GASTRO PROTECTIVE EFFECTS OF δ-TOCOTRIENOL ON STRESS INDUCED GASTRIC MUCOSAL INJURY

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ABSTRACT

This study aims to investigate the gastric protective effects of δ-tocotrienol (T3) concentrate (90% δ-tocotrienol, and 10% γ-tocotrienol) supplementations on gastric injury of rats induced by water-immersion restraint stress. Fourteen male *Sprague-Dawley* rats (200-250 g) were divided into two equal sized groups; a control group and a treatment group. The treatment group received δ-tocotrienol concentrate at 60 mg/kg body weight for 35 days. The body weights of rats were recorded daily before the treatment was given. At the end of the treatment period, all rats were subjected to water-immersion restraint stress (WIRS) for 3.5 hours, following which, the rats were euthanized. The stomachs were isolated and opened along the greater curvature for the examination of lesions and measurements of gastric parameters such as gastric malondialdehyde (MDA) and prostaglandin E_2 (PGE_2). The severity of gastric mucosal lesions was graded by macroscopic observation using a semiqualitative scale by independent examiners. The findings showed that the mean gastric mucosal lesion index in the treated rats were lower ($P<0.05$) than that of the control rats. This suggests that the tocotrienol concentrate has the ability to confer protection to the gastric mucosa against gastric injury induced by acute restraint stress. No significant difference was observed on changes in rats body weight before and after the treatment. The gastric PGE_2 content in both groups were comparable. We also found that the gastric MDA content was significantly higher in the treatment group compared to the control group rats which indicates that pure tocotrienol supplementation (60kg/kg bw) was not able to reduced the lipid peroxidation process. This study concludes that the δ-tocotrienol concentrate has the ability to protect the gastric mucosa from stress-induced injury. The gastric protection, however is mediated through a non-antioxidants mechanism.

CONTENTS

CHAPTER 1

INTRODUCTION

It is well known that stress has been implicated as a risk factor of various major health problems (Vere *et al* 2009, Kane 2009, Tawatsupa *et al* 2010). In particular, this include on the formation of gastric lesion, also known as stress-induced gastric mucosal injury (SIGMI) (Konturek *et al.* 1998). Among various animal models of stress, water immersion restraint stress (WIRS) has been widely accepted for studying SIGMI. Previous studies had demonstrated an immediate appearance of multiple gastric lesions in the gastric mucosa in rats subjected to WIRS for 3.5 hours (Konturek *et al* 2001, Hidemi *et al* 2001, Ibrahim IA *et al* 2008, Chen *et al* 2010) confirming the reproducibility of this model.

The pathological basis for the development of stress induced gastric injury is multifactorial. Stress had been shown to cause overstimulation of sympathetic activity and activation of hypothalamic-pituitary adrenal axis (HPA-axis) leading to the hypersecretion of catecholamine. This increased in catecholamine levels will result in direct vasoconstriction of gastric mucosal vessels which in turn leads to local hypoxia and ischemia. Under this hypoxic-ischemic condition, the reactive oxygen species (ROS) such as superoxide anion, hydrogen peroxide and hydroxyl radical are rapidly generated.