

SYNTHESIS AND ANTIFUNGAL ACTIVITY OF NEW 3(5)-METHYL-5(3)-(2-THIOPHENYL AND -2-FURANYL)- 1H-1-R-4-CYANOPYRAZOLES

Stefania Aiello^a and Enrico Aiello^a

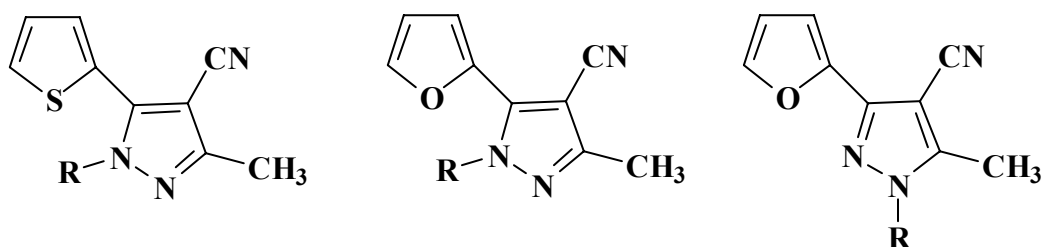
^aDipartimento Farmacochimico Tossicologico e Biologico
Università degli Studi, Via Archirafi 32, 90123 Palermo, Italy
stefania.aiello@unipa.it

We have reported that 4-nitrosopyrazoles derivatives displayed *in vitro* potent antifungal activity at no cytotoxic concentrations and that some of these compounds were 4 times more potent than Amphotericine B and Fluconazole respectively against *Cryptococcus neoformans*. We reported also that the absence of NO group or its replacement with NO₂ or NH₂ groups gave compounds devoid of antimycotical activity.^[1-2]

With the final aim to gain a deeper insight into the mechanism of action, we studied the *in vivo* metabolism of some 4-nitrosopyrazoles in rat liver and a rapid metabolization, with formation of the corresponding amines, was observed.^[3]

These findings and need for novel antifungal agents lead us to synthesize and to investigate the antifungal activity of title compounds in which the 4-NO group was replaced with 4-CN group having, these last, similar steric and electronic features, but different routes by which may be metabolised *in vivo*.

Synthesis, SAR, *in vitro* and *in vivo* biological test of title compounds will be reported.



a:R=H; b:R=CH₃

[1] Aiello, E.; Aiello, S.; Mingoia, F.; Bacchi, A.; Pelizzi, G.; Musiu, C.; Setzu, M. G.; Pani, A.; La Colla, P. and Marongiu, M. E. Synthesis and Antimicrobial Activity of New 3-(1-R-3-methyl-4-nitroso-1H-5-pyrazolyl)-5-methylisoxazole derivatives. *Bioorganic and Medicinal Chemistry*, 2000, 8, 2719-2728.

[2] Stefania Aiello, Antonio Macchiarulo, Maria Milici and Enrico Aiello, Sintesi e studi QSAR di nuovi derivati 3(5)-(2-X)-1R-1H-4-nitrosopirazoli: una classe di composti con potente attività antifungina *in vitro*. Parte VI XVII Convegno Nazionale della Divisione di Chimica Farmaceutica della SCI, Pisa 6-10 settembre 2004.

[3] Stefania Aiello; Enrico Aiello, Marica Orioli, Marina Carini, 3-(1-R-3-methyl-4-nitroso-1H-5-pyrazolyl)-5-methylisoxazoles: a new class of antifungal compounds. *In vitro* metabolism by rat liver: LC and LC-MS studies. Convegno Nazionale, Sorrento 18-22 Settembre 2002.