CHAPTER - I

INTRODUCTION
INTRODUCTION

1.1 HISTORICAL PERSPECTIVE

In recent years, micellar reaction media\textsuperscript{1-12} have attracted considerable attention as means of controlling the rates of reactions of chemical, industrial and biological interest. In most cases, simple electrostatic considerations suffice for prediction of whether a reaction will be catalyzed or inhibited by cationic, anionic, or non-ionic micelles, but several quantitative theories based on the pseudophase model\textsuperscript{13-15} have also been developed. According to this model, a micellar pseudophase is distributed uniformly through the bulk (generally) aqueous phase of a micellar system, and reactions take place in both phases. The relative importance of these two pathways depend on the reaction rates in each phase and the distribution of reagents between the two.

Twenty four years after Fendler's\textsuperscript{16} challenge on biomimetic media, it seems that organic chemistry has not gained very much from microorganized media, except from some spectacular experiments which specifically designed reaction systems. With usual micelles, interesting catalytic effects on reactions between hydrophilic and hydrophobic reagents can be expected if the hydrophilic reagent can be forced into the Stern layer but much work on ion-exchanges is still to be done before this condition can be readily achieved.

The transfer of a reactive solute into a micelle, changes several features of its existence that can alter its inherent stability. In the micelle the molecular environment of the solute molecules will have changed drastically, from an aqueous to a relatively non-polar environment, depending on the depth of insertion into the micelle. The simple fact that the solute may be protected from attacking species such as H\textsuperscript{+} or OH\textsuperscript{-} ions will give rise to stabilization of labile molecules such as esters; in some charged micelles, the surface characteristics will be such that there is a concentration of ions which would result in a more rapid breakdown in simple aqueous solution.

The micellar environment is sufficiently different from the simple aqueous environment, that reaction rates may sometimes be dramatically changed. Because of this, there has built a number of schools throughout the World in which micellar systems are used deliberately to alter the rates and directions of chemical reactions. In pharmaceutical formulations the influence of surfactant on the stability of the
pharmaceutical is generally secondary to its main purpose, but surfactants may be used to stabilize labile pharmaceuticals, and an understanding of the mode of action and interactions can avoid the problem of destabilization which might unwittingly occur. Most studies in this field have concerned reactions between an organic substrate and a reactive ion in the presence of surfactants. A large effort has been directed toward understanding the reactivity in surfactant systems, and a great deal of progress has been made in the last decade, both theoretically and experimentally. Several reviews, monographs and books cover the substantial literature on chemistry in amphiphilic aggregates, structure and reactivity in micelles and, quantitative treatment of chemical reactivity. These are excellent starting points for deep immersion in the field.

Mechanistic information obtained at interfaces is more representative of complex biochemical reactions than that studied in dilute aqueous solutions.

This worldwide interest in micelles originates from scientists with diverse specialities; organic chemistry, physical chemistry, biochemistry, pharmaceutical chemistry and polymer chemistry. Thousands of patents on micelles and micelle-forming compounds testify to the commercial importance of the subject. Micelles have been scrutinized by an unusually wide variety of techniques including X-rays, NMR, ESR, fluorescence, light scattering, small angle neutron scattering and colorimetry. The group of Raipur have gained experience in the chemistry of hydroxamic acids in microorganized media recently. In particular, alkaline and acidic hydrolysis of hydroxamic acids were investigated by Ghosh et al. Despite extensive efforts by many investigators, the reactions in mixed micelles remain only partially understood. The multitude of publications has not resolved questions of micelle shape, water penetrations, ion-binding and reactivity in mixed and polymer-surfactant micelles. It was, therefore, thought worthwhile to investigate the acidic and alkaline hydrolysis of hydroxamic acids in micellar and mixed micellar media. The primary objective of the work presented in this thesis has been to study the reaction in binary surfactants. An attempt was made to study the hydrolysis reaction in surfactant-polymer mixtures. A knowledge of hydroxamic acid and mixed micelles is required for conceptual and quantitative understanding. Therefore, a brief description of hydroxamic acid is presented first, followed by a discussion on mixed micelles.
1.2 CHEMISTRY AND BIOLOGIC ACTIVITY OF HYDROXAMIC ACIDS

The hydroxamic acids (HAs) having paired carbonyl and hydroxylamino functional groups (I) are an important family of organic compounds.

\[
\begin{align*}
\text{O} & \quad \text{OH} \\
\text{I} & \quad \text{C} \quad \text{N} \\
\end{align*}
\]

Many hydroxamic acids have been found to be biologically active and they are useful as a variety of drugs. Both hydroxamic acids and their N-substituted derivatives serve as bidentate ligands towards many metal ions are therefore useful in analytical chemistry. One of the recent elegant applications in this field is the use of hydroxamic acid metal complexes in DNA cleaving. Both hydrolytic and oxidative cleavage of DNA have been accomplished by use of the hydroxamic acid-metal ion systems. This simple cleavage system may be useful for the development of artificial metalonucleases, especially artificial hydrolytic nucleases.

