



# Research Journal of Pharmaceutical, Biological and Chemical Sciences

## Protective Impacts of Zinc against the Toxicity of Smoking Induced Fluctuated Levels Of testosterone, Estrogen and Zinc in Smoker Men.

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### ABSTRACT

Smoking has multiple effects on sex hormone secretion, some of which are associated with important clinical implication. This study was to evaluate the protective effects of zinc against the toxicity of smoking induced testosterone, estrogen and zinc levels fluctuated in smoker men. Blood samples were collected from 112 students male in Aljouf, 78 subjects were smokers compared with 34 subjects were non-smokers. The mean levels of zinc was significantly decreased in smokers than non-smokers ( $p \leq 0.05$ ), also the level of zinc increased significantly ( $p \leq 0.05$ ), in test group after using zinc tabs compared to before using zinc tabs. Testosterone and Estrogen hormones were significantly decreased in smokers compared to non-smokers. Cigarette smoking decreased zinc, testosterone hormone and Estrogen hormone levels significantly, zinc treatment significantly compensates zinc level, but failed to compensate testosterone and Estrogen hormones in one month of treatment. No association between BMI and smoking.

**Keywords:** Sex hormones binding globulin, zinc, smoking, BMI.

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## INTRODUCTION

The health consequences of cigarette smoking and the use of the other tobacco products are well known. They are an important cause of the increase of mortality and morbidity in developed countries and the prevalence is increased in developing world as well [1]. Tobacco smoke contains numerous compounds; the important substance of material is being the carcinogen (such as poly cyclic aromatic hydrocarbons), irritant substances, nicotine, carbon monoxide and other gases. [2] Each puff of a tobacco contains  $10^{14}$  oxidants in the tar phase and  $10^{15}$  in the gas phase. [3] The high production of these multiple types of oxidant and reactive oxygen species (ROS) associated with smoking may exceed the capacity of the oxidant defense system, resulting in oxidative damage to select proteins, lipids and DNA. [4] Smoking has an effect on the various metabolic and biological processes in the body including secretion of hormones. [5] Cigarette smoking has major effects on the reproductive potential of humans; it has anti-estrogenic effect in women. [6] Smoking in Saudi Arabia is increasing rapidly, particularly among the young, partly due to aggressive marketing by tobacco companies and financial reasons were less important for quitting smoking, probably because of the low price of cigarettes; [7] although around 160 \$ million is used for purchasing tobacco in Saudi Arabia every year. [8] In males, the effect of smoking is on androgen levels; given the recent interest in the association between androgen levels and metabolic syndrome and coronary heart disease, [9] the prevalence of smoking in Saudi Arabia is 25% (equal 6 million people) and the prevalence of current smoking is much higher in males than in females at different ages and more research is needed in the area of prevention and treatment of smoking. [10] Cigarette smoking may be associated with sub-fertility in males and may result in decreased sperm concentration, low sperm motility and reduce percentage of morphologically normal sperm respectively. [11] This is probably due to changes in hepatic estrogen metabolism induced by smoking. Smoking has a powerful effect on the 2-hydroxylation pathway of estradiol metabolism leading to increased production of 2-hydroxyestrogens. [12] These compounds have minimal estrogenic activity and are rapidly cleared from the circulation. Furthermore, in the circulation estrogens bind avidly to sex hormone binding globulin (SHBG) (38%), loosely to albumin (60%) and the remainder is the free unbound fraction. In smokers, concentrations of SHBG are higher and lower concentrations of biologically active estrogens are thus seen. [13] Nicotine-addicts usually have the risk of depletion/deficiency in important nutrients and minerals including zinc. The zinc deficiency leads to decrease number of sperm and impotence in males. Zinc also inhibits the aromatase enzyme that converts testosterone into excess estrogen; the high estrogen activity results in increased risk of heart disease, weight gain and obesity in male. The low levels of zinc lead to lower sperm count, lower sex drive and can aid in producing prostate cancer. [14] Zinc is involved in numerous aspects of cellular metabolism [15] and it plays a role in immune function, protein synthesis, cell division, DNA synthesis, [16] and wound healing. [17] Zinc also supports normal growth and development during pregnancy, childhood, and adolescence [18] and is required for proper sense of taste and smell. [19] A daily intake of zinc is required to maintain a steady state because the body has no specialized zinc storage system. [20] The aim of this study is to evaluate the protective effects of zinc against the toxicity of smoking induced testosterone, estrogen and zinc levels fluctuated in smoker men.

## SUBJECTS AND METHODS

### Subjects

A group of 112 Saudi male students at Aljouf University (Aljouf-Saudi Arabia) (age range 18-30 years old) in different colleges; during the period from 1/10/2012 to 20/1/2013, 78 subjects were smokers with daily consumption of 20 cigarettes for a different period (ranging from 3-8 years), were enrolled in this study and compared with 34 non-smokers. All test groups were clinically healthy. Both participant (smoker and non-smoker) had been volunteers and an informed consent were filled with a questionnaire from them. Exclusion criteria for both groups were any history of cardiovascular, hypertension, endocrine, oral diseases and alcohol consumption. They did not take any medications continuously or therapy at least for last three months. This study conducted under consultation of medical doctors.

