INTRODUCTION

Propolis, having hundreds of polyphenols, is a mixture produced by the honeybee. This sticky, greenish-brown product has different compositions depending on the location of the bees and what trees and flowers they have access to. Propolis from Turkey or Egypt will not have the same chemical properties as propolis from Europe or Brazil. This is because it is very difficult for researchers to come to general conclusions about its health benefits. Caffeic acid phenethyl ester (CAPE) [Figure 1] is one of important compounds found in propolis that has antiviral [1], antioxidant, anti-inflammatory, antiproliferative, antitumor, and immunomodulatory effects [2]. This marvelous compound has been used to prevent oxidative stress-based deterioration in cells/tissues/organs in both cell culture and experimental animals. Lately, the protection of CAPE on central and peripheral nervous system as well as a reproductive system have been extensively reviewed [3-5]. Cyclophosphamide (CP) is an anticancer chemotherapeutic drug classified as an alkylating agent. It has extensively been used to treat a broad of malignancies including Hodgkin’s and non-Hodgkin’s lymphoma, Burkitt’s lymphoma, chronic lymphocytic leukemia, Ewing’s sarcoma, breast cancer, testicular cancer, etc. It may cause several side effects after treatment. In this mini review, the protective effects of propolis and CAPE were compared each other in terms of effectiveness against CP-induced injuries.

ABSTRACT

Propolis is a mixture having hundreds of polyphenols including caffeic acid phenethyl ester (CAPE). They have been using in several medical conditions/diseases in both in vitro and in vivo experimental setup. Cyclophosphamide (CP) has been used to treat a broad of malignancies including Hodgkin’s and non-Hodgkin’s lymphoma, Burkitt’s lymphoma, chronic lymphocytic leukemia, Ewing’s sarcoma, breast cancer, testicular cancer, etc. It may cause several side effects after treatment. In this mini review, the protective effects of propolis and CAPE were compared each other in terms of effectiveness against CP-induced injuries.

KEY WORDS: Caffeic acid phenethyl ester, cyclophosphamide, propolis
ameliorative effect of propolis against CP-induced toxicity in mice was studied by El-Naggar et al. [6]. It throws light on the side effects of a common anticancer agent, CP, used in the treatment of various malignancies and possible remedies to prevent that type of side effects in vital organs such as liver and kidney. The proposed natural compound propolis has been found to be protective against CP toxicity. Uysal et al. [7] conducted an experimental animal study to determine protective role of CAPE on CP-induced hemorrhagic cystitis (HC). While CP-induced HC lead to increase in superoxide dismutase, catalase, and malondialdehyde activities/levels, CAPE significantly reduced these parameters showing the protective effects. In addition to this biochemical effects, CAPE also ameliorates edema, hemorrhage, inflammation, and mucosal ulceration of CP-induced HC.

We published a review article about toxicities of some therapeutic compounds and the protective effect of CAPE on chemotherapy- and radiotherapy-induced toxicity [8]. We have shown that CAPE has protective effects on oxidative stress-induced toxicities by doxorubicin (nephrotoxicity) [9], cisplatin (neurotoxicity, ototoxicity, and hepatotoxicity) [10-13], and bleomycin (lung fibrosis) [14].

It has been shown that CAPE application to the rats modifies the enzyme activity of cytochrome P450 (CYP) isoforms involved in the activation of diethylnitrosamine such as CYP1A1/2 and CYP2B12 [18]. Furthermore, treatment with CAPE of carbon tetrachloride-induced hepatotoxicity in mice blocks CYP2E1-mediated CCl₃ bioactivation and protects against fas/FasL-mediated apoptosis [19]. It will be very interesting to see the effect of CAPE on CYP2B6, which constitutes 3-6% of total hepatic CYP content and metabolizes several pharmaceuticals mediated CYP2B12 [18]. Furthermore, treatment with CAPE of carbon tetrachloride-induced hepatotoxicity in mice blocks CYP2E1-mediated CCl₃ bioactivation and protects against fas/FasL-mediated apoptosis [19]. It will be very interesting to see the effect of CAPE on CYP2B6, which constitutes 3-6% of total hepatic CYP content and metabolizes several pharmaceuticals including CP [20]. To achieve this, further studies on the every single bioactive constituent of propolis such as CAPE and some other polyphenols are necessary to identify interactions mediating their biological effects on CYP2B6, since there are roughly 150 different polyphenolic compounds within propolis.

As a conclusion, studying propolis to prevent CP-induced oxidative stress in animals has several limitations since the proposed effect cannot be specified to one or several molecules within the mixture. In that case, every single bioactive constituent of propolis needs to be studied to show the source of real effects and the molecular mechanisms of this effects.

REFERENCES


acid phenethyl ester (CAPE), an active compound of propolis, in neurological disorders and emergencies. spatula DD 2011;1:37-42.


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