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EVALUATION OF SUPEROXIDE DISMUTASE LEVELS IN RODENT VISCERAL ORGANS AND TISSUES AFTER FEEDING A DIET FORTIFIED WITH CHILLI FOR THREE MONTHS

Korra Mangthya[1,2*], Pradeep B. Patil[1*], R. Ananthan[#], K. Subash[#], T Longvah[#], SSYH Qadri[*]

**NIN animal Facility, [#] NIN Food Chemistry Department*
ICMR-NIN, Hyderabad, India -500007

[1] *Shared First Authors*
[2] *Corresponding Author*

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ABSTRACT

Purpose: *It is known that chilli has untoward effects on the living being on taste buds, gastric mucosa, and other organs. It could lead to gastric cancer through severe acid production. However, we could not blame all chillies (hot, bell, red, cayenne, and sweet) as their capsaicin (CAP) and other capsaicinoids vary in different regions and chilli varieties. This study measured the effect of three chillies (Naga King, Bird's Eye, and Guntur) on superoxide dismutase (SOD) levels of visceral and vital organs.*

Design/methodology/approach*: In this study, a diet fortified with chilli powder was used for feeding Sprague Dawley rats which contained standard 20% protein and chilli powder (0.005% of CAP equivalent) over three months to measure superoxide dismutase levels in six vital, visceral organs/tissues (Adipose, Brain, Heart, Lung, Kidneys and Testes).*

Finding: *Heart tissue followed by brain and lung have shown more SOD levels in the CEG group, whereas in the rest of the groups' lung tissue had shown a notable increase in SOD levels. NKC and BEC showed a three-fold increase in SOD levels of the lung, whereas the CEG group had a 1.25-fold increase compared to standard diet normal control (SNC).*

Research limitations/implications: *Active components of the chilli have to be tested separately to reach a reproducible conclusion. Oral dosing of chilli's active component instead of feeding through diet would provide more reliable data.*

Originality/value: *Vital organs like the brain, lungs and kidneys are also affected through chilli consumption; however, its severity and protective role can be understood through oxidative enzymes like SOD.*

KEYWORDS: *Naga King Chilli, Guntur Chilli, Bird's Eye Chilli, Capsaicin, Sprague Dawley rat*
Paper type: Original article

1. INTRODUCTION

Literature suggests that chilli could lead to dyspepsia and peptic ulcers; however, on the other hand, it is also claimed that consumption of chilli capsaicin (CAP) increases gastric mucosal [1, 2] and dermal blood flow [3] along with an increase in nitric oxide [4, 5] release. Increased gastric acid secretion through chilli ingestion assists in assimilating sugar, fibre, fat, amino acids, and dietary trace metals. Other studies suggest that it could be gastro-protective to prevent haemorrhagic shocks [6] or gastric ulcers [7]. Chilli could also enhance the essential cations of trace elements solubilisation from food matrix using gastric acid secretion and suppressing gastric acid [8].

The risk of gastric cancer in humans is correlated to chilli consumption. However, scientists also look forward to CAP's role in cardiovascular risks/protection [9], obesity [10], neural protection [11], mucosal ailments or production [12], and modulating absorption and metabolism of lipoproteins [13] and other nutrients [14].

Several events causing stress in living beings could cause oxidative stress, free radical formation, mitochondrial dysfunctions, DNA damage, and inflammation. Diet is considered one of the essential factors that contribute to these events. Moreover, dietary patterns, habits, or diet customs have also been correlated to these factors. The perspective toward eating habits could be flawed *vs* good, superior *vs* inferior. Although such information is accurate for particular locations or environments, it affects ordinary people when they copy the culture and eating habits resulting in oxidative stress. In a nutshell, oxygen used during anabolic and catabolic reactions leads to the production of free radicals in the form of superoxide anion, H2O2, OH-, and singlet oxygen (1O2), which is not a free radical. However, it can trigger free radical formations. These free radicals depend on oxidative stress damage in cells, including several types of liver injuries through lipid and protein peroxidation. Such lipid peroxidation products from different biochemical reactions will be nullified or modified with the help of the antioxidant system either by scavenging free radicals or suppressing the actions of reactive oxygen species. There are different antioxidants widely

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distributed through our body in all cells, either in the form of nonenzymatic forms like vitamins (like A, C & E), bilirubin, reduced glutathione, or ceruloplasmin, and enzymatic forms (like superoxide dismutase, glutathione-S-transferase and catalase etc.).

