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# Evaluation of ameliorative potential of selenium on carbendazim induced oxidative stress in male goats

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ABSTRACT

In the present investigation, ameliorative effect of selenium on carbendazim induced oral sub chronic toxicity in bucks was assessed by studying various indices of antioxidant defense system. Bucks were randomly divided into four groups of four animals each. Group I served as control, Group II was orally drenched carbendazim at the dose rate of 50 mg/kg body weight for 90 consecutive days. Group III was orally administered selenium in the form of sodium selenite at the dose rate of 0.05 mg/kg body weight for 90 consecutive days. Group IV was orally administered carbendazim along with selenium at the same dosages as Group II and III. Prolonged administration of carbendazim produced oxidative stress in goat bucks as evidenced by increase in lipid peroxidation and decline in total antioxidant capacity. The increase in the activity of antioxidant enzymes was not sufficient to prevent pesticide induced oxidative stress. Selenium supplementation provides some amelioration against this effect. Further study is needed to prove ameliorative potential of this antioxidant against carbendazim induced toxicity in goat bucks.



## 1. Introduction

Carbendazim (CBZ) (methyl-2-benzimidazole carbamate) is a broad spectrum benzimidazole fungicide extensively used on fruits, vegetables, field crops and ornamental plants for the control of molds, rot, and blight (Vettorazzi, 1976). Carbendazim presents a low potential risk for causing acute illness and has relatively low toxicity in tested mammalian species (Krieger, 2001). However, at higher doses carbendazim has been reported to produce reproductive and developmental effects (Cummings et al., 1990; Gray et al., 1990; Nakai et al., 1992; Perreault et al., 1992). Carbendazim acts by binding to the colchicine binding site of fungal tubulin (Devidse, 1986) and thus disrupting microtubules and consequently inhibiting mitosis (Burland and Gull, 1984; Devidse and Flach, 1977). A similar mechanism of toxicity has been postulated in mammalian testicular microtubules (Devidse and Flach, 1977; Russel et al., 1992). In contrast to high affinity for fungal tubulin, carbendazim has been shown to bind with low affinity to mammalian tubulin (Devidse and Flach, 1977). Carbendazim induces oxidative stress leading to the generation of free radicals and alteration in antioxidant or oxygen free radical scavenging enzymes such as superoxide dismutase,

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catalase, glutathione peroxidase, glutathione reductase and glutathione transferase (Rajeswary et al., 2007a).

Oxidative stress is a term used to describe various deleterious processes resulting from an imbalance between excessive formation of ROS and/or reduced antioxidant defenses (Sordillo, 2013). Antioxidants are the first line of choice to take care of this oxidative stress produced by free radicals in the animal body. When free radical generation exceeds the body's antioxidant defense following exposure to exogenous environmental factors, produces oxidative stress and subsequently cellular injury and tissue damage (Zhao et al., 2013; Rahal et al., 2014). The various enzymatic and non-enzymatic antioxidants are necessary for maintenance of intracellular redox balance and thus lessening undesirable cellular damage caused by ROS (Durackova, 2010). Lipid peroxidation is oxidation of polyunsaturated fatty acids present in the membrane lipid producing hydroxyl radicals and damaging cell membrane.

Proteins that are sensitive to covalent and/or oxidative modification of their thiol groups include the enzyme of energy metabolism, DNA repair enzymes, caspases, transcription factor AP, etc. The inactivation of these proteins by thiol-reactive chemicals, results in impaired maintenance of the cell's energy and metabolic homeostasis and/or altered signal transduction. The covalent and/or oxidative modification of thiol groups in proteins like Keap1 triggers the adaptive electrophile stress response, which is cytoprotective. Two proteins KEAP-1 (Kelch-like ECH related protein) and Nrf2 (nuclear factor E2 p45-related factor-2) function as xenosensors and induce enzymes in response to oxidative stress (Dinkova-Kostova et al., 2005). Binding of the transcription factor Nrf2 to the region of DNA known as the antioxidant response element (also known as the electrophilic response element) induces enzymes that detoxify electrophiles and metabolites that generate reactive oxygen species (ROS), including glutathione transferase (GSTA1), glutamate-cysteine ligase (GCL), etc. GCL catalyzes the rate-limiting step in glutathione synthesis. Induction of GCL increases the rate of glutathione synthesis under conditions of oxidative stress and a decrease in glutathione concentration (Lee et al., 2004).

Selenium is an essential component of the rare amino acid selenocysteine (Sec) and is incorporated at the catalytic site of various selenium-dependant enzymes such as glutathione peroxidase (GPx), thioredoxin reductases, and one methionine-sulfoxide-reductase. These selenoenzymes play important roles in regulating metabolic activity, immune function, antioxidant defense and intracellular redox regulation and modulation (Tinggi, 2008; Papp et al., 2010). Plasma Glutathione peroxidase (GSH-PX) protects cellular membranes and lipid containing organelles from peroxidative damage by inhibition and destruction of endogenous peroxides, acting in conjunction with vitamin E-an antioxidant to maintain integrity of these membranes (Van Metre and Callan, 2001). Selenium supplementation in the form of sodium selenite have been reported to protect the cells through expression of oxidative stress related genes and improving the activities of antioxidant enzymes (Zhao et al., 2013). The trace element has been shown to protect the organs and tissues from oxidative damage through suppression of ROS generation and thus exhibiting antioxidant property (Wang et al., 2013). Research done by Khera et al. (2013) proved that selenium supplementation protects cardiac tissues from the damaging effects of the oxidative stress. Study by Mehta et al. (2012) reported that selenium protect neurons against hypoxic/ischemic damage by reducing oxidative stress, restoring mitochondrial functional activities and stimulating mitochondrial biogenesis. Selenium supplementation can maximizes anti-oxidant expression in preparation of an oxidative insult (Munaza and Tahir, 2012). Selenium has been reported to be most protective against oxidative stress in conjunction with vitamin E (Srivastava et al., 2010).

The antioxidant roles of vitamin E and selenium are linked which can be explained as vitamin E is thought to inhibit the production of lipid peroxides, whereas selenium destroys any lipid peroxides that are formed via glutathione peroxidase (Hoekstra, 1975). Vitamin E and selenium through glutathione peroxidase function as part of multicomponent antioxidant defense system (National Research Council, 1987). Vitamin E readily reduces alkyl peroxy radicals of unsaturated lipids and generate hydroperoxides that are further reduced by the selenoperoxidases, in particular by phospholipid hydroperoxide glutathione peroxidase (Flohe and Traber, 1999).

Carbendazim has been reported to alter antioxidant defence system, in mammalian species and antioxidants have been proved protective against the carbendazim induced toxicosis (Rajeswary et al., 2007b). Selenium, a well known antioxidant have not yet been studied to see any amelioration against this fungicide, so the present investigation was undertaken in goat bucks to evaluate the ameliorative potential of selenium against carbendazim induced oxidative stress.

## 2. Materials and methods

### 2.1. *Chemicals*

Bavistin$^{R}$ (Carbendazim 50%, w/w) was purchased from the local pesticide shop. Sodium selenite was purchased from Loba chemicals Mumbai. All other chemicals for enzyme estimation were purchased from Sigma, Merck, SRL, SD fine chemicals depending upon purity required.

### 2.2. *Experimental animals*

The experiment was conducted on sixteen Beetal goat bucks of one and half years of age procured from Department of Animal Nutrition, GADVASU Ludhiana. The animals were acclimatized in the animal shed of the department of Veterinary Pharmacology and Toxicology. The animal house of department fulfills all measures of husbandry to ensure healthy and homogenous ambient conditions throughout the study period. Prior to the experimentation, animals were dewormed and vaccinated against major diseases. Bucks were fed with Berseem (4–5 kg) mixed with chopped wheat straw (1.5–2 kg) along with 500 g concentrate per animal per day and water was provided ad libitum. All the animals were weighed at weekly intervals to make necessary changes in dosage.

Bucks were randomly divided into four groups of four animals each in which group I served as control. Carbendazim (BavistinR) weighed daily, mixed in distilled water and