Thesis title Synthesis of Chroman Amide and Nicotinyl Amide Derivatives as Inhibitors of Lipid Peroxidation II.

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ABSTRACT

A series of chroman amides and nicotinyl amides was designed and synthesized as lipid peroxidation inhibitors using the carbodiimide coupling method. Their structures are modified by varying the chemical function of both sides of amides. The acid parts were trolox, nicotinic acid and 6-hydroxynicotinic acid; the amine parts were 2-amino-6-methoxyquinoline, 3-(2-aminoethyl)indole and 1-(2-aminoethyl)piperazine. The seven newly synthesized compounds and the six previously prepared compounds of the same series were tested for inhibitory activity against lipid peroxidation using the thiobarbituric acid method. The lipophilicity value was determined using two methods, calculation with program C log P and reversed phase thin-layer chromatography. It was found that chroman amides and hydroxynicotinyl amides were active whereas nicotinyl amides were inactive. Chroman amides, the more lipophilic, were more potent than hydroxynicotinyl amides. [(3,4-Dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2yl)carbonyl]-2'-amino-6'-methoxyquinoline (XI), the most lipophilic compound in this series, was the most active. Percent inhibition of lipid peroxidation by this compound was

46.93% at 1μM which was significantly more potent than trolox, the reference compound ($p < 0.01$). The inhibitory action against lipid peroxidation of antiradical agents was related to the electron donating property of the molecule to scavenge radicals and to the lipophilicity of the molecule for penetratation of membrane lipids. The log P value for the maximal inhibition of lipid peroxidation was between 4.5 and 5.