STUDIES ON POTENTIAL STAT-3 INHIBITORS:
REACTIVITY AND BEHAVIOUR OF FURAZAN DERIVATIVES

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Signal transduction and activator of transcription 3 (STAT-3) is a latent cytosolic protein member of STAT family that transmits cytoplasmic signals (e.g. from growth factors, polypeptide cytokines) to the nucleus\textsuperscript{1}. The mechanism of activation provides the STATs recruitment to phosphorilated receptors \textit{via} their SH2 domain. STAT-3 is involved in cell growth and survival but STAT-3 signalling might contribute to malignancy by preventing apoptosis: even if the molecular mechanism of oncogenesis by STAT-3 must be clearly defined, STAT-3 is constitutively activated by aberrant upstream tyrosine kinase activities in a broad spectrum of human solid and blood tumours. As reported, the blocking of constitutively activated STAT-3 signalling leads to apoptosis of tumour cells\textsuperscript{2-4} but does not affect normal cells\textsuperscript{5-6}. Therefore, inhibition of STAT-3 could be a leading target for cancer therapy.

Our preliminary studies were focused at the discovery of new small molecules as potential STAT-3 inhibitors. On these bases, we decided to explore the reactivity of a relatively poorly studied heterocycle, namely furazan (1,2,5-oxadiazolic) ring and we planned the synthesis of a new series of compounds:

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\begin{align*}
\text{R} & = \text{CH}_3, \text{CH}_2\text{OH}, \text{COOCH}_3, \text{C}_6\text{H}_5 \\
\text{X} & = \text{NHCO}, \text{NHSO}_2, \text{NHCN}\end{align*}
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The synthetic procedures applied for the preparation of the new derivatives as well as the results of their biological evaluation, modelling and crystallographic studies will be presented.