SYNOPSIS OF THE THESIS TO BE SUBMITTED TO KARNATAK UNIVERSITY, DHARWAD FOR THE AWARD OF DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY

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Title of the Thesis : “Synthetic, analytical and mechanistic investigations of some carbohydrates and bioactive compounds by unusual oxidants”

Registration No. : SC/2009-10/4034

Date of Registration : 26-05-2009
Kinetics studies

Kinetic studies are receiving much importance in the recent years since they provide us the most powerful method of investigating the detailed reaction mechanisms. It is one of the most intriguing and challenging areas of chemistry, which deals with the mechanisms of reactions. To many chemists the real heart of chemistry is the study of mechanisms. Thus, chemical kinetics can be defined as that branch of chemistry concerned with the study and prediction of time dependent systems. To understand the mechanism of any reaction we must know a reaction as a function of time, the exact positions of all the atoms as the reactants are converted into product molecules. Virtually all information regarding reaction mechanism comes by inference of indirect evidence. Hence, it is the important job of chemists to device the proper experiments to generate most conclusive evidence.

The experimental part of the subject deals with ways of measuring precisely the rates of reactions at various varying conditions of the experiments. The interpretation of results leads to an understanding of the mechanism of the reaction. The combination of the results of a large number of experiments gives rise to general theories of chemical reactivity. The important steps in any kinetic investigations are: (1) collection of kinetic data, (2) establishment of relationships between the rate and reaction mixture composition, (3) study of structural effects and (4) interpretation of the collected data to arrive at reaction mechanism.
Development of Analytical methods

1. HPLC Method

HPLC provides reliable quantitative precision and accuracy, along with a linear dynamic range sufficient to allow for the determination of the active pharmaceutical ingredients and related substances in the same run using a variety of detectors, and can be performed on fully automated instrumentation. HPLC provides excellent reproducibility and is applicable to wide array of compound types by judicious choice of HPLC column chemistry. Separation of chiral molecules into their respective enantiomers is possible by HPLC. This involves precolumn derivatisation to form diasteriomers or addition of the derivatization reagents to the chromatographic mobile phase to form dynamic diasteriomers during separation processes.

2. Cyclic voltammetric methods

Cyclic voltammetry is the most versatile electroanalytical techniques for the study of electroactive species. It is used in all field of Chemistry as a means of studying redox states. The electrode potential at which a drug, a metal ion or complex or some other compound undergo reduction (acceptance of electrons) or oxidation (removal of electrons) can be rapidly located by cyclic voltammetry (CV). The versatility of CV combined with its simplicity has resulted in its rapid growth in popularity.
Nano-particles

Nanotechnology wants to control the smallest structures built of atoms and molecules. It is connected with colloidal chemistry and physics, biology, medicine, pharmacy and engineering (materials and processes).

Nanoparticles are particles that have one dimension that is 100 nanometers or less in size. The properties of many conventional materials change when formed from nanoparticles. This is typically because nanoparticles have a greater surface area per weight than larger particles; this causes them to be more reactive to certain other molecules. There are number of techniques available to synthesize different types of nonmaterial in the form of colloids, clusters, powders etc in that important methods are physical, chemical, biological, and hybrid method but we have selected biological methods

In the present thesis, some redox reactions in alkaline medium have been studied. Reactions were followed conveniently by spectrophotometer in the UV-visible region. Some analytical methods like cyclic voltammetry, HPLC method and biosynthesis of Ag nano-particles were also done. The details of such studies are given below.

The thesis is divided in to three parts and is presented in seven main chapters including the general introduction.
I. **General introduction**

This chapter introduces about the kinetics, mechanism, analytical methods and biosynthesis of nano-particles of reactions in general.