As mentioned and described in our earlier publications [15, 16], CAP and other nutrient analyses from three types of chillies were carried out before initiating an animal study where a chilli-fortified diet was fed for three months, followed by visceral organ harvesting for tissue level antioxidant enzymes quantification. In this article, effect on tissue level of SOD is estimated and compared in fold change with various controls.

2. OBJECTIVES

To evaluate the change in vital, visceral organs/tissues SOD levels in a rodent model fed with a chilli fortified powder diet.

3. METHODOLOGY

Three types of chillies were used for analysis and diet preparation. The powder diet for the rodent study was prepared using a standard 20% protein diet fortified with capsaicin equivalent chilli powder. Study design, sample collection, processing, animal study and the analysis of Superoxide Dismutase (SOD) activity were described in detail in our earlier publication [15].

4. RESULTS

The SOD levels in Adipose (Graph 1): In the current study, the BEC had elevated SOD levels in adipose tissue (3.13-fold), and it is followed by the Ethanol group (2.16-fold) and the NKC group (1.71) compared to the SNC group. Similarly, the BEC group also had an increase in SOD levels of adipose tissue (3.56-fold), followed by the Ethanol group (2.46-fold) and NKC group (1.95-fold) compared to the CEG group. However, the GC group had a slight decrease (0.75 and 0.85-fold) in SOD levels of adipose tissue than the SNC group and the CEG group, respectively.

The inverse correlation between SOD activity and weight in visceral adiposity has shown adipocyte death, adipose tissue inflammation in mouse model [17, 18], and metabolic stress [19]. Literature also suggested that SOD reduces adipose tissue inflammation [20, 21] by reducing macrophage accumulation and triglyceride metabolism. *In vitro* studies have provided evidence about improvement in bone repair through SOD which helps in differentiation [22] compared to other antioxidant systems. Obesity increases oxidative stress and decreases SOD activity [20, 21]. Interestingly, similar results were obtained in the current study as NKC and BEC had 18% decrease in body weight compared to SNC whereas GC group had just 15% more weight than NKC.

The SOD levels in the Brain (Graph 2): *In vitro* studies suggest that dopamine exposure to astrocytes causes the release of SOD mRNA. Interestingly, SOD levels of the brain have increased more than two-fold in two chillies, BEC (3.17-fold), NKC (2.56-fold), and Ethanol group (2.96-fold), whereas no significant variation was observed in the CAP group (1.39-fold) and GC group (0.94-fold). This results in SOD protein enzyme activity and NF-κB activation [23]. Knock-in and transgenic mice study suggested that overexpression of EC-SOD may have a protective effect in the chronic hypoxia model [24] with a dual role in controlling and regulating ROS signalling [25].

The SOD levels in living mammalian cells will have Zn and Mn as co-factors, whereas intracellular pathogens like protozoa will have Fe as a cofactor; however, bacteria will have Zn and Mn cofactor similar to mammalian cells [26], which affects the quantification of SOD. It was also found that a decrease in SOD level results in the induction of hypertension and peripheral inflammation in the CNS [27].

The SOD levels in the Heart (Graph 3): The heart tissue SOD levels were doubled in BEC (2.42-fold), and NKC (2.25-fold) compared to the SNC group, whereas the Ethanol group (1.25-fold) and CEG (1.58-fold) had an almost similar level of increase in SOD. Usually it is said that SOD plays a role of shepherd for heart [28]. Elevated levels of SOD in plasma is also indicator of coronary heart diseases [29]. The SOD overexpression increases NO bioavailability, whereas it reduces infarct intensity in ischemia or reperfusion studies [30]. SOD activity is also used to predict outcomes in non-ischaemic dilated cardiomyopathy patients [31]. The SOD has been correlated with cardiac malfunction, fibrosis [32], and cardiovascular disease [33].