Many diseases or their symptoms originate from the deficiency or excess of a specific metabolite, which is either substrate or product of an enzymatic reaction. Therefore, researches on enzyme inhibitors as potential drugs is a successful approach in medicinal chemistry. Especially mechanism-based inhibitors, compounds activated during interaction between target protein and inhibitor have the potential to lower side effects in drug administration. Knowledge of the hydrolytic decomposition pathway of prolyl (II) and glycyl hydroxamate (III) might help in design of protease inhibitors with increased hydrolytic stability.

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{N} \quad \text{O} \\
\text{II} & \quad \text{O} \\
\text{H}_3\text{C} & \quad \text{N} \quad \text{O} \\
\text{III} & \quad \text{O} \\
\end{align*}
\]

In recent times hydroxamic acids have attracted attention because of their properties as iron-chelators (siderophores) with therapeutic potential. Siderophores are produced by microorganisms to acquire and transport ferric iron under iron...
stress conditions\textsuperscript{88-90}. Hydroxamate siderophores form the largest structural type and have been isolated from bacteria, fungi and algae. The hydrolysis of hydroxamic acids to hydroxylamine is an important first step in the quantitative analysis of hydroxamate siderophores\textsuperscript{91}. Because of the potential application in the treatment of iron overload disease, there is great interest in the development of new ligands for the effective complexation with iron. A currently used drug, methanesulfonate salt of desferrioxamine B (Desferal \textregistered DFB) (IV) is derived from a natural trihydroxamate siderophore\textsuperscript{92}. Patients with B Thalassaemia major comprise the largest group of patients who have benefited from Desferal. Research is also continuing to determine the role of Desferal in other conditions such as Alzheimer's disease, aluminium overload, cerebral malaria, tissue perfusion injury and as adjunctive therapy in malignant diseases.

\[ \text{CH}_3\text{SO}_3^-\text{NH}_3\text{C} \quad \begin{array}{c} \text{CONH} \\ \text{(CH}_2\text{)}_5 \end{array} \quad \begin{array}{c} \text{CONH} \\ \text{(CH}_2\text{)}_5 \end{array} \quad \text{CH}_3 \]

(IV) Desferrioxamine B (Desferal)

However, it cannot be administered orally and has several side effects such as septicemia\textsuperscript{93}. In the course of searching for new chelators to replace DFB, nitrogen containing heterocycles such as pyridinone derivatives (V) have received much attention because of their potential for clinical use\textsuperscript{94}.

\[ \begin{array}{c} \text{N} \\ \text{N} \end{array} \quad \begin{array}{c} \text{C} \\ \text{N} \end{array} \quad \text{OH} \]

(V) Cyclic Hydroxamic acids
One can predict the oxidized nitrogen in the π electron deficient ring systems may lead to remarkable acidity on the part of the OH group. Therefore, three intrinsic properties are expected: (1) a low pKₐ value, (2) high water solubility, and (3) metal chelating ability.

The hydroxamic acid-based inhibitor of zinc dependent matrix metalloproteinases Ro 31-9790 (VI) completely prevented shedding of cell surface L-selection from leucocytes in mouse, rat and man.

The biological importance of hydroxamic acids has been proved beyond doubt and increased interest in their chemistry. For the last few years the studies on the mechanisms of chemical carcinogenesis by N-arylhydroxamic acids are going on. But we still have much to learn about the chemistry of nitrenium ion and the relationship of that chemistry to their carcinogenicity. Extracts of certain Gramineae such as rye, wheat and maize contain hydroxamic acids which inhibit growth and development of plant pathogens and are involved in cereal resistance to various insects. Knowledge of the reactivity of these compounds in solution is essential for the molecular interpretation of their widespread toxicity. Many of hydroxamic acids are powerful mutagens and carcinogens.

Hydroxamic acids have also received considerable attention as reagents in analytical chemistry for gravimetric analysis and for the solvent extraction and spectrophotometric determination of metals.

