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Evaluation of The Acute Nephrotoxicity and Cardio Toxicity of Commonly Used Herbs for Treatment of Sexual Dysfunction.

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ABSTRACT

Erectile dysfunction it's a condition in which a man cannot achieve or maintain an erection in sexual performance , around one in ten men will experience recurring impotence problems at some points in their life's, erectile dysfunction supplements and other natural remedies have long been used in Chinese , Africa and other cultures . Erectile dysfunction herbs and supplements haven't been well studied or tested. Some can cause side effects or interact with other medications .we aim in this work to evaluate the nephrotoxicity and cardio toxicity of commonly used herbs for treatment of sexual dysfunction (ginseng, piper cubeba & ginger) in experimental rats both laboratory & pathologically.

Keywords: ginseng, piper cubeba, ginger ,cardio toxicity and nephrotoxicity.

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INTRODUCTION

Erectile dysfunction (also known as ED or "(male) impotence") is a sexual dysfunction characterized by the inability to develop and/or maintain an erection(1,2).

Erectile dysfunction can occur due to both physiological and psychological reasons, most of which are amenable to treatment. Common physiological reasons include diabetes, kidney disease, chronic alcoholism, multiple sclerosis, atherosclerosis, vascular disease, and neurologic disease which collectively account for about 70 percent of ED cases. Some drugs used to treat other conditions, such as lithium and paroxetine, may cause erectile dysfunction.[2, 3]

Erectile dysfunction, tied closely as it is to cultural notions of potency, success and masculinity, can have devastating psychological consequences including feelings of shame, loss or inadequacy;[4] There is a strong culture of silence and inability to discuss the matter. In fact, around one in ten men will experience recurring impotence problems at some point in their lives.[5]

Erectile dysfunction supplements and other natural remedies have long been used in Chinese, African and other cultures. But unlike prescription medications for erectile dysfunction, such as sildenafil, vardenafil, tadalafil and avanafil, erectile dysfunction herbs and supplements haven't been well-studied or tested. Some can cause side effects or interact with other medications. And the amount of the active ingredient can vary greatly from product to product.(6,7)

Aim of the work:

To evaluate nephrotoxicity and cardio toxicity of commonly used herbs for treatment of sexual dysfunction (ginseng, piper cubeba & ginger) in experimental rats both laboratory & pathologically

MATERIAL AND METHODS

For this study 40 male rats with average weight 200 + 50 were used .rats were healty with normal kidney and cardiac function tests and were kept in separate cages at room temperature for one week before starting the study then were dinided into four main groups each group ten rats with the same feeding like the control group, of All experimental procedures were conducted in accord with the principles for the care and use of laboratory animals in research and approved by the local ethics committee. All efforts were made to minimize animal suffering and reduce the number of animals used.(8)

After a quarantine period of 7 days, 40 male rats were randomly divided into four groups, each consisting of 10 rats.

Group A was used as control .
Group B receive ginseng powder dissolved in water orally 200mg/kg for one month as by conversion of adult human dose (8) to animal dose(9).
Group C receive piper cubeba at a dose of 500mg/kg orally for one month (10).
Group D received ginger at a dose of 100mg/kg for one month (11).

All this groups was evaluated for penile size measurements, at start and at the end of the study

The rats were sacrificed 24 h following the last herbal dose, blood samples were collected, and serum was separated by centrifugation at 3000 g for 10 min. A longitudinal section from the left kidney and the heart was excised from each animal for histological examination.

1- **Laboratory :**
   - Kidney function tests:
     - Blood Urea & creatinine
     - Urine test for albuminuria
   - Cardiac function test:
     - Creatinine kinase (CK)

- CK-MB
- Aspartate transaminase (AST)
- Lactate dehydrogenase (LDH)
- Troponin I

2- Histo pathological Examination

Kidney and heart samples of control group and treated groups were taken from sacrified rats and fixed in 10% buffered formaline solutions . the samples were prepared in paraffin wax blocks and sectioned (5 micron thick sections). The sections were stained with hematoxylin and eosin stain. Kidney and heart sections were microscopically examined to evaluate the histopathological toxic changes (13).