The SOD levels in Lung (Graph 4): Lung SOD levels were found elevated in the BEC (3.08-fold) and NKC (3.00-fold), followed by the Ethanol group (2.17-fold), whereas the GC group had slight variations (1.25-fold) compared to the SNC group. Similarly, an increase in SOD values of lung tissue was observed in the BEC (2.31-fold) and NKC (2.25-fold), followed by the Ethanol group (1.63); however, the GC group had minimal variations (0.94-fold) compared to the CEG group. The superoxide dismutase family is downregulated in lung diseases, and many external antioxidant therapies failed, whereas some studies with intravenous SOD showed promising protection against barometric lung impairment [34]. However, SOD mimetics showed promising results [35]. Similarly, upregulation of SOD by chilli diet could be an attractive diet-based therapy. Oxidant/antioxidant balance is pivotal in pulmonary disease, and SOD is one of the essential pillars in preventing airway oxidative stress [36]. However, the proteolytic processing of SOD decreases its affinity for the extracellular matrix [37] during inflammation.

Certain studies also suggest that Sirtuin (SIRT3) increases Mn-SOD activity so that such gene therapy might help prevent lung damage [38], however, the success of gene therapy is subject-oriented, and hidden side effects are unknown. Still, using chilli to activate endogenous SOD is an easy option. The sepsis model of caecal perforation or ligation has shown an increase in the release of endogenous SOD. However, it is not sufficient to rescue where SOD mimetics might help [39]; here, we also believe that activating such endogenous SOD routinely by the bird's eye chilli or Naga king chilli will protect or prevent such sepsis-related mortality, which should be further tested in animal models.

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The SOD levels in Kidneys (Graph 5): Similar to other organs and tissues, the SOD levels of kidneys elevated in two chillies (NKC - 2.30-fold, BEC - 1.90-fold) and Ethanol group (1.40-fold) compared to the SNC group, whereas the GC group (0.70-fold) and CEG group (0.90-fold) had minimal variations. Experimental results from mice suggest that Extracellular SOD levels are decreased in chronic kidney diseases [40], whereas plays a protective role in ischemia-reperfusion injury of the kidney [41]. Another study in mice suggests that inactivation of the gene related to EC-SOD, elevated hypoxia-induced Epo gene expression almost 100-fold [42], indicating it has a significant role in maintaining kidney health. Many studies have a typical relationship between SOD dysfunction in mitochondria and renal disease [43].

The SOD levels in the Testes (Graph 6): Testes have more SOD as an antioxidant system superoxide dismutase than other tissue, and the germ cell line regulates its level [44]. The SOD levels in testes were found high in the BEC group (1.56-fold), NKC (1.38-fold), and Ethanol group (1.38-fold) than in the SNC group, whereas they were low in GC (0.36-fold); however, the CEG control group had no change in testes SOD levels. Other studies on rats fed a high-fat diet with CAP revealed that SOD levels increase in testicular and hepatic tissue, known as oxidant-antioxidant status [45]. However, there was merely no difference between the testes-SOD levels of CEG group and the SNC group in this study. This could be because, in the current study, we fed less CAP, which is 0.005% in the powder diet (Graph 1), compared to the study mentioned above, i.e., 0.015% CAP in the powder diet. Another interesting study reveals that the SOD activity decreases with chronic stress in adult model [46]; however, in our study, SOD was increased in BEC, NKC, and Ethanol groups and decreased in Guntur chilli.

Organ-wise comparison of SOD (Graph 7 - 11): Interestingly, it was found that a chronic but small amount of alcohol consumption increases the SOD levels [47]; in this study, we found similar results as our dose (80% average 1mL/250 of rat) was even smaller than the one used in the study as mentioned above (0.05g/kg). SOD levels in GC and CAP groups did not increase much. Ironically GC group had decreased SOD compared to CAP and the normal group in all vital, visceral organs except the lung. It reflects that Guntur chilli could be a stress inducer and need to be used in diet with caution. However, NKC, BEC and Ethanol groups showed a 2-3-fold increase in SOD compared to normal control group (SNC).

5.0. SUGGESTIONS

Chilli in the diet is utilised as a spice and added for the tastebud's sake. However, the literature suggests that it has high medicinal and cosmetic applications. Although the data available is not adequate, here in this manuscript, efforts were made to find out which chilli has the potential to be a suitable candidate for therapeutic potential and what proportion it should be consumed. It was also surprising that the CAP-fed group did not do better than NKC and BEC-fed groups. This could be due to either the biphasic nature of CAP or the lower dose in this study than in most other studies. Similarly, the Ethanol group has performed well in all tissues along with BEC and NKC, which could be because its lower dose works as a chronic challenging study to cells. A further detailed study on individual active components of chilli is warranted to reach a suitable conclusion.

