4-NITROPHENYL-1,4-DIHYDROPYRIDINES – A NEW GROUP OF INHIBITORS OF PEROXIDE OXIDATION

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1,4-Dihydropyridine derivatives have antioxidant activity that depends on both the structure of the 1,4-dihydropyridine and the substrate of peroxide oxidation [1, 2]. However, in the 3,5-dialkoxycarbonyl-1,4-dihydropyridine series antioxidant activity thus far has been uncovered only for 4-unsubstituted compounds, while compounds even with electron-donor substituents in this position were inactive. We have found that the known 4-nitrophenyl-1,4-dihydropyridines and their three-ring analogs – 4-nitrophenyl-5-oxo-1,4-dihydroindeno[1,2-b]-pyridines – have antioxidant activity that significantly exceeds the activity of the corresponding 4-unsubstituted compounds. Thus in the inhibition of the peroxide oxidation of methyl oleate (50°C) 4-(2-nitrophenyl)-2,6-dimethyl-3,5-dimethoxycarbonyl-1,4-dihydropyridine and 2-methyl-3-ethoxycarbonyl-4-(2-nitrophenyl)-5-oxo-1,4-dihydroindeno[1,2-b]pyridine in concentrations of $7.5 \cdot 10^{-4}$ mole-liter^{-1} increase the induction period by factors of 80 and 51, respectively. The most active of the 4-unsubstituted 1,4-dihydropyridines, viz., 2,6-dimethyl-3,5-bis(cyclohexyloxycarbonyl)-1,4-dihydropyridine in a concentration of $3 \cdot 10^{-3}$ mole-liter^{-1}, increases the induction period by a factor of only two. It must be emphasized that high antioxidant activity is peculiar only to o-nitrophenyl derivatives and that the corresponding meta and para derivatives are much less active.

The antioxidant activity of 4-nitrophenyl derivatives of 1,4-dihydropyridine is also displayed in the inhibition of the hemolysis of erythrocytes induced by both dialuric and hydrochloric acids. 1,4-Dihydroindenopyridines are less effective in this case, possibly as a consequence of their lower capacity for bonding with the membrane of the erythrocyte.

Thus 4-(2-nitrophenyl)-1,4-dihydropyridines and 1,4-dihydroindeno[1,2-b]pyridines are new groups of synthetic antioxidants, the properties of which are determined by the presence of a strong electron-acceptor nitro group in the molecule.

LITERATURE CITED

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