Statistical analysis:

Data were analyzed using Statistical Program for Social Science (SPSS) version 20.0. Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- A one-way analysis of variance (ANOVA) when comparing between more than two means.
- Chi-square (X^2) test of significance was used in order to compare proportions between two qualitative parameters.
- Probability (P-value)
  - P-value <0.05 was considered significant.
  - P-value <0.001 was considered as highly significant.
  - P-value >0.05 was considered insignificant.

RESULTS

Table 1: Comparison between groups according laboratory data.

	Group A	Group B	Group C	Group D	ANOVA	p-value
Urea						
Mean±SD	27.50±7.62	40.90±9.34	40.30±8.30	37.40±5.13	6.410	**<0.001**
Range	17-38	27-51	28-51	30-45		
Creatinine						
Mean±SD	0.59±0.08	0.50±0.06	0.51±0.11	0.48±0.05	3.580	**0.020**
Range	0.48-0.68	0.42-0.58	0.32-0.68	0.43-0.55		
AST						
Mean±SD	54.05±8.78	158.80±29.86	63.00±20.14	50.00±11.83	70.990	**<0.001**
Range	38-65.3	80-192	48-100	40-70		
CK						
Mean±SD	119.80±33.38	675.00±352.52	270.80±90.42	216.00±78.06	17.120	**<0.001**
Range	88-170	200-1292	100-380	100-320		
CKMB						
Mean±SD	0.27±0.12	0.16±0.12	0.03±0.05	0.07±0.05	14.250	**<0.001**
Range	0.1-0.4	0-0.3	0-0.1	0-0.1		
LDH						
Mean±SD	429.50±63.19	1537.30±843.25	327.60±106.70	440.00±54.77	17.900	**<0.001**
Range	280-488	800-3087	188-450	380-500		
Troponin I						
Mean±SD	0.20±0.11	0.20±0.11	0.20±0.11	0.20±0.11	0.000	1.000
Range	0-0.3	0-0.3	0-0.3	0-0.3		

This table Shows statistically significant difference between groups according laboratory data, while troponin I non significant.

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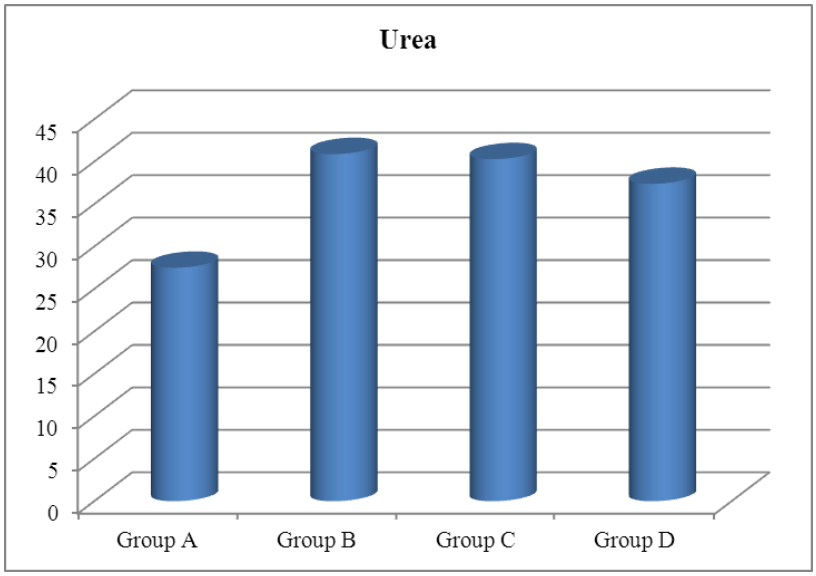

