Hydroxamate, a key pharmacophore exhibiting a wide range of biological activities

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Résumé en anglais	Naturally occurring hydroxamic acid derivatives are biosynthesized by microorganisms (siderophores) and plants (benzoxazinoids). Recent developments in drug discovery have highlighted the numerous biological and pharmacological properties that the hydroxamic acid function may possess, leading to therapeutic applications. These properties may be explained by its ability to chelate metals via the presence of two oxygen atoms. Their pharmacological activities can be divided into three groups. The first concerns the ability of these hydroxamic acid derivatives to scavenge metals (particularly iron), which leads to antioxidant, antimicrobial and metal detoxification activities. The latter is largely used to treat iron overload in patients. The second group of activities is related to their ability to inhibit metallo-enzymes, which gives them a wide range of pharmacological effects: antimicrobial, anti-inflammatory and antitumor. The third group is linked to the capacity of these compounds to generate nitric oxide, which confers hypotensive activity. However, hydroxamates exhibit relatively low stability in vivo, which can be overcome by the synthesis of appropriately designed analogs. For this purpose, many different strategies have been proposed. In this review, we compare and discuss the various synthetic pathways used to obtain the most complex of them, the N-substituted hydroxamic acids. We conclude that among numerous protocols reported so far, the direct N-substitution of hydroxamic acids, the acylation of the appropriate N-O derivative and the direct oxidation of the corresponding amide allow for the synthesis of a wide range of new biologically active compounds.
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