

## Effect of Acute Administration of 3-Butyl-1-Phenyl-2-(Phenyltelluro)Oct-En-1-One on Oxidative Stress in Cerebral Cortex, Hippocampus, and Cerebellum of Rats

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Received: 23 May 2010 / Accepted: 10 July 2010 / Published online: 29 July 2010  
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**Abstract** Organotellurium compounds have been synthesized since 1840, but pharmacological and toxicological studies about them are still incipient. Therefore, the objective of this study was to verify the effect of acute administration of the organochalcogen 3-butyl-1-phenyl-2-(phenyltelluro)oct-en-1-one on some parameters of oxidative stress in the brain of 30-day-old rats. Animals were treated intraperitoneally with a single dose of the organotellurium (125, 250, or 500 µg/kg body weight) and sacrificed 60 min after the injection. The cerebral cortex, the hippocampus, and the cerebellum were dissected and homogenized in KCl. Afterward, thiobarbituric acid reactive substances (TBARS), carbonyl, sulfhydryl, catalase (CAT), superoxide dismutase (SOD), nitric oxide (NO) formation, and hydroxyl radical production were measured in the brain. The organotellurium enhanced TBARS in the cerebral cortex and the hippocampus, and increased protein damage (carbonyl) in the cerebral cortex and the cerebellum. In contrast, the compound provoked a reduced loss of

thiol groups measured by the sulfhydryl assay in all the tissues studied. Furthermore, the activity of the antioxidant enzyme CAT was reduced by the organochalcogen in the cerebral cortex and the cerebellum, and the activity of SOD was inhibited in all the brain tissues. Moreover, NO production was increased in the cerebral cortex and the cerebellum by this organochalcogen, and hydroxyl radical formation was also enhanced in the cerebral cortex. Our findings indicate that this organotellurium compound induces oxidative stress in the brain of rats, corroborating that this tissue is a potential target for organochalcogen action.

**Keywords** Organochalcogen · Tellurium · Oxidative stress

### Introduction

Chalcogen metalloids such as tellurium (Te) have found many uses in the manufacture of ceramics, glass, semiconductors, and metals (Ogra et al. 2008). Recently, Te has been used as an alloy with germanium (Ge), antimony (Sb), and/or bismuth (Bi) in phase-change optical magnetic disks, such as digital versatile disk-random access memory (DVD-RAM), and DVD-recordable disk (DVD-RW) (Yamada et al. 2002). Therefore, exposure to Te is expected to increase in everyday life.

Despite the growing use of organotellurium compounds in the chemical and biochemical fields and the increased risk of occupational and environmental human exposure to these elements, there has been little concern about their toxicity. In fact, these compounds have been shown as promising and useful alternatives for numerous synthetic operations in

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organic synthesis (Petraghani, 1994; Comasseto et al. 1997; Zeni et al. 2003, 2006).

Previous studies have indicated that organotellurium compounds are potentially toxic and lethal to rodents at low doses (Meotti et al. 2003; Savegnago et al. 2006). Indeed, tellurides can cause cytotoxicity (Sailer et al. 2003, 2004; Iwase et al. 2004; Rooseboom et al. 2002), hepatotoxicity (Meotti et al. 2003), glutamatergic system alterations (Nogueira et al. 2001, 2002), teratogenic effects (Stangherlin et al. 2005), and alterations of cytoskeletal proteins phosphorylation (Moretto et al. 2005; Funchal et al. 2006a). In addition, organotellurium compounds can inhibit cysteinyl-containing enzymes, such as Na<sup>+</sup>/K<sup>+</sup> + ATPase (Borges et al. 2005),  $\delta$ -ALAD (Maciel et al. 2000; Nogueira et al. 2003), and squalene monooxygenase (Laden and Porter, 2001). Thus, the toxicity of organotellurides may be related to the interaction with thiol groups of important biomolecules (Nogueira et al. 2004); the replacement of selenium in selenoproteins, such as thioredoxin (Engman et al. 2000; and the capacity of the Te compounds to induce formation of reactive species (RS) (Chen et al. 2001).