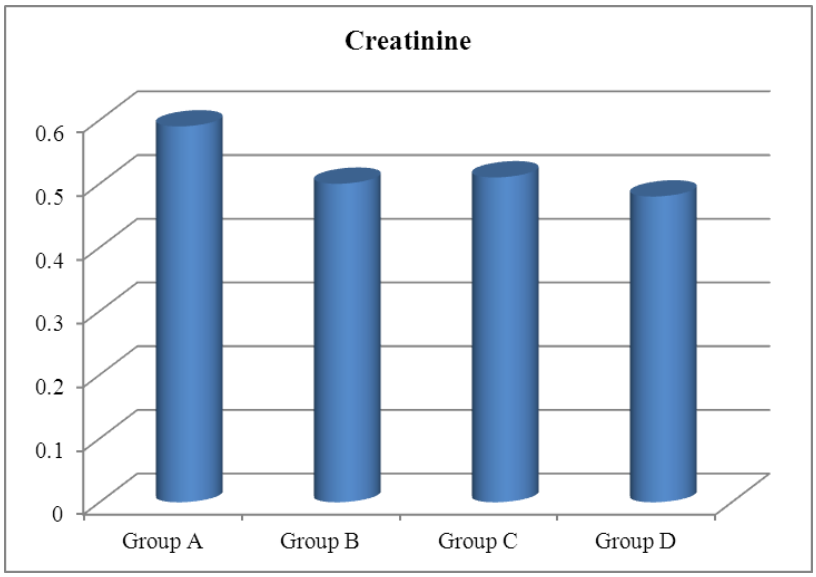

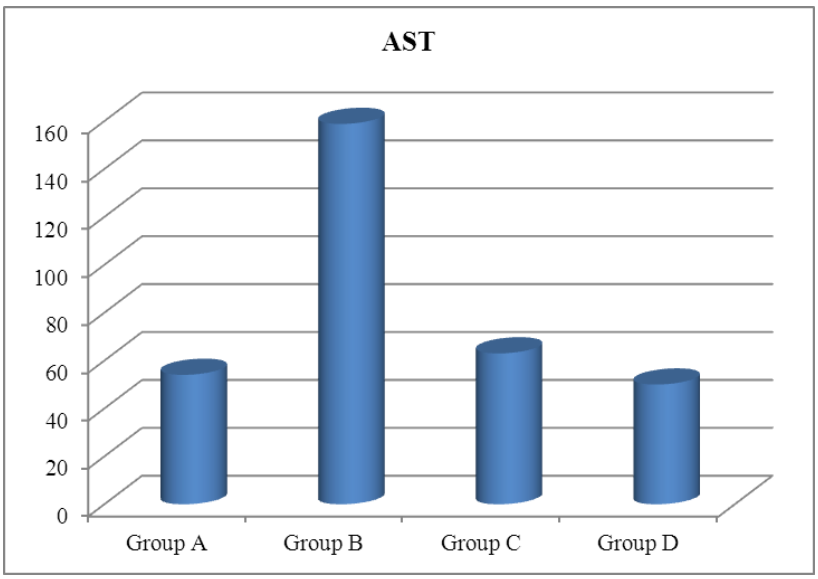

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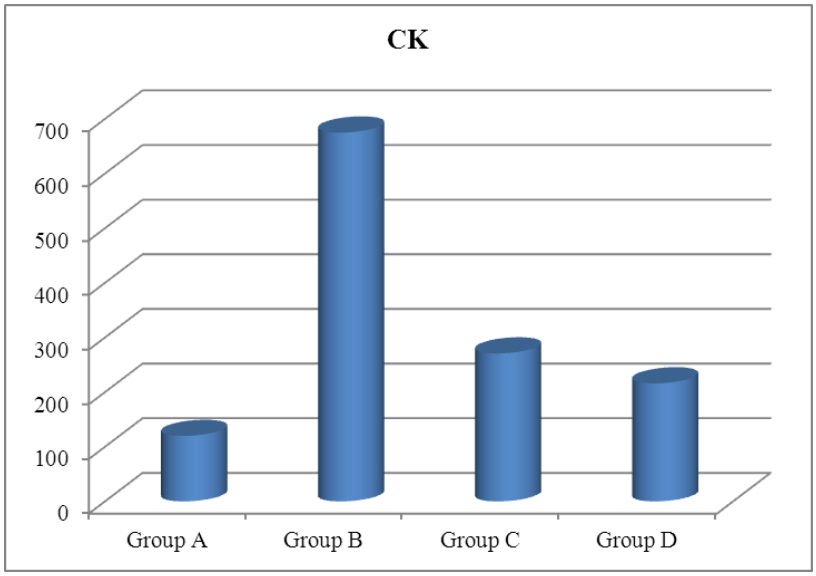