**Part A: KINETICS STUDIES**

II. **Oxidation of D-Glucose by silver(III) periodate complex in presence of Ru(III)/Os(VIII) as a homogeneous catalyst: a comparative mechanistic Study**

The kinetics of the oxidation of ruthenium(III) (Ru(III)) and osmium(VIII) (Os(VIII)) catalysed oxidation of D-Glucose (D-Glu) by silver(III) periodate complex (DPA) in aqueous alkaline medium at 298K and constant ionic strength 0.003 mol dm\(^{-3}\) was studied spectrophotometrically. The reaction between DPA and D-glucose in alkaline medium exhibits 1:2 Stoichiometry in both catalysed reactions (D-Glu: DPA). The main products were identified as D-arabinonic acid and formic acid by spot test and chromatographic techniques. Probable mechanisms were proposed and discussed. The activation parameters with respect to slow step of the mechanism were computed and discussed and thermodynamic quantities were also calculated. It has been observed that the catalytic efficiency for the present reaction is in the order of Os(VIII)>Ru(III). The active species of catalyst and oxidant have been identified.
III. Mechanistic investigations of uncatalysed and ruthenium(III) catalyzed oxidation of D-mannitol by diperiodatoargentate(III) complex in aqueous alkaline medium

The kinetics of oxidation of D-Mannitol (D-Manni) by diperiodatoargentate(III) (DPA) both in the absence and presence of ruthenium(III) catalyst in alkaline medium at 298 K and at a constant ionic strength of 0.10 mol dm$^{-3}$ was studied spectrophotometrically. The reaction exhibits a 1:2 stoichiometry ([D-Manni]:[DPA] and first order in [DPA], less than unit order in [D-mannitol] in both the cases. The alkali had retarding effect and added periodate had no effect on the rate of the reaction in both the cases. The order with respect to [Ru(III)] was unity. The main products were identified by spot tests, FT-IR, LC-MS spectral studies. Based on the experimental results possible mechanisms were proposed. The reaction constants involved in the different steps of the mechanisms were evaluated. The catalytic constant ($K_C$) was also calculated for Ru(III) catalysis at different temperatures. The values of activation parameters with respect to the catalyst have been evaluated. The activation parameters with respect to slow step of the mechanisms were computed and discussed and thermodynamic quantities were also determined. Kinetic studies suggest that the active species of DPA and ruthenium(III) were found to be $[\text{Ag(H}_3\text{IO}_6\text{)}_2]^{-}$ and $[\text{Ru(H}_2\text{O})_5\text{OH}]^{2+}$ respectively.
Part B: Development of Analytical methods

IV. RP-HPLC Method for the determination of 5-Flourouracil in pharmaceutical formulations and spiked human plasma

A simple, rapid and accurate reverse phase high-performance liquid chromatographic method for the determination of 5-Flourouracil (5-FU) in pharmaceutical formulations and human plasma samples has been developed and validated. The assay of the drug was performed on a CLC C_{18} (5 \mu m, 25 cm \times 4.6 mm i.d.) with UV detection at 266 nm. The mobile phase consisted of methanol-water mixture in the ratio of 98:2, and a flow rate of 1 ml/min was maintained. The standard curve was linear over the range of 0.9-18.4 \mu g/ml \ (r^2=0.9966). Analytic parameters have been evaluated. Within-day and between-day precision as expressed by relative standard deviation was found to be less than 2%. The method has been applied successfully for the determination of 5-FU in spiked human plasma samples and pharmaceutical formulations. The method will be useful for routine quality control analysis.

V. Voltammetric oxidation and determination of 5-flourouracil and its analysis in pharmaceuticals and biological fluids at glassy carbon electrode mediated by surfactant cetyltrimethyl ammonium bromide

The voltammetric oxidation and determination of 5-Fluorouracil 5-(FU) was studied at a glassy carbon electrode (GCE) in the presence of cetyltrimethyl ammonium bromide (CTAB) by cyclic and differential pulse voltammetry at pH-7. The results indicated that the voltammetric responses of
5-Flurouracil are drastically increased in the low concentration of CTAB, suggesting that CTAB exhibits observable enhancement effect to the determination of 5-Flurouracil. Under the optimal conditions the peak current was proportional to 5-Flurouracil concentration in the range of $2.0 \times 10^{-8}$ to $6.0 \times 10^{-7}$ M with detection limit of 20.13nM by differential pulse voltammetry. The proposed method was applied to the determination of 5-Fluorouracil in pharmaceuticals. The analytical performance of this sensor has been evaluated for detection of analyte in human serum and urine as real samples.

