Quantitative Relation between Surface Active Properties and Antibiotic Activity of 1-Alkyl-3-alkylthiomethylimidazolium Chlorides

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The critical micelle concentration (CMC) values were determined by surface tensiometry, and the hydrophobicity index (HI) was calculated. The quantitative relation between the minimum inhibitory concentration (MIC) and the CMC, and the HI was calculated.

Key words 1-alkyl-3-alkylthiomethylimidazolium chloride; minimum inhibitory concentration; critical micelle concentration; hydrophobicity index

In earlier papers we reported the synthesis of 1-alkyl-3-alkylthiomethylimidazolium chlorides and their biological activity.[1,2] The present study attempts to evaluate the relationship between the surface and antibiotic activities of 1-alkyl-3-alkylthiomethylimidazolium chlorides.

The critical micelle concentration (CMC) was determined by means of surface tension isotherms at 20 °C. The surface tension values of aqueous solutions of imidazolium chlorides were measured by the ring method. A platinum ring of 10.4 mm ring radius and 0.2 mm wire radius and a Teflon vessel 10 cm diameter were used. The solutions were prepared by weight, using freshly boiled doubly distilled water stored under nitrogen.

The correction factors, which are dependent on the solution properties, have been determined experimentally according to the theory of Harkins and Jordan[3] as well as Freud and Freud.[4] To eliminate any error due to the formation of a finite contact angle at the ring, it was necessary to take off the ring after measurement of the solution and to rinse it with pure water.[5] The reproducibility of surface tension measurements was within 2%. In the micellar region, the surface tension of aqueous of 1-alkyl-3-alkylthiomethylimidazolium chlorides decreased to 29.5—24.7 [mN/m].

In the course of systematic studies, we have arrived at a formula for the quantitative relation between surface active properties and the antibiotic activity of aqueous 1-alkyl-3-alkylthiomethylimidazolium chlorides. The correlation is as follows:

$$\log(1/\mathrm{MIC}) = A \log \mathrm{CMC} + B(\log \mathrm{CMC})^2 + C \log \mathrm{HI} + D(\log \mathrm{HI})^2 + E$$

where MIC is the minimum inhibitory concentration, HI is the hydrophobicity index, and A, B, C, D and E are regression parameters.

The hydrophobicity index is defined as a ratio of the effective length, n_{eff}, to the actual number of carbon atoms, n, of the chain.[6]

$$\mathrm{HI} = n_{\mathrm{eff}}/n$$

The following relationship may be used for the calculation of the n_{eff} values of studied chlorides

$$\log \mathrm{CMC} = a - bn_{\mathrm{eff}}$$

For the 1-alkyl-3-alkylthiomethylimidazolium chlorides, a and b equal 1.582 and 0.292, respectively. The values of a and b were obtained from 1-alkylimidazole hydrochlorides. The n value is the number of carbon atoms plus 0.88 (sulfur atom) in the alkylthiomethyl chain. The value of 0.88 represents the sulfur atom in the length as the equivalent to one methylene group, and was estimated from thermochemical study of an aqueous micellar solution of 1-alkyl-3-alkylthiomethylimidazolium chlorides at 20 °C.

All the described models are linear. The estimates of the parameters of these models are obtained using the least squares method. Accuracy of the models and the significance of the parameters were tested using the methods of regression and variance analyses.[7] The computer program was described by Bogacka and Bogacki.[8] Table 1 shows the values obtained for A, B, C, D, E, R (correlation coefficient) and α (confidence interval) of 3-alkylthiomethyl-1-octylimidazolium chloride, where alkyl = C_4H_9, C_6H_{13}, C_8H_{17}, $C_{10}H_{21}$, $C_{12}H_{25}$, and $C_{14}H_{29}$. The confidence interval for all models obtained is very low ($\alpha <$

Table 1. Values for the Parameters A, B, C, D and E of 3-Alkylthiomethyl-1-octylimidazolium Chlorides

	Strain	Parameters						
		A	B	C	D	E	α	R
Rods	*Klebsiella pneumoniae*	−40.72	−7.992	1.964	179.1	−47.46	0.0000	0.9995
	Serratia marcescens	−45.11	−9.127	−15.58	223.4	−49.42	0.0000	0.9999
Cocci	*Staphylococcus aureus*	−58.08	−11.75	−25.73	300.8	64.70	0.0000	0.9999
	Gaffkya tetragena	−5.449	−0.0803	−2.346	52.06	−5.029	0.0000	0.9996
	Sarcina lutea	−6.177	−0.8699	−1.102	7.021	−2.892	0.0000	0.9999
Fungi	*Rhodothorula glutinis*	−24.76	−4.650	−11.63	127.3	−25.82	0.0000	0.9999
Bacilli	*Bacillus substilis*	−55.08	−10.80	−25.16	305.2	−627.3	0.0000	0.9994

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0.05) and the correlation coefficient in many cases is greater than 0.99. Such values of these two parameters suggest that the obtained models are very significant.

The present results demonstrate the quantitative relation between the minimum inhibitory concentration and the critical micelle concentration as well as hydrophobicity index of 1-alkyl-3-alkylthiomethylimidazolium chlorides. The most important factor governing the adsorption of the molecules in the studied interphase is the alkylthiomethyl chain.

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