Mutation Research 768 (2014) 69–73

Contents lists available at ScienceDirect

Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis

journal homepage: www.elsevier.com/locate/molmut
Community address: www.elsevier.com/locate/mutres

Review

Free radical scavenging, antioxidant and cancer chemoprevention by grape seed proanthocyanidin: An overview

Debasis Bagchi[a,b,*], Anand Swaroop[b], Harry G. Preuss[c], Manashi Bagchi[b]

[a] Department of Pharmacological and Pharmaceutical Sciences, University of Houston College of Pharmacy, Houston, TX, USA
[b] Research & Development Division, Cepham Inc., Piscataway, NJ, USA
[c] Department of Medicine, Georgetown University Medical Center, Washington, DC, USA

ARTICLE INFO

Article history:
Available online 19 April 2014

Keywords:
Grape seed proanthocyanidins
Free radicals
DNA damage
Apoptosis
Necrosis
Multiorgan toxicity
Cancer
Vitamins C, E and β-carotene
Idarubicin
4-Hydroxyperoxycyclophosphamide
Amiodarone
Doxorubicin
Dimethylnitrosamine

ABSTRACT

A large number of investigations have demonstrated a broad spectrum of pharmacological and therapeutic benefits of grape seed proanthocyanidins (GSP) against oxidative stress and degenerative diseases including cardiovascular dysfunctions, acute and chronic stress, gastrointestinal distress, neurological disorders, pancreatitis, various stages of neoplastic processes and carcinogenesis including detoxification of carcinogenic metabolites. GSP exhibited potent free radical scavenging abilities in both in vitro and in vivo models. GSP exerted significant in vivo protection against structurally diverse drug and chemical-induced hepatotoxicity, cardiotoxicity, neurotoxicity, nephrotoxicity and spleentoxicity. GSP also protected against idarubicin and 4-hydroxyperoxy-cyclophosphamide-induced cytotoxicity toward human normal liver cells. GSP exhibited selective cytotoxicity toward selected human cancer cells, while enhancing the growth and viability of normal cells. GSP exhibited potent modulatory effects of pro-apoptotic and apoptotic regulatory bcl-XL, p53, c-myc, c-JUN, JNK-1 and CD36 genes. Long-term exposure to GSP may serve as a novel chemoprotectant against three stages of DMN-induced liver carcinogenesis and tumorigenesis including initiation, promotion and progression. GSP may selectively protect against oxidative stress, genomic integrity and cell death patterns in vivo. These results demonstrate that GSP may serve as a novel therapeutic intervention against carcinogenesis.

© 2014 Elsevier B.V. All rights reserved.

Contents

* Corresponding author at: University of Houston College of Pharmacy, 141 Science & Research Building 2, Houston, TX 77204-5000, USA. Tel.: +1 925 948 6951.
E-mail address: debasisbagchi1@gmail.com (D. Bagchi).

http://dx.doi.org/10.1016/j.mrfmmm.2014.04.004
0027-5107/© 2014 Elsevier B.V. All rights reserved.

1. Cancer chemoprevention and grape seed proanthocyanidins

Cancer and chemoprevention have caused a major challenge to the health professionals around the world [1–3]. A significant number of drugs and pharmaceuticals have been developed, however, most of these drugs exhibit potential cytotoxicity and caused the induction of a broad spectrum of degenerative diseases [2,4,5]. Thus, development of a safe, non-toxic, phytopharmaceutical is warranted.

It has been well demonstrated that the development of cancer occurs in three stages [1–5]:

1. Initiation: This step is initiated when a carcinogen modulates the genetic integrity of a cell and initiates the cell to divide more rapidly.
2. Promotion: In this Phase, the genetically damaged cells fail to fix the damage and promotes uncontrolled growth
3. Progression: In this step, the system builds up a blood supply network through angiogenesis and induces the incremental growth of the tumor and carcinogenesis.

A number of phytopharmaceuticals including resveratrol, curcumin, green tea extract, oligomeric proanthocyanidins, etc. have demonstrated significant benefits in cancer chemoprevention [2,6,7].

It has been well demonstrated that higher dietary intakes of flavonoids and proanthocyanidins are associated with a lower risks of cancers [6–8]. Wang et al. [8] examined selected epidemiological studies from 2002 to 2009 on the efficacy of total flavonoids, flavan-3-ols, and proanthocyanidins in prostate cancer. Wang et al. [8] reported inverse trends with higher total flavonoids (P for trend = 0.05) and proanthocyanidins (P for trend = 0.04) with high-grade prostate cancer, but not with advanced prostate cancer [8].

This short review will highlight the beneficial and pharmacological effects of GSP in cancer chemoprevention.

2. Grape seed proanthocyanidins (GSP) and free radicals

The concentration-dependent free radical scavenging abilities of GSP, vitamin C and vitamin E were assessed against biochemically generated superoxide anion and hydroxyl radicals using cytochrome *c* reduction and chemiluminescence assays. At a concentration of 50 mg/l, GSP exerted 84 and 98% greater free radical scavenging abilities against superoxide anion and hydroxyl radicals, respectively, as compared to vitamin E [9]. GSP also demonstrated superior free radical scavenging abilities as compared to vitamin C, and superior peroxyl radical scavenging abilities as compared to Trolox [10].

