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A COMPARATIVE STUDY AND BEHAVIOUR OF A SERIES OF CATIONIC SURFACTANTS TOWARDS THE DEGREE OF THE BASIC HYDROLYSIS OF p-NITROPHENYL ACETATE

FOUZIA HASSAN AND A.E. BEG*
Department of Pharmaceutics, Faculty of Pharmacy
University of Karachi, Karachi-75270, Pakistan

ABSTRACT

The surfactant effect of cationic micelles of Dodecyl, tetradecyl and hexadecyl trimethyl ammonium bromide, Cetyl pyridinium bromide, Cetyldimethyl ethyl ammonium bromide and benzalkonium chloride on the hydrolysis of p-nitrophenyl acetate (PNPA), was studied. The effect of cationic surfactants was within concentration range of 1×10^{6}M - 1×10^{-1}M, with the exception of benzalkonium chloride, where the concentration effect was investigated between 1×10^{6}M - 3×10^{-1}M. All cationic micelles in-creased the rate of hydrolysis of PNPA upto their concentration of 1×10^{-2}M and then the rate decreased while benzalkonium chloride showed this maximum at 5×10^{-2}M. Orientation and adsorption of substrate at the micelle surface are put forwarded to explain this catalytic behaviour. An attempt has also been made to interprete the influence of cationic micelles on the basis of ion exchange model.

Introduction

During the past two decades there has been considerable interest in reactions which can be carried out at interfaces. Among them the catalysis and inhibition by submicroscopic entities, such as micelles, have attracted increasing attention (Kafarski & Lejczak, 1987). Numerous surfactants have been used to catalyse alkaline hydrolysis of phenylesters (Broxton et al., 1988; Ihara et al., 1987) and most of these have been quarternary ammonium systems. The effect of cationic micelles on the rate of these bimolecular reactions is considered on the basis of the increased concentration of ester and hydroxide ions in the small volume of the micellar Stern layer (Fendler et al., 1975). Simple electrostatic consideration predict that these micelles will enhance reaclion rates.

*For correspondence:
Prof. Dr. Anwer Ejaz Beg, Philadelphia University, P.O. Box 1101, Sweileh, Jordan

The catalytic property of micelle is an interesting behaviour to study and has been the subject of many investigations (Braxton et al., 1989; Rav-Acha 1988). Much of the reported work in micellar catalysis has been done on the hydrolysis of esters by hydroxyl ions.

The purpose of this work is to determine the effect of substrate and surfactant structure on hydrolysis in order to understand better the nature of substrate surfactant interactions and Stellar reaction in general. We selected PNFA as model for study because it can be followed spectrophotometrically at very low concentration where the structure of the micelles, formed by the surfactants is not perturbed. Moreover basic hydrolysis of FNPA is thoroughly understood reaction and one that is free from complication. U is also used very frequently as a probe for determining the esterase activity of may enzymes (Connor & Wallace, 1984).

Materials:

All the reagents used in this study were of A.R. grade.

p-nitrophenyl acetate (PNPA), supplied by Sigma Laboratories was twice recrystallized from 50% ethanol. M.P. 773°C (Lit. 77°- 78°C) (Chattaway, 1931). Throughout the work the concentration of the ester was kept as 4×10^{-S}M. Reagent grades of Dodecyl, Tetradecyl, Hexadecyl trimethyl ammonium bromides, Cetyl pyridinium bromide, Cetyl di-methyl ethyl ammonium bromide and Benzalkonium chloride supplied by Sigma Laboratories, were purified according to the process given elsewhere (Fendler & Fendler, 1975). Water used in this study was double distilled from all glass still with a specific conductivity $< 10^{-7}$ Ohm^{-1} cm^{-1} and surface tension of 7105 m Nm^{-1} at 25°C.

Experimental:

Hydrolysis of the drug was followed at 400 nm in visible spectrophotometer in carbonate-bicarbonate buffer at pH 9.2 and 35°C in the absence and presence of various concentrations of cationic surfactants i.e. from 1×10^{6}M - 1×10^{-1}M. The first order rate constants were obtained in the usual manner as reported previously (Beg & Meakin, 1986).