The reagents are also useful in the analysis of trace metals by flow injection analysis and high performance liquid chromatography. The properties and behaviour of hydroxamic acid resins have been studied. Discovery of oscillation phenomena in the fluorescence intensity of some aromatic hydroxamic acids suggests that they can undergo photochemical reactions.
In spite of these interesting properties and diverse applications, hydroxamic acids remain one of the less well-characterized classes of organic compounds. In future studies, there is a great deal more to be learned about the structure of hydroxamic acids and their mechanistic aspects.

The chemical approach to biological problems through investigations of models rests upon the ability of the chosen system to mimic some functions of the biological ensemble. Surfactants in aqueous media have been extensively used as model systems. Interest in micellar chemistry has been prompted by the proposed similarities between the structures of globular proteins and spherical micelles and between micellar and enzymatic catalyses.

Recently some works on micellar and solvent effects of hydroxamic acids have been initiated. The surface complex stoichiometry and structure change to reflect different solution condition and affect the mechanism, rate and extent of the subsequent surface reactions.

Adsorption of organic solutes to mineral surfaces is critical to understanding solute transport in aquatic environments because many key chemical reactions are enhanced by adsorption. Recently Holmen et al. established the structure of the goethite, a simple analogue compound for the high - molecular weight hydroxamate siderophores produced by soil microbes to sequister iron from the environment.

Hydroxamate ions are α - effect nucleophiles, i.e. their reactivity is higher than that predicted by Bronsted relations between nucleophilicity and basicity. They are effective deacylating and dephosphorylating agents, and reactivities of amphiphilic hydroxamate ions are increased by co-micellization with inert surfactants in water. Hydroxamic acids exist as E- and Z- isomers and the equilibrium composition is medium dependent. Charge delocalization, as in simple amides, generates partial double bond character and should increase on deprotonation. 

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6
Scheme - I

Interfacial regions of aqueous micelles and similar association colloids are somewhat less polar than water, and effects on the rate constants of reactions in these regions are often interpreted on the assumption that polarities are similar to those of medium chain length alcohols. Bunton et al. examined micellar and solvent effects on the geometrical isomerism of hydroxamic acids and their anions. During the last 10 years, much more detailed information on synthesis and therapeutic potential of hydroxamic acids has been published. Exploitation of the tremendous therapeutic potential of hydroxamic acids, their analogues, and derivatives requires access to sufficient quantities of materials for preliminary and long-term study. It is the goal of the thesis to develop concise formulations of micellar catalysis in pure and mixed systems through the study of some simple hydroxamic acids.

In the present investigation following hydroxamic acids have been used for detailed investigation.

\[ R = H, R' = CH_3 \]
\[ R = H, R' = C_6H_5 \]
\[ R = C_6H_5, R' = C_6H_5 \]
\[ R = 4-CH_3C_6H_4, R' = C_6H_5 \]

Acetohydroxamic acid (AHA)
Benzohydroxamic acid (BHA)
N-phenylbenzohydroxamic acid (PBHA)
N-p-tolylbenzohydroxamic acid (p-TBHA)

Benzohydroxamic acids (hydroxy and amino substituted) have been found to inhibit mammalian ribonucleotide reductase and inhibit antineoplastic activity in...
L1210 leukemic mice. Benzohydroxamic acid and acetoxyhydroxamic acid can be utilized as a new type of DNA scission agent in the presence of metal ions. N-phenylbenzohydroxamic acid (PBHA) is the most studied and widely used N-substituted hydroxamic acid. This reagent is widely used as a colorimetric reagent, especially for the vanadium (V) in industrial analysis. Besides that, PBHA have found numerous applications for solvent separation of metal ions. Several metals such as thorium, uranium, plutonium of interest in nuclear energy programme have been separated from commonly associated metals by solvent extraction using PBHA.

The other N-substituted hydroxamic acid, N-p-tolylbenzohydroxamic acid (p-TBHA) is proved a good analytical reagent. The effects of several experimental variables on quantitative colour development were examined. The method gives precise and accurate results. The method is fairly sensitive and is useful for determining micro quantities of p-TBHA. Carbon tetrachloride, o-dichlorobenzene, chlorobenzene, benzene, toluene, xylene, ethyl acetate and several solvents do not interfere in the procedure recommended for determining p-TBHA.

