SYNTHESIS OF PYRIMIDINES BEARING HYDROXAMIC ACID AND 1,3,4-OXADIAZOLE-2-THIONE MOIETIES AS POTENTIAL HDAC INHIBITORS

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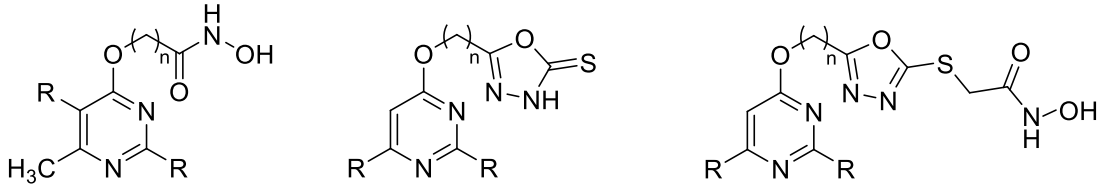
Histone deacetylases (HDACs) are a family of enzymes that modulate the acetylation of histones and non-histone proteins. HDACs play an essential role in many biological processes such as gene regulation, transcription, cell proliferation, angiogenesis, migration, differentiation and metastasis [1]. HDACs have been proven to be promising therapeutic targets for cancer treatment, particularly of hematological malignancies, based on the successful clinical approval of six HDAC inhibitors to date: vorinostat, romidepsin, belinostat, panobinostat, pracinostat, and chidamide [2]. Pyrimidines are widely spread in nature and occupy an exclusive place, mainly due to their importance for living organisms and wide range of biological activities of their derivatives [3, 4]. Pyrimidine moiety is a building block for several new drugs introduced to the marked every year [5]. In this context and continuing our work dedicated to the development of efficient methods for the synthesis of functionalized pyrimidines [6, 7], we present herein the synthesis of pyrimidine-based hydroxamic acids and 1,3,4-oxadiazole-2-thiones **1**–**3**.



1 **2** **3**

The inhibitory activity of ompounds **1–3** against HDAC4 and HDAC8 isoforms were tested. Several compounds were micromolar HDAC inhibitors.

References

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