Hydroxamic acids, which can be represented by a general formula RCONR'OH, where R, R' may be aryl or substituted aryl moiety, constitute a very unique family of chemicals that possess a wide spectrum of biological activities. They act as selective inhibitors of many enzymes, such as matrix metalloproteinases (MMPs), peroxidases, hydrolases, ureases, lipoxygenases, cyclooxygenases, histone deacetylase and peptide deformylases, and consequently possess hypotensive, anti-cancer, anti-malarial, anti-tuberculosis and anti-fungal properties. Their CONHOH moiety has been identified as a key functional group to develop potential therapeutic agents targeting cardiovascular diseases, HIV, Alzheimer’s disease, allergic diseases, metal poisoning and iron overload. Hydroxamic acids are also used industrially as anti-oxidants, inhibitors of corrosion, for the extraction of toxic elements, as a means of flotation of minerals and even for their ability to serve as redox switches for electronic devices. They can also act as nitric oxide donors. This versatility of hydroxamic acids depends on their ability to act as a bidentate ligand to chelate with metal ions such as Fe$^{2+}$ and Zn$^{2+}$ at the active site of the enzymes. Their hydroxamic acid moiety, CONHOH, is not only a strong metal-binding group but also possesses multiple sites for potential hydrogen bond interactions with the enzymes. Thus, the metal-chelating property and multiple hydrogen-bond formation ability of hydroxamic acids have made them an intriguing family of compounds with a wide spectrum of therapeutic roles. One of the first therapeutic roles of hydroxamic acids was associated with their use as siderophores, a class of low molecular weight iron-sequestering agents. Siderophores have vast therapeutic potential to deal with iron overload in transfusion-dependent patients, such as those suffering from thalassemia. Because of these enormous therapeutic applications, the hydroxamic acids have greatly drawn the attention of both theoretical and experimental chemists to make studies on them for the design and development of drugs against a number of diseases. This book therefore presents some very interesting chapters on them, written by experts, covering their various chemical and pharmaceutical aspects.

The book contains 11 chapters in total. Since the multi-faceted activity of hydroxamic acids depends on the chemical aspects of these compounds, the very first chapter written by Gupta and Anjana describes in detail The Chemistry of Hydroxamic Acids covering their synthesis, structure, chelating, hydrogen-bonding
and nitric oxide releasing properties, and general mechanism of inhibition of various enzymes. The second chapter written by Kakkar on Theoretical Studies on Hydroxamic Acids further adds to their chemistry, discussing their conformation, tautomerism, metal ion selectivity, and complexation.

Among the various enzymes which have been found to be inhibited by hydroxamic acids, the carbonic anhydrases (CAs), MMPs and histone deacetylases (HDACs) have been most widely studied. Therefore, the three consecutive Chaps. 3–5, namely Hydroxamic Acids as Carbonic Anhydrase Inhibitors by Supuran, Structure–Activity Relationships of Hydroxamic Acids as Matrix Metalloproteinase Inhibitors by Patil and Gupta and Hydroxamic Acids as Histone Deacetylase Inhibitors by Thaler et al. describe vividly the different types of hydroxamic acids inhibiting these enzymes and their structure–activity relationships. However, no less important have been hydroxamic acids acting as inhibitors of ribonucleotide reductase, as the inhibitors of this enzyme have been developed as potent anticancer agents. Therefore, Chap. 6 Hydroxamic Acids as Ribonucleotide Reductase Inhibitors written by Basu and Sinha presents a few kinds of hydroxamates that inhibit carbonucleotide reductase, their mode of action, and progress in computer-aided SAR studies on them leading to the development of anticancer drugs.

Inhibitors of MMPs, HDACs, and ribonucleotide reductase have been developed as potent anticancer drugs. Therefore, a discussion of the inhibitors of these enzymes that belong particularly to hydroxamic acid class and have been evaluated against cancers have been nicely presented by Gupta et al. in Chap. 7 entitled as Hydroxamic Acid Derivatives as Anticancer Agents. These authors also discuss in this chapter the future prospects of design of potent anticancer agents based on hydroxamic acids.

Since HDAC inhibitors have been most attractive as anticancer agents, detailed quantitative structure–activity relationship (QSAR) studies have also been made on them in order to find the physicochemical and structural properties of the compounds governing their activity, so that the design of potent anticancer drugs may be rationalized. Hadjipavlau-Litina and Pontiki, therefore, presented in Chap. 8 entitled as Quantitative Structure-Activity Relationship Studies on Hydroxamic Acids Acting as Histone Deacetylase Inhibitors a detailed account of QSAR studies on hydroxamic acids acting as HDAC inhibitors. All 2D and 3D QSAR studies pointed out that anticancer activity of these compounds are basically controlled by their hydrophobic and steric properties.

The activity of the enzyme urease, which is produced in the body by a bacterium called Helicobacter pylori (H. pylori), plays a critical role in the pathogenesis of several diseases, such as urinary tract infections, urolithiasis, pyelonephritis, hepatic encephalopathy, hepatic coma, cancer, etc. Therefore, the inhibitors of urease have been greatly studied and hydroxamic acids have occupied the foremost position among the urease inhibitors. Thus Chap. 9 Hydroxamic Acids as Inhibitors of Urease in the Treatment of Helocobactor pylori Infections written by Muri and Barros gives a detailed account of hydroxamic acids acting as urease inhibitors and of their structure–activity relationships. The chapter also
describes the new technologies for the delivery of effective urease inhibitors in the body.

Hydroxamic acid derivatives have recently been recommended for the therapeutic treatment of several diseases, such as hypertension, cancer, as well as inflammations and infectious diseases, due to their ability to chelate metals, especially in metalloenzymes. In Chap. 10 entitled as Therapeutic Potential of Hydroxamic Acids for Microbial Diseases, Rodrigues et al. therefore present the potential use of hydroxamates and their derivatives for the treatment and control of such diseases, along with a general overview of their structure, synthesis and inhibition mechanism. Application of hydroxamic acids as chelating mineral collectors for ore beneficiation is a unique area of their use and has attracted the attention of limited workers in this unique area. Therefore, a review of the use of alkyl and aryl hydroxamic acids in mineral processing is finally presented by Natarajan in Chap. 11 entitled as Hydroxamic Acids as Chelating Mineral Collectors. In this chapter, basic information on mineral flotation chemistry is provided for the non-expert.

Thus an attempt has been made to cover all aspects of hydroxamic acids, a unique class of chemicals having multiple biological activities. Articles covered in this book are not only of interest to those working in this area but also to general readers. As an editor of this book, I have greatly enjoyed reading all the chapters and also hope the readers will do so. I greatly acknowledge the interest and zeal of all the authors for contributing such interesting and useful chapters.

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