Results and Discussion

First order rate constant for base catalysed hydrolysis of PNPA in presence of varying concentration of all cationic surfactants in terms of "Surfactant Effect Ratio" (SER) (Winterborn, 1972) are shown in Figure 1.

This profile indicates that the "SER" increases with increase in the concentration of all surfactants upto a maximum (10^{2}M) with the exception of benzalkonium chloride where this maximum occurs at 5×10^{-2} then "SER" falls.

The increase in the rate of hydrolysis upto maximum follows the simple Hartley rules (Martely,1934). Starting from the CMC their occurs rather an abrupt increase in "SER", reflecting a highly efficient uptake of the substrate by these cationic micelles. Then the rate goes to a maximum and decreases at still higher concentration of cationic surfactants. This behaviour is normal for some of the substrates like Alkyl arene sulfonates and phenyl esters in presence of CTAB (Langkruis & Engberts, 1984).

Base-catalysed hydrolysis proceeds by bimolecular attack of the OH ion on the carbonyl group of the ester forming a tetrahedral intermediate followed by elimination of alcohol. As the intermediate is negatively charged it is, therefore, suggested that cationic micelles may enhance base-catalysed hydrolysis not only increasing the attraction of OH ion but also estabilizing the intermediate. Also bimolecular reactions are generally faster when micelles are present. This enhancement of the reaction rate is probably due largely to increased concentration of the two reactants in micellar pseudophase (Fendler et al., 1975; Menger et al., 1967; Bunton, 1979).

The orientation of substrate solubilized by micelles and the consequences of this orientation on the magnitude of micellar catalysis are concerning the dependence of the magnitude of micellar catalysis on orientation exist. In general two approaches have been used to influence the substrate orientation within the micelles. Firstly, hydrophobic alkyl groups in the substrate have been assumed to be anchored in the hydrophbic cores of the micelles. Secondly, the substrate containing anionic groups such as the carboxylate group -COO', has been used and it is assumed that these ionic groups would preferentially be found protruding from the micelles surface into the aqueous intermicellar pseudophase. These influences have been assumed to orient the reaction center of the subtrate in predictable ways. Few of these studies have been supported by spectroscopic studies to confirm the actual orientation of the substrate in the micelles. Recently reports of the orientation of salicylate ions (Manohar et al., 1986; Rao et al., 1987) in micelles, on the basis of NMR studies in D2O and in CTAB have led to some studies of substrate orientation in micelle (Broxton et al., 1988; Broxton et al., 1987). The study of aspirin derivatives 1-3 makes use of both approaches described above to influence substrate orientation in micelles (Broxton et al., 1987).

As a result of NMR and viscoelasticity studies it has been concluded that for compound 1 and 3 the reaction centers is either at the interface or in aqueous internilcellar pseudophase (a possibility with could also exist for PNPA - cationic surfactant systems), while for compound 2 the reaction center is pulled further into the micelles (Broxton et a1., 1987). On the basis of these studies here it is, therefore, suggested that concentration of reactants into small volume at the micelle-water interface may be the main factor in rate enhancement of such bimolecular reaction.

The micelle surface is another possible site of substrate adsorption. The ionic portion

of surfactant molecules forms highly charged surfaces which attract small counter ions from the solution in order to relieve electrostatic repulsion. Thermal motion which tends to produce uniform distribution of the ions, disturbs the ionic array resulting in the well-known diffused electrical double layer. Basic ester hydrolysis is not very sensitive to ionic strength changes, so that the high concentration of ions at the double layer would not in itself greatly affect the reaction (Menger et al., 1967). However, ad-sorption at the surface of cationic micelles could result in considerable rate enhancement (as in this study) because hydroxide ions (along with other ions) collect in this region.