Although, a previous acute study on rats for seven days where an aqueous extract of chillies and ethanol (80%) fed using oral gavage provided mixed results where the ethanol group and CAP group ranked high in stomach tissue-SOD levels, followed by NKC + Ethanol group and CAP + NKC group in comparison with vehicle control and saline control. Similarly, performing a chronic challenge study for three months using a powder diet on all six visceral organs/tissues would provide a piece of valuable information on its protective role in the ethanol consumption population.

The limitation of the existing study is that the SOD in serum was calculated for acute study (published in NIN annual report 2014-15). However, serum SOD levels were not estimated in this study. The blood parameters like differential count and other inflammatory markers have not been studied, which would have been confirmatory for the present observation. Measurement of free radicals using chemiluminescence tagging (imaging) and challenge study could have been helpful to draw therapeutic conclusions. The bone mineral density using DEXA and lean body mass analysis using TOBEC would have provided more evidence to support the results.

6.0. CONCLUSIONS

SOD levels are indicators of stress and the capacity to fight stress. An acute increase in tissue level SOD may indicate stress; however, after chronic study, if the SOD levels are increased at the tissue level, it means it has adequate antioxidants ready for use. It indirectly means it can cope better with the higher stress level due to the availability of more SOD in tissue. Guntur chilli has shown opposite results compared to the CAP control group. In contrast, bird's eye chilli and Naga King chilli have a 2-3-fold increase in SOD compared to the usual or CAP group indicating that other capsaicinoids present in chilli also play a significant role in activating the antioxidant system.

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7.0. FIGURES, TABLES AND REFERENCES

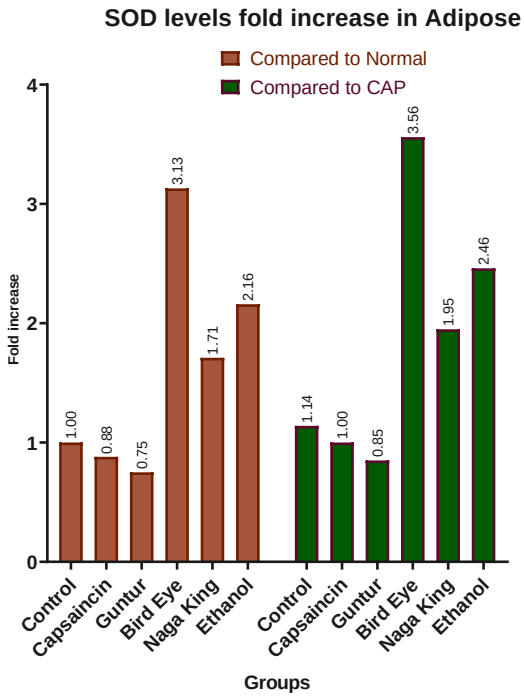

Figure 1: Change in SOD levels of Adipose tissue after 90 days of feeding trial (fold increase)

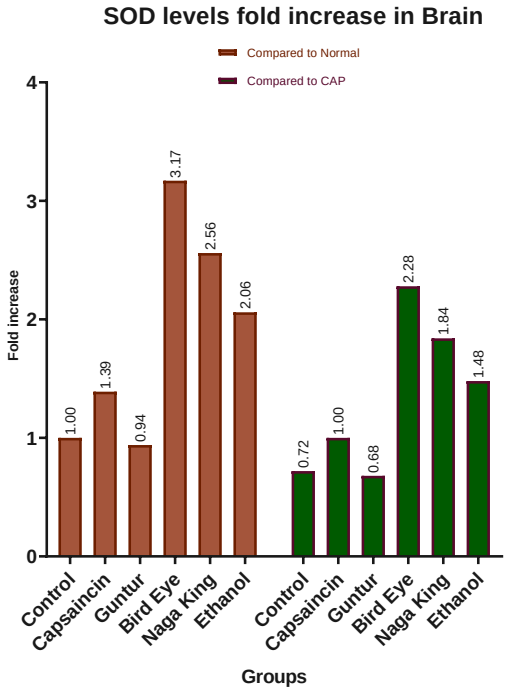

Figure 2: Change in SOD levels of Brain tissue after 90 days of feeding trial (fold increase)