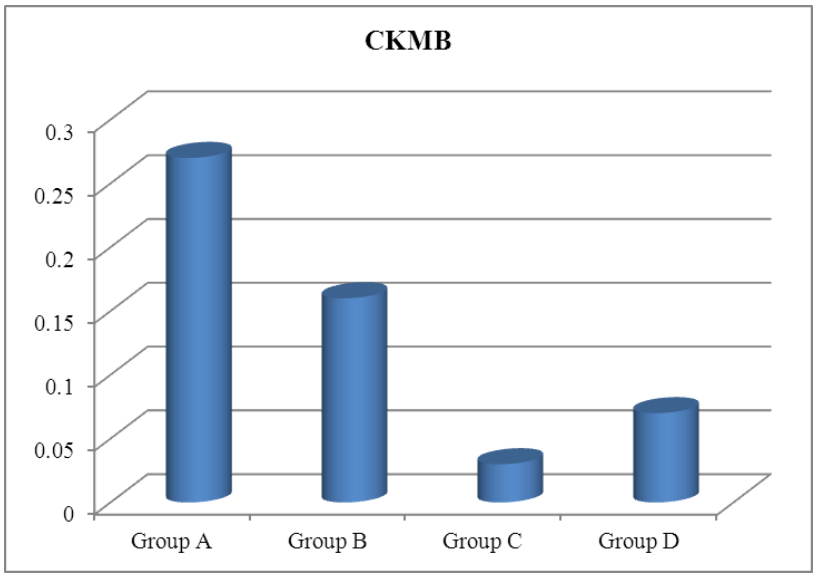

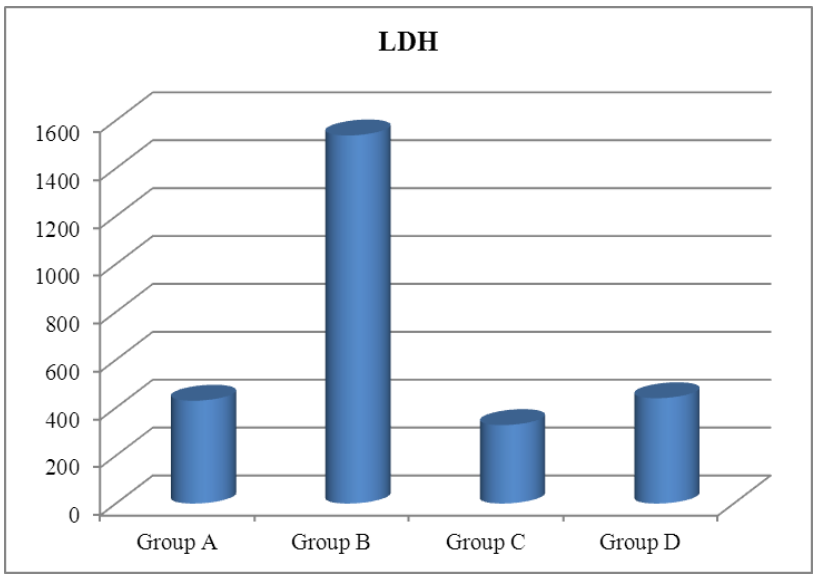

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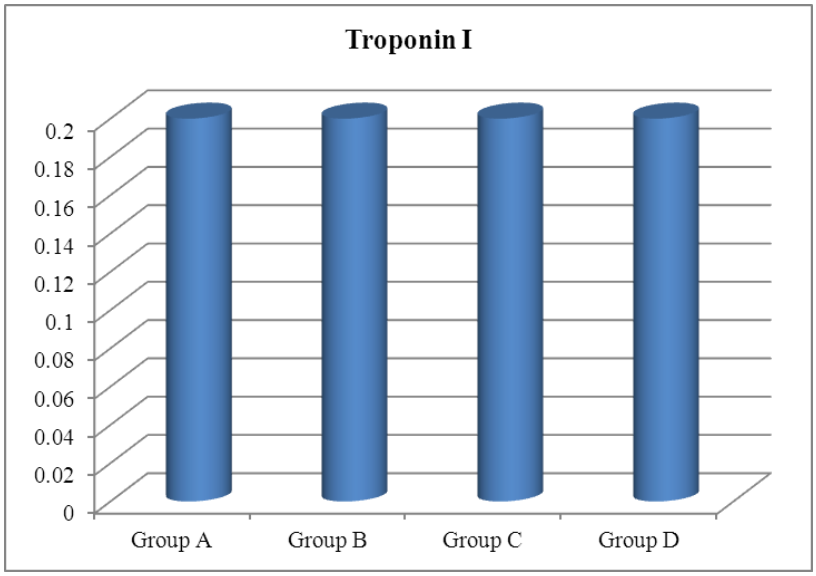

Table 2: Comparison between groups according pathology on penis.

Pathology on penis	Group A	Group B	Group C	Group D	Chi-square	p-value
Un remarkable pathological changes	10 (100%)	0 (0%)	4 (40%)	10 (100%)	30.000	**<0.001**
Vasodilatation +congestion	0 (0%)	10 (100%)	6 (60%)	0 (0%)		
Total	10 (100%)	10 (100%)	10 (100%)	10 (100%)		