### Biochemical Measurements

First blood samples were collected from them and they were started to use zinc tablets (50mg), 1 tab/day (under consultation of medical consultants). The second blood samples were collected from the participating after 1 month of using zinc tabs, then 5ml of Venous blood were collected in plain containers using disposable syringes. All blood samples were allowed to clot at room temperature and then centrifuged at 4000 R.P.M to obtain the serum. The samples were centrifuged for 15 min at 2000 rpm and laboratory analysis started immediately. Testosterone and Estrogen were measured by using (RIA) technique. Zinc level was measured by using atomic absorption spectrophotometer. Body mass index (BMI, kilograms per meter squared) was calculated from measurements of weight and height. Ethical considerations: The objectives of the study were explained to all students participating in this study, blood samples before and after zinc tabs were collected after an informed consent from all participating.

### Statistical analysis

Statistical analysis was performed using SPSS 11.5 software. T-test was used to analysis and a p value less than 0.05 were considered as significant.

## RESULTS

Table 1 show the characteristics of the study group smoker and non-smoker, in which there were insignificant difference noticed in testosterone levels among smokers and non-smoker ( $P= 0.126$ ),

**Table 1: Characteristics of the study populations**

Characters	Test group (smokers)	Control (non-smokers)
N	78	34
Age/year	22.2±3.3	22.8±4.8
Body max index (kg/m <sup>2</sup> )	22.8 ± 2.1	23.1 ± 3.4
Zinc (µmol/L)	12.2 ± 1.9	14.1± 1.6*
Estrogen (pg/mL)	69.4± 11.2	70.7±12.4*
Testosterone (ng/ml)	16.6 ± 1.9	17.3± 2.1*

- n = number of group
- The table show data as Mean ± SD
- \* Significant at (p ≤ 0.05)

**Table 2: levels of Zinc, Estrogen and Testosterone hormones in 2 subgroup of Test group (smokers) according to use of Zinc tabs:**

	Before zinc tabs	After zinc tabs
N	78	78
Zinc (µmol/L)	12.2 ± 1.9	13.3± 1.3*
Estrogen (pg/mL)	69.4 ± 11.2	70.4 ± 10.2
Testosterone (nmol/L)	16.6 ± 1.9	17.0± 1.2

- n = number of group
- The table show data as Mean ± SD
- \* Significant at (p ≤ 0.05)

**Table 3: levels of Zinc, Estrogen and Testosterone hormones in control (non-smokers) group compared to test group (smokers) after use of Zinc tabs:**

	Non-smoker	Smoker (After zinc tabs)
N	34	78
Zinc (µmol/L)	14.1± 1.6*	13.3± 1.3
Estrogen (pg/mL)	70.7±12.4	70.4 ± 10.2
Testosterone (nmol/L)	17.3± 2.1	17.0± 1.2

- n = number of group
- The table show data as Mean ± SD
- \* Significant at (p ≤ 0.05)

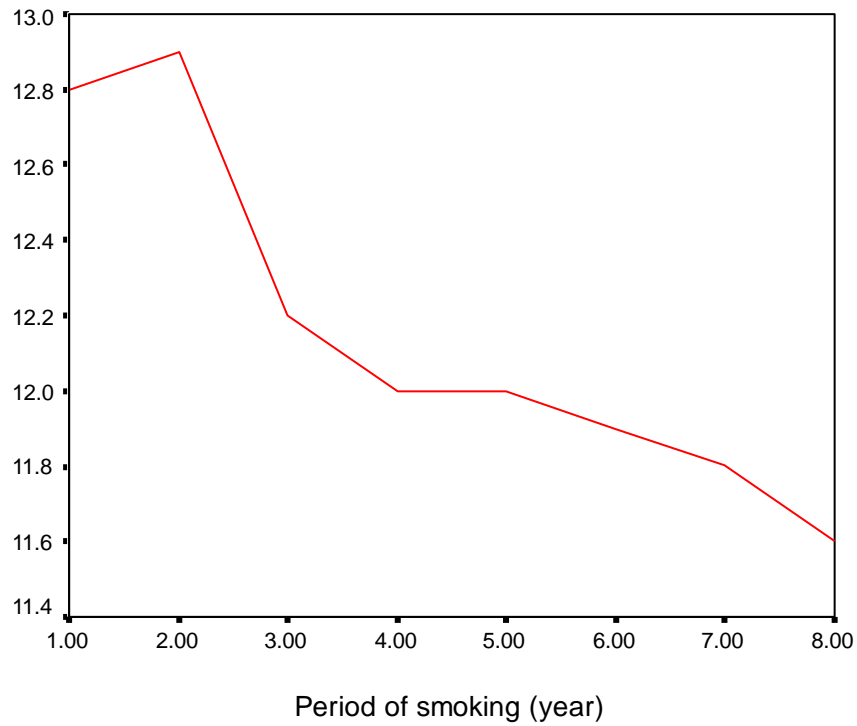


Figure 1: decreased Zinc level in smoker/year (in last 8 years)

