

STUDY ON THE CHARACTERIZATION OF BIOACTIVE COMPOUNDS USED IN THE THERAPY OF NEUROLOGICAL DISORDERS BY COMPLEX PHYSICOCHEMICAL SCREENING

Doctoral Thesis – Summary

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This doctoral thesis, entitled “*Study of the Characterization through Complex Physicochemical Screening of Bioactive Compounds Used in the Therapy of Neurological Disorders*”, aims to investigate the physicochemical properties, stability, and compatibility of atypical antipsychotic agents, in order to support preformulation studies and optimize modern strategies for the development of solid dosage forms.

The importance of physicochemical characterization lies in its direct influence on the bioavailability and therapeutic efficacy of active pharmaceutical ingredients. In this context, the research focuses on aripiprazole and risperidone, widely used in the treatment of neurological disorders, and addresses two major research directions: (i) the evaluation of solid-state compatibility with pharmaceutical excipients and (ii) the improvement of physicochemical properties through the formation of supramolecular host–guest systems with cyclodextrins.

Preformulation studies demonstrated that the crystalline structure of the active substances is preserved in binary mixtures with excipients under ambient conditions, without the occurrence of polymorphic transformations. However, specific incompatibilities were identified: aripiprazole showed interactions with magnesium stearate and colloidal silicon dioxide, while risperidone exhibited incompatibilities with lactose, mannitol, magnesium stearate, and colloidal silicon dioxide. The combined use of spectroscopic (UATR-FTIR), diffractometric (PXRD), and thermoanalytical techniques enabled a detailed assessment of these interactions.

A central aspect of the thesis is the preparation and characterization of inclusion complexes of aripiprazole and risperidone with methylated β -cyclodextrins. Aripiprazole formed stable complexes with a 1:2 stoichiometry, resulting in a significant enhancement of solubility (up to approximately 38-fold), particularly in the presence of RAMEB and DIMEB. In the case of risperidone, inclusion complexes with variable stoichiometries (1:1 and 2:1) were obtained depending on the type of cyclodextrin, also leading to a marked increase in solubility, with DM- β -CD showing the highest efficiency.

Compatibility studies of the supramolecular systems with pharmaceutical excipients indicated that most excipients are suitable for formulation, with some specific incompatibilities, such as those between ARP/DIMEB and magnesium stearate, or between risperidone-based systems and lactose.

Overall, the results highlight the importance of integrating spectroscopic, diffractometric, and thermoanalytical techniques in the evaluation of complex pharmaceutical systems, contributing to the development of stable and efficient solid formulations with improved biopharmaceutical profiles.