1.3 MICELLAR CATALYSIS

Micellar catalysis has attracted considerable interest with regard to fundamental studies of catalysis and for its relationship to enzymatic processes. The hydrolysis of amide like substances is of interest, because of their relationship to peptides. Micelles and other types of surfactant aggregates are quite effective catalysts for many organic reactions. Recently micellar catalysis of hydroxamic acids have been studied by Ghosh et al. In this connection Berndt et al. also documented investigations on micellar hydrolysis of hydroxamic acids in pure surfactants. Surprisingly, there appear no paper analysing the influence of mixed surfactant systems on hydrolysis of hydroxamic acids. Mixed micellar aggregates are composed of two or more different surfactants in equilibrium with the surfactant monomers. The superior properties of mixed surfactants as compared to a single surfactant and their relatively lower production cost have been brought out in several cases. Therefore, it would be quite illustrative to investigate acidic and alkaline hydrolysis of hydroxamic acids in mixed surfactants and surfactant-polymer mixed systems. The following section will throw a brief focus on the mixed surfactants and polymer system, to point out features that are still to be fully understood, and to consider some recent developments. The basic understanding of solution and interfacial behaviours of surfactants is necessary for the art of management of their surface chemical applications.
1.31 MICELLAR PROPERTIES OF BINARY MIXTURES (MIXED MICELLES)

Solutions containing mixtures of surfactants (mixed micellar solutions) are currently a subject of considerable practical and industrial importance\textsuperscript{120-130}. They can be produced at a relatively lower cost than that of isomerically pure surfactants. In addition, in many surfactant applications, mixtures of dissimilar surfactants often exhibit properties superior to those of the constituent single surfactants due to the synergistic (attractive) interactions between the surfactants molecules. Moreover, in general, synergistic interaction between different surfactant species can be, and have been, exploited by the surface scientists in designing solution of surfactant mixtures which display unique desirable properties. Detergent and cleaning formulations often include both anionic surfactants, to maximize solubilization, and non-ionic surfactants to maximize water hardness tolerance\textsuperscript{131}. In skin care applications synergism in a surfactant mixture can minimize the total surfactant monomer concentration, which in turn has been shown to reduce skin irritation\textsuperscript{132}. In addition, as environmental impact regulations on producing and releasing new materials become more restrictive, it may be preferable from a regulatory perspective to combine existing surfactants rather than to introduce new ones.

Developing a fundamental understanding of the behaviour of mixed micellar solutions, including a rationalization of the nature of interactions, constitute a problem of great practical importance. In solutions containing mixtures of surfactants, the tendency to form aggregated structures (mixed micelles) can be substantially different than in solutions containing only the constituent single surfactants. For example, the critical micellar concentration of a mixture of anionic and cationic surfactants in aqueous solution is considerably lower than the CMC's of each individual surfactant\textsuperscript{133}. On the other hand, antagonistic interactions, in mixtures of hydrocarbon-based and fluorocarbon-based surfactants in aqueous solution, result in mixture CMC's that can be considerably higher than the CMC's of the constituent single surfactant\textsuperscript{134}. In general, specific interactions between (synergistic or antagonistic) between surfactants result in solutions of surfactant mixtures having micellar and phase behaviour properties which can be significantly different from those of the constituent single surfactants\textsuperscript{135}. Indeed, in order to tailor surfactant mixtures to a particular application, the surfactant technologist has to be able to predict and manipulate,
the tendency of surfactant mixtures to form mixed micelles, and other self assembling aggregates in solution.

(ii) the properties of the formed aggregates such as their shape and size.

(iii) the distribution of the various surfactant species between monomers and aggregates.

(iv) the phase behaviour and phase equilibria of solutions containing surfactant mixtures, and

(v) reaction kinetics in mixed systems.

In spite of their considerable practical importance as well as the challenging theoretical issues associated with the description of these complex fluids, solutions of surfactant mixtures have not received the full attention that they deserve. Very little effort has been devoted to understand the kinetics of chemical reactions in mixed micellar systems. In view of this, it is quite clear that there is an immediate need to develop a concise formulations of chemical reactivity in mixed micelles. Before doing kinetics it is necessary to characterise the reaction medium. Formation of a micelle and its dependence on environmental factors (pH, temperature, additives etc.), thermodynamics of micellization, counterion binding, aggregation number and catalysing functions, etc., are important physicochemical aspects that need detailed and intensive attention for both fundamental understanding and application prospects. In the present work micellar properties of pure and mixed surfactants have been investigated. We hope that the comparative and quantitative description of the mixed surfactant systems of diverse characters (taken from literature and obtained from studies on ionic-ionic and ionic-non-ionic in our laboratory) will reveal the scope and limitations of the theoretical models and help in the development of more appropriate future mixed micellar models besides providing a useful guidance in the design and selection of non-ideal surfactant combinations for practical purposes. Mixed micellar effects upon rate constants of some organic reactions are shown in Table 1.1.

