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Design and synthesis of new neuroprotective agents as a potential aid to smoking cessation

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Background: According to the world health organization (WHO) statistics, there is about one third of male adult smokers, which can lead to four million deaths per year. Tobacco addiction could be potentiated by monoamine oxidase (MAO) inhibition as several MAO inhibitors were identified in tobacco smoke. Bupropion exhibits antismoking activity in addition to its known anti-depressant effect. The primary goal of this project was to synthesize new bupropion analogs with potent MAO inhibitory activity.

Methods: We synthesized new bupropion analogs using 3'-chloropropiophenone as a starting material. The first step was the synthesis of α -bromoderivative using bromine in glacial acetic acid followed by amination with different amines. We converted these obtained products immediately to the corresponding fumarate salts. We monitored all reactions by thin layer chromatography (TLC) and purified them by crystallization, solvent-solvent extraction and column chromatography. We elucidated the structures of the prepared compounds by nuclear magnetic resonance (NMR), Fourier-transform infrared spectrophotometry (FT-IR) and mass spectrometry (MS). Nowadays, the MAO-B inhibitory activity is being evaluated against recombinant human MAO-B using 96-well microtitre plate reader.

Results: We prepared several bupropion analogs and confirmed the structure of the purified compounds using with FT-IR and LC/MS. Currently, we are investigating the prepared compounds in relation to their MAO inhibition activity.

Conclusion: We successfully were able to achieve the synthesis and structural elucidation of the several compounds. These derivatives, which have potent MAO inhibitory activity, will potentiate the anti-smoking effect of the Bupropion and will have a pronounced impact on the future of the smoking cessation pharmacotherapies alternatives.

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