On the basis of dynamic light scattering studies, it has recently been recorded (Broxton et al., 1988) that micelles of quarternary ammonium salts have a higher fractional charge (a = 0.22) for CTAB) which could also be another reason for the rate enhancement. It is also known that aqueous solution of micellized cationic surfactants speed decomposition of Dinitrophenylphosphate (DNPP) di-anions (Bunton et al., 1968; Buist et al., 1970; Bunton et al., 1975) which is akin 10 a submicroscopic solvent effect. Rate of spontaneous dephosphorylations and decarboxylations increase (Kemp et al., 1975) as the polarity of solvent is decreased and micellar polarities as given by the apparent dielectric constant are lower than those of water (Cordes et at, 1913; Mukergee, 1979).

The rate enhancement of hydrolysis of PNPA by cationic micelles in this study could also be interpreted on the basis of interaction of the nitro group, of PNPA with the cationic micellar head group. Probably the combined electronic effects of Br and Cl counter ions of cationic surfactants and the nitro group of PNPA assist in protons release in the transition state so that it carries a negative charge and so these micelles enhance base catalysed hydrolysis by stabilizing the transition state.

"SER" profile (Fig. 1) shows maximum ranging from 1 x 10^{-2}M - 5 x 10^{-2}M. The subsequent fall in the ratio is probably attributable to an increase in counter ions concentration causing displacement of hydroxyl-ions from the area immediately surrounding the micelle surface as postulated by Romsted and Cordes (Romsted & Cordes, 1968) for their surfactant ester study in buffer system. The decrease in the rate of hydrolysis after maxima in this study also agrees with the result of the study of Funasaki (Funnasaki, 1978) who found that as the concentration of CTAB was in-creased above the CMC the surface hydroxide ion concentration decreased and bromide counter-ions were bound to the surface of the micelle in place of carbonate and hydrogen carbonate ions (of buffer). The rate constant at the micellar surface was found to be proportional to surface OH ion concentration and the decrease with in-creasing BF concentration at the surface as in bulk phase. This he suggests explains the profile for p-nitrophenylbutyrate hydrolysis in CTAB-carbonate buffer systems. Maxima at this concentration are also apparent in the SER-CFAB profiles for the hydrolysis of 2, 4-dinitrochloro benzene and PNPA and p-nitrophenyloctanoate (Menger & Portnoy, 1967). No such maximum in "SER" profiles of

anionic and non-ionic surfactants was observed (Hassan, 1989) and therefore this could be taken as characteristic features of cationic surfactants accelerated processes.

The development of the ion exchange model by Romsted (Romsted, 1977) involved several assumptions: counter ions competing for ionic micelles and large, low-charge density ions binding more strongly than small, high charge density ions reaction occurring at micelle- water interface where ions bind specifically and the fractional ionization of the micelles essentially independent of the nature or concentration of the counter ions. The concentration of the micellar bound ions is, therefore, proposed to be directly related to fractional of micellar head groups neutralized by counter ions. Ions not specifically bound to the micelles but in diffuse layer are assumed not to react with micellar bound substrate.

This general model explains the widely observed rate maxima for bimolecular ionic reactions with increasing surfactant concentration.

Various theories and suggestions have been but forwarded for the distribution of OH ions between water and micelles (Romsted, 1977, Romsted, 1984) and these help in die understanding of rate maxima appearing in SER-surfactants profiles. In the light of these theories interaction between x and OH for micellized cetyltrimethyl ammonium ions (CTA) can be shown as:

$$\overline{OH}_M + \overline{X}_W \rightleftharpoons \overline{OH}_W + \overline{X}_M \quad \ldots (1)$$

where X = fraction of counter ions.

W and M denote the aqueous and micellar pseudophases respectively and

$$K_X^{OH} = [\overline{OH}_W][\overline{X}_M] / [\overline{OH}_M][\overline{X}_W] \quad \ldots (2)$$

Equation 2leads to the prediction of a maximum in the first order rate constant of a bimolecular reactions at constant [OH] with increasing surfactant concentration (Bunton et al., 1968; Buist et al., 1970; Bunton et al., 1975) as is observed in this study. However, the continuing increase in the "SER" with increasing length of the alkyl chain of surfactant as evidenced from Fig. l is not clearly understood at this stage. It must involve either an unexpectedly high sensitivity of the electrostatic forces to curvature of the micellar surface, or else a rearrangement of micellar structure as the length of the alkyl chain is being extended. The magnitude of this increase in the "SEW with increase in alkyl chain length resembles with the results of a series of anionic micelles where inhibition in the rate of hydrolysis has been shown (Kurz, 1962; Menge et al, 1968). Also the study of Dunlap and Cordes on the effect of the chain length of sodium alkyl sulphate

on the add catalysed hydrolysis of methylorthobenzoate sup-ports our observations where some change in micellar structure has been observed (Dunlap & Cordes, 1968).