This table shows statistically significant difference between groups according to pathology on penis.

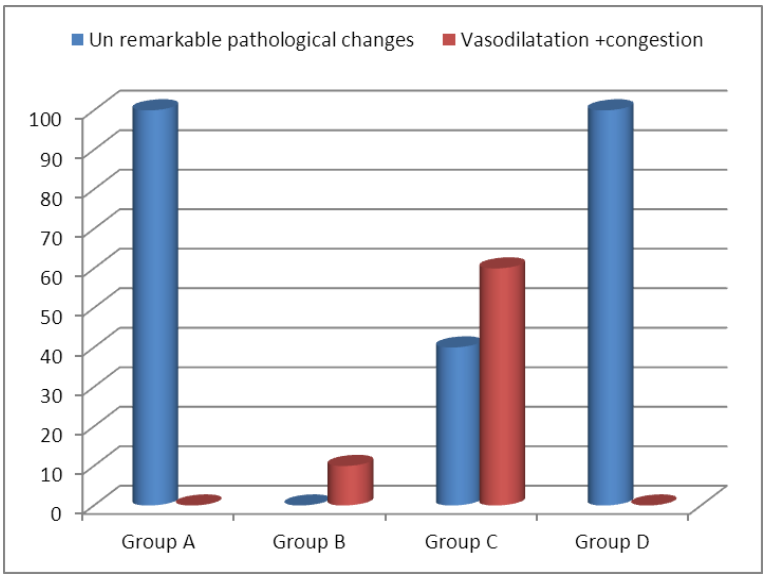

Table 3: Comparison between groups according pathology on kidney.

Pathology on kidney	Group A	Group B	Group C	Group D	Chi-square	p-value
Mild congestion	0 (0%)	1 (10%)	0 (0%)	0 (0%)	3.077	0.380
Un remarkable pathological changes	10 (100%)	9 (90%)	10 (100%)	10 (100%)		
Total	10 (100%)	10 (100%)	10 (100%)	10 (100%)		

This table shows no statistically significant difference between groups according to pathology on kidney.

