

Metal ion mediated photolysis reactions of riboflavin: A kinetic study



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ABSTRACT

The effect of metal ion complexation on the photolysis of riboflavin (RF) using various metal ions (Ag^+ , Ni^{2+} , Co^{2+} , Fe^{2+} , Ca^{2+} , Cd^{2+} , Cu^{2+} , Mn^{2+} , Pb^{2+} , Mg^{2+} , Zn^{2+} , Fe^{3+}) has been studied. Ultraviolet and visible spectral and fluorimetric evidence has been obtained to confirm the formation of metal-RF complexes. The kinetics of photolysis of RF in metal-RF complexes at pH 7.0 has been evaluated. The apparent first-order rate constant (k_{obs}) for the photolysis of RF and the formation of lumichrome (LC) and lumiflavin (LF) (0.001 M phosphate buffer) and LC, LF and cyclodehydroriboflavin (CDRF) (0.2–0.4 M phosphate buffer) have been determined. The values of k_{obs} indicate that the rate of photolysis of RF is promoted by divalent and trivalent metal ions. The second-order rate constants (k') for the interaction of metal ions with RF are in the order: $\text{Zn}^{2+} > \text{Mg}^{2+} > \text{Pb}^{2+} > \text{Mn}^{2+} > \text{Cu}^{2+} > \text{Cd}^{2+} > \text{Fe}^{2+} > \text{Ca}^{2+} > \text{Fe}^{3+} > \text{Co}^{2+} > \text{Ni}^{2+} > \text{Ag}^+$. In phosphate buffer (0.2–0.4 M), an increase in the metal ion concentration leads to a decrease in the formation of LC compared to that of CDRF by different pathways. The photoproducts of RF have been identified and RF and the photoproducts have simultaneously been assayed by a multicomponent spectrometric method. The mode of photolysis of RF in metal-RF complexes has been discussed.

1. Introduction

Riboflavin (RF) (1) (Fig. 1) is a photosensitive compound [1] which undergoes degradation in aqueous solution on exposure to light [2–4]. The degradation takes place by different mechanisms depending upon the reaction conditions (pH, buffer kind and concentration, light intensity and wavelengths, aerobic or anaerobic) [5–7]. The photolysis of RF in aqueous solution leads to the formation of a number of compounds including formylmethylflavin (FMF) (2), lumichrome (LC) (3), lumiflavin (LF) (4), carboxymethylflavin (CMF) (5) and cyclodehydroriboflavin (CDRF) (6) by photoreduction and photoaddition pathways [2,8–14] (Fig. 1). The kinetics of photolysis reactions of RF has been evaluated [2,10,12–16] using specific spectrometric methods [2,11,12,17,18].

Flavins are known to interact with metal ions to form complexes. For example, 10-methylisoalloxazine forms a complex with Cu^+ ions [19,20], RF with monovalent ions (Ag^+) [21,22], divalent ions (Fe, Cu, Cd, Mg, Mn, Co, Ni, Zn, Ru) [23–30] and trivalent ions (Cr^{3+} , Fe^{3+}) [31,32], flavin mononucleotide (FMN) with divalent ions (Mg, Ca, Sr, Ba, Mn, Co, Cu, Zn, Cd) [33] and trivalent ions (Fe^{3+}) [34], flavin dinucleotide with Hg^{2+} and Cd^{2+} ions [35] and flavin analogues (3-methyl-10-phenylisoalloxazine and 3-methyl-10-phenyl-5-deazaisoalloxazine) with Mg^{2+} and Zn^{2+} ions [36,37]. Structural

characteristics [22,24,28,38,39] and redox reactivity [28,37,40] of the metal-flavin complexes have been studied in detail.

It has been shown [28,37,38] that metal centers can bind to flavin in the N(5)-C(4a)-C(4)-O(4) site to form a planar five-membered chelate ring (Fig. 2). Electrochemical and spectroscopic data on the structural features of these complexes have been reported [28,37,38]. The metal-flavin interactions have important implications in the electron transfer reactivity of flavins in biological systems [28].

