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# Studies on the potential protective effect of cinnamon against bisphenol A- and octylphenol-induced oxidative stress in male albino rats

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ABSTRACT

Among the numerous chemicals discharged into the surrounding environment, bisphenol A (BPA) and octylphenol (OP) have been shown to increase oxidative stress in body by disturbing the prooxidant/antioxidant balance of cells. Cinnamon aqueous extract (CAE) is a natural product rich in polyphenolic compounds that have antioxidant activity. This study was designed to investigate the protective efficacy of CAE against oxidative disorders induced by BPA and OP in male albino rats. Animals were divided into 6 groups (10 rats each) and treated orally, 3 times weekly for 50 days. Group 1: control vehicle (olive oil); group 2 (25 mg BPA/kg b.wt./day); group 3 (25 mg OP/kg b.wt./day); group 4 (200 mg CAE/kg b.wt./day); group 5 (CAE 2 h before BPA administration); and group 6 (CAE 2 h before OP administration). BPA- and OP-exposed groups showed insignificant elevation in the final body weight; weight gains and significant reduction only in the relative kidneys weight. Also, BPA and OP exposure resulted in significant increase in serum urea, creatinine and kidney, brain, testicular malondialdehyde (MDA) levels. Significant reduction in tissues reduced glutathione (GSH) contents; catalase (CAT) and superoxide dismutase (SOD) activities were also recorded in BPA and OP exposed animals compared to the control vehicle group. Pretreatment with CAE 2 h either before BPA or OP administration ameliorated the BPA- and OP-induced body weight; weight gains and relative organs weight changes and biochemical adverse effects. CAE pretreatment also protected against the recorded pathological changes in kidney, brain and testis. In conclusion, CAE could ameliorate the oxidative toxic effects of BPA and OP indicating its protective antioxidant effect.


## 1. Introduction

Environmental pollution with hazardous chemicals and metals can arise from natural as well as anthropogenic sources; many of them cause oxidative stress. Oxidative stress has long been linked with pathogenesis of various diseases in humans. It takes place due to unregulated production of free radicals or reactive oxygen/nitrogen species. Reactive oxygen species (ROS) are cytotoxic agents that lead to damage of nucleic acid bases, lipids and proteins, thereby leading to cell death [6,43].

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Bisphenol A (BPA) and octylphenol (OP) are endocrine disrupting chemicals (EDCs) that are of scientific interest due to their widespread use and ubiquitous exposures. Beside their endocrine disrupting effect [28,34,56] they are also known to induce oxidative stress [2,3,25,26].

BPA is the building block of polycarbonate plastics, a hard plastic used to make numerous consumer products, including most baby and water bottles. Its final product includes adhesives, coatings, paints and building materials [57]. BPA waste may enter the environment during handling, loading and unloading, heating or releases. BPA can enter the human body through reusable baby bottles [8], food packing materials [27], liquid of canned vegetables [10] and dental sealants [41].

OP is one of the final degradation products of alkylphenol polyethoxylates (APEOs), which are nonionic surfactants used as intermediates or as additives for a wide range of industrial products and processes [19,47]. OPs are used as tackifiers in tire rubber, in recovery of oil in offshore processes, and in printing inks, pesticide formulations (as a dispersant), water based paints, textile auxiliaries, and emulsion polymerization processes [37]. These are generally discharged in large quantities to aquatic environments either directly from untreated effluent or indirectly from sewage treatment plants [33]. Exposure to OPs may occur through ingestion of contaminated foods (*e.g.* fish) and drinking contaminated water. It may occur also from contact with some personal care products and detergents [12].

Generation of free radicals and antioxidant capacity of the body have been observed to be modulated by environmental, physiological and nutritional factors [31,44]. For example, physiological factors such as aging, alteration of body mass index and obesity and life style confounding factors such as smoking, drinking and high calorie diet have enhancing effect on oxidative stress and suppressive effect on antioxidants [44,48,49].

Natural plant-derived antioxidants are in high demand than synthetic antioxidants because of their potential in health promotion, disease prevention, and their improved safety and consumer acceptability [20,54].

Cinnamon is one of the most widely used plants in herbal medicines with diverse bioactive effects. It is obtained from the inner bark of several trees from the genus *Cinnamomum*. The used species in this study, *Cinnamomum aromaticum* (*C. cassia* or Chinese cinnamon) is an ever green tall tree with thick leathery leaves and yellow flowers [35].

Su et al. [58] indicated that cinnamon may serve as potential dietary source of natural antioxidants for improving human nutrition and health. It is rich in natural polyphenolic compound. Polyphenols act as reactive oxygen and nitrogen species scavengers, redox-active transition metal chelators and enzyme modulators [45].

Previous studies reported that cinnamon stimulates the increase of antioxidant enzymes activities, including SOD and CAT in rat's liver and heart [15,24].

The present study was designed to assess the potential protective effect of *Cinnamon cassia* aqueous extract against bisphenol A- and octylphenol-induced oxidative stress in the kidney, brain and testis of male albino rats.

## 2. Materials and methods

### 2.1. Animals

A total of 60 adult male albino rats weighing between 120 and 150 g were used in this study. They were obtained from the AL-Zyade Experimental Animals Production Center, Giza, Egypt. All animals were housed in polypropylene cages with mesh wire tops in well ventilated room and provided with balanced ration and clean water *ad libitum*. They were kept under observation for two weeks before the beginning of experiments for atmospheric and handling accommodation.

### 2.2. Chemicals

Bisphenol A (CAS No. 80-05-7; purity of 97%) and 4-Tert-octylpenol (CAS No. 140-66-9; purity of 97%) were purchased from Sigma–Aldrich Company, Germany. Chemicals were dissolved in olive oil (vehicle).

*C. cassia* bark was purchased from Harraz market, EL-Azhar, Cairo, Egypt. It was identified and authenticated in Botany Department, Faculty of Science, Cairo University.

Diagnostic kits for assaying serum urea and creatinine levels; MDA, GSH levels and CAT, SOD activities in renal, brain and testicular tissue homogenates were purchased from the Biodiagnostic Company, Dokki, Giza, Egypt.

### 2.3. Preparation of cinnamon aqueous extract (CAE)

The *C. cassia* aqueous extract (CAE) was prepared from the air dried powdered cinnamon bark according to Azab et al. [4]. The aqueous extract was freshly prepared by soaking 10 g of the grinded bark in 100 ml distilled water at 90 °C for 2 h followed by filtration. The filtrate was then dehydrated in oven at 80 °C overnight. The resulting dark reddish brown dry extract was weighed and the dry yield was then calculated.

### 2.4. Experimental design and animal grouping

Sixty male albino rats were weighed and divided into six equal groups; all were treated orally three times a week for 50 days [25,26].

Group 1: control vehicle (olive oil); group 2 (25 mg BPA/kg b.wt./day); group 3 (25 mg OP/kg b.wt./day); group 4 (200 mg CAE/kg b.wt./day); group 5 (CAE 2 h before BPA administration) and group 6 (CAE 2 h before OP administration). BPA and OP dose was selected according to that previously used by Aydogan et al. [2,3] and Korkmaz et al. [25,26]. However, CAE was given orally at 200 mg/kg/day according to Kim et al. [24] and Azab et al. [4].

### 2.5. Collection of serum and tissue samples

At the end of the experiment, the animals were fasted overnight and weighed then anaesthetized and sacrificed for samples collection. Blood samples were collected without anticoagulant and centrifuged at 3000 rpm for 15 min for serum separation.