**VI. Studies based on the electrochemical oxidation of orphendrine hydrochloride at gold electrode and its analytical applications**

This work describes a novel type of working electrode for use in voltammetric methods. The electrochemical oxidation of orphendrine hydrochloride has been investigated for the first time by cyclic, linear sweep and differential-pulse voltammetry at different pH at gold electrode. Cyclic voltammetric studies were performed in a wide range of sweep rates and various concentrations of orphendrine hydrochloride. The effects of surfactants were studied. The anodic peak was characterized and process was adsorption-controlled. The probable oxidation mechanism was proposed. According to the linear relation between the peak current and the orphendrine hydrochloride concentration, differential-pulse voltammetric method for the quantitative determination in pharmaceuticals was developed. The linear response was obtained in the range 0.1-20µM with a detection limit (LOD) of 1.27nM and
limit of quantification (LOQ) of 4.24nM under the physiological condition i.e. pH 7.0. The proposed method was successfully applied to orphendrine hydrochloride determination in pharmaceutical samples and for the detection of orphendrine hydrochloride in urine as a real sample.

**Part C: Biosynthesis of Ag Nano-particles**

**VII.** Biosynthesis, characterization and activity studies of Ag nano particles

by (Costus Ingneus) Insulin plant extract

Nanotechnology is receiving much importance in the present century due to its capability of modulating metals in to their nanoparticles. Research in nanotechnology highlights the possibility of their green chemistry pathways to produce important nanomaterials. We report in this chapter on the biological synthesis of silver nano-particles using Costus Ingneus extract and its activity studies on antidiabatic, antibacterial and antifungal activities. Characterization of newly synthesized silver nanoparticles was made using TEM and XRD studies. The results showed that silver nanoparticles from Costus Ingneus extract showed good antidiabatic activity than plant extract themselves.

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**Signature of the Research Candidate**

**Signature of the Research Supervisor**
Research Publications

1. RP-HPLC method for the determination of 5-Flurouracil in pharmaceutical formulations and spiked human plasma.
   S R Sataraddi and S T. Nandibewoor
   IJPSR.1, 164-169 (2010)

2. Voltammetric-oxidation and Determination of 5-Flurouracil and its Analysis in Pharmaceuticals and Biological Fluids at Glassy Carbon Electrode Mediated by surfactant cetyltrimethyl ammonium bromide
   S R Sataraddi and S T. Nandibewoor
   Der Pharma Chemica. 3, 253-265 (2011)

3. Biosynthesis, characterization and activity studies of Ag nanoparticles, by (Costus ingneus) insulin plant extract
   S R Sataraddi and S T. Nandibewoor
   Der Pharma Lettre. 152-158 (2012)

4. Oxidation of D-Glucose by silver(III) periodate complex in presence of Ru(III)/Os(VIII) as a homogeneous catalyst: a comparative mechanistic study
   S R Sataraddi and S T. Nandibewoor
   J. Soln. Chem. (Revised submitted)

5. Mechanistic investigations of Uncatalysed and Ru(III) catalysed oxidation of D-Mannitol by Diperiodatoargentate(III) complex in aqueous alkaline medium
   S R Sataraddi and S T. Nandibewoor

6. Development of electrochemical method for the determination of anticholinergic drug Orphendrine hydrochloride and its applications to pharmaceuticals Dosage form and human biological fluids.
   S R Sataraddi and S T. Nandibewoor
   J. Anal. Chem. (communicated)

7. Electrochemical Behavior and Determination of Indomethacin in Pharmaceuticals, and Biological Fluids at Multi Walled Carbon Nano-Tubes Modified Glassy Carbon Electrode.
   S R Sataraddi and S T. Nandibewoor
   J. Solid State Chem.(Communicated)