



UNIVERSITÀ DEGLI STUDI DI SALERNO



UNIVERSITÀ DEGLI STUDI DI SALERNO
Dipartimento di Farmacia

PhD Program
in **Drug Discovery and Development**
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PhD Thesis in

*Chemical and Biological study
of natural substances active
on the Central Nervous System*

Candidate

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Abstract

The research project "Chemical and biological study of natural substances active on the Central Nervous System" has been focused on the possible effects of essential oils, their main constituents (in particular monoterpenes), plant extracts and/or their fractions and/or their constituents on the expression of some proteins involved in the adenylate cyclase 1 pathway, on cell electrophysiology and their potential effect on *in vivo* models.

Eight species were selected including three aromatic plants (*Lavandula angustifolia*, *Coriandrum sativum*, *Laurus nobilis*); two *Citrus medica* cultivars (cv '*liscia*' and cv '*rugosa*'); two species of *Ipomea* genus known because also *Ipomea violacea*, a famous 'smart drugs', belongs to this genus; and *Hypericum hircinum* belonging to the same genus of *Hypericum perforatum* known for its antidepressive properties. Essential oils have been obtained from the aerial parts of *L. angustifolia* and *L. nobilis*, from *C. sativum* fruits and from the two cultivars of *C. medica* flavedo, while from the aerial parts of the two *Ipomea* species and *H. hircinum* we obtained different extracts by using solvents with increasing polarity.

We analyzed the chemical composition of essential oils and the extracts by GC-MS for the first one, and by thin-layer chromatography (TLC), adsorption chromatography and HPLC for the second one. With this procedure it was possible to identify the main constituents of essential oils and the fractions with a chemical profile of interest.

Subsequently, were performed several *in vitro* and *in vivo* assays following a bioassay guided fractionation.

We evaluated the cytotoxicity of the substances on human neuroblastoma cells (SH-SY5Y) in order to determine the most appropriate concentrations to treat the cells to study the effect on adenylate cyclase 1, protein kinase A, pERK and ERK protein expression.

In collaboration with the University of Genoa, we evaluated the possible effects on cellular electrophysiology of *L. angustifolia* essential oil, its main constituent and of *H. hircinum* methanolic extract.

Finally, in the period of research carried out at the Department of Psychobiology of the University of Valencia in Spain, we evaluated the effects of the essential oil of *L.*

angustifolia and of the linalool on stress and social interactions with different experimental procedures *in vivo*.