The formation of RS is a natural consequence of aerobic metabolism and is associated with the balance between constitutive oxidants and antioxidants (Seifried et al. 2007). Oxidative stress arises when the balance between pro-oxidants and antioxidants is shifted toward the pro-oxidants (Halliwell and Gutteridge, 2007). The imbalance could either be caused by exogenous sources (air pollutants, tobacco smoke, and radiation), through metabolism of xenobiotics, or by endogenous sources. Due to their high reactivity, the pro-oxidants may cause damage to cellular constituents or important biomolecules, such as DNA, proteins, lipids, or carbohydrates (Valko et al. 2007). In order to prevent undesired, radical induced damage, the organism is equipped with elaborate antioxidant systems, such as vitamin E, ascorbate, glutathione, uric acid, catalase, glutathione peroxidase, and superoxide dismutase (Halliwell and Gutteridge, 2007). Free radicals have been implicated as important pathologic factors in cardiovascular diseases, pulmonary diseases, autoimmune diseases, inherited metabolic disorders, cancer, and aging (Heffner and Repine 1989; Alho et al. 1998; Funchal et al. 2006b).

Considering that our group recently reported that the organochalcogen 3-butyl-1-phenyl-2-(phenyltelluro)oct-en-1-one was able to induce *in vitro* oxidative stress in the cerebral cortex of rats (Penz et al. 2009), and that Te compounds are highly toxic to the central nervous system (CNS) of rodents (Maciel et al. 2000; Nogueira et al. 2001; Widy-Tyszewicz et al. 2002; Stangherlin et al. 2005). The purpose of this study is to evaluate the effect of an acute *in vivo* treatment with this organochalcogen in the cerebral cortex, the hippocampus, and the cerebellum of 30-day-old Wistar rats.

## Methods

### Chemicals

3-butyl-1-phenyl-2-(phenyltelluro)oct-en-1-one was synthesized according to Silveira et al. 2002. Thiobarbituric acid was purchased from Merck (Darmstadt, Germany). 2,4-dinitrophenylhydrazine (DNPH), 5,5'-dithiobis (2-nitrobenzoic acid), sulfanilamide, and N-(1-naphthyl)ethylene-diamine were from Sigma (St. Louis, MO, USA). All other chemicals were of analytical grade and were purchased from local suppliers.

### Animals

Thirty-day-old Wistar rats were obtained from our own breeding colony. They were maintained at approximately 25 °C, on a 12-h light/12-h dark cycle, with free access to food and water. The ‘‘Principles of laboratory animal care’’ (NIH publication no 80–23, revised 1996) were followed in all experiments and our research protocol was approved by the Ethical Committee for Animal Experimentation of the Centro Universitário Metodista. All efforts were made to minimize animal suffering and to use only the number of animals necessary to produce reliable scientific data.

### Acute *in Vivo* Treatment

The animals were treated intraperitoneally with a single dose of 3-butyl-1-phenyl-2-(phenyltelluro)oct-en-1-one (125, 250, or 500  $\mu$ g/kg body weight). Control rats were chosen randomly and received saline solution (0.85% NaCl) in the same volumes. Rats were sacrificed 60 min after the injection.

### Tissue Preparation

After 60 min of the drug administration, the animals were killed by decapitation without anesthesia, and the brain was rapidly excised on a Petri dish placed on ice. The olfactory bulb, pons, and medulla were discarded, and the cerebral cortex, the hippocampus, and the cerebellum were dissected and kept chilled until homogenization which was performed using a ground glass type Potter-Elvehjem homogenizer.

### Brain Preparation for Measurement of Oxidative Stress Parameters

Brain tissue was homogenized in 1.5% KCl. The homogenates were centrifuged at 800 g for 10 min at 4 °C, the pellet was discarded, and the supernatants were kept at –70 °C until the determinations.