Finally, the role of surfactant hydrophobicity in determination of catalytic efficiency cannot be eliminated. It is generally true that more hydrophobic the surfactant the better catalyst it is (Bendier & Fendler, 1975). This behaviour may reflect the partitioning of substrate between micellar bulk phase or the precise localization of substrate with respect to the micellar surface which may lead to a direct contribution of hydrophobic forces to the activation energy for the reaction. It is not possible to access the relative contribution of each of these factors to the observed rate effect at this time.

Also the increased hydrophobicity conferred by an increase of chain length causes an increase in micellar size. In many cases a linear relationship has been established between log of micellar weight and hydrocarbon chain length (Arnarson and Elworthy, 1981) and this could probably affect the rate of hydrolysis as the hydrocarbon chain length of surfactants is increased.

"SEW profiles (Fig.l) indicate that all cationic surfactants studied in this work increase the rate of hydrolysis of PNPA in the following order: Dodecyl < tetradecyl < Hexadecyl trimethyl ammonium bromides < Cetyldimethylethyl ammonium bromide < Pyridinium bromide < Benzalkonium chloride.

This change in the degree of hydrolysing ability of the above surfactants for PNPA could be attributed to the modification or change in the hydrophilic group i.e. from trimethyl ammonium bromide to ethyldimethyl ammoniumbromide, pyridinium and dimethyl benzonium groups of benzalkonium chloride. The effect of the nature of polar group of ionic surfactants on micellar properties has been studied in detail by Anacker and Coworkers (Geer et al., 1971). These researchers concluded that an important factor controlling the micellar size was the mean distance of closest approach of a counter ion to the charge center of the surfactant. Solvent interaction may also be an influential factor (Anacker & Geery, 1977). Hydrogen bonding between oxygen atom of surfactant such as that of decyl morpholinium bromide and water is thought to be responsible for smaller micellar size of this compound as compared to cetyl pyridinium bromide which does not interact with solvent in this way. The cause of this effect has been ascribed to changes in the effective dielectric constant produced when polar head structure is changed and intermolecular hydrogen bonding between the polar head hydroxy ethanol group and water.

The effect of changing the charge bearing atom in the polar head has been reported (Anacker et al., 1977). In most cationic surfactants the charge is localized on a single N atom which is typically located at the end of hydrocarbon chain (as in the case of cetyl pyridinium bromide). However, when the polar group is a pyridinium ring the mode of

delocalization of the charge around the ring may affect the aggregation number. An increase in the positive charge on that particular atom of the ring to which the hydrocarbon chain is attached leads to a decrease in aggregation numberQacobs & Anacker, 1973) producing a bigger micelle which could be accounted for a very high degree of hydrolysis of PNPA by cetyl pyridinium bromide in this study. The most dramati effect of the hydrophobic group of benzalkonium chloride on the rate of hydrolysis of PNPA is not *very* clear at this time. This could be associated with aromatic grouping which is present in the hydrophilic part of this surfactant. Further work on this line is in progress in this laboratory and is expected to be published in due course of time.

Conclusion

The main conclusion which may be drawn from the present work may be summarized as follows:

(1) In the absence of cationic surfactants the hydrolysis of PNPA is subject to general catalysis by carbonate-bicarbonate buffer.
(2) SER-concentration profiles indicate maxima in the region of (10^{-2}M) in all cases except benzalkonium chloride where this maximum occurs at 5 x 10^{-2}M.
(3) Increase in the "SER" with increasing the length of the alkyl chain is in the order dodecyl < tctradecyl < hexadecyl < trimethyl ammonium bromide < cetyldimethylethyl ammonium bromide < cetylpyridinium bromide < benzalkonium chloride.
(4) The dramatic increase which is found in the rate of hydrolysis for benzalkonium chloride is to be explored.