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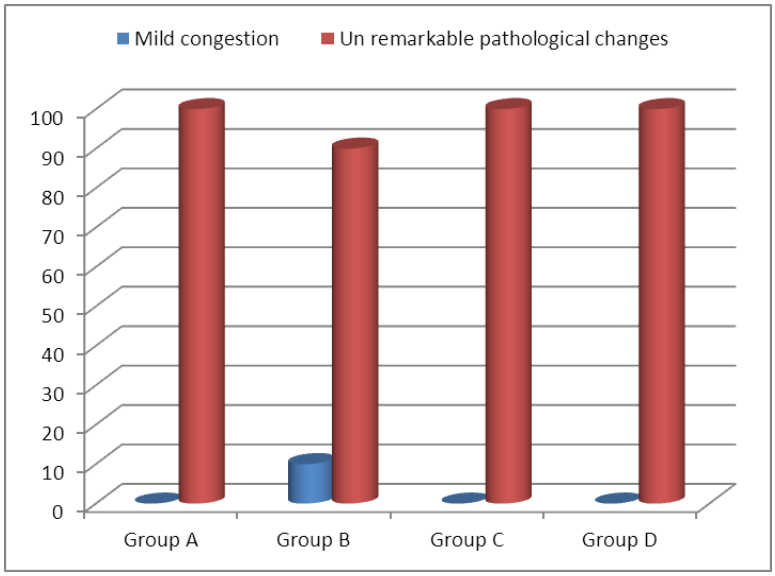
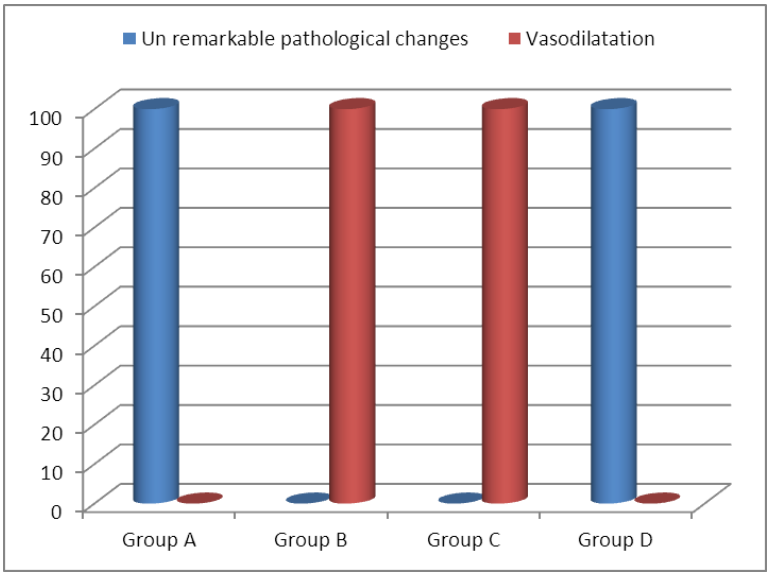


Table 4: Comparison between groups according pathology on heart.

Pathology on heart	Group A	Group B	Group C	Group D	Chi-square	p-value
Un remarkable pathological changes	10 (100%)	0 (0%)	0 (0%)	10 (100%)	40.000	**<0.001**
Vasodilatation	0 (0%)	10 (100%)	10 (100%)	0 (0%)		
Total	10 (100%)	10 (100%)	10 (100%)	10 (100%)		

This table shows statistically significant difference between groups according to pathology on heart.



DISCUSSION

By evaluation of chronic toxicity of commonly used herbs for sexual dysfunction specially in Egyptian market we find:

Regarding kidney function tests that creatinine with normal range in all studied groups , urea with normal range in group A control group and group D ginger group , but with high normal in group B ginsing group and group C piper cubeba .

Regarding urine test for albuminuria by test strip no proteinuria in all groups

This is going with Afshari et al., Ebru et al., who suggests a renal protective effect of ginger and vijayakumar prove an antioxidant effect of piper. Zidan et al., Kalkan et al., found a renal protective effect of ginseng

In regard to histopathology no abnormality detected in all groups except one case 10% mild congestion who received ginseng

By conclusion no evidence of significant nephrotoxicity with ginseng , piper cubeba and ginger.

Regarding chronic cardiotoxicity laboratory we notice significant rise of AST,CK and LDH in group B ginsing group with normal CK-MB and troponin I , so changes considered non specific to the heart .

Regarding pathology no pathological changes in group D ginger group but regarding group B ginseng group and group C piper cubeba we find 100% vasodilatation of the coronary arteries with no ischemic changes . This goes with Li et al., Zheng et al., who states a protective effect of ginseng on heart and shanmugam et al who proved protective effect of ginger on antioxidant enzymes.

Regarding penile patology, no vasodilatation in control group and group D ginger group. And there is 100% vasodilatation in group B ginseng group and group C piper cubeba which is considered beneficial for penile erection process**.**

REFERENCES

[1] Milsten, Richard (et al.), The Sexual Male. Problems And Solutions. London, 2000.