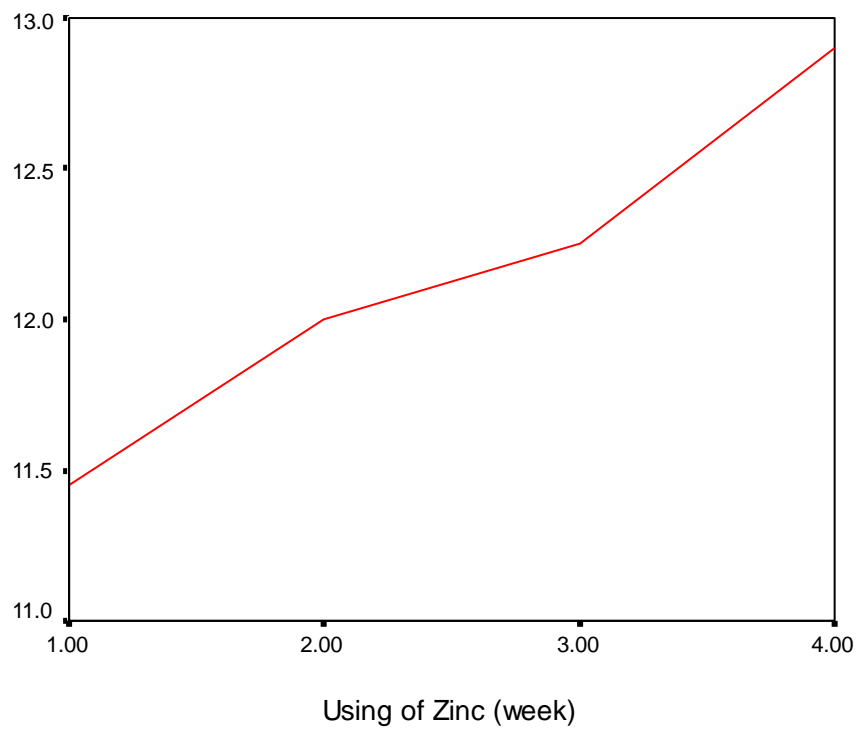


Figure 2: increased Zinc level/week of using Zinc tabs (in one month)

## DISCUSSIONS

Cigarette smoking is an important modifier of hormones and a detailed smoking history is essential when assessing patients with endocrine disorders. [21] The direct toxic effect of environmental toxins present in cigarette smoking which contains a lot of known toxins that may have detrimental effects on fertility in both sexes. [22] Some of the chemicals in cigarette's smoke generate a large number of free radicals, which may be related to the etiology of cancer and various diseases. [23]

Garcia [23] *et al*, 2012 said that Zinc treatment protected against the toxic of smoking in which it is an antioxidant and stimulant of cell division, can be indicated as a promising treatment in men with infertility caused by the toxic components of cigarette smoke. In our study the test group using zinc tabs to test the effect on zinc serum levels and testosterone and estrogen hormones, zinc level decreased significantly in smokers compared to non-smokers, and results in table 2, figure 2 documented that. This finding agrees with the finding of Oldereid *et al*, 1994 [24] and disagrees with Al-Azzawy 2011. [13] The effect of zinc tabs significantly increased the zinc serum levels and table 2 showed that ( $P \leq 0.05$ ), in which the level of zinc increased in smokers after one month of zinc treatment, this indicated the highly significant of zinc treatment, so our study suggested that zinc treatment compensates decreased zinc level caused by smoking.

In our study, the data suggest that tobacco smoking has a significant effect on the biological active function of testosterone and estrogen hormones in smokers compared with non-smokers group, this finding agrees with the finding of Svartberget *et al*, 2003 [21] who have observed a positive significant correlation between testosterone level and tobacco smoking. While, disagree with English *et al* 2001 study [22] who found no significant effect of cigarette smoking on the active fraction of testes in smoker but may influence the levels of total testosterone through the change in the levels of sex hormone binding globulin (SHBG). After zinc treatment the levels of both hormones (testosterone and estrogen) were increased although it is not statistically significant (table 2) ( $P \geq 0.05$ ), the suggestion of this case is that low period of treatment (just one month of using zinc) which does not lead to increase the level of both hormones significantly. Table 3 indicated significant difference between zinc serum level in controls compared to test group after using zinc treatment, and insignificant difference in the level of testosterone and estrogen hormones, and the suggestion of this case is that low period of zinc treatment. In regarding to BMI and smoking status, no association between the mean concentration of BMI and smoking; our results are similar to the result of Marc 2007, [25] who found that smoking was positively associated with physical inactivity, which mediated the association between tobacco use and BMI. This finding is different from the finding of other studies who found that smoking was positively associated with BMI and this is due to the poor behavioral habits among smoking. [26]

## CONCLUSION

There was a significant association between zinc level and smoking status, in which it is decreased significantly; zinc treatment significantly compensates serum levels of zinc. Smoking status decreased the levels of testosterone and estrogen hormones concentration,

while zinc treatment failed to compensate serum levels of both hormones in one month of treatment. There was no significant association between smoking status and BMI.

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