Overall intracellular oxidized states of cultured murine macrophage J774A.1 and adrenal pheochromocytoma PC-12 cells were assessed following incubation with H_2O_2 (0.5 mM for 24 h) and/or GSP at an excitation wavelength of 513 nm using 2,7-dichloro-fluorescein diacetate as the probe [10]. H_2O_2-induced 5.8- and 4.5-fold increases in fluorescence intensity in J774A.1 and PC-12 cells, while 50 mg/l GSP decreased H_2O_2-induced fluorescence intensity by 36% and 50%, respectively [11].

In another independent study, Jia et al. [12] demonstrated that oxidative damage caused by H_2O_2 treatment can irreversibly damage lens epithelium, resulting in cell death and cataract, while GSP has the ability to significantly scavenge H_2O_2-induced free radicals and oxidative stress in human lens epithelial B-3 (HLEB-3) cells. Cell viability was monitored by 4,5-dimethylthiazol-2-yl-2,5-diphenyltetrazolium bromide (MTT) assay, while apoptosis rate and oxidative stress were detected by flow cytometric analysis, and expression of NF-κB/P65 and mitogen activated protein kinase (MAPK) proteins were measured by western blot. GSP substantially reduced H_2O_2-induced cell apoptosis, oxidative stress and activation and translocation of NFκβ/p65 in cultured HLEB-3 cells [12]. Furthermore, GSP also depressed H_2O_2-induced phosphorylation of the p38 and c-Jun N-terminal kinase (JNK) proteins of the MAPK family at various time points. Thus, GSP has potential protective effect against H_2O_2-induced oxidative stress, activation of NFκβ and MAPK signaling, and indices of cataractogenesis in HLEB-3 cells [12].

3. Protection of GSP against 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced oxidative stress and DNA fragmentation in mice

TPA-induced significant lipid peroxidation and DNA fragmentation in the brain and hepatic tissues of mice and the comparative protective abilities of GSP (100 mg/kg body weight) and vitamins C (100 mg/kg body weight), E (100 mg/kg body weight), a combination of vitamins C plus E (100 mg/kg body weight each) and β-carotene (50 mg/kg body weight) were assessed. Pre-treatment of mice with the above dosages of GSP, vitamin E, vitamin C, β-carotene and a combination of vitamins C plus E decreased TPA-induced DNA fragmentation by 50, 31, 14, 11 and 40%, respectively, in the brain tissue, and 47, 30, 10, 11 and 38%, respectively, in the hepatic tissue, while lipid peroxidation was reduced by 61, 45, 13, 8 and 48%, respectively, in the brain tissue, 46, 36, 12, 7 and 39%, respectively, in the hepatic mitochondria, and 59, 47, 14, 12 and 53%, respectively, in the hepatic microsomes compared to controls [13]. Similarly, TPA-induced massive production of reactive oxygen species in the peritoneal macrophages as determined by chemiluminescence response and cytochrome *c* reduction, while GSP, vitamin E, vitamin C, β-carotene and a combination of vitamins C plus E provided similar protection. These studies demonstrate the bioavailability of GSP to the target organs and exhibit superior protection against oxidative stress and oxidative DNA damage as compared to vitamin C, vitamin E, a combination of vitamins C and E, and β-carotene [13] (Tables 1 and 2).

4. Smokeless tobacco extract (STE)-induced oxidative stress and apoptotic cell death in human oral keratinocyte cells and protection by GSP

Oral cancer accounts for approximately 3% of all cancers in USA and seventh most leading cause of cancer death. It has been demonstrated that STE-induced oxidative stress and programmed cell death (apoptosis) in a primary culture of human oral keratinocytes have been significantly protected by GSP and exhibited superior protection as compared to a combination vitamins C and E. The oral cells were isolated from human oral tissue and treated with STE (0–300 μg/ml) for 24 h. Apoptotic cell death was measured by flow cytometry [14]. STE-induced a 9, 29 and 35% apoptotic cell death in these oral cells following treatment with 100, 200 and 300 μg/ml of STE. Pretreatment of the 300 μg/ml smokeless tobacco-treated cells with 100 mg GSP/ml reduced tobacco-induced apoptotic cell death by approximately 85%, while only 46% reduction was observed with a combination of vitamins C and E (75 μM each) as assessed by flow cytometric analysis. Similar protective abilities were also observed in lipid peroxidation and DNA fragmentation assay [14].

In another study, it was observed that the protective role of GSP was superior as compared to vitamins C and E against STE-induced oxidative stress in a primary culture of human oral keratinocytes. Approximately 11%, 26%, 28% and 50% protection were observed following incubation with vitamin C, vitamin E, and a combination of vitamins C plus E, and GSP, respectively as demonstrated by laser

Download English Version:

https://daneshyari.com/en/article/2146296

Download Persian Version:

https://daneshyari.com/article/2146296

Daneshyari.com