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Hemolysis of human red blood cells by combination of riboflavin and aminophylline

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Abstract

The effect of aminophylline on human red blood cells (RBC) has been studied. Under in vitro condition, aminophylline alone does not hemolyse RBC. However, in the presence of riboflavin and visible light, aminophylline causes hemolysis of RBC. This hemolysis depends on the concentration of both riboflavin and aminophylline. Using different free radical scavengers we show that RBC hemolysis is caused by reactive oxygen species. Studies using bovine serum albumin show that riboflavin–aminophylline combination can also cause protein degradation in vitro.

Keywords: Riboflavin; Aminophylline; Oxygen radicals; RBC; Hemolysis

Introduction

There is a growing body of evidence that prooxidant species can contribute to lung injury in a variety of pulmonary diseases including asthma [1,2]. Enhanced production of free radicals has been reported particularly in asthmatic patients. This oxidant load has been found to correlate with the clinical severity of the disease and the entity of the airway obstructions [2,3]. Theophylline, and its more soluble form, aminophylline, are bronchodilator drugs commonly used for the treatment of asthma [4,5]. Both these drugs are administered

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intravenously during treatment. Both aminophylline and theophylline are xanthine compounds structurally related to uric acid [4], which has significant antioxidant property [1]. Recent studies have shown that theophylline, at therapeutically used concentrations, can decrease oxygen radical release from alveolar macrophages and mononuclear cells [6], suggesting that some indirect antioxidant mechanisms may also be operative in its therapeutic action [7]. On the other hand, theophylline, in combination with riboflavin, was also found to enhance bilirubin degradation in vitro. Therefore, a riboflavin–aminophylline combination was recommended for the effective treatment of jaundice in neonate [8].

We have recently shown that photoactivated riboflavin induces hemolysis of human red blood cells (RBC) in the presence of Cu(II) [9]. As aminophylline is administered intravenously, it was of interest to study whether the recommended riboflavin–aminophylline combination had any effect on human RBC. Unexpectedly, it was observed for the first time that a riboflavin–aminophylline combination causes hemolysis of fresh human RBC in the presence of visible light and in absence of Cu(II). However, neither riboflavin nor aminophylline was able to cause any hemolysis alone, either in the presence or absence of light.

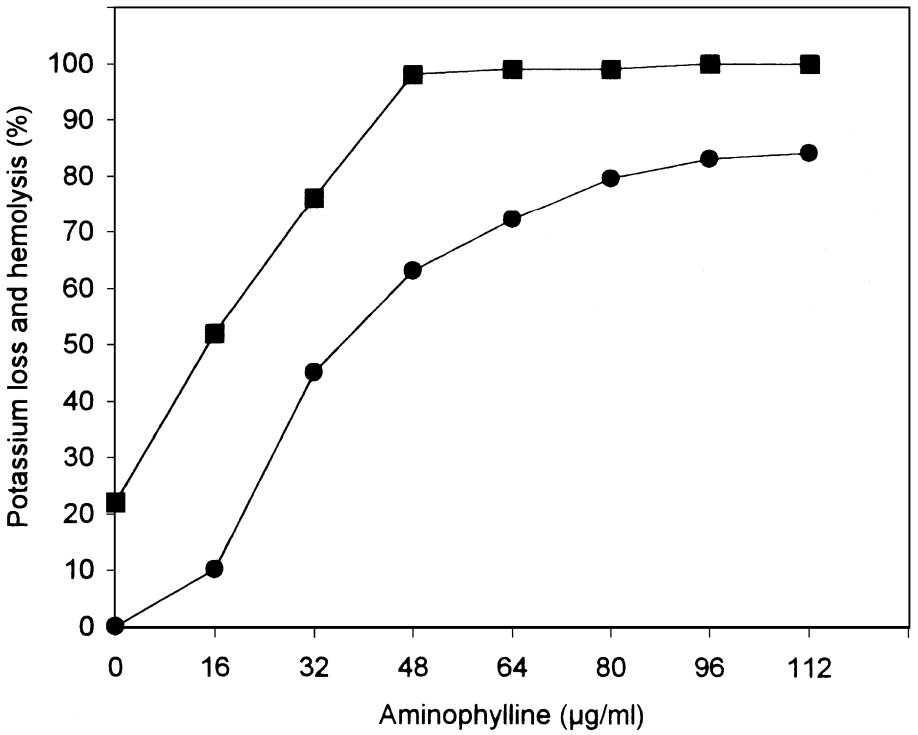

Fig. 1. Riboflavin–aminophylline induced K^+ loss and hemolysis of human RBC. Cells were incubated in 3 ml of buffer containing 10 mM Tris–HCl, pH 7.4, 0.15 M NaCl, 50 μM riboflavin and 16–112 μg/ml aminophylline to give 0.5% hematocrit. The percent of K^+ loss (■) and hemolysis (●) was measured after 2 hours of incubation in visible light.