## Oxidative Stress Measurements

### *Thiobarbituric Acid Reactive Substances (TBARS) Measurement*

For the TBARS assay, trichloroacetic acid (10% w/v) was added to the homogenate to precipitate proteins and to acidify samples (Buege and Aust, 1978). This mixture was then centrifuged (1000 g, 3 min). The protein-free sample was extracted, and thiobarbituric acid (0.67% w/v) was added to the reaction medium. Tubes were placed in a water bath (100 °C) for 30 min. Absorbance was read at 535 nm in a spectrophotometer. Commercially available malondialdehyde was used as a standard. Results were expressed as nmol/mg of protein.

### *Carbonyl Assay*

Homogenates were incubated with 2,4 dinitrophenylhydrazine (DNPH 10 mmol/l) in 2.5 mol/l HCl solution for 1 h at room temperature, in the dark. Samples were vortexed for every 15 min. Then, 20% TCA (w/v) solution was added in tube samples, left in ice for 10 min, and centrifuged for 5 min at 1000 g to collect protein precipitates. Another wash was performed with 10% TCA. The pellet was washed three times with ethanol:ethyl acetate (1:1) (v/v). The final precipitates were dissolved in 6 mol/l guanidine hydrochloride solution, left for 10 min at 37 °C, and read at 360 nm (Reznick and Packer 1994). The results were expressed as nmol/mg protein.

### *Sulphydryl Assay*

This assay is based on the reduction of 5,5'-dithio-bis(2-nitrobenzoic acid) (DTNB) by thiols, generating a yellow derivative (TNB) whose absorption is measured spectrophotometrically at 412 nm (Aksenov and Markesbery, 2001). In brief, 0.1 mM DTNB was added to 120 µl of the samples. This was followed by 30 min incubation at room temperature in a dark room. Absorption was measured at 412 nm. The sulphydryl content is inversely correlated to oxidative damage to proteins. Results were reported as mmol/mg protein.

### *Determination of Antioxidant Enzyme Activities*

Superoxide dismutase (SOD) activity, expressed as units per milligram of protein, was based on the inhibition of superoxide radical reaction with pyrogallol (Marklund, 1985). Catalase (CAT) activity was determined by following the decrease in 240 nm absorption of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>). It was expressed as nanomols of H<sub>2</sub>O<sub>2</sub> reduced per minute per milligram of protein (Aebi, 1984).

## *Nitric Oxide Production*

Nitric oxide was determined by measuring the stable product nitrite through the colorimetric assay described by Hevel and Marletta (1994). In brief, the Griess reagent was prepared by mixing equal volumes of 1% sulfanilamide in 0.5 N HCl and 0.1% N-(1-naphthyl)ethylenediamine in deionized water. The reagent was added directly to the homogenates and incubated under reduced light at room temperature for 30 min. Samples were analyzed at 550 nm on a microplate spectrophotometer. Controls and blanks were run simultaneously. Nitrite concentrations were calculated using a standard curve prepared with sodium nitrite (0–80 mM). Results were expressed as mmol/mg protein.

### *Measurement of 2-Deoxy-D-Ribose Degradation*

The hydroxyl radical scavenging activity of 3-butyl-1-phenyl-2-(phenyltelluro)oct-en-1-one was determined by assaying the malondialdehyde chromogen originated from 2-deoxy-D-ribose degradation (Halliwell and Gutteridge, 1981). The reaction medium contained 3 mM 2-deoxy-D-ribose, 20 mM FeCl<sub>3</sub>, 100 mM EDTA, 500 mM H<sub>2</sub>O<sub>2</sub>, 100 mM ascorbate, and the sample containing the organotellurium (1, 10, or 30 µM) in 20 mM sodium phosphate buffer, pH 7.4 containing 140 mM KCl. After 1 h incubation at 37 °C, 2.8% trichloroacetic acid and 1% thiobarbituric acid were added, followed by 30 min incubation in boiling water. The mixture was allowed to cool on running tap water for 5 min. The resulting pink-stained TBARS was determined in a spectrophotometer at 532 nm. The results were expressed in units of absorbance.

### *Protein Determination*

Protein concentrations were determined by the method of Lowry et al. (1951) using bovine serum albumin as standard.

### *Statistical Analysis*

Data from the experiments were analyzed statistically by one-way analysis of variance (ANOVA) followed by the Tukey test, where the *F* value was significant. Values of *P* < 0.05 were considered to be significant. All analyses were carried out in an IBM compatible PC using the Statistical Package for Social Sciences (SPSS) software.

## **Results**

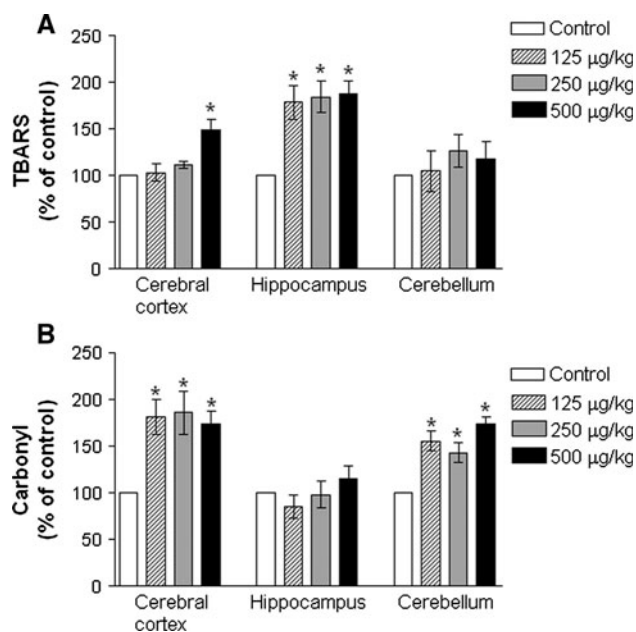
Thirty-day-old rats were treated intraperitoneally with a single dose of 3-butyl-1-phenyl-2-(phenyltelluro)oct-en-1-one

(125, 250, or 500  $\mu\text{g}/\text{kg}$  body weight), and after 1 h they were killed and various parameters of oxidative stress, such as TBARS, carbonyl, sulphhydryl, the activities of the antioxidant enzymes CAT and SOD, nitrite formation, and hydroxyl radical production were measured in the cerebral cortex, the hippocampus, and the cerebellum.

Our results showed that the organotellurium produced both lipid and protein damage according to the brain area (Fig. 1). Figure 1a shows that the organotellurium was able to produce lipid damage in the cerebral cortex (500  $\mu\text{g}/\text{kg}$ ) and in the hippocampus (250 and 500  $\mu\text{g}/\text{kg}$ ) of the 30-day-old rats. Figure 1b demonstrates that the compound enhanced protein damage at all doses in the cerebral cortex and the cerebellum of rats.

Then, we verified the effect of the  $\alpha,\beta$ -unsaturated ketone on the non-enzymatic antioxidant defenses by measuring protein sulphhydryl groups. Figure 2 shows that sulphhydryl groups were markedly reduced by the compound in all the tissues tested, [the cerebral cortex (125, 250 and 500  $\mu\text{g}/\text{kg}$ ), the hippocampus (500  $\mu\text{g}/\text{kg}$ ), and the cerebellum (250 and 500  $\mu\text{g}/\text{kg}$ )]. These results indicate that the organochalcogen reduced the non-enzymatic antioxidant defenses in the rat brain.

Next, the enzymatic antioxidant defenses were investigated by measuring CAT and SOD activities in the brain tissue (Fig. 3). Figure 3a shows that CAT activity was



**Fig. 1** Effect of the  $\alpha,\beta$ -unsaturated ketone 3-butyl-1-phenyl-2-(phenyltelluro)oct-en-1-one on thiobarbituric acid reactive substances (TBARS) (a) and carbonyl formation (b) in the cerebral cortex, the hippocampus and the cerebellum of rats. Values are means  $\pm$  S.D. for 8–10 samples in each group expressed as percent of control. Statistically significant differences from control were determined by ANOVA followed by Tukey test: \*  $P < 0.01$

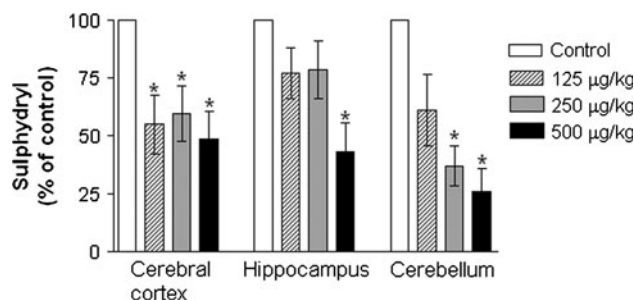
reduced by 250 and 500  $\mu\text{g}/\text{kg}$  treatments in the cerebral cortex and by 250  $\mu\text{g}/\text{kg}$  treatment in the cerebellum. Moreover, SOD activity was significantly reduced by all concentrations of the organochalcogen in the cerebral cortex, and by 250 and 500  $\mu\text{g}/\text{kg}$  treatment in the hippocampus and the cerebellum (Fig. 3b). These findings indicate that the enzymatic antioxidant defenses were significantly reduced by exposing cerebral tissue to 3-butyl-1-phenyl-2-(phenyltelluro)oct-en-1-one.

We also evaluated the effect of the organotellurium on NO production and on hydroxyl radical formation by measuring 2-deoxy-D-ribose degradation (Fig. 4). Figure 4a demonstrates that the organochalcogen enhanced NO production in the cerebral cortex and in the cerebellum at 250 and 500  $\mu\text{g}/\text{kg}$ , and 500  $\mu\text{g}/\text{kg}$  treatment, respectively. Figure 4b shows that hydroxyl radical formation was increased by 250 and 500  $\mu\text{g}/\text{kg}$  treatment of the organotellurium only in the cerebral cortex. Both results evidence the diverse pro-oxidant mechanisms of this organochalcogen.

## Discussion

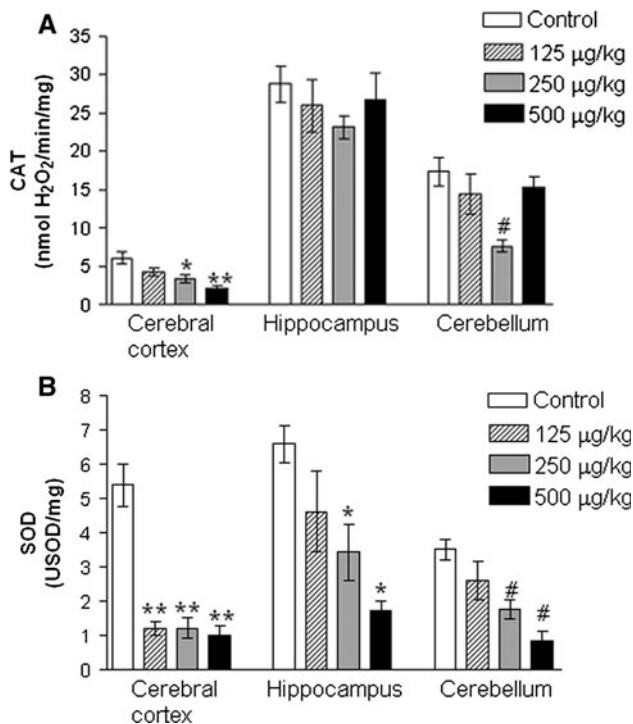
Considering the increasing exposure of humans to organotellurium compounds due to their role as important intermediates in organic synthesis, which can provoke occupational and environmental risk to human health (Zeni et al. 2006), in this study, we investigate whether an acute treatment with the organotellurium 3-butyl-1-phenyl-2-(phenyltelluro)oct-en-1-one induces oxidative stress in the brain of 30-day-old rats.

Reactive species such as superoxide radical anion ( $\text{O}_2^{\bullet-}$ ), hydroxyl radical ( $\text{OH}^{\bullet}$ ), hydrogen peroxide ( $\text{H}_2\text{O}_2$ ), and NO are produced in metabolic and physiological processes, and harmful oxidative reactions may occur in organisms (Halliwell, 2006). The oxidative effects of RS are controlled by non-enzymatic antioxidants, such as ascorbic acid and



**Fig. 2** Effect of the organochalcogen 3-butyl-1-phenyl-2-(phenyltelluro)oct-en-1-one on protein sulphhydryl groups in the cerebral cortex, the hippocampus and the cerebellum from 30-day-old rats. Values are means  $\pm$  S.D. for 8–10 samples in each group expressed as percent of control. Statistically significant differences from control were determined by ANOVA followed by Tukey test: \*  $P < 0.001$



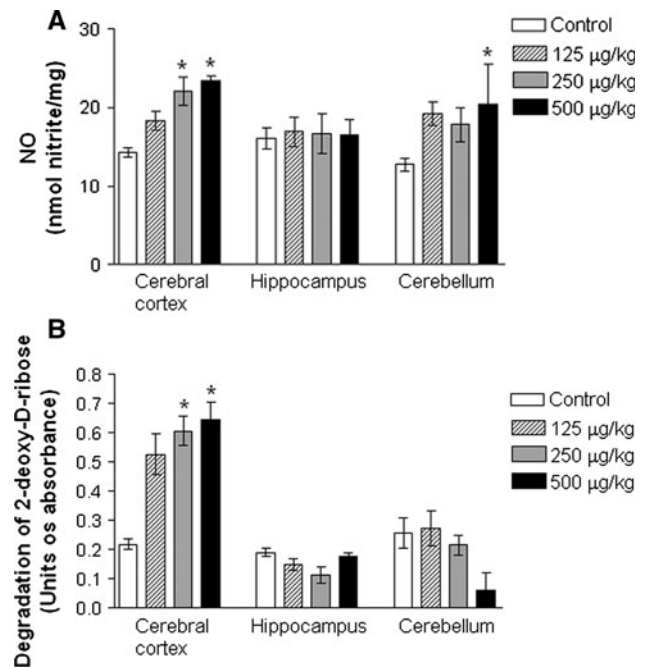


**Fig. 3** Effect of 3-butyl-1-phenyl-2-(phenyltelluro)oct-en-1-one on the activities of the antioxidant enzymes catalase (a) and superoxide dismutase (b) in the cerebral cortex, the hippocampus and the cerebellum from 30-day-old rats. Values are means  $\pm$  S.D. for 8–10 samples in each group. Statistically significant differences from control were determined by ANOVA followed by Tukey test: \*  $P < 0.01$ ; \*\*  $P < 0.001$ ; #  $P < 0.005$

glutathione, and also by enzymatic antioxidants (SOD, CAT, GPx). Under some conditions, the increase in oxidants and the decrease in antioxidants cannot be prevented, and the oxidative/antioxidative balance shifts toward the oxidative status (Halliwell, 2001, 2006). Consequently, oxidative stress is associated with the onset and pathogenesis of several prominent CNS disorders (Lehtinen and Bonni, 2006).

In this context, the CNS has an extraordinary high metabolic rate, as it consumes about 20% of oxygen inspired at rest, while accounting for only 2% of the body weight (Kann and Kovács, 2007). Therefore, the brain may be particularly vulnerable to free radicals due to its high rate of oxidative metabolic activity, high content of polyunsaturated fatty acids, regions rich in iron concentration, high extra cellular concentration of glutamate, and low levels of antioxidants (Halliwell and Gutteridge, 2007). In fact, oxidative stress has been implicated in the pathophysiology of common neurodegenerative disorders, such as Parkinson's disease and Alzheimer's disease, as well as in epileptic seizures and demyelination (Bogdanov et al. 2001; Behl and Moosmann, 2002; Berg and Youdim, 2006).

In this study, we initially tested the effect of the  $\alpha,\beta$ -unsaturated ketone on TBARS and protein carbonyl



**Fig. 4** Effect of 3-butyl-1-phenyl-2-(phenyltelluro)oct-en-1-one on nitric oxide (NO) production (a) and hydroxyl radical activity (b). Values are means  $\pm$  S.D. for 8–10 samples in each group. Statistically significant differences from control were determined by ANOVA followed by Tukey test: \*  $P < 0.001$

groups, biochemical markers of lipid and protein oxidative damage, respectively, and we verified that the compound was able to enhance lipid peroxidation in the cerebral cortex and the hippocampus of the rats and to increase protein damage in the cerebral cortex and the cerebellum of rats. This is in agreement with a study, where diphenyl ditelluride [(PhTe)<sub>2</sub>] induced increased lipid peroxidation levels in the hippocampus and striatum of young rats (Stangherlin et al. 2009). Furthermore, our group recently reported that the 3-butyl-1-phenyl-2-(phenyltelluro)oct-en-1-one enhances lipid peroxidation in human serum (Carvalho et al. 2009). However, the diethyl-2-phenyl-2-tellurophenyl vinylphosphonate (DPTVP), another organochalcogen, was not able to modify cerebral TBARS in mice (Ávila et al. 2007). Considering that TBARS measurement reflects the amount of malondialdehyde formation, an end product of membrane fatty acid peroxidation (Halliwell and Gutteridge, 2007); the increased values of this parameter elicited by the organotellurium strongly indicate that this compound causes lipid peroxidation in the brain of rats. On the other hand, 3-butyl-1-phenyl-2-(phenyltelluro)oct-en-1-one was not able to increase carbonyl in our in vitro model in the cerebral cortex of rats (Penz et al. 2009) and in human serum (Carvalho et al. 2009).

Thiols (SH) are recognized to play a fundamental antioxidant role by protecting cellular and extracellular functions against oxidative stress (Aksenov and Markesbery,

2001). In this context, here we observed that 3-butyl-1-phenyl-2-(phenyltelluro)oct-en-1-one markedly reduced the sulfhydryl groups in all the tissues studied, indicating that the organochalcogen reduced the non-enzymatic antioxidant defenses in the brain of rats. This is in line with our previous *in vitro* studies, demonstrating that this organochalcogen reduced the SH groups in the cerebral cortex of rats (Penz et al. 2009). It is also described in the literature that tellurite, the most toxic and soluble oxyanion among Te compounds, decreased the cellular content of reduced thiols with a consequent increase in the production of ROS and stimulation of SOD activity (Tremaroli et al. 2007).

Mammalian cells from different tissues, including the brain, possess a system that regulates redox status of cellular thiols and protects SH-containing proteins from excessive oxidation. It includes low molecular weight donors of SH groups and enzymes, which can catalyze the reduction of SH groups in proteins and detoxify prooxidants by conjugation with glutathione (GSH) (Zugno et al. 2008). In this context, (PhTe)<sub>2</sub> inhibited Na<sup>+</sup>, K<sup>+</sup>-ATPase, a sulfhydryl-containing enzyme that is an enzyme embedded in the cell membrane and responsible for the active transport of sodium and potassium ions in the CNS (Borges et al. 2005). Ávila et al. (2006) described that the activity of  $\delta$ -ALAD, another thiol-containing enzyme that catalyzes the condensation of two aminolevulinic acid molecules with the formation of porphobilinogen, which is a heme precursor (Jaffe 1995), was decreased by diethyl 2-phenyl-2-tellurophenyl vinyl-phosphonate in brain, liver, and kidney of rats. At this point, we propose that the decrease of SH groups observed in our model could provide evidence for increased oxidative damage of proteins in the brain of rats.

Antioxidant enzymes such as CAT and SOD represent the first barrier against RS and are essential to cell survival (Halliwell 2001). SOD activity catalyzes the dismutation of O<sub>2</sub><sup>•-</sup> to oxygen and hydrogen peroxide, while CAT activity converts H<sub>2</sub>O<sub>2</sub> to water and molecular oxygen (Halliwell and Gutteridge, 2007; Valko et al. 2007). Here we showed that the organotellurium reduces the activity of the antioxidant enzymes, CAT in the cerebral cortex and the cerebellum and SOD in all brain areas studied. The decreasing of the antioxidant system could cause the accumulation of H<sub>2</sub>O<sub>2</sub> or products of its decomposition and of O<sub>2</sub><sup>•-</sup> (Halliwell and Gutteridge, 2007). This is in line with previous studies, demonstrating that sodium tellurite depleted the activity of CAT in brain of mice (Kaur et al. 2003), and that (PhTe)<sub>2</sub> reduced the activity of CAT and SOD in the hippocampus and striatum of young rats (Stangerlin et al. 2009).

We next investigate whether NO synthesis could be induced by this organochalcogen, since SOD activity can be altered by peroxynitrite, the most harmful NO derivative (Ischiropoulos et al. 1992; Yamakura et al. 2005). We found that 3-butyl-1-phenyl-2-(phenyltelluro)oct-en-1-one

markedly increased NO levels in the cerebral cortex and the cerebellum of rats, showing that in these brain areas this compound could be really harmful.

Increases in RNS production result from excess or deregulated NO reacting with ROS. NO is a signaling molecule that reacts with O<sub>2</sub><sup>•-</sup> to generate RNS, including peroxynitrite, which is a very reactive molecule that can modify biomolecules, including DNA, lipids, and proteins (Ischiropoulos et al. 1992; Yeo et al. 2008).

Glial cells are known to protect neurons against oxidative stress and cell death by releasing GSH extracellularly and keeping it in the reduced form (Sagara et al. 1993; Stone et al. 1999). Considering that GSH is the major naturally occurring non-enzymatic antioxidant in the brain (Lissi et al. 1995; Evelson et al. 2001), the decrease of sulfhydryl groups observed by the 3-butyl-1-phenyl-2-(phenyltelluro)oct-en-1-one administration is related to the decrease of this non-enzymatic antioxidant defenses in the brain of 30-day-old rats used in this study. It is, therefore, presumed that GSH levels were reduced intracellularly because of the excess of free radical formation, including NO or its derivative peroxynitrite forming nitrosoglutathione or by regenerating the nitrosyl groups and, thus, limiting NO deleterious effects (Stamler and Toone, 2002; Rodriguez-Martin et al. 2002).

Considering that the antioxidant enzymes SOD and CAT are the first line of defense against oxidative injury and that alterations in the antioxidant system may cause the accumulation of H<sub>2</sub>O<sub>2</sub> or products of its decomposition (Strayo et al. 2008), we tested whether the organotellurium could enhance OH<sup>•</sup> production and verified that the compound was able to increase this parameter only in the cerebral cortex. These data probably indicate that the organochalcogen induces oxidative damage by overproduction of OH<sup>•</sup> in the cerebral cortex.

Taken together, the organic compound-induced lipid peroxidation, protein damage, significantly compromised the non-enzymatic (sulfhydryl assay) and the enzymatic antioxidant defenses (CAT and SOD) and increased the levels of RS in the brain of rats. As a result, there was an unbalance between prooxidants and antioxidants, a situation defined as oxidative stress (Sies, 1991; Halliwell and Gutteridge, 2007).

In conclusion, this is the first article showing that the  $\alpha,\beta$ -unsaturated ketone 3-butyl-1-phenyl-2-(phenyltelluro)oct-en-1-one elicits *in vivo* oxidative damage in the CNS. Therefore, it is tempting to speculate that RS may act synergistically with other susceptibility factors, contributing, at least in part, to the biochemical mechanisms involved with the toxicity provoked by this organochalcogen.

**Acknowledgments** This study was supported by Centro Universitário Metodista IPA and Universidade de Caxias do Sul.

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