1.4 REACTIVITY IN POLYMER-SURFACTANT SYSTEMS

Polymer-surfactant interactions are currently the subject of extensive investigations in view of the number of formulations and processes where they are utilized simultaneously, and the topic has been recently reviewed. It is not
<table>
<thead>
<tr>
<th>S.NO</th>
<th>REACTION</th>
<th>MIXED MICELLAR EFFECTS UPON RATE CONSTANTS OF SOME REACTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>MIXED-MICELLAR SYSTEM</td>
</tr>
<tr>
<td>1.</td>
<td>Acid hydrolysis of alkyl nitrites</td>
<td>Non-ionic-anionic decrease</td>
</tr>
<tr>
<td></td>
<td>Hydrolysis of 2,4-dinitrophenyl acetate and benzoic anhydride (pH</td>
<td>136</td>
</tr>
<tr>
<td>2.</td>
<td>S^2 reaction of Br^- with methyl</td>
<td>Non-ionic-cationic mediated reaction</td>
</tr>
<tr>
<td></td>
<td>naphthalene-z-sulfonate (MeO2N)</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Hydrolysis of 2,4-dinitrophenyl acetate</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Alkaline hydrolysis of ethyl benzoate</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Hydrolysis of ethyl benzoate and benzoic anhydride (pH</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>Acid hydrolysis of alkyl nitrites</td>
<td></td>
</tr>
</tbody>
</table>

TABLE 1.1
surprising, that aqueous solutions containing both surfactants and polymers exhibit complex interaction patterns, with the number of variations in the interactions apparently as numerous as the number of systems itself. Because of the importance of polymer-surfactant systems a variety of applications including pharmaceutical, and cosmetic preparations, oil-drilling fluids, detergents, etc., and because of the fundamental interest in these systems, research in this field has increased rapidly in recent years. An understanding of these systems is also of fundamental importance in many biological processes and systems, including biomembrane, vesicles, and the binding of small molecules to biopolymers. In most studies "interaction" is used to mean "binding" of surfactant to polymer. The morphology of the complex formed between a non-ionic water soluble polymer and surfactant molecules has puzzled chemists from the first study of Saito\textsuperscript{149} in 1957 onwards. Cabane\textsuperscript{150} in 1977 established the model that is now quite generally accepted. According to this model segments of the polymer bind to the surface region of the surfactant micelles. Stabilization of the interface between the hydrophobic core and water is considered to be a major driving force for polymer-micelle interaction.

Although, the morphology of polymer-micelle complexes thus seems to be known in some detail, the subtle way in which the chemical structure of the surfactant and the morphology of the unperturbed micelle influence the tendency for association with nonionic polymers remains a challenging problem. In the case of water soluble nonionic polymers with medium chain length surfactants several modes of interaction (hydrophobic interaction, dispersion forces, hydrogen bonding, hydration of the polymer and head groups etc.) may contribute in the same order of magnitude to the total energy of the system. The polymer-surfactant reaction media is very interesting. There have been few studies of the characterization and properties of polymer-micelles as a reaction medium\textsuperscript{151-159}.

Polymer-surfactant mixed solutions form surfactant aggregates in the polymer domain and thus provide a hydrophobic micropseudophase in the bulk aqueous phase. It may be expected that reactants dissolved in these systems are in an unusual organized environment influencing their reactivity. While increasing numbers of paper have been published on chemical reactions in organized assemblies such as micelles, membranes, vesicles and microemulsions, such studies have been limited in polymer-surfactant mixed systems. We have initiated research on hydrolytic stabilities of hydroxamic acids in polymer surfactant systems. The field is still need of high quality data for systematically varied polymer and surfactant structures. Our work then is an attempt to contribute to this field.
1.5 THE PRESENT INVESTIGATION

Self organized association colloids, i.e., micelles, microemulsions, liposomes, vesicles, etc. are compartmentalized liquid which may show special performance towards reaction equilibria and reaction dynamics. Chemical and biochemical reactions have been reported to be fairly as well as extraordinary influenced under compartmentalized conditions. One important aspect is the catalysis or inhibition reactions by submicroscopic entities such as micelles, that now are considered as models for enzymes action because they are similar in size and shape, both have polar surfaces and hydrophobic interiors. Although the kinetic aspects of hydrolysis of hydroxamic acids\textsuperscript{169-172} have been studied by our group at Raipur, a comprehensive work in the mixed-micellar medium is lacking, in particular, the acidic and alkaline hydrolysis have not been examined in such media.

