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List of Abbreviations

AD .....Alzheimer's disease

AGEs.....advanced glycation end-products

ALEs .....advanced lipoxidation end-products

Ca^{2+} .....Calcium

CAR .....Carnosine

Cd.....cadmium

$CdCL_2$.....cadmium chloride

cGMP.....guanosine 3', 5'-monophosphate

CN .....carnosinase

DNA.....Deoxyribonucleic acid

EC-SOD .....extracellular Super oxide dismutase

eNOS .....endothelial nitric oxide synthase

ER .....endoplasmic reticulum

Fe^{2+}.....Ferrous

GABA.....gamma-aminobutyric acid

GFR .....glomerular filtration rate

GSH .....glutathione

H_2O_2.....Hydrogen peroxide

HCD.....histidine-containing dipeptides

HNE.....hydroxynonenal

I/R.....ischemia/reperfusion

IL-10.....Interleukin 10

IL-4.....Interleukin 4

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IL-6.....Interleukin 6

iNOS .....Induced nitric oxide synthase

MAPK .....mitogen-activated protein kinases

MDA .....malondialdehyde

MPO.....Myeloperoxidase

MT.....metallothionein

NADPH .....nicotinamide adenine dinucleotide phosphate

NO .....nitric oxide

NOS .....nitric oxide synthase

O_2 .....oxygen

POT .....proton-coupled oligopeptide transporter

ROS .....Reactive oxygen species

SH .....Sulfhydryl

SOD .....Super oxide dismutase

STAT .....signal transducer and activator of transcription

TNF-α .....tumor necrosis factor-α

UV.....Ultraviolet

Zn^{2+} .....Zinc

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Abstract

Introduction: Cadmium (Cd) is one of the most toxic non-essential toxic metals, an environmental and occupational pollutant endangering human and animal health. **Aim of the study:** Due to carnosine's multifunctional properties, the present study was designed to study the effect of carnosine as potential antioxidant agent on cadmium–induced lipid peroxidation and renal oxidative stress in aged rats. **Materials and Methods:** The present study was performed on 45 female Wistar rats, weighing at the start of the study between 280-380 g. During the experimental protocol the animals were maintained in the animal room at the physiology department with 12 hours periods of light and darkness under standard conditions of boarding with environmental temperature 20-25°C, and received food and tap water ad libitium. Animals were left for 10 days to acclimatize, housed in animal acrylic cages (45x38x18cm). **Results:** The results encountered in the present study reflect the changes in serum urea, creatinine, albumin, superoxide dismutase, malondialdehyde, nitric oxide, tumor necrosis factor-α and interleukin 10 levels, as well as blood and renal tissue cadmium levels, renal tissue superoxide dismutase, tumor necrosis factor-α and nitric oxide levels in control, cadmium, and carnosine treated groups. **Summary and Conclusion:** Due to carnosine's multifunctional properties, the present study was designed to study the effect of carnosine as potential antioxidant agent on cadmium–induced renal oxidative stress and lipid peroxidation.

Keyword: Protective Effect, Cadmium-Induced

INTRODUCTION

Cadmium (Cd) is one of the most toxic non-essential toxic metals, an environmental and occupational pollutant endangering human and animal health ***(El-Boshy et al., 2014; Satarug et al., 2003).*** Cigarette smoking is a significant source of environmental Cd exposure ***(Elinder et al., 1983).*** The kidney, skeleton and lungs are the tissues most affected by chronic Cd toxicity, with chronic exposure to Cd, approximately 50% of the accumulated dose is stored in the kidneys ***(Johri et al., 2010)***.

Aging in most species associates with impaired adaptive and homeostatic mechanisms that leave an individual susceptible to environmental or internal stress followed by increasing rates of disease and death ***(Anderson et al., 2009; Ning et al., 2013).*** Kidney is a typical target organ of age-associated tissue damage, and the increased incidence of chronic kidney disease in the elderly is a health problem worldwide ***(Coresh et al., 2003).***

Histidine-containing dipeptides like carnosine and arnesine have protective functions in both health and disease ***(Peters et al., 2015).*** The best-characterized histidine-containing dipeptide is carnosine ***(Boldyrev et al., 2013; Budzen and Rymaszewska, 2013),*** which is stored in

several tissues ***(Bex et al., 2014)***, it plays many roles in maintaining health, including antioxidant activity ***(Babizhayev et al., 2013; Boldyrev, 1993; Mozdzan et al., 2005)*** and the ability to scavenge carbonyls ***(Barski et al., 2013; Negre- Salvayre et al., 2008; Vistoli et al., 2009),*** inhibits glycation ***(Alhamdani et al,. 2007)***, and inhibits angiotensin-converting enzymes ***(Hou et al., 2003; Nakagawa et al., 2006)***.

Thus, it was important to probe the possible role of carnosine in protecting the kidneys from cadmium exposure in aged individuals.