

Biological Evaluation of Some Selected Cyclic Imides: Mitochondrial Effects and *in vitro* Cytotoxicity

Silvia Regina Tozato Prado^{a,b}, Valdir Cechinel-Filho^b, Fátima Campos-Buzzi^b, Rogério Corrêa^b, Silvia Maria Correia Suter Cadena^a, and Maria Benigna Martinelli de Oliveira^{a,*}

^a Department of Biochemistry and Molecular Biology, Federal University of Paraná, Curitiba, Paraná, Brazil. Fax: +55-41-2662042. E-mail: mbmo@ufpr.br

^b Núcleo de Investigações Químico-Farmacêuticas (NIQFAR)/CCS, Universidade do Vale do Itajaí (UNIVALI), Itajaí, Santa Catarina, Brazil

* Author for correspondence and reprint requests

Z. Naturforsch. **59c**, 663–672 (2004); received February 16/April 21, 2004

Cyclic imides such as succinimides, maleimides, glutarimides, phthalimides and their derivatives contain an imide ring and a general structure -CO-N(R)-CO- that confers hydrophobicity and neutral characteristic. A diversity of biological activities and pharmaceutical uses have been attributed to them, such as antibacterial, antifungal, antinociceptive, anticonvulsant, antitumor. In spite of these activities, much of their action mechanisms at molecular and cellular levels remain to be elucidated. We now show the effects of several related cyclic imides: maleimides (S2, S2.1, S2.2, S3), glutarimides (S4, S5, S6), 4-aminoantipyrene derivatives (L1, F1, AL1, F1.14, F1.2) and sulfonated succinimides (RO1, FA, FE, FD, MC, DMC) on isolated rat liver mitochondria, B16-F10 melanoma cell line, peritoneal macrophages and different bacterial streams. The effects on mitochondrial respiratory parameters, cell viability and antibacterial activity were also evaluated.

The results indicated that S3, S5 and S6 caused an increased oxygen consumption in the presence of ADP (state III) or its absence (state IV), while all other compounds decreased those parameters at different degrees of inhibition. All the compounds decreased the respiratory control coefficient (RCC). Loss of cell viability of peritoneal macrophages and the B16-F10 cell line was observed, L1 and S2.1 being more effective. S1, S2, S3, L1 and F1 compounds showed antibacterial activity at experimental concentrations.

Key words: Cyclic Imides, Mitochondrial Respiratory Chain, Cytotoxicity