[2] Sadeghipour H, Ghasemi M, Ebrahimi F, Dehpour AR (2007). "Effect of lithium on endothelium-dependent and neurogenic relaxation of rat corpus cavernosum: role of nitric oxide pathway". Nitric Oxide **16** (1): 54–63.

[3] Sadeghipour H, Ghasemi M, Nobakht M, Ebrahimi F, Dehpour AR (2007). "Effect of chronic lithium administration on endothelium-dependent relaxation of rat corpus cavernosum: the role of nitric oxide and cyclooxygenase pathways". BJU Int. **99** (1): 177–182.

[4] Tanagho, Emil A. (et al.), Smith's General Urology. London, 2000.

[5] NHS Direct – Health encyclopaedia -Erectile dysfunction

[6] Shin YS, et al. Current status and clinical studies of Oriental herbs in sexual medicine in Korea. World Journal of Men's Health. 2015;33:62.

[7] 7-Hidden risks of erectile dysfunction "treatments" sold online. U.S. Food and Drug Administration. http://www. fda.gov/For Consumers/ConsumerUpdates/ucm048386.htm. Accessed Nov. 1, 2015.

[8] DAVID KIEFER, M.D., TRACI PANTUSO, B.S., (2003): Panax Ginseng, Am Fam Physician. 2003 Oct 15;68(8):1539-1542

[9] FASEB J., Reagan-Shaw S[1], Nihal M, Ahmad N.: (2008) Dose translation from animal to human studies revisited. Epub ;22(3):659-61

[10] Mansour AlSaid, Ramzi Mothana, Mohammad Raish, Mohammed Al-Sohaibani, Mohammed Al-Yahya, Ajaz Ahmad, Mohammed Al-Dosari,[1] and Syed Rafatullah: (2015) Evaluation of the Effectiveness of Piper cubeba Extract in the Amelioration of CCl_4-Induced Liver Injuries and Oxidative Damage in the Rodent Model BioMed Research International, Volume 2015

[11] Khaki, Arash, et al. “The effects of Ginger on spermatogenesis and sperm parameters of rat.” Iranian Journal of Reproductive Medicine 7.1 (2009): 7-12.

[12] A. Buege and S. D. Aust, “Microsomal lipid peroxidation,” Methods in Enzymology, vol. 52, pp. 302–310, 1978.

[13] Rosai and Ackermans (2011)b: surgical pathology 10th edition editor (mosby)- kidney1224-1229.

[14] Shanmugam K. R. , Mallikarjuna K. , Nishanth K., et al., (2010):Protective effect of dietary ginger on antioxidant enzymes and oxidative damage in experimental diabetic rat tissues.food chemistry 124 (4) :1436-1442.

[15] Vijayakumar R. S., Surya D., and Nalini N. (2013): antioxidant efficacy of black pepper and piperine in rats with high fat diet induced oxidative stress. Communications in free radical research 9 (2).

[16] Li J., Lchikawa T., Jin Y. , et al., (2010): An essential role of Nrf2 in American ginseng –mediated anti-oxidative actions in cardiomyocytes. Journal of Ethnopharmacology 130 (2): 222-230.

[17] Afshari A. T. , Shirpoor A., Farshid A., et al., (2006): The effect of ginger on diabetic nephropathy , plasma antioxidant capacity and lipid peroxidation in rats .Food chemistry 101 (1)148-153.
[18] Zidan R., A., Elnegris H., M., Wahdan R., A., (2015): Evaluating the protective role of ginsing against histological and biochemical changes induced by Aflatoxin B1 in the renal convoluted tubules of adult male aibino rats .journal of clinical and experimental pathology.
[19] Kalkan Y., Kapakin T., et al., (2012): protective effect of panax ginseng against serum biochemical changes and apoptosis in kidney of rats treated with gentamycin sulphate. Journal of molecular histology.
[20] Zheng S., Wu H., Wu D., (2012): roles and mechanisms of ginseng in protecting heart . Chinese journal of integrative medicine 18(7): 548-555.