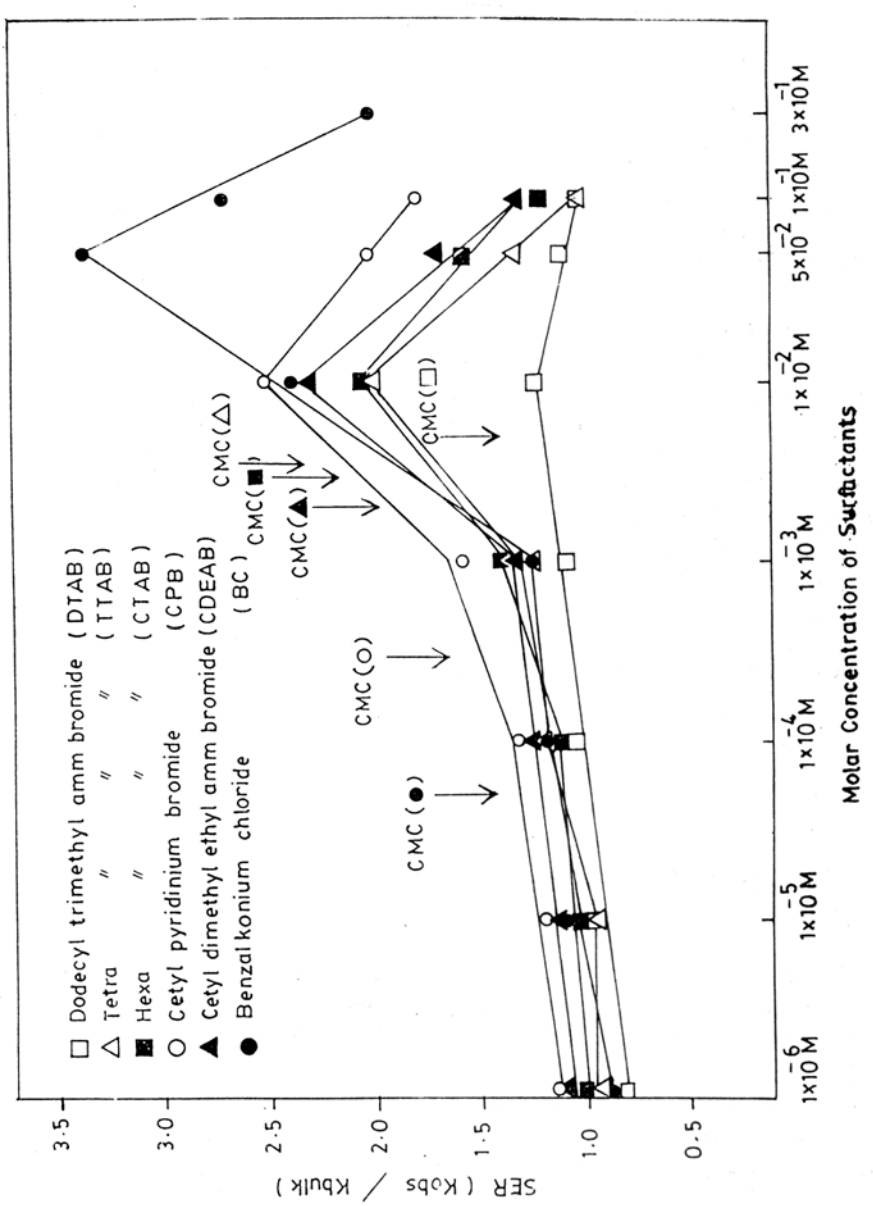

Fig. 1: The effect of various cationic surfactants on the hydrolysis of 4 x 10-5M PNPA at pH 9.2 and 35oC as a ratio of (Kobs/Kbuylk).

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