilage, fast setting rates of dental filling, rate at which steel rusts and so on [8]. Tandem mass spectrometry is another tool which is used extensively for investigating the identities and the sites of post-translational modifications. This approach is exploited while performing kinetic studies on the Real-Time HD Exchange Kinetics of Proteins from buffered aqueous solutions. The rate constants for HDX (hydrogen-deuterium exchange) of ubiquitin were shown to be obtained as a result of partial resolution of approximately 1.3 residues under the aid of Endothermal supercharging (ETS) HDX with NMR, thereby explaining that the high spray potentials are necessary to avoid HD scrambling and allowing ETS [9].

High- Throughput interaction Kinetics for Cyclodextrins

Determination of rate constants to evaluate the rate of various reactions is a tedious process which requires separate tests and immense data entries. These however, are not sufficient to produce the equilibrium constants and the association constants. Equilibrium constants determine the value of the reaction quotient where the reaction attains equilibrium. Investigation of such rate constants is done extensively by High Performance Affinity Chromatography (HPAC). In studying the kinetics of specific cyclodextrins, a combination of HPAC-MS/MS is employed to determine the cyclodextrin interaction kinetics with low sample loading ~10 ng per injection for individual compound. The study proved that this sample loading provided a high output which is equal to ~20 drugs. This determines that when the rate constants are known, they provide an overview regarding the output. Quantitative association and equilibrium constants can be further measured by peak profiling method. These constants are also shown to be sensitive towards the acidity and the basicity of the drugs. In this manner (Figure 1), high-throughput HPAC-MS/MS is proven to be highly efficient in the investigation of the drug- CD interaction kinetics. This now is a novel screening technique for the solubilization of cyclodextrins [10].

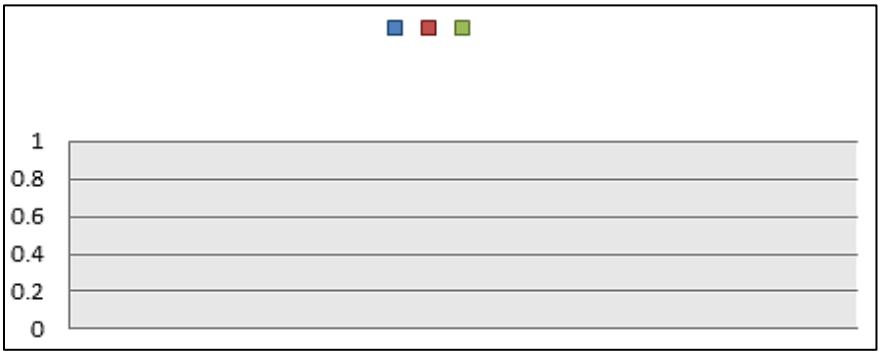

Figure 1: Graphical representation of equilibrium constants of cyclodextrins (CD)

Release Kinetics of Encapsulated Paclitaxel and its Intercellular Delivery

Naturally present halloysite tubules are highly compatible to be incorporated with drugs. This facilitates easy and safe delivery of drugs at concentrations of 0.5 mg/ml. Experiments prove that the encapsulated anticancer drug paclitaxel evaluated the release kinetics in stipulated gastric and intestinal parameters. In order to bring about maximum drug release in the intestinal region, the halloysite tubes are coated with a polymer such as methacrylic acid-co-methyl methacrylate. Results have proved that the release kinetics suggested a release pattern at higher pH.

Paclitaxel is an efficient excipient when designed as a tablet as these have a sustained drug release rate (Figure 2). Anticancer effects of paclitaxel loaded with halloysite nanotubules are also investigated on human cancer cells. These showed that such cell volumes contain chromatin and polyploid nuclei of varied sizes therefore exhibit an increased therapeutic effect of halloysite designed paclitaxel [11].

