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ORIGINAL ARTICLE

Kinetics, mechanistic and synergistic studies of Alpha lipoic acid with hydrogen peroxide

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Abstract Alpha lipoic acid (ALA) holds redox behavior that was observed in the presence of different metals utilizing hydrogen peroxide (H_2O_2) as a strong oxidizing agent. The effects of different parameters like temperature, pH and concentrations were also monitored.

ALA in the presence of hydrogen peroxide (H_2O_2) showed oxidation as well as degradation processes. To monitor the oxidation kinetics of ALA in the presence of different essential metals to find its reaction pathway using salt affect parameters.

The redox behavior of Alpha lipoic acid (ALA) was found to be significant at pH ranging from 4 to 10, at 29 °C in a given pseudo first order reaction conditions. The values of the rate constant in the presence of different essential metals such as Mo, Se, Co, Cr, Fe, and Zn were also obtained. Furthermore, synergistic effects were observed in the presence of Mo^{6+} and Fe^{2+} at all applied conditions.

Activation energy of ALA oxidation is 36.7 kJ whereas in the presence of Fe^{2+} its activation energy went up to 48 kJ; however, in the presence of Mo^{6+} the activation energy drops to 18.3 kJ. In the presence of Fe^{2+} and Mo^{6+} the synergistic effect works and its activation energy became 36.5 kJ. The reaction mechanism was also proposed.

1. Introduction

Alpha lipoic acid (ALA) derives its name because of its higher degree of solubility in lipid and its acidic nature (p*K*a = 4.7). It helps in a number of in vivo reactions, like in a transfer of hydrogen and acyl groups in oxidative decarboxylation of α-keto acids. ALA acts as the chelator for metal in lead toxicity [1].

ALA and its reduced fellow di-hydro alpha lipoic acid (DHLA) hold all the necessary characteristics of an ideal anti-oxidant such as early quenching of free radicals, [2] chelate metals have an amphiphilic nature with no side effects [3]. Within the time period of 30–60 min maximum absorption was achieved when its single dose of 50–600 mg was administered [4].

ALA and DHLA are not only potent quenchers but also quench different oxygen species [1]. ALA neutralizes free radicals such as free OH, hypochlorous acid, singlet oxygen, but

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not hydrogen peroxide [5]. ALA and DHLA, hold an ability to reduce oxidative stress by regenerating other antioxidants (vitamins C, E and glutathione), serving as a Reactive Oxygen Species (ROS) scavenger, and also chelate transition metals (Cu and Fe) [6,7]. Preferential metals being chelated by ALA and DHLA are Cu^{+2}, Zn^{+2}, and Pb^{+2} whereas Fe^{+3} is chelated by DHLA only [8]. ALA when supplied exogenously shows its antioxidant properties and prevents the cause of damage due to ROS [1]. On the other hand H_2O_2 is an environmentally friendly oxidizing agent due to the presence of only hydrogen and oxygen atoms which promotes the photo-catalysis in two possible ways;

1. Hydroxyl free radicals produced by H_2O_2 reduction at the conduction band.
2. Hydroxyl radical produced by photolytic cleavage in the presence of UV radiations [9]. It is having many physiological and non-physiological uses so its trace concentration determination is also very important [10].

Iron an abundant metal in human physiology is redox active in nature and has great potential to generate free radicals mediated by Fenton chemistry. In aqueous medium ferrate is an energetic oxidizing agent, where its oxidation potential ranges from 2.20 V in acidic medium to 0.7 V in basic medium [11]. H_2O_2 plays a vital role in the death of osteoblast which is sensitive against ROS [12]. Among the elements, iron holding a redox active properties, exacerbates oxidative stress by OH generation by Fenton chemistry, ALA chelation with Fe in vivo has not been determined as yet [1]. Cells convert ALA into DHLA which in-turn can interact with Fe, although Fe chelation in vitro is possible with both ferric and ferrous.

The aim of the study was to find the kinetic aspects of ALA at various kinetic conditions. The behavior of ALA on the interaction with redox active specie (H_2O_2), and then to see its oxidation behavior in the presence of different metals with which it can easily interact. Software was used to prove the scavenging and synergistic properties on the described reaction.

2. Material and methods

2.1. Equipment

All the absorbance was recorded with a path length of 1 cm quartz cuvette using UV–Visible Spectrophotometer UV-1601 Shimadzu Japan. pH was adjusted by the help of a pH meter (Precisa 900) with accuracy of ± 0.003 pH. Temperature was maintained by using Memmert water bath (WB 14) with accuracy of ± 0.1 K.

2.2. Chemicals

Hydrogen peroxide (H_2O_2) of Riedel-de Haën and for a pH maintenance, Hydrochloric acid (HCl) of REANAL and sodium hydroxide (NaOH) of Alpha aesar were used. lipoic acid and all metal salts of Sigma Aldrich, were purchased from a local supplier of Analytical Grade (AG). All the chemicals were used directly as received bases without purification. The *Compusyn* software was used for analyzing the combined effects of Fe and Mo on the reaction and reported in Table 1. The symbols Fa and CI represent, Fraction affected and Combination Index respectively. CI > 1 means the combination effect is antagonistic in nature while CI = 1 means it is an additive, whereas CI < 1 shows synergism.

2.3. Procedure

ALA is almost insoluble in aqueous medium; therefore, sodium salt of ALA was used for the preparation of ALA aqueous solution, using the reported method [13].

Table 1 Thermodynamic parameters.

Temperature T (K)	Activation energy E_a (kJ/mol)	Frequency factor A (1/s) $\times 10^5$	Enthalpy $\Delta H°$ (kJ/mol)	Entropy $\Delta S°$ (kJ/mol)	Gibbs energy $\Delta G°$ (kJ/mol)	Microstates W
Thermodynamic parameters of ALA						
302	36.7	1.28	34.82	−157.0	82.5	6.5×10^{-69}
307				−157.5	83.2	
313				−157.8	84.2	
319				−157.8	85.2	
Thermodynamic parameters of ALA with Fe^{2+}						
302	48	0.0191	47.82	−119.1	83.0	2.08×10^{-52}
307				−120.5	84.0	
313				−119.2	85.0	
Thermodynamic parameters of ALA with Mo^{6+}						
291	18	560	16.84	−206.8	77.0	3.43×10^{-90}
297				−206.7	78.2	
302				−206.6	79.2	
308				−206.8	80.5	
Thermodynamic parameters of ALA with synergistic effects						
285	36.5	0.4	22.51	−188.7	76.2	2.2×10^{-82}
292				−189.0	77.7	
302				−188.7	79.5	