The aerobic photolysis of RF is promoted by Fe^{2+} , Fe^{3+} , Cu^{2+} , Sn^{2+} , Co^{2+} , Mn^{2+} , Cr^{2+} , Al^{3+} in the decreasing order of reactivity. The anaerobic photolysis of RF is promoted by Fe^{3+} ions and inhibited by Fe^{2+} and Cu^{2+} ions [25]. RF catalyzes the photooxidation of Fe^{2+} (oxygen dependent) and photoreduction of Fe^{3+} (inhibited by oxygen). Both ions have been found to quench the fluorescence of RF [31]. Metal-flavin complexes presumably involve extensive charge transfer from metal d orbitals to flavin π^* orbitals [32]. The fluorescence of RF is quenched by Ag^+ ions, various divalent ions and Fe^{3+} ions due to the formation of non-fluorescent metal-RF complexes [21,23,24,31]. The quenching of excited singlet states of organic molecules by metal ions has been observed [41]. Fe^{2+} ions promote photolysis of RF strongly followed by the effect of Fe^{3+} , Cu^{2+} , Al^{3+} , Sn^{2+} , Co^{2+} , Mn^{2+} , Cr^{3+} and Zn^{2+} ions. Ag^+ ion inhibits the photolysis of RF [25].

Trace quantities of metallic impurities in pharmaceuticals may

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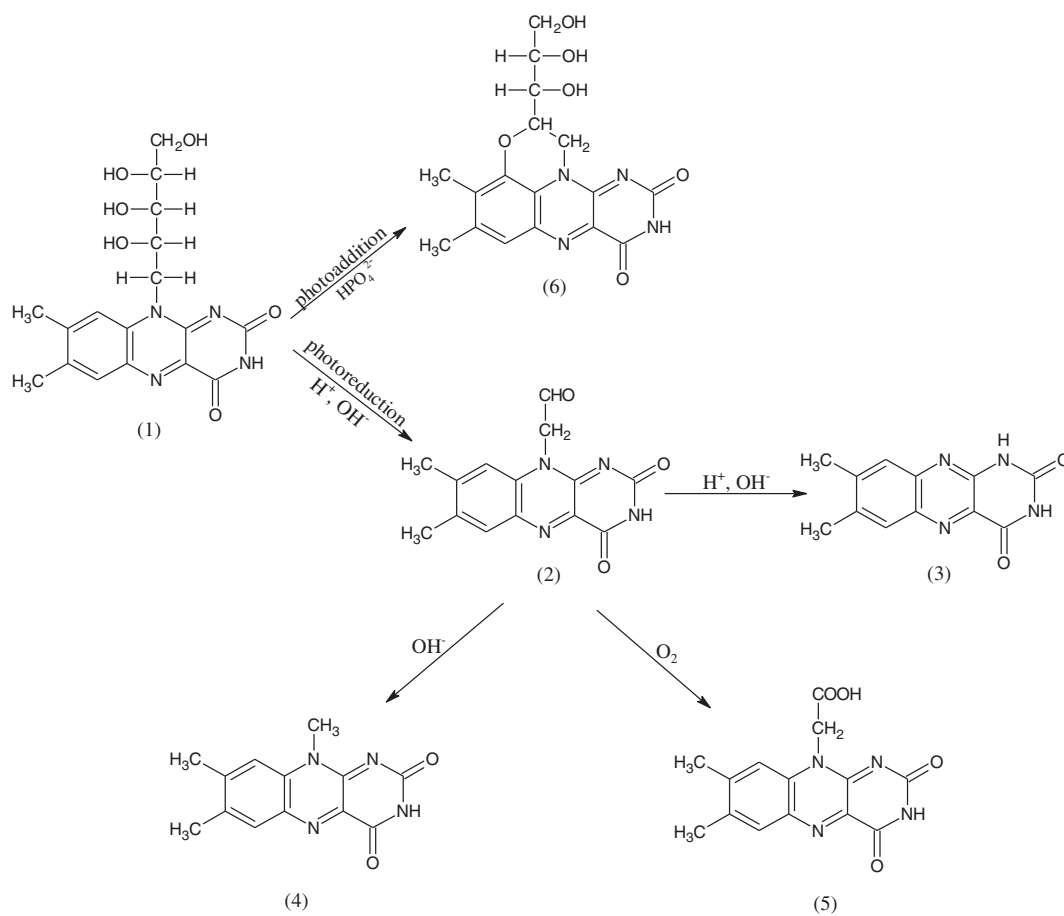
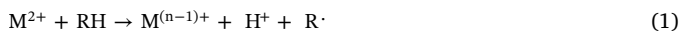


