ABSTRACT

Since their discovery by Wahlroos and Virtanen in 1959, and over the past decades, the chemistry and biochemistry of hydroxamic acids and their derivatives have attracted considerable attention, due to their pharmacological, toxicological and pathological properties. Hydroxamic acids generally have low toxicities and have a wide spectrum of activities in all types of biological systems, as such they act variously as growth factors, food additives, tumor inhibitors, antimicrobial agents, antituberculous, antileukemic agents, key pharmacophore in many important chemotherapeutic agents, pigments and cell-division factors. Several of them have been advanced into human clinical trials as pharmaceutical drugs, for the treatment of several diseases. The design and synthesis of ligands for biomedical applications in fields such as anticancer applications has become of great importance. One of these important ligands is hydroxamate molecules. Hydroxamic acids have been found to react with both proteins and nucleic acids. The reactivity of hydroxamic acids towards sulfhydryl groups of proteins has been suggested to be the reason for their inhibitory effect on various enzymes.

Quite recently, there have been articles concerning the biochemistry of anticancer activity of naturally occurring and synthetic class of organic compounds containing the hydroxamic acid functional group (-CONHOH). Hydroxyurea containing that group, is a well-known anticancer drug. It inhibits the DNA synthesis by impairing the activity of enzyme ribonucleotide reductase. Though it is clinically used as anticancer agent, it perturbs the hematological parameters and depresses the bone marrow. Subsequently anticancer properties of some aliphatic and aromatic hydroxamic acids (such as acetohydroxamic acid, benzohydroxamic acid and salicylhydroxamic acid) have been studied.

Kinetic studies on oxidation of the prepared binary complex of Salicylhydroxamate and its ternary complex involving Cysteine ligand have been investigated. The rate of oxidation of both [Cr(ShiH₂)(H₂O)₄]²⁺ and [Cr(ShiH₂)(cys)(H₂O)₃]⁺ by periodate were increased with [periodate], [complex], pH of the medium and temperature. Thermodynamic activation parameters were determined. From these studies, it was concluded that the reaction of [Cr(ShiH₂)(H₂O)₄]²⁺ obeys the rate law:

\[
d\frac{\text{[Cr}^{VI}] }{dt} = K_1 k_2 [\text{Cr (ShiH}_2) (\text{H}_2\text{O})_4 ^{2+}] [\text{H}_3\text{IO}_6] / (K_4 [\text{H}^+])
\]

Whereas the rate of oxidation of [Cr(ShiH₂)(cys)(H₂O)₃]⁺ was increased with [periodate], [complex], pH of the medium and temperature according to the rate law:

\[
d\frac{\text{[Cr}^{VI}] }{dt} = (k_2 + k_3/[\text{H}^+]) [\text{IO}_4^-] [\text{Cr(ShiH}_2)(\text{cys})(\text{H}_2\text{O})_3]^{+}
\]

Two alternative mechanisms may be considered for the oxidation of [Cr(ShiH₂)(cys)(H₂O)₃]⁺ by periodate. The first alternative inner-sphere mechanism may be accommodated through replacement of coordinated H₂O by periodate species and the second alternative mechanism may be accommodated through reactive species IO₄⁻ coordinates to form the precursor complex. The rate law is consistent with a mechanism including two electron transfer paths; one is first order while the second is second order in periodate. The enthalpy of activation ΔH° and entropy of activation ΔS° also are calculated.