COMPUTATIONAL STUDY OF PYRAZOLINE DERIVATIVES PROVIDED WITH POTENT AND SELECTIVE MONOAMINOXIDASE ACTIVITIES

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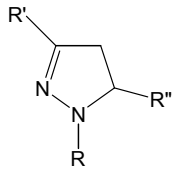
In this communication we present a computational study conducted with the aim to rationalize the structure-activity relationships of potent inhibitors of monoamine oxidases (MAO) based on the pyrazoline scaffold.



Most of the new synthesized compounds proved to be more reversible, potent, and selective inhibitors of MAO-A than of MAO-B.[1] This feature is particularly important for the development of new antidepressant and antianxiety drugs.
The 30 most active compounds show inhibitory activity on MAO-A in the range 8.6×10^{-8} - 9.0×10^{-9} M. Moreover, most of them are characterized by a Selectivity Index $_{\text{MAO-B/MAO-A}}$ in the range 10,000 - 12,000.
The computational work has been conducted developing new pharmacophore models for the pyrazoline derivatives following an approach previously reported.[2]

[1] Chimenti, F.; Bolasco, A.; Manna, F.; Secci, D.; Chimenti, P.; Befani, O.; Turini, P.; Giovannini, V.; Mondovi', B.; Cirilli, R.; La Torre, F. *J. Med. Chem*. **2004,** *47*, 2071.
[2] Gritsch, S.; Guccione, S.; Hoffmann, R.; Cambria, A.; Raciti, G.; Langer, T. *J. Enz. Inhib*. **2001,** *16,* 199.