BioFactors

# Vitamin E protects against stress-induced gastric mucosal lesions in rats more effectively than vitamin C

*Yoshiji Ohta,[1]* Yoichiro Imai,[2] Shingo Kaida,[3] Yoshio Kamiya,[4] Minoru Kawanishi,[3] and Ichiro Hirata[4]*

*[1]Department of Chemistry, Fujita Health University School of Medicine, Toyoake, Aichi 470-1192, Japan*

*[2]Department of Clinical Biochemistry, Fujita Health University College, Toyoake, Aichi 470-1192, Japan*

*[3]Department of Internal Medicine, Fujita Health University School of Medicine, Toyoake, Aichi 470-1192, Japan*

*[4]Department of Anesthesiology, Second Teaching Hospital, Fujita Health University, Nagoya, Aichi 454-0012, Japan*

## Abstract.

In this study, we examined the protective effects of vitamin E (VE) against gastric mucosal lesions induced by water immersion restraint stress (WIRS) in rats in comparison with that of vitamin C (VC). The gastric mucosa of rats with 6 h of WIRS showed lesions with bleeding, decrease in nonprotein SH, VC, VE, and adherent mucus concentrations and constitutive nitric oxide synthase activity, and increase in lipid peroxide and NOx (nitrite/nitrate) concentrations and myeloperoxidase, xanthine oxidase, and inducible nitric oxide synthase activities. Either VE (0.05 or 0.5 mmol/kg) or VC (0.5 or 1.5 mmol/kg) was orally administered to rats with 6 h of WIRS just before the onset of the stress. Both doses of preadministered VE prevented gastric mucosal lesion development and attenuated all these changes in gastric mucosal components and enzymes studied, whereas only the higher dose of preadministered VC suppressed the changes in all parameters studied. These results indicate that orally administered VE protects against WIRS-induced gastric mucosal lesions in rats more effectively than orally administered VC. These results also suggest that the administered VE protects against gastric mucosal lesions in rats with WIRS through its antioxidant and anti-inflammatory actions in the gastric mucosa in the same way as the administered VC.

© 2010 International Union of Biochemistry and Molecular Biology, Inc.

Volume 36, Number 1, January/February 2010 , Pages 60–69 •

E-mail: yohta@fujita-hu.ac.jp

**Keywords:** gastric mucosal lesion, water immersion restraint stress (rat), vitamin E, vitamin C, oxidative damage

## 1. Introduction

Vitamin C (VC) (or ascorbic acid) is a water-soluble antioxidant. This vitamin scavenges reactive oxygen species (ROS) such as superoxide radical ($O_2^{\bullet -}$), hydroxyl radical ($^{\bullet}OH$), hydrogen peroxide ($H_2O_2$), singlet oxygen, hypochlorous acid (HOCl), and peroxyl radical by itself and also supports the chain-breaking antioxidant action of vitamin E by reducing vitamin E radical to vitamin E in the liquid/aqueous interface [1–7]. VC reduces ROS generation by activated neutrophils [8] and prevents neutrophil adherence to endothelium by scavenging ROS derived from activated neutrophils [9]. Vitamin E (VE) is a lipid-soluble antioxidant. This vitamin functions as a chain-breaking antioxidant for lipid peroxidation in cell membranes and also as a scavenger of ROS such as $O_2^{\bullet -}$, $^{\bullet}OH$, and singlet oxygen [10]. VE exerts an anti-inflammatory action by inhibiting the production of $O_2^{\bullet -}$ in activated neutrophils, adhesion of neutrophils to endothelial cells, and transendothelial migration of neutrophils [11–14]. Thus, there are many similarities in antioxidant and anti-inflammatory actions between VC and VE, although the cellular localization of both vitamins is different.

It has been reported that ROS generated by infiltrated neutrophils and the xanthine–xanthine oxidase (XO) system and/or lipid peroxidation caused by the generated ROS are involved in the development of gastric mucosal lesions induced by water immersion restraint stress (WIRS) in rats [15–20]. We have shown in rats exposed to WIRS over 6 h that gastric mucosal lesions appear at 1 h of WIRS and develops time-dependently thereafter and that the gastric mucosal ascorbic acid level decreases at 3 h of WIRS with its further decrease at 6 h, whereas the gastric mucosal VE level decreases at 6 h [21]. Furthermore, we have shown that oral administration of L-ascorbic acid (250 mg/kg) to rats with 6 h of WIRS just before the onset of the stress prevents lesion development with attenuation of decreased

*Address for correspondence: Yoshiji Ohta, Ph.D., Department of Chemistry, School of Medicine, Fujita Health University, Toyoake, Aichi 470-1192, Japan. Tel.: +81-562-93-4593; Fax: +81-562-93-4593; E-mail: yohta@fujita-hu.ac.jp

Received 7 June 2009; accepted 2 December 2009
DOI: 10.1002/biof.73
Published online 20 January 2010 in Wiley InterScience (www.interscience.wiley.com)