Correlation between Experimentally Obtained and Theoretically Predicted Activities of New Bio-antioxidants

Adriana Slavova-Kazakova[a], *Silvia Angelova*[a], *Jordan Nechev*[a], *Vessela D. Kancheva**[a], *Ashok Prasad*[b], *Virinder Parmar*[b]

[a]*Institute of Organic Chemistry with Centre of Phytochemistry,Bulgarian Academy of Sciences, "Acad. Georgi Bonchev" Str., Block 9, 1113 Sofia, Bulgaria,vedeka@abv.bg;*

[b]*Chemistry Department, University of Delhi, Delhi, India*

The aim of this study was to test the correlation between experimentally obtained radical scavenging (antiradical) and chain-breaking (antioxidant) activities with theoretically calculated (predicted) activity of 26 recently synthesized set of hydroxyl-4-methyl-coumarins and 7 related compounds. These nature-like biologically active compounds, synthesized from the Chemical Department, University of New Delhi, India, demonstrated anti-inflammatory and anticancer activity, as well as some of them, i.e. 7,8-dihydroxy-4-methyl coumarins are effective as reducing agents of cholesterol.

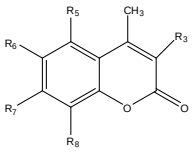

Abb	R_3	R_5	R_6	R_7	R_8	RSA	AOA	BDE $_{O-H}$
a1	H	H	H	OH	OH	strong	moderate	moderate/strong
a2	CH_2COOEt	H	H	OH	OH	strong	moderate	moderate/strong
a3	CH_2CH_2COOEt	H	H	OH	OH	strong	moderate	moderate/strong
b1	H	H	OH	OH	H	moderate	strong	strong
b3	CH_2CH_2COOEt	H	OH	OH	H	moderate	strong	strong
c1	H	OH	H	H	H	weak	weak	weak
d1	H	H	H	OH	H	weak	weak	weak

New order of radical scavenging activity (RSA) was obtained by applying one of the most popular tests (DPPH test) in ratio of [AH]/[DPPH]=0.40. Compounds of 7,8-dihydroxy-4-methyl-coumarins (a3 and a1) showed the strongest activity (RSA>40%) and their activity is comparable with the most powerful antioxidants like α-tocopherol, caffeic acid and gallic acid. 6,7-dihydroxy-4-methyl-coumarins (b1 and b3) showed moderate activity (40%>RSA>15%). Chain-breaking antioxidant activity (AOA) was studied during lipid autoxidation kinetics monitoring on the base of lipid hydroperoxides determination as primary oxidation products and determination of the main kinetically parameters – protection factor (PF) and inhibition degree (ID). There are also compounds with acetoxy and methoxy groups instead of hydroxyl groups in 6,7 and 8 positions. For that reason they are without capacity as radical scavengers or antioxidants. Taking into account however the interesting biological activities of these compounds, they were studied by applying theoretical approaches. Diacetoxy derivatives in methanolic solutions showed capacity to scavenge free radicals, as a result of some hydrolysis to free hydroxyl groups. Excellent correlation has been found between experimental and theoretically predicted activities. All compounds of the present study are in agreement with the *Lipinski's Rule of Five*, which is of importance for further development of drugs based upon these substances, and their analogs.