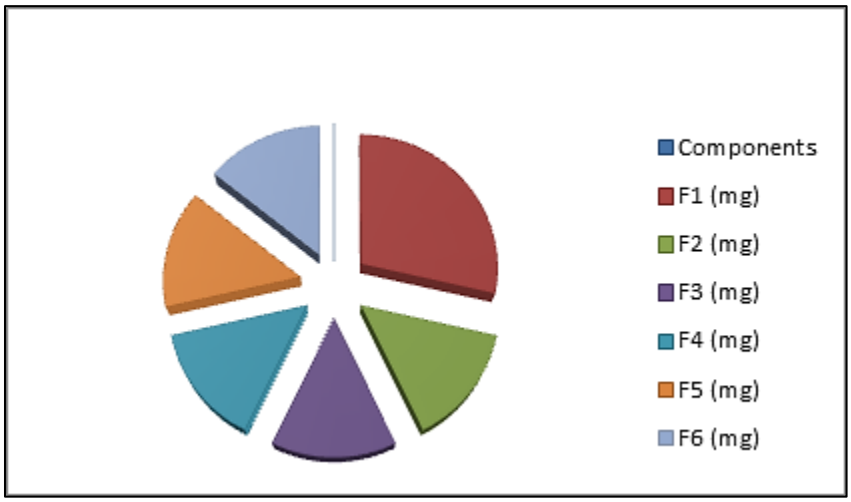

Figure 2: Pie chart representing drug release rates of paclitaxel, polycaprolactone, poly (lactic co glycolic acid)

DISCUSSION AND CONCLUSION

Kinetic multilayer model resolves chemical transformations and mass transport at the layers of the skin. It is therefore important to understand the evolution of the products under varied environmental conditions. It is observed that the ozone reacts with lipids present in the skin such as squalene, which in turn generates varied organic compounds. The method enables the determination of temporal and spatial concentrations of various labels of the skin oil present between the layers. The kinetics of ozonolysis of squalene in the gas phases when exposed to ~30 ppb ozone, showed the formation of breakdown products in an order of ~10 mmol/m^3. Ozone kinetics also showed that different concentrations can exponentially decrease due to the reactions of skin lipids. Investigations proved that ozone spontaneously react with the upper layers of the skin, hence reaching the blood [12]. This review concentrates on the chemical kinetics of some of the drugs and its applications as well as the rate at which the prescribed drug is released into the body and how different drugs react once they are entered into the body. The fashion in which the drug metabolizes once the drug enters is also understood. Kinetics of cyclodextrins in various forms have been analyzed most specifically in the formation of a water-soluble anchor dyes which act as an auxiliary unit to facilitate strong binding to macroscopic molecules. The dye is a component of 7-nitrobenzofurazan and a cluster of dodecaborate which is globular. Kinetics of this dye has shown that they present an increased sensitivity for indicator displacement advantages [13]. Drug competitions for different metabolizing enzymes are a usual mechanism for drug interaction studies. This can usually lead to altered kinetics while the drug is being metabolized. In an effort to prevent this, FDA employs methods to assay drug interactions so as to result in uniform kinetic values as this in turn contributes the rate of the reactions. Through this technique catalytic activity of CYP2C9 was investigated using high-throughput self-assembled layers of SAMDI (matrix assisted laser desorption- ionization mass spectrometry). The kinetics of CYP450 metabolism determined a set of drugs which inhibits CYP2C9 and hence determined the K_i values for the actual inhibitors. This study proves as a scaffold for drug metabolism and drug interactions to be interpreted at a prescribed scale [14]. Skin cancer represents one of the growing ailments in the world and UV radiation can be considered as the primary cause. Application of paclitaxel is considered to be one of the most significant treatments as it is recommended immensely. Kinetic studies of this drug proved to have a particle size in the range of 78.8-590 nm and the synthetic yield were found to be ~65%. *In vitro* drug release was seen to be biphasic having its effect which followed a slow release. The histopathological kinetic study proves this drug to have the highest efficacy in the treatment of cancer as the permeability quotient and the enhancement ratio using increases in every formulation [15]. Drug kinetics and ligand protein binding are gaining immense importance in drug release and formulation studies. In order to evaluate the efficacy of the drug it is very vital to study the drug profile this sometimes becomes very laborious. Over the past decade, computational techniques have been employed to provide a potential in the drug discovery process of which SAMDI is a classic example [16]. The main purpose of

this review is to summarize the state of the art of computational strategies for estimating the kinetic and thermodynamic parameters of a ligand–protein binding.

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