From the preceding discussion it is evident that mixed surfactants are of great importance because of fundamental interest as well as extensive scientific and technological applications\textsuperscript{165,166}. Out of three types (nonionic, ionic, and zwitterionic) of surfactants, it is known that in the mixed state nonionics show ideal behaviour, while other combinations exhibit nonideality resulting from synergistic (attractive) or antagonistic (repulsive) interactions between the surfactants of different types.

The factors guiding the interactions are of various origin, their quantitative accounting remains a matter of continued research interest. It may be mentioned that similarly charged amphiphiles of different molecular architecture may exhibit both ideal and non-ideal\textsuperscript{167} behaviours in solutions forming micelles. A literature survey shows that significant efforts have been made on the study of mixed surfactant systems to characterize micelles and their formation. The significant contributions of Rosen et al.\textsuperscript{167-168} and Moulik et al.\textsuperscript{169-171} deserve special mention in this context. Extensive investigations on the thermodynamics of micellization and adsorption, counterion binding, polarity, and aggregation number have been reported\textsuperscript{165-171}, but systematic studies are limited. Moreover, fundamental investigations on hydrolysis reactions in mixed systems most probably have not yet been addressed. In view of
this, it is quite clear that there is an immediate need to study influence of various mixed micelles and polymer-micelles on the following hydrolysis reactions of hydroxamic acids:

\[
\begin{align*}
\text{Acidic Hydrolysis} \\
\text{Alkaline Hydrolysis}
\end{align*}
\]

By using a micellar mediated system (simple or complex), whose solvation properties are adjustable, the selectivities of these reactions achieved and controlled.

With this goal in mind, the present investigation is divided into following parts:

(I) Physicochemical properties and thermodynamic description of micellization of aqueous solutions of pure and binary surfactant mixtures.

(II) Kinetics of acidic and alkaline hydrolysis of hydroxamic acids in pure and mixed micelles.

(III) Kinetics of hydrolysis of hydroxamic acids in surfactant/polymer mixed micelles.

(IV) Quantitative treatment of micellar and mixed micellar rate effects.

I. PHYSICOCHEMICAL PROPERTIES AND THERMODYNAMICS OF MICELLIZATION

The structure and thermodynamics of formation of mixed micelle is of great theoretical interest. It is an enormous challenge to understand the interactions between different surfactant components in the various applications in which surfactants are used. Individual surfactants vary in their tendency to form aggregated structures. Examples of such aggregates are micelles, precipitate, and monolayers. In solutions containing mixtures of surfactants, the tendency to form aggregated
structures can be substantially different than in solutions containing only the pure surfactants involved. The mixtures of surfactants can achieve great synergisms in various processes by manipulation of the relative tendency to form various aggregated structures. Often, the formation of certain aggregate will inhibit the formation of a less desirable aggregate. For example, addition to nonionic surfactants to anionic surfactants enhance the formation of micelles, resulting in a reduced tendency for the anionic surfactant to precipitate. The distribution of surfactant components between micelles and monomeric state in aqueous solutions depends on surfactant structures as well as on overall solution composition. The total monomer concentration of a binary mixture of two similarly structured surfactants of like charge (on ideal system) lies between the critical micelle concentrations of the individual surfactants involved for total surfactant concentration at or above the mixture CMC. In the present investigation the physicochemical properties of following systems have been studied [Table - 1.2A]

[i] Pure surfactant
[ii] Binary Mixed Surfactants
[iii] Surfactant-Polymer

Cationic, nonionic, anionic, zwitterionic.
Cationic - Cationic
Cationic - Nonionic
Anionic - Nonionic
Cationic - Nonionic Polymer (PEG)
Nonionic-Nonionic Polymer

All the results have been discussed in Chapter III. There are some large gaps in our knowledge of mixed micelles which is seriously impending progress toward understanding and quantifying their behaviour. In this section (Chapter III) the critical micelle concentration, counterion binding, and thermodynamics of micellization etc. have been quantitatively estimated by surface tension and conductometric methods. An attempt has been made to study surfactant-nonionic, water soluble polymer (PEG, mol. wt. = 400). The critical association concentration and polymer saturation point have also been measured.

