A New Series of Chalcone Analogs as Potential Selective and Reversible Monoamine Oxidase-B Inhibitors
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Purpose
Monoamine oxidases (MAO-A and MAO-B) are flavoenzymes responsible for the oxidative deamination of neurotransmitters and xenobiotic monoamines. MAO inhibition is useful for the treatment of neurological disorders; such as depression, Parkinson’s disease and Alzheimer’s disease. The chronic nature of these diseases raises a compelling need for new MAO inhibitors with improved bioavailability and safety profiles. The aim of this project is to synthesize new chalcone analogs and evaluate their inhibition towards both MAO isoforms.

Methods
A series of chalcone analogs was proposed and chemically synthesized by reacting various acetophenones with substituted benzaldehydes, using Claisen-Schmidt condensation. The products were purified by crystallization. Structures were confirmed by FT-IR, GC/MS, and NMR. Compounds were screened for MAO inhibition; those exhibited ≥70% inhibition at 10 μM underwent Ki determination experiments. Molecular docking was performed to understand the mechanism of their activities.

Results
Ten novel chalcones analogs were designed, synthesized, purified and evaluated for their both hMAO-A and B inhibitory activities. Their structures were confirmed by pertinent spectroscopic techniques. Five out of the ten compounds appeared to be selective MAO-B inhibitors with Ki values in the micromolar to submicromolar range. Molecular modeling studies gave insight into the binding mode of the synthesized compounds, that suggests a reversible mode of inhibition.

Conclusion
Our findings demonstrate that most of the synthesized chalcone analogs reversibly and selectively inhibit MAO-B, and thus represent potential therapeutic agents to treat Parkinson’s disease and other neurodegenerative disorders.