Fig. 1. The photoreduction and photoaddition pathways of riboflavin (RF).

catalyze the degradation of drug substances [1], particularly in the presence of light. These processes occur by one-electron oxidative reactions and result in an increase in the rate of formation of radicals that lead to the degradation products. Oxidative reactions are often initiated by metal ions such as Fe^{3+} , Cu^{2+} , Co^{3+} , Ni^{2+} , Mn^{2+} . These metal ions act as initiators since they are capable of acting as radicals in their oxidation states, for example, Cu^{2+} ion has 27 electrons and it requires one electron to complete the electron pair. The metal ion can react with a drug to form radicals (Eq. 1).



The radical can then participate in the propagation cycle or can react with a hydroperoxide to catalyze the degradation (Eq. 2).



$\text{R}'\text{OOH}$ could be a hydroperoxide of the drug (e.g. RF) itself or of some other component present in the system [42]. Thus the metal ion can directly react with oxygen to form an oxygen radical which can then initiate an autoxidation reaction. The metal ion can also form a complex with oxygen to produce a peroxy radical or it can react with a drug (e.g. RF) to form a radical to initiate a photochemical chain reaction.

The object of this work is to conduct a study of the photolysis of RF in metal-RF complexes using various metal ions, to identify the photoproducts, to determine the absorption and fluorescence characteristics and to evaluate the influence of metal ions on the kinetics of photolysis reaction at different buffer concentrations. It may have

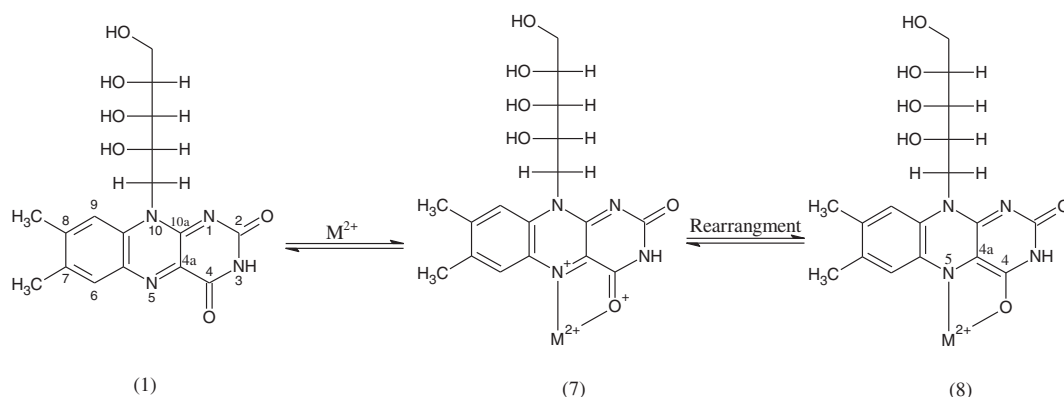


Fig. 2. Formation of the metal-RF complex.

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