Plant Physiology and Biochemistry 118 (2017) 643–652

Contents lists available at ScienceDirect

Plant Physiology and Biochemistry

journal homepage: www.elsevier.com/locate/plaphy

Research article

Exploration of acute genotoxic effects and antigenotoxic potential of gambogic acid using *Allium cepa* assay

Abhishek Shetty [a], Thejaswini Venkatesh [b], Padmanaban S. Suresh [a, *], Rie Tsutsumi [c]

[a] Department of Biosciences, Mangalore University, Mangalagangothri, 574199, India
[b] Department of Biochemistry and Molecular Biology, Central University of Kerala, Kasaragod, India
[c] Division of Nutrition and Metabolism, Institute of Biomedical Science, Tokushima University, Tokushima, Japan

ARTICLE INFO

Article history:
Received 20 June 2017
Received in revised form
31 July 2017
Accepted 4 August 2017
Available online 5 August 2017

Keywords:
Gambogic acid
Root tip
Genotoxic
Clastogenic

ABSTRACT

The plant derived xanthanoid gambogic acid (GA) is well known for its anticancer activity. To date, biological actions of GA on plant system have not been reported. In the present study, we evaluated the potential acute genotoxic activity of GA, and its antigenotoxic potential against H_2O_2 induced genetic damage using *Allium cepa* root chromosomal aberration assay under hydroponic conditions. There was a significant decrease in the percentage of mitotic index/prophase index with the increase in clastogenicity percentage in a dose and time-dependent manner when *Allium cepa* bulbs were exposed to GA at 0.1 mM and 1 mM concentration for 1 h, 2 h, and 4 h. Total genomic DNA integrity analyzed by agarose gel electrophoresis and cell viability revealed pronounced DNA degradation and loss of viability when treated with 1 mM GA for 4 h. In situ histochemical localization by Schiff's staining and 3, 3-diaminobenzidine confirmed increased levels of lipid peroxide and H_2O_2 in GA treated roots respectively. Scanning electron microscopy and FT-IR suggested surface damage and biomolecular intervention of GA in root cells. In addition, possible antigenotoxic effect of GA at lower concentration was explored by employing standard assays using H_2O_2. We observed a higher percentage of nuclear lesions upon treatment with 3% H_2O_2 (97.21 ± 0.76) that reduced significantly after modulatory treatment with 0.01 mM GA (70.44 ± 4.42). The results suggest that GA is a Janus-faced compound as it demonstrates a genotoxic activity at higher doses and genoprotective action at lower precise doses.

1. Introduction

Garcinia hanburyi plant species belongs to the genus *Garcinia*. The gamboge trees are native to tropical Asian regions especially Cambodia, Laos, Thailand, and Vietnam. The active constituents of Garcinia species include xanthones, benzophenones, bioflavonoids, and biphenyls. The gamboge resin derived from these plants is used as a folk medicine (purgative and anti-microbial) and majorly constitutes of gambogic acid (GA) and other polyprenylated xanthones. In the past few decades, plant-derived natural bioactive substances have been searched extensively for their potential antitumor activities. In this regard, several studies have demonstrated GA-mediated inhibitory activities both in vitro and in vivo against various malignant cells derived from lung cancer (Zhang et al., 2016, 2017), leukemia (Shi et al., 2014), gastric carcinoma (Zou et al., 2012), and breast cancer (Zhen et al., 2015). Also, its low toxicity on normal tissues has further enhanced the interest in its use as a possible therapeutic agent for cancer (Zhang et al., 2016, 2017). GA exerts its anticancer effects primarily through cell cycle arrest, apoptosis, topoisomerase II inhibition, and telomerase down-regulation (Qin et al., 2007; Yu et al., 2007). DNA damage caused by oxidative stress is a crucial event in cancer genesis, and medicinal herbs with antioxidant properties are attractive agents to scavenge free radicals in normal cells thus preventing cancer induction. Certain medicinal herbs mediate apoptotic cell death through the generation of reactive oxygen species (ROS) or by antioxidant depletion. Similarly, GA mediates apoptotic cell death in SMMC-7721 and MDA-MB 231 cell lines by elevating ROS levels (Li et al., 2012; Nie et al., 2009). The structure of GA incorporates an, β-unsaturated ketone moiety and the anticancer drugs with unsaturated ketones moieties are known to induce apoptosis through ROS generation. GA-induced apoptosis through ROS generation was

* Corresponding author. Department of Biosciences, Mangalore University, Mangalagangothri, 574199, Mangalore, Karnataka, India.
E-mail addresses: surepadman@gmail.com, surepadman@rediffmail.com (P.S. Suresh).

http://dx.doi.org/10.1016/j.plaphy.2017.08.005
0981-9428/