

Antimicrobial Activity of N,N'-bis(decylmethyl)- α,ω -alkanediamine Dioxides [1]

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Antimicrobial activity of N,N'-bis(decylmethyl)- α,ω -alkanediamine dioxides determined on *Staphylococcus aureus*, *Escherichia coli*, and *Candida albicans* is presented as minimal inhibitory concentration (MIC). The effect of the length of linking alkylene chain on this activity has been followed.

Non-aromatic amine oxides involving in their molecules at least one long aliphatic chain were found to have marked surface active properties and found wide application possibilities in industry [2–4]. However, there are few data on biological effects of these substances and particularly on their antimicrobial activities [5–7]. It was found in these studies that monoamine oxides with surface active properties also showed a distinct antimicrobial activity. In case of bisamine dioxides derived from tetramethyl- and tetraethyl- α,ω -alkane diamines [8] their weak antistaphylococcal effect has been observed. The authors have found that the above mentioned substances showed a remarkably lower toxicity than analogous organic ammonium salts.

Papers [9, 10] describe antimicrobial effects of some N,N'-bisdialkyl- α,ω -alkanediamine dioxides in the case of which marked effects were found on both grampositive and gramnegative bacteria and yeasts. The maximum activity of these compounds was found if their long alkyl chain contained 9 to 11 atoms of carbon. Therefore, N,N'-bis(decylmethyl) derivatives were used in this study: there are the best available products from the aspects of their synthesis, and the effect of the length of the linking alkylene chain on antimicrobial activity was followed.

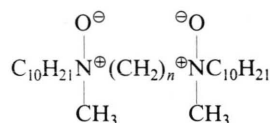
Experimental

Synthesis of these compounds has been described elsewhere [11, 12], the antimicrobial activity was determined by the inhibition method directly in the cultivation media [13]. For testing we used microorganisms: *Staphylococcus aureus* Oxford Mau 1/45; *Escherichia coli* Eck 61/59, and *Candida albicans* 45/53. Results are presented as minimal inhibitory concentration (MIC) which is the lowest concentration inhibiting visible growth in the media.

Results and Discussion

The results of the tests are given in the Table. From these data is evident that all diamine dioxides tested are active against the microorganisms used. The course of the activity depending on the length of the linking alkylene chain is not linear. The activity increases from $n = 2$, reaches maximum at $n = 6$ and drops to $n = 10$. The presence of the long alkyl chain and the polar N–O groups is decisive for the activity [6, 9]. A significant role is played by stereochemistry of the molecules and their hydrophile-hydrophobic balance. In case of the derivative of 1,2-ethanediamine ($n = 2$; No. 1) there is a limited possibility of the formation of conformation isomers which results in decreased molecule solva-

Antimicrobial activity of N,N'-bis(decylmethyl)- α,ω -alkanediamine dioxides (MIC in $\mu\text{g ml}^{-1}/\text{mmol l}^{-1}$, respectively).



No.	n	<i>S. aureus</i>	<i>E. coli</i>	<i>C. albicans</i>
1	2	40 0.0998	100 0.250	40 0.0998
2	3	40 0.0924	60 0.139	30 0.0693
3	4	30 0.0645	50 0.108	20 0.0430
4	5	10 0.0217	30 0.0651	5 0.0109
5	6	5 0.0101	20 0.0406	3 0.0061
6	8	20 0.0412	80 0.165	20 0.0412
7	10	50 0.0975	200 0.390	30 0.0585

tation and thus also in more difficult transport to the active sites of the cells. Elongation of the connecting alkylene chain results in improved possibilities of the formation of other conformation isomers (due to increased possibilities of rotation around the σ -bonds of the linking chain) and at the same time hydrophobic properties of the whole molecule are increased.

Regarding the effects followed the optimum arrangement is probably reached in the derivative of 1,6-hexanediamine ($n = 6$), as further elongation of the alkylene chain still increases the hydrophobic

character of the molecule, suppressing thus its hydrophile character and disturbing the optimum hydrophile-hydrophobic balance of the molecule.

Diamine dioxides studied can be compared as for their antimicrobial character with structurally similar organic ammonium salts [14], however, the former were found less toxic and irritant. In comparison with monoamine oxides, the bisamine dioxides studied are more active on gramnegative bacteria *E. coli*, their activity on *S. aureus* and *C. albicans* can be compared with that of monoamine oxides.

- [1] Paper No. 9 of the series: Amine Oxides. Paper No. 8: F. Devínsky, D. Mlynarčík, I. Lacko, and Ľ. Krasnec, Chem. Zvesti, in press.
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