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

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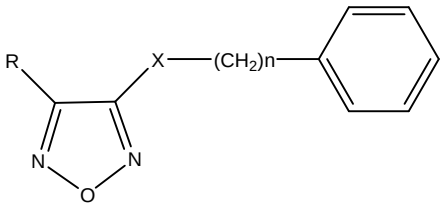
Signal transduction and activator of transcription 3 (STAT-3) is a latent cytosolic protein member of STAT family that transmits cytoplasmic signals (e.g. from growth factors, polypeptide cytokines) to the nucleus[1].
The mechanism of activation provides the STATs recruitment to phosphorilated receptors *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[2-4] but does not affect normal cells[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:



n = 0, 1

R = CH_3 , CH_2OH, $COOCH_3$, C_6H_5

X = NHCO, $NHSO_2$, NHCONH

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.

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