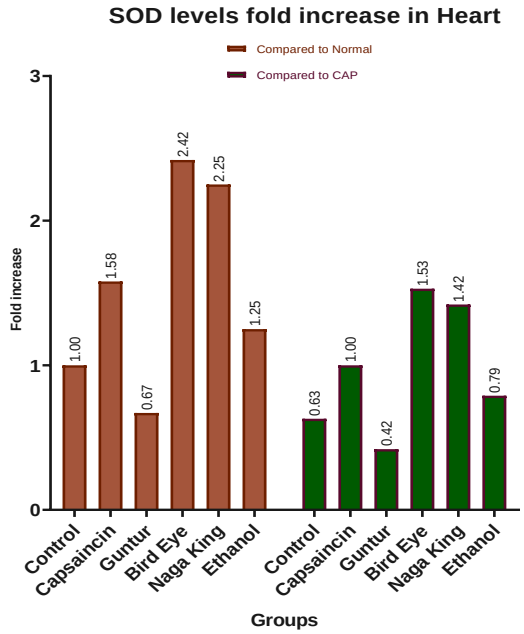

Figure 3: Change in SOD levels of Heart tissue after 90 days of feeding trial (fold increase)

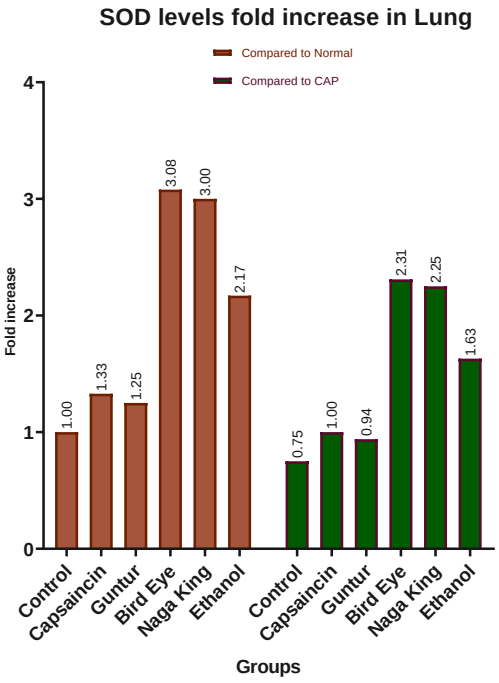

Figure 4: Change in SOD levels of Lung tissue after 90 days of feeding trial (fold increase)

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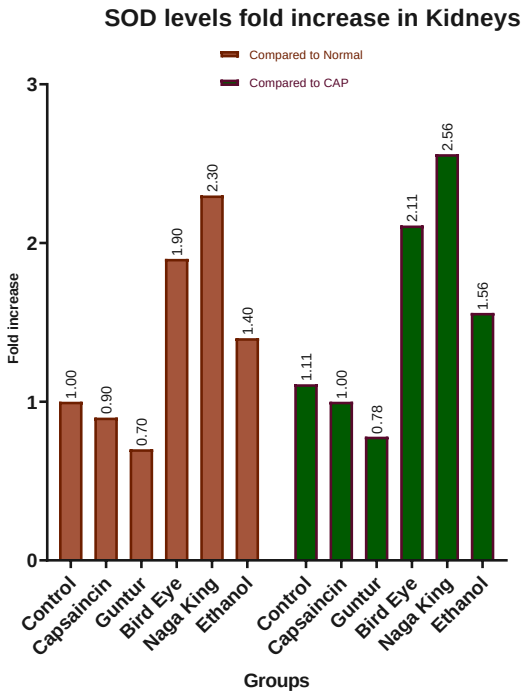

Figure 5: Change in SOD levels of Kidneys tissue after 90 days of feeding trial (fold increase)

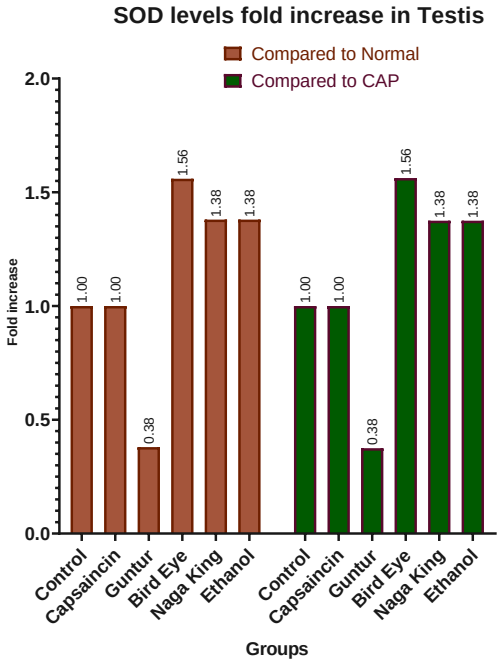

Figure 6: Change in SOD levels of Testes tissue after 90 days of feeding trial (fold increase)