II. KINETICS OF ACIDIC AND ALKALINE HYDROLYSIS OF HYDROXAMIC ACIDS IN MIXED MICELLES

One of the most encouraging aspects of this field is the increasingly international nature of work in the area of hydroxamic acids. These are indispensable compounds in the development of siderophores, analytical reagents
TABLE - 1.2
SUMMARY OF THE PRESENT INVESTIGATION
[A] CMC & THERMODYNAMICS OF MICELLIZATION

<table>
<thead>
<tr>
<th>SURFACANTS</th>
<th>BINARY MIXED SURFACANTS</th>
<th>SURFACANT-POLYMER MIXED-SYSTEMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTAB'</td>
<td>CTAB - Brij-35(^{1,2})</td>
<td>CTAB-PEG</td>
</tr>
<tr>
<td>TTAB'</td>
<td>CTAB - TX - 100(^{1,2})</td>
<td>TTAB-PEG</td>
</tr>
<tr>
<td>CPC'</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPB'</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CTAS'</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SDS'</td>
<td>TTAB - Brij-35(^1)</td>
<td></td>
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<tr>
<td>SDOD'</td>
<td></td>
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</tr>
<tr>
<td>DSOD'</td>
<td>TTAB - TX - 100(^1)</td>
<td></td>
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<tr>
<td>Brij-35'</td>
<td></td>
<td></td>
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<tr>
<td>TX-100'</td>
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<tr>
<td>SB3-16'</td>
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<tr>
<td>SB3-12'</td>
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<tr>
<td>BHAC(^2)</td>
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<tr>
<td>NaC(^2)</td>
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<tr>
<td>NaDC(^2)</td>
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<tr>
<td></td>
<td>CTAB - CPC(^{1,2})</td>
<td></td>
</tr>
</tbody>
</table>

1 - Room temp. (30\(^\circ\)C), surface tension method & conductance method.
2 - 35\(^\circ\)C, 45\(^\circ\)C, 55\(^\circ\)C, 65\(^\circ\)C, Surface tension method.
The structure and full name of the surfactants are given in Chapter II (Experimental section)
<table>
<thead>
<tr>
<th>Surfactant System</th>
<th>Medium</th>
<th>Reaction</th>
<th>Catalyst</th>
<th>Temperature</th>
<th>Surfactant Systems</th>
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<tr>
<td>Pure Surfactants</td>
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<tr>
<td>1. I.</td>
<td>0.1 M NaOH</td>
<td>Alkaline</td>
<td>PBHA·p-TBHA</td>
<td>55°C</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.35 M HCl</td>
<td>Acid</td>
<td>PBHA·p-TBHA</td>
<td>55°C</td>
<td></td>
</tr>
<tr>
<td>II. Polyelectrolyte-Surfactant Mixed Systems</td>
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<tr>
<td>2.</td>
<td>0.1 M NaOH</td>
<td>Alkaline</td>
<td>PBHA·p-TBHA</td>
<td>55°C</td>
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<tr>
<td></td>
<td>0.35 M HCl</td>
<td>Acid</td>
<td>PBHA·p-TBHA</td>
<td>55°C</td>
<td></td>
</tr>
<tr>
<td>III. Polyelectrolyte-Surfactant Mixed Systems</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>3.</td>
<td>0.1 M NaOH</td>
<td>Alkaline</td>
<td>PBHA·p-TBHA</td>
<td>55°C</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.35 M HCl</td>
<td>Acid</td>
<td>PBHA·p-TBHA</td>
<td>55°C</td>
<td></td>
</tr>
</tbody>
</table>

**Kinetics of Hydrolysis of Hydroxamic Acids**

- 0.35 M HCl 55°C
- 0.1 M NaOH 55°C

**Effect on PBHA, BHA & AHA (in acid medium, 0.35 M HCl)**
and pharmaceuticals. Micelles provide a reaction medium apparently distinct from the bulk solvent. One of the most important properties of aqueous micellar solutions is their ability to solubilize a wide variety of organic solutes normally not dissolvable in water. The hydrophobic molecules can reside anywhere, starting from the purely nonpolar inner core (a hydrocarbon like solvent) and to the partially polar surface hydrophobic sites. This gamut of solubilization environments, inherent to microheterogeneous micellar solutions, plays an important role in determining chemical reactivity. The present work analyzes the influence of pure and mixed-micellar solutions on the acidic and alkaline hydrolysis of hydroxamic acids [Table - 1.2B]. The micellar effects on hydrolysis of hydroxamic acids have frequently been a matter of study in the past few years, nevertheless, further efforts have not been dedicated to investigating mixed micellar and polymer-surfactant effects on hydrolysis of hydroxamic acids or to determining the mechanism. This study aims at addressing this oversight in past. In these experiments various cationic, non-ionic and anionic surfactants have been employed to produce micelles. All the data will be compared with similar data obtained in the absence of surfactants.

The hydrophobicity of the hydroxamic acids can be controlled by varying the substituent on the C or N atom.

\[
\begin{align*}
\text{O} & \quad \text{OH} \\
R & \quad \text{C} \quad \text{N} \quad R'
\end{align*}
\]

For example, changing the C substituent from \(-\text{CH}_3\) (acetohydroxamic acid, hydrophilic), to \(-\text{C}_6\text{H}_5\) (benzohydroxamic acid, hydrophobic) to \(R = \text{C}_6\text{H}_5, R' = \text{C}_6\text{H}_5\), and \(R = \text{C}_6\text{H}_5, R' = 4\text{CH}_3\text{C}_6\text{H}_4\) (hydrophobic) provides for a wide range of hydrophobic control.

Chapter IV deals with acidic hydrolysis in pure and mixed micellar systems. Similarly in Chapter V is described alkaline hydrolysis of hydroxamic acids in mixed micelles. The development of a quantitative understanding of chemical reactivity in solution has depended on the willingness of chemists to use models that are no more than crude approximations. For this reasons it is useful to accept the pseudophase model, despite its imperfections, until it either fails to fit the data, or is replaced by a better model.
III. KINETICS OF HYDROLYSIS OF HYDROXAMIC ACIDS IN SURFACTANT/ POLYMER MIXED MICELLES.

Although mixed-micelles are frequently used for chemical kinetics, there is little reliable information on reactivity in polymer-surfactant aggregates. The addition of polymers to surfactant micellar solution modifies micellar properties, when the polymer chains and micelles interact. Polymer-surfactant interactions are relevant to several biological applications, for example they may simulate protein-membrane systems, and these complexes are also important in the pharmaceutical and cosmetics industries, paints and detergent manufacturing, and even enhanced oil recovery. In the present study, acidic and alkaline hydrolysis of hydroxamic acids have been investigated in cationic and neutral water soluble polymer (polyethylene glycol, PEG, mol. wt. = 400) and nonionic–PEG systems [Table - 1.2B]. Chapter VI is devoted for this study.

An important section of this thesis (Chapter II) outlines the synthesis of hydroxamic acids and experimental procedure etc.

1.6 IMPORTANCE OF THE STUDY

Research into the chemistry of surfactant mixture behaviour has seen a rapid increase in activity over the last decade. New technological applications involving surfactants have evolved, many of which are dependent on the use of surfactant mixtures. There is no reason to doubt that now applications of surfactant mixtures will continue to be discovered. As a result of the growing awareness of the wealth of fascinating scientific phenomena occurring in mixed surfactant systems, research into surfactant mixture behaviour will also continue to increase in intensity. Our work consists in the investigation of the effects of micro-organized media on the hydrolysis of hydroxamic acids. It is expected that by using a reaction media, (pure, mixed, or polymer – micelles) whose solvation properties are adjustable, to achieve and control the selectivities of these reactions. Three kinds of benefits are expected.

[A] FUNDAMENTAL KNOWLEDGE

Acquisition of data on local reactivity at surfaces and their interpretation in terms of physicochemical properties of these interfaces: microscopic polarity, hydrophilicity - lipophilicity balance, electrostatic and London forces, local hydration and solvation ability in particular.
APPLICATIONS IN ENVIRONMENTAL CHEMISTRY

Design of surfactant systems which provide extremely fast destruction of pollutants and, in particular, organophosphorous esters under biocompatible conditions.

OTHER POTENTIAL APPLICATIONS

Hydroxamic acids have been successfully used for a large variety of applications in analytical, biological and medicinal fields, such as drug-delivery systems, DNA cleavage, iron-transport, etc. It is our intention to investigate how the incorporation of these chemicals in molecular assemblies can improve their interest in these fields. The primary objective of the work presented in this thesis has been to study the micellar mediated hydrolysis of hydroxamic acids. Hopefully these investigations will make the achievement of this goal close at hand. Furthermore, extensive efforts were made at each phase of this research to understand the basic chemical principles involved in mixed surfactant systems. These studies have provided answers for old questions and raised new horizons. There are unanswered questions regarding mathematical models of mixed micellization, polymer-surfactant interactions, position of substrate within the micelle etc. More detailed studies are needed which are at present being done in our laboratory by other workers. The coming years promise to be times of exciting progress in mixed surfactant systems.

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