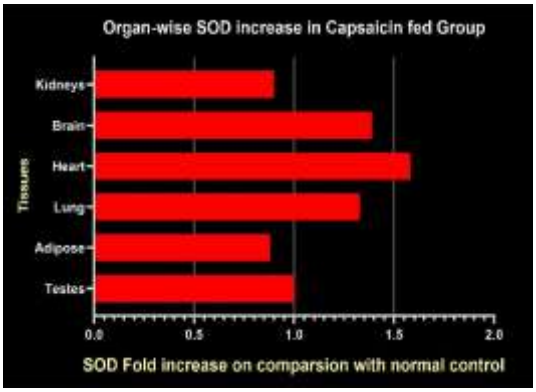

Figure 7: Organ-wise change in SOD levels in various tissues upon feeding of CAP

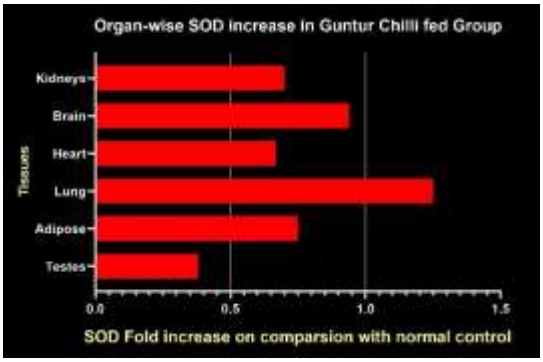

Figure 8: Organ-wise change in SOD levels in various tissues upon feeding of Guntur Chilli

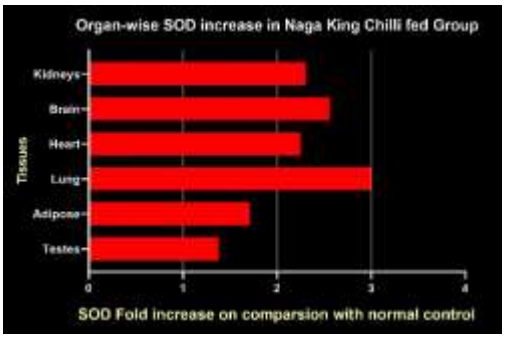

Figure 9: Organ-wise change in SOD levels in various tissues upon feeding of NKC

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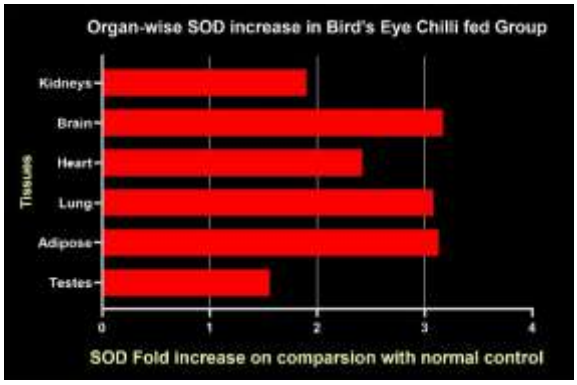

Figure 10: Organ-wise change in SOD levels in various tissues upon feeding of BEC

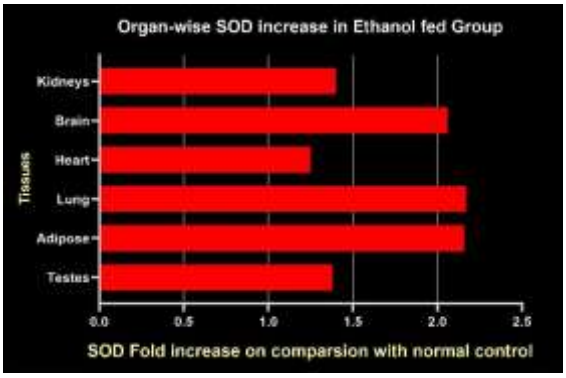

Figure 11: Organ-wise change in SOD levels in various tissues